### **10th Anniversary**

International IMBMC Medical Congress

# Bio-medical Scientific Cyprus

18 Credits of Continued Education will be awarded by the CYMA

> 18 Credits of Continuing Professional Development by the CBS

- 3rd to 5th November 2022
- Cultural Center, European University Cyprus

Organized & Supervised by: Professor Dr Ioannis Patrikios



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### Index

| Welcome Address by Professor Andreas Efstathiou                         | 4   |
|---|-----|
| Welcome Address by the Dean Professor Dr. Elizabeth O. Johnson          | 6   |
| Welcome Address by the Congress Chairman Professor Dr Ioannis Patrikios | 8   |
| Welcome Address by the Dr Petros Agathangelou Chairman of the CyMA      | 11  |
| Organizing Committee  | 16  |
| Program   | 20  |
| Clinical Faculty Inauguration   | 44  |
| Speakers CVs  | 46  |
| Abstracts   | 117 |
| Invited Abstracts   | 118 |
| Selected Abstracts  | 168 |
| Poster Abstracts  | 180 |
| Names of Participants in Alphabetical Order                             | 228 |
| Names of Volunteeres Medical Students                                   | 230 |

"Some men see things as they are and say why,

I dream things that never were and say why not"

George Bernard Shaw (1856 - 1950)





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### Welcome Address

By Professor Andreas Efstathiou



Distinguished guests and participants

It is my great pleasure and honor to welcome you today to European University Cyprus, on the occasion of the opening ceremony of the 10th International Multi-thematic Scientific Bio-Medical Congress organized by our School of Medicine.

The annual International Multi-thematic Scientific Bio-Medical Congress, which this year celebrates its 10th anniversary, ranks as one of the most significant international scientific meetings held in Cyprus and has already made a significant contribution in developing research and innovation activity in the fields of study it covers on the island.

The congress has already acquired a reputation for attracting to Cyprus distinguished scholars, academics and researchers in the field of Bio-Medical Sciences and Medicine from all over the world and this year's congress is no exception.

On this important day for our University please allow me to say a few words about its history, our achievements and our vision.

Our University has its roots in Cyprus College which was founded in 1961, only one year after the establishment of the Republic of Cyprus. It therefore ranks as one of the most historic academic institutions in Cyprus.

Our institution has come a long way since its founding more than sixty years ago. An ever-increasing number of our faculty, collaborate with scientists in some of the finest universities in the world. Our faculty also coordinate or participate in a number of prestigious projects which are funded by the European Commission, the Research and Innovation Foundation here in Cyprus and other funding agencies. Our research activity in the last five years increased at the average rate of around 30% per year quadrupling external research funding and publications in peer-reviewed journals. As a result, the University already fulfills the criteria for entering prestigious rankings such as the Times Higher Education World University rankings.

The establishment of the School of Medicine in recent years, operating in concert with our School of Dentistry and the School of Sciences, which is offering numerous programs in the area of Health and Life Sciences, has given a new impetus to the research activity of our University with new achievements. The organization of the annual International Multi-thematic Scientific Bio-Medical Congress gives the opportunity to our faculty to contribute to the establishment of Cyprus as a leading center for teaching and research in Medicine in the region.

At a time when international security and stability are at risk following the first major conflict in Europe after the second world war, European University Cyprus reaffirms its commitment for international collaboration and welcomes students and academics from all over the world. We are also very proud of the fact that our University last month began the offer of its program in Medicine at the branch of our School of Medicine in Frankfurt, Germany.

I would like to conclude with my warm thanks and congratulations to all those who worked for the organization of this year's congress and especially Prof. Ioannis Patrikios, Deputy Dean of our School of Medicine and founder of the congress. I would also like to acknowledge Bayer / Novagem Ltd, the diamond sponsor of the congress and all the other sponsors and supporters for their contribution.

Best wishes to all for a successful congress.

Professor Andreas Efstathiou

Rector, European University Cyprus

November 2022

### Welcome Address

By the Dean Professor Dr Elizabeth O. Johnson



Dear Friends & Colleagues,

It is a sincere pleasure to welcome you to European University Cyprus and to the 10th International Bio-Medical Scientific Congress.

This year, the School of Medicine of European University Cyprus has completed its first full decade. Just 10 short years ago, we 1<sup>st</sup> opened our doors of our new medical school. We opened our doors to our 1<sup>st</sup> cohort of medical students that came from 2 countries, Cyprus and Greece. Today, after one decade, we now open our doors to students from over 40 countries around the world, who come to us because they trust us for their medical education.

While our medical program has evolved with current thought in medicine, we have not stayed within the borders of this great Republic of Cyprus. This year, EUC, School of Medicine - Frankfurt Branch opened in October with its inaugural cohort of students, marking a true celebratory milestone for our 10-year Anniversary.

Not only has our School completed one full decade, but our Multi-thematic Congress has also closed a full decade and evolved. The Multithematic Congress was the vision and dream of Professor Ioannis Patrikios, one of the first faculty members of our School. While the first congress was humble, and more of an internal affair with a few guests, our small faculty and friends to fill the auditorium, today we step forward to our second decade with a with a resounding impact. In our celebratory 10-year Anniversary Congress, Prof. Patrikios has opened our doors to over 75 international speakers, among whom are internationally renowned scientists and clinicians, such as Prof. Kypros Nicolaides, Prof. Nikolai Korpan, Prof. Amanda Varnava, Prof Philippe Menasche', Prof. Stylianos Antonarakis, Prof. Paolo Madeddu, Prof. Paul Moss, Prof. Vasso Apostolopoulos, Prof. Graier Wolfgang, Prof. Kevin Harrington... a list that is as long as it is impressive.

Three Nobel Laureates will share their expertise at this year's 10 Year Anniversary Meeting, Prof. Gregg Leonard Semenza, Johns Hopkins School of Medicine, Nobel Prize in Medicine in 2019, for his groundbreaking work on discoveries of how cells sense and adapt to oxygen availability, Professor Sir Martin Evans, Cardiff University, Nobel Prize in Medicine in 2007 for his groundbreaking discoveries concerning embryonic stem cells, and Professor Sir Gregory Winter, Cambridge University, Nobel Prize in Chemistry in 2018 impact on the therapeutic use of monoclonal antibodies. Both Prof Sir Evans and Prof Sir Winter will be awarded Honorary Professorships of Medicine by European University Cyprus on Saturday, November 4<sup>th</sup>, 2022.

EUC continues to step to the forefront of global medical and health education. We are dedicated to preparing the healthcare leaders of tomorrow, with outstanding clinicians and scientists who will contribute to the advancement of science and medicine across the globe.

It is in this spirit that Professor Ioannis Patrikios, the Program Director, has constantly across

the last decade created an excellent scientific program for our Multi-thematic Congresses, including plenary lectures, keynote lectures, and poster sessions designed to provide an innovative and comprehensive overview of the latest research developments in bio-medical sciences, across a wide gamma of topics. Distinguished scientists and clinicians have joined us to take part in the plethora sessions, assuring that this event will remain one of the major scientific events in Cyprus.

Congratulations to Professor Patrikios, whose inspiration was the incentive for creating this meeting. A sincere word of gratitude to our sponsors, Bayer Novagem (Diamond), Energon (Platinum), Novartis (Platinum), Deputy Ministry of Tourism (Platinum), Cyprus Athletic Association (KOA)(Gold), PMI Science/ Philip Morris International (Gold), Mundipharma (Bronze), and the Sponsors Medochemi, Paploizou, Alector Pharma, Ardius Hellas, WinMedica Hellas, and Genesis. The Sigma TV / Dias Publishing House are the media sponsors. We are proud that the Congress is under the auspices of the Ministry of Health, the Cyprus Medical Association (CYMA), among many others. The quality of the congress ensures that participants can earn 18 CME credits from CYMA and 18 CPD (Continued Professional Development) from the Biological Society.

The scope and quality of the scientific exchange makes the Multi-thematic Congress a premier scientific forum in Cyprus. In addition to the rich program, I have no doubt that you will also enjoy your stay in beautiful Cyprus and exciting city of Nicosia.

Sincerely,

Dean School of Medicine European University Cyprus

### Welcome Address

By the Congress Founder and Chairman Professor Dr Ioannis Patrikios

Dear Congress participants and guests

It is my great pleasure to welcome you to the 10th International Multythematic Bio-Medical Scientific Cyprus Congress that is organized by the School of Medicine of the European University Cyprus (EUC) with the Cyprus Medical Association as a co-organizer, that is taking place in Nicosia, Cyprus on the 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> of November 2022.

The School of Medicine of the EUC and Myself personally welcome all distinguished, invited keynote and plenary speakers and the medical/scientific community of Cyprus as well as the delegates from all over the world (Greece, Poland, UK, Israel, Lebanon, Egypt, Italy, Germany, France, Austria, Spain and other) that are attending this exceptionally high quality and high caliber Multidisciplinary Scientific Symposium.

As the founder and general organizer of the congress, I would like to thank the Ministry of Health and the Cyprus Medical Association (CYMA) for their support and recognition. It is worth saying that our congress has been institutionalized by CYMA and this means a lot for the event itself, our School and University but also for me and I would like very much to thank Dr Petros Agathaggelou the president of CYMA but also the rest of the committee members for their decision. Moreover, CYMA is a co-organizer for this congress since 2019.

Once more, I would like to thank all of my fellow colleagues and friends that accepted the invitation to participate, travel, attend and share with us their unique and innovative scientific work of excellence as well as the executives of the European University of Cyprus (EUC) for their support and trust in me to organize this event at the highest possible level.

I thank all of our colleagues participating as chairmen/moderators of the session committees or the highly specialized round table workshops and satellites. It is worth saying that for this year and like never before and for no any other event, our IMBMC congress is endorsed and under the auspices of the Ministry of Health, Deputy Ministry of Tourism, Anesthesiology Society of Cyprus and Cyprus Resuscitation Society that organized 4 workshop sessions free of any charge for us, the Biological Society of Cyprus, Cyprus Cardiology Society, Cyprus Society of Atherosclerosis, Cyprus Medical Student Association, Cyprus Diabetic Association, Cyprus Endocrinology Society, Cyprus Perigenetic Society, Cyprus Society of Genetic Medicine, Medical Society of Nicosia-Kyrenia Ippokratis, Nicosia Cancer Society, Cyprus Pediatric Society, Karaiskakio Foundation, Cyprus Sports Organization (KOA), Cyprus Oncology Society, the Unique Smiles for rare diseases, The Cyprus Association of Cancer Patients and Friends, the Charity Organization Elpida and The American Hellenic Educational Progressive Association (AHEPA). I thank you all by heart.

Furthermore, I thank the abstract /poster participants from local higher Institutions as well as from Institutions abroad, but also my colleagues here at the School of Medicine for their

support and willingness to help making this an unforgettable date of our calendar.

"Biomedical Scientific Cyprus, (BSC)" has now been established as an annual event with global recognition. We are here for 10 consecutive years. The target has been accomplished. Now the only thing we need to do is to keep this congress at the level it deserves. The level of excellence as a medium of a Continued Medical Education for the professionals in Medicine but also as an international arena of dissemination of novelties, networking and scientific excellence in Medical Science.

Our congress is now a three-days event with participation and submission of more than 250 abstracts with 150 been selected and published in the ISBN International libraries number referenced congress abstract book; numbers that well exceeded all expectations and any previous participation.

Endorsing congresses by the level of original scientific work presented is not happening every day. Our congress has been internationally recognized by one of the most trustable and reputable publishers in the world; through Meeting Reports in the Nature-Publisher-journal "Cell Death & Disease" for six consecutive years.

This alone indicates the quality, seriousness and scientific prestige of the conference that was first organized exactly with the opening of the Medical School ten years ago and became an ordinance ever since.

Our Congress will not only remain one of the major scientific events in Cyprus, but it will continue serving as a primary forum for global academic exchange. In addition to reviewing the latest scientific developments and best clinical practices across the basic, clinical and translational contents presented at the meeting, the rich social program provides the opportunities for networking with colleagues from around the world in an exciting environment. The EUC Multi-thematic Congress indubitably provide the opportunity to interact with colleagues and stimulate the creative and productive exchange of ideas for a personally and professionally rewarding experience. Its overall mission is to promote the advancement of Science/Medicine, knowledge and its humane and benevolent applications Globally, accounting the role of Cyprus as a gateway of knowledge and innovation.

Finally, for once more I would like also to thank the sponsors of the congress, the diamond sponsor for 10 years continuously, Bayer/ NOVAGEM LTD and especially Mr. Mario Christodoulou, the General Director of the aforementioned companies in Cyprus, for his genuine support; investing on continued learning, knowledge, innovation and excellence. Bayer/NOVAGEM is the sponsors of this event since our first meeting, and we hope to have them for the ones to come. Our thanks extend to our platinum sponsors Energo lab equipment and Novartis pharma, the gold sponsors, PMI Science of Philipp Morris International, Metochemi, bronze sponsors, our Bronze sponsors Mundipharma and Alector/Papaloizou, Remedica, the sponsors and the supporters, Cyprus Biological Society, Winmedica Hellas, Medochemi, Ardius Hellas, and Genesis. Our thanks extend to the Cyprus Sports Organization and especially the president Mr Andreas Michaelides for supporting, endorsing and participating with a satellite session organized by the Cyprus Institute of Cardiology - Research and Study of Cardiovascular Diseases and Other Hereditary Cardiovascular Diseases (KIKEMM).

The conference is being held in November one of the best times to visit the island and enjoy its natural beauty as well as history. I thank each and every one of you for being here with us.

I feel confident that you will enjoy both, the scientific program and the unique Mediterranean Island of Cyprus.

I wish you all the best and a productive Congress

Professor Dr Ioannis Patrikios Deputy Dean, Faculty of Medicine, School of Medicine, European University Cyprus

Founder, Chairman and General Congress Supervisor

### Welcome Address

By the Congress Co-Chairm Dr Petros Agathangelou, Chairman of the Cyprus Medical Association (CyMA)



Dear Colleagues, Distinguished guests,

It is a distinct honour to welcome you all, to the 10th International Multi-thematic Scientific Bio-Medical Cyprus Congress, organized by the School of Medicine of the European University Cyprus and co-organized by the Cyprus Medical Association. We are privileged to co-organize the Biomedical Scientific Cyprus, which has been established as an annual event with international recognition. We all understand the importance of medical science, technology and innovation in our day-to-day lives and the ways in which they are transforming the world.

A glance through the list of presentations planned reveals the important significance of this Multi-thematic Congress. They range from Infectious diseases and immunization after the Covid-19 pandemic, to genetics as a diagnostic and therapeutic tool, cancer genetics, oncology, advances in cardiology & cardiovascular disease, atherosclerosis and modern therapies, robotic surgery, research in medicine, diabetes and many more fields and specialties. The medical field is as expansive and multifaceted as the intricacies of the human body. Fields of interest within the medical specialties exist to serve the needs of a particular realm of care. Foreseeable, demand for specialists will likely continue to rise.

Medical practice is evolving rapidly as new information supplants obsolete. The Cyprus Medical Association strongly supports initiatives and scientific events like this Congress. Our aim is to provide our members with the tools for lifelong learning and continuing professional development. We all need to be lifelong learners so that we continue to adapt to the changing ecology of the medical environment.

The Congress brings together experts, researchers, scientists, physicians, Professors, pharmaceutical industry representatives, providing us, with all the ammunition to develop our science further, exchange knowledge, share experiences and research results, discuss challenges encountered. It is imperative for us all to sustain and empower the scientific exchange on knowledge.

The multi-thematic and multi-lateral approaches of the objectives of this Congress have great importance. We are eager to learn more about the innovations in the field of medicine which are applicable today globally and interact among a great team of well-known specialized Professors and Physicians in their fields.

Our practice requires a permanent update, in accordance with the advances in medicine, which as a science, implies innovation and creativity and research to invent new drugs, treatments and diagnostic techniques that alleviate human pain, restore lost health, and allow the prevention of multiple diseases that afflict the community.

Unquestionably, the International Multi-thematic Scientific Bio-Medical Congress, brings for

the 10th year, an excellent networking platform for experts to share their latest research and advancements in their fields.

I'm certain that the Congress will stimulate scientific debate, increase network between scientists, physicians, professors, representatives of pharmaceutical industry and policy makers and encourage further research.

So, let me conclude by congratulating the European University School of Medicine and by thanking all our supporters and all the participants.

Looking forward for a successful Congress.

# Όλα για την υγεία

Στη φαρμακευτική εταιρεία **Χρ. Γ. Παπαλοϊζου** γνωρίζουμε την αξία της υγείας και την υπηρετούμε εδώ και 60 χρόνια. Φροντίζουμε να προσφέρουμε στην κυπριακή αγορά σύγχρονα φάρμακα που ικανοποιούν σημαντικές ιατρικές ανάγκες στην καρδιολογία, τη γαστρεντερολογία, την ψυχιατρική, τη νευρολογία, την ογκολογία, την πνευμονολογία, τη δερματολογία, την ενδοκρινολογία, τη γονιμότητα.

Διατηρούμε μακρόχρονες στρατηγικές συνεργασίες με διεθνούς φήμης φαρμακευτικές εταιρείες όπως η AstraZeneca, n Merck, n Lundbeck, n Recordati, n Grunenthal, n Galderma και η WinMedica, που αφιερώνουν μεγάλο μέρος των εσόδων τους στην έρευνα για την ανακάλυψη και ανάπτυξη νέων αποτελεσματικών και ασφαλών θεραπειών. Παράλληλα, με καταρτισμένο επιστημονικό προσωπικό είμαστε δίπλα στον ιατροφαρμακευτικό κόσμο στον τομέα της ενημέρωσης και, μέσω ενός άρτιου δικτύου διανομής, εξυπηρετούμε και το πιο απομακρυσμένο φαρμακείο της Κύπρου.

Όλοι αναγνωρίζουμε ότι η υγεία είναι ύψιστο αγαθό και εμείς κάνουμε όλα όσα μπορούμε για την προαγωγή της.



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In a randomised, doubleblind clinical trial; treatment with Neuroaspis® PLP10 significantly reduced the relapse rate and the risk of sustained disability progression without any reported serious adverse events in patients with Multiple Sclerosis (1). An additional study was published by Aristotelous et al., 2021, supporting the hypothesis that Neuroaspis® PLP10 can act protectively against functional deterioration of patients with a progressive disease such as Relapsing-Remitting Multiple Sclerosis (3).

Another study by Stavrinou et al., 2020 demonstrated that a high-dose of specific omega-3 and omega-6 fatty acids supplementation, in combination with specific antioxidant vitamins, can possibly prevent or treat cognitive impairment and functional decline; therefore, improve independence and quality of life of older individuals with mild cognitive impairment (2).

Furhtermore, Neuroaspis® PLP10 was shown to improve the symptoms of Parkinson's disease and possibly play a major role in delaying the progression of the disease when used as an adjuvant to the conventional treatment (4).

In general, Neuroaspis® PLP10 can help support

- Brain & Memory
- Heart
- Joints & Bone
- Immune System
- Antioxidant & Skin
- Eye & Vision

 Pantzaris MC, Loukaides GN, Ntzani EE, Patrikios IS. A novel oral nutraceutical formula of omega-3 and omega-6 fatty acids with vitamins (PLP10) in relapsing remitting multiple sclerosis: a randomised, double-blind, placebo-controlled proof-of-concept clinical trial. BMJ Open. 2013 Apr 17;3(4):e002170. doi: 10.1136/bmjopen-2012-002170. PMID: 23599375; PMCID: PMC3641495.

 Stavrinou PS, Andreou E, Aphamis G, Pantzaris M, Ioannou M, Patrikios IS, Giannaki CD. The Effects of a 6-Month High Dose Omega-3 and Omega-6 Polyunsaturated Fatty Acids and Antioxidant Vitamins Supplementation on Cognitive Function and Functional Capacity in Older Adults with Mild Cognitive Impairment. Nutrients. 2020 Jan 26;12(2):325. doi: 10.3390/nu12020325.
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4.Pantzaris M, Loukaides G, Paraskevis D, Kostaki EG, Patrikios I. Neuroaspis PLP10<sup>™</sup>, a nutritional formula rich in omega-3 and omega-6 fatty acids with antioxidant vitamins including gamma-tocopherol in early Parkinson's disease: A randomized, double-blind, placebo-controlled trial. Clin Neurol Neurosurg. 2021 Nov;210:106954. doi: 10.1016/j.clineuro.2021.106954. Epub 2021 Sep 17. PMID: 34607196.

### Organizing Committee

#### Master of Ceremony

#### Ms. Evgenia Karampesini

#### **Organizing Committee**

Chairman:Ioannis PatrikiosDeputy Dean, School of Medicine European University CyprusVise Chairman:Petros Agathaggelou<br/>Adj. Assoc Prof.School of Medicine European University Cyprus &<br/>President of the Cyprus Medical AssociationMembers:Elizabeth Johnson<br/>Dean, School of Medicine European University<br/>Cyprus

Anastasis Stephanou School of Medicine European University Cyprus

Emmanouil Nikolousis School of Medicine European University Cyprus Konstantinos Lambropoulos School of Medicine European University Cyprus

#### **Independent Poster Award Committee**

Professor Dr Graier Wolfgang Nikon-Center of Excellence, Medical University of Graz, Austria

> Professor Dr Achilleas Gravanis School of Medicine, University of Crete

Professor Dr Kyriakos Kypreos School of Medicine, University of Patras





Βοηθήστε να γίνουν τα φάρμακα πιο ασφαλή και Αναφέρετε ΟΛΕΣ τις ανεπιθύμητες ενέργειες για ΟΛΑ τα φάρμακα Συμπληρώνοντας την "ΚΙΤΡΙΝΗ ΚΑΡΤΑ" ΟΝΟΜΑΣΙΑ ΤΟΥ ΦΑΡΜΑΚΕΥΤΙΚΟΥ ΠΡΟΙΌΝΤΟΣ: Ferinject 50 mg σιδήρου ανά ml ενέσιμο διάλυμα/διάλυμα για έγχυση. ΠΟΙΟΤΙΚΗ ΚΑΙ ΠΟΣΟΤΙΚΗ ΣΥΝΘΕΣΗ: Ένα ml διαλύματος περιέχει 50 mg σιδήρου, ως ένωση καρβοξυμαλτόζης με σίδηρο. ΚΑΘε φιαλίδιο των 10 ml περιέχει 500 mg σιδήρου, ως ένωση καρβοξυμαλτόζης με σίδηρο. ΚΑΤΟΧΟΣ ΤΗΣ ΑΔΕΙΑΣ ΚΥΚΛΟΦΟΡΙΑΣ: Vifor France 100-101Terrasse Boieldieu, Tour Franklin La Defense 8, 92042 Paris La Defense Cedex, Γαλλία. Για περατέρω πληροφορίες παρακαλώ απευθυνθείτε στη Genesis Pharma



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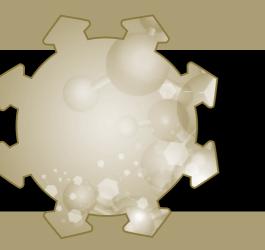




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### Bio-medical Scientific Cyprus

### Program



10th International Multithematic Scientific Bio-Medical Congress (IMBMC) "Bio-medical Scientific Cyprus" THURSDAY, 03 NOVEMBER 2022

### Program

- 8:00 9:00 Registration / Coffee
- 8:50 8:55 EUC School of Medicine
- 8:55 9:00 Masters of Ceremony
  - Ms. Evgenia Karampesini



Short Introduction and Kick-off Prof Dr. Ioannis Patrikios Founder and Organizing/Scientific Committee Chairman

#### **SESSION I**

#### POST-COVID-19 EPOCH: CONSEQUENCES OF THE PANDEMIC WHAT WE HAVE LEARNED AND WHAT IS COMING UP NEXT? IS THIS THE END?

#### 9:00 - 9:20 "The One Health Approach in the Post Covid Era"



#### Ass Prof. Dr. Zoi Dorothea Pana

Specialist in Pediatrics, Faculty Member (European University, Cyprus), Specialized in Hospital Epidemiology/ Infection Control/Stewardship (Johns Hopkins Hospital, USA); COVID-19 Advisory Committee/ Consultant (Ministry of Health, Cyprus) Chairs: Manolis Nikolousis. Christina Kousparou

#### 9:20 - 9:40 "Evolution of SARS-Cov2 Since the Start of the Pandemic"



#### Prof Dr. Peter Karayiannis

Professor of Microbiology/Molecular Virology at the University of Nicosia Medical School; COVID-19 Advisory Committee/ Consultant (Ministry of Health, Cyprus) Chairs: Manolis Nikolousis, Christina Kousparou

9:40 - 10:00 "The Enemy of Your Enemy is Your Friend - The Reintroduction of Bacteriophages for Resistant and Persistent Infections"



#### Prof. Dr. Ran Nir-Paz

Professor of Medicine, Chair Executive committee ESGNTA – ESCMID study group for Non-Traditional Antimicrobial agents Department of Clinical Microbiology and Infectious Diseases Hadassah-Hebrew University Medical Center, Jerusalem, Israel

Chairs: Giorgos P. Georgiou, Anastasis Stephanou

#### **SESSION II**

NEUROLOGY, NEUROIMMUNOLOGY, NEUROPHARMACOLOGY CHRONIC DISEASES

- Genetics as a Diagnostic and Therapeutic Tool
- Novelties and Emerging Targets

#### 10:00 - 10:20 "The Role of miRNAs in Signaling and Use as Biomarkers in Myotonic Dystrophy Type I"



**Prof. Dr. Leonidas Phylactou** CEO and Medical Director, The Cyprus Institute of Neurology & Genetics Chairs: Antonia Sophocleous, Stephanos Christodoulides



"Viruses in Multiple Sclerosis" Prof. Dr. Nikolaos Grigoriadis Aristotle University of Thessaloniki, AHEPA University Hospital, Thessaloniki, Greece Chairs: Dimitrios Papadopoulos, Marios Pantzaris



 11:00 - 11:20
 "Stress Impact on Hepatic Drug Metabolism"

 Prof. Dr. Maria Konstanti
 Pharmacology Faculty of Medicine School of Health Sciences, University of Ioannina

 Chairs: Iva Tzvetanova, Carsten Werner Lederer

11:20 - 11:45 SATELLITE SESSION PMI (HYBRIT) 🐼 MISCENCE



"How New Technologies can Benefit Public Health- The Role of Harm Reduction in the Area of Smoking" Prof. Dr. R. Zimlichman Director of The Brunner Institute for Cardiovascular Research Sackler Faculty of Medicine,

Chairs: Iva Tzvetanova, Carsten Werner Lederer

11:45 - 12:25 Lunch Buffet

#### **POSTER SESSION**

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#### **SESSION III**

CARDIOLOGICAL IMAGING & NEW GENERATION ANTITHROMBOTIC ANTICOAGULANT THERAPIES: TWO SIDES OF THE SAME COIN?

#### Effectiveness and Safety of Direct Oral Anticoagulants (DOACs)

#### 12:25 - 12:45 "Imaging Coronary Artery Disease" (HYBRID)



#### Prof. Dr. Jeroen Bax

Director of Noninvasive Imaging, Department of Cardiology, Leiden University Medical Centre (LUMC), Leiden, The Netherlands, Immediate Past-President, European Society of Cardiology (ESC) 2018-2020

Chairs: Konstantinos Lampropoulos, Stephanos Christodoulides



12:45 - 13:05

#### Dr. Charalampos (Haris) Kartsios

Thromboembolism (VTE)"

Consultant Haematologist, Royal Derby Hospital, University Hospitals of Derby and Burton, NHS Foundation Trust, UK

"Effectiveness and Safety of Doacs for the Prevention of Recurrent Venus

Chairs: Marios Antoniades, Manolis Nikolousis





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#### ADVANCES IN CARDIOLOGY / CARDIOVASCULAR DISEASES

- Focus on today to enlighten the Future
- Atherosclerosis: Cardiometabolism Dysfunction and Inflammation in the Vessels

13:05-13:25 "High Density Lipoprotein: Guardian Angel or Indifferent Bystander?"



**Prof. Dr. Kyriakos Kypreos** School of Medicine, University of Patras Chairs: Viky Zeniou, Giorgos Miltiadous

#### 13:25 - 13:45 "Atherosclerosis: The Crucial Role of Hypercholesterolemia and Inflammation"



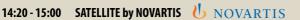
**Dr. Phivos Symeonides** Consultant Cardiologist, President of the Cyprus Society of Atherosclerosis Chairs: Viky Zeniou, Giorgos Miltiadous

#### 13:45 - 14:05 "Lipid Management in 2022. Is There a Reasonable Gap Between Guidelines and Clinical Practice?"



#### **Dr. Dimitri Richter** Consultant Cardiologist, Euroclinic Hospital, Athens, Greece Chairs: Giorgos Miltiadous, Costas Economides

#### 14:05 - 14:20 Coffee Break



"Pharmacological Lipid-Modification Therapies for the Prevention of Ischaemic Heart Disease: Novel Options"



Assoc. Prof. Dr. Konstantinos Lambropoulos, School of Medicine, European University Cyprus



Dr. Theodoros Christodoulides Consultant Cardiologist

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Chairs: Giorgos Miltiadous, Costas Economides

#### SESSION V **INTERVENTIONAL CARDIOLOGY** New Frontiers in an old Game: What is new out there?



#### 15:00 - 15:20 "ST-Elevation Myocardial Infarction (STEMI) Today, What We Need to Know!"

#### Dr. Christos Christou

Consultant Interventional Cardiologist, Medical Director, American Heart Institute Chairs: Savvas Constantinides, Giorgos M. Georgiou

#### 15:20 - 15:40 "Imaging to Select and Guide TAVI"



Prof. Dr. Kostas Toutouzas Consultant Interventional Cardiologist, National and Kapodistrian University of Athens Chairs: Savvas Constantinides, Giorgos M. Georgiou

#### **SESSION VI**

NEW IDEAS FOR ANTICOAGUI ANT APPLICATION IN CLINICAL MANAGEMENT OF **CARDIOVASCULAR RISK FACTORS DOACs in Venous Thromboembolism and in perioperative setting** 

15:40 - 16:00

"Effectiveness and Safety of Direct Oral Anticoagulants (Doacs) in the Treatment of Venous Thromboembolism (VTE)"; with real case presentations.

Prof. Dr. Miltiadis (Miltos) Matsagkas Vascular Surgery, School of Medicine, University of Thessaly Chairs: Stelios Papas, Neophytos Zambas

16:00 - 16:20 "Effectiveness and Safety of direct oral anticoagulants (DOACs) in the perioperative setting"; with real case presentations



Prof. Dr. Eleni Arnaoutoglou Anesthesiology, School of Medicine, University of Thessaly Chairs: Stelios Papas, Neophytos Zambas

#### 16:20 - 16:45 **KEYNOTE SPEAKER**



#### "Cells for Heart Failure: Replacement Therapy or Paracrine Signaling?"

#### Prof. Dr. Philippe Menasche'

Prof. at UAB Department of Biomedical Engineering; Clinical cardiac surgeon at the Hôpital Européen Georges Pompidou; Professor of Thoracic and Cardiovascular Surgery at the University of Paris Descartes; and leader of an INSERM (National Institute of Health and Medical Research) team devoted to cell therapy of cardiovascular diseases

Chairs: Ioannis Tzanavaros, Konstantinos Lampropoulos



#### **OPENING CEREMONY**

- 17:00 17:05 School of Medicine Virtual presentation
- 17:05 17:20 Musical Interlude with the Joint Saxophone Ensemble of the Escuola Superior di Musica di Lisboa (ESML) and the Cyprus Saxophone Association Saxophonia

Conductor: Associate Professor Yiannis Miralis, European University Cyprus

#### 17:20 - 17:40 Welcome Addresses

Prof. Dr Ioannis Patrikios Deputy Dean of the School of Medicine, European University Cyprus & Congress founder and Committee Chairman

**Prof. Dr Elizabeth Johnson** Dean, School of Medicine, European University Cyprus

**Prof. Andreas Efstathiou** Rector, European University Cyprus

**Dr Petros Agathaggelou** President, Cyprus Medical Association & Congress Committee Vise Chairman

Cyprus Sport Organization (KOA/CSO) Andreas Michaelides, President of CSA

Cyprus Depudy Ministry of Tourism Representative

Ministry of Health Mr Michael Hadjipantelas, Minister of Health

#### 17:40 - 18:00 OPENING CEREMONY LECTURE



"Human Genome and the Evolution of Medicine" Prof. Dr. Stylianos Antonarakis Prof. of Genetic Medicine at the University of Geneva Medical School in Switzerland

"Closing Remarks of 1<sup>st</sup> Day End of Sessions"



### 10th International Multithematic Scientific Bio-Medical Congress (IMBMC) "Bio-medical Scientific Cyprus"

FRIDAY, 04 NOVEMBER 2022

### Program

- 8:00 8:45 Registration / Coffee
- 8:45 8:50 EUC School of Medicine

#### 8:50 - 9:50 SELECTED ABSTRACTS

 (10 min each presentation)
 Oral Presentations

 (The Presenting Authors are underlined)



"Chemical Characterization and Biological Evaluation of Nasturtium Officinale (Watercress) in an Experimental Model of Human Malignant Melanoma" <u>Nikoleta Dimosthenous</u><sup>1</sup>, Mihalis I. Panayiotidis, Sotiris Kyriakou

1. Department of Cancer Genetics, Therapeutics & Ultrastructural Pathology, The Cyprrus Institute of Neurology & Genetics, Nicosia, Cyprus



"A personalized Risk Assessment Tool for Colorectal Cancer Prevention through 3'mRNA Sequencing of Normal-Appearing Mucosa in the Cypriot Population" (MoCo Project) <u>Katsaounou Kyriaki</u>

University of Cyprus, Department of Biological Sciences, Infection and Cancer Laboratory "Effective Bedside Prognostic Tools for Septic and Septic Shock Patient – A Necessity"





Bianca-Liana Grigorescu, <u>Oana Coman<sup>1</sup>, Georgescu Anca Meda, Bacârea Anca,</u> Alexandra Elena Lazăr, Petrișor Marius, Irina Săplăcan 1. Department of Anesthesiology and Intensive Care, University of Medicine, Pharmacology,

1. Department of Anesthesiology and Intensive Care, University of Medicine, Pharmacology Sciences and Technology, Târgu Mureş, 540142 Mureş, Romania

"Investigation of the aetiology of community acquired pneumonia in Cyprus and characterization of host factors in viral/bacterial co-infections" <u>Petros Ladas 1</u>, Ilias Porfyrides, Christina Christodoulou, Jan Richter 1. The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus, Department of Virology

"Amygdalin as a Chemoprotective Aagent in Co-Treatment with Cisplatin" <u>Panayiota Christodoulou 1,</u> Panagiotis Boutsikos, Christiana M. Neophytou, Theodora-Christina Kyriakou, Maria-Ioanna Christodoulou, Panagiotis Papageorgis,





Anastasis Stephanou, Ioannis Patrikios 1. School of Medicine, European University Cyprus, Nicosia, Cyprus "VITAMIN D – Hormone of the Modern Age as Adjuvant Therapy in Skin Diseases" <u>Andrija Stanimirović<sup>1</sup></u>, Tea Štrbac, Josip Rešetar

1. Dermatology & Venereology, University of Applied Health Sciences, Mlinarska cesta, Croatia

Chairs: Anastasis Stephanou, Charalambos Michaeloudes



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#### SESSION VII MEDICAL GENETICS AS A TOOL FOR NEW THERAPIES Chronic and Rare Diseases



9:50 - 10:10

"Adaptation and Cancer Genes: From Cells to Populations" Assoc. Prof. Dr. Constantinos Voskarides Genetics and Molecular Biology, University of Nicosia Medical School Chairs: Pavlos Neophytou, Elpida Nikolousi



#### "Pseudomonas Aeruginosa: An Opportunist with a Cause" Assoc. Prof. Dr. Yiorgos Apidianakis Biological Science, University of Cyprus Chairs: Pavlos Neophytou, Elpida Nikolousi



10:40 "Bioinformatics Insights to Post-Analysis of Computational Drug Repurposing Results" Prof. Dr. Giorgos Spyrou The Cyprus Institute of Neurology & Genetics Chairs: Kyriakos Felekkis, Stephanos Christodoulides



10:50 - 11:10

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**Prof. Dr. Evangelos Manolopoulos** Pharmacology, School of Medicine, University of Alexandroupolis Chairs: Kyriakos Felekkis, Stephanos Christodoulides

11:10 - 11:30 "How a Mendelian Monogenic Disease Behaves as a Multifactorial Phenotypic Chameleon: Inherited Hematurias"



#### Prof. Dr. Constantinos Deltas

Director, Center of Excellence in Biobanking and Biomedical Research & Molecular Medicine Research Center, University of Cyprus, Medical School Chairs: Soteroula Christou, Manolis Nikolousis

#### 11:30 - 11:50 CANCER UPDATES

## "Cancer in children and adolescents in Cyprus: Incidence rates among the highest in the world, cancer type distribution differences, temporal trends and the search for the causes"



#### Prof. Dr. Loizos Loizou

Clinical Professor of Pediatrics, Pediatric Oncology - Hematology, Medical School, University of Nicosia. Fmr. Director of the Pediatric Oncology - Hematology Clinic, Archbishop Makarios III Hospital, Nicosia. President of the ELPIDA Foundation for children and adolescents affected by cancer or leukemia

Chairs: Soteroula Christou, Manolis Nikolousis

11:50 - 12:30 Lunch Buffet

#### **POSTER SESSION**

#### SESSION VIII

**CANCER: New Frontiers** From Genetics to Clinical Trials to Clinical Practice: Novel and Pioneer Strategies for Treating Patients



12:30 - 12:50

"From Radiomics to Clinical Trial to Clinical Practice: Novel and Pioneer Strategies for Treating Patients"

**Dr. Costantinos Zamboglou** Radiation Oncology, Vice Medical Director, German Oncology Center Chairs: Adamos Hadjipanayis, Vasiliki Danilatou



13:10 - 13:30

12:50 - 13:10 "Lung Fibrosis and Cancer- Distinct Horns of the Same Devil" Assoc. Prof. Dr. Aravris Tzouvelekis Respiratory Medicine University of Patra, Greece

"Management of Colorectal Cancer in Elderly Patients"

Chairs: Adamos Hadjipanayis, Vasiliki Danilatou

Assist. Prof. Dr. Demetris Papamichael Director, Bank of Cyprus Oncology Centre, Assist. Professor at St. George's Hospital-Medical School, University of London / UNIC Campus

Chairs: Charis Charalambous, Pantelis Kountourakis

#### 13:30 – 13:55 KEYNOTE SPEAKER

#### "Vaccines in the New Era: What Have We Learnt in the Last 30 Years?"



**Prof. Dr. Vasso Apostolopoulos** Pro Vice-Chancellor, Research Partnerships at Victoria University, Australia Expertise with development of drugs and vaccines (First vaccine against breast cancer) Chairs: Charis Charalambous, Pantelis Kountourakis

#### **SESSION IX** BLOOD MALIGNANCIES: CURRENT STATUS AND ADVANCES



and Beyond" Assoc. Prof. Dr. Carsten Werner Lederer The Cyprus Institute of Neurology & Genetics Chairs: Loizos Loizou, Dimitris Papadopoulos

14:15 - 14:35

Assoc. Prof. Dr Manolis Nikolousis Assoc. Prof. of Hematology, Chairman, School of Medicine, European University Cyprus Chairs: Loizos Loizou, Dimitris Papadopoulos

"CAR-T Cells in Haematological Malignancies - A Key to Success?"

"Novel Tools and Approaches for Translational Research in Haematopoietic Cells

14:35 - 14:55 Coffee Break

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#### **SESSION X** GENETIC AND MOLECULAR MEDICINE: NEW FRONTIERS FOR HUMANITY S' HEALTHY BEING

14:55 - 15:20 HONORARY KEYNOTE SPEAKER



"Hypoxia-Inducible Factors in Physiology and Medicine" (HYBRIT)
Prof. Dr. Gregg L. Semenza - (Nobel 2019)
Pediatrician and Professor of Genetic Medicine at the Johns Hopkins School of Medicine Nobel Prize in Physiology or Medicine, 2019
Chairs: Petros Agathaggelou, Christodoulos Kaisis

 15:20 - 15:40
 "Metabolic rewiring: instigator or consequence of cellular dysfunction?"

 Prof. Dr. Graier Wolfgang
 Head of the NIKON-Center of Excellence; Medical University of Graz, Austria

 Chairs: Petros Agathaggelou, Christodoulos Kaisis

#### 15:40 - 16:05 KEYNOTE SPEAKER



"How to Make an External Ear: The Story of FOXI3" Prof. Dr. Stylianos Antonarakis Genetic Medicine at the University of Geneva Medical School in Switzerland Chairs: Anastasis Stephanou, Charalambos Michaeloudes

#### SESSION XI IMMUNITY

**Antibodies: A Revolution that Led to Modern Therapeutics** 

### 16:05 - 16:25 "Is there a Rationale for Combining Radiotherapy and Immunotherapy in Patients with Head and Neck Cancer?"



**Prof. Dr. Kevin Harrington** Honorary Consultant Clinical Oncologist at The Royal Marsden NHS Foundation Trust and at St George's Hospital

Chairs: Manolis Nikolousis, Konstantinos Lampropoulos

#### 16:25 - 16:50 KEYNOTE SPEAKER



"From Diagnostics to Therapeutics; Antibodies Take Center Stage in COVID-19"

#### Prof. Dr. Paul Moss

Prof. of Haematology and Deputy Head of the College of Medicine at the University of Birmingham, UK. Chief Investigator of the UK Coronavirus Immunology Consortium

Chairs: Manolis Nikolousis, Konstantinos Lampropoulos

#### 16:50 - 17:20 HONORARY KEYNOTE SPEAKER

"Antibodies and Antibody Mimics as Pharmaceutical Drugs"



#### Prof. Sir Gregory Winter-(Nobel 2018)

Laboratory of Molecular Biology, Medical Research Council; Master, Trinity College, Cambridge University, Cambridge, UK. Best Known for the engineering of humanized monoclonal antibodies and their widespread use in medical therapy, particularly for treatment of cancer and immune disorders

Chairs: Elizabeth Johnson, Zoi Dorothea Pana

17:20 - 17:55 Coffee Break

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#### SESSION XII ENCOUNTER WITH THE PIONEERS

State of the Art Therapeutic Surgical Methods - The Robotic "DaVinci" & Cryosurgery

17:35 - 17:55

#### "Robotic Thoracic Surgery: From Science Fiction to Everyday Practice" Assoc. Clin. Prof. Dimitrios Kyparissopoulos



University of Nicosia, Medical School & Harefield Hospital, Royal Brompton and Harefield NHS Foundation Trust, London, UK

Chairs: Panos Hountis, Lefteris Karapashis

#### 17:55 - 18:15



### "The Role of the Robotic Surgery in the Evolution of the Minimal Invasive Surgical Oncology: Where We Stand"

#### Assoc. Prof. Dr. Athanasios Petrou

Associated Professor in Surgery, European University CY, School of Medicine Director of the Advanced Laparoscopic Hepatobiliary-Pancreas and Surgical Oncology Center at Mediterranean Hospital, EU, Cy

Chairs: Panos Hountis, Lefteris Karapashis

#### 18:15 - 18:40 KEYNOTE SPEAKER

### Lecture Title: "Robotic General Surgery 16 Years of Experience at Athens Medical Centre"



#### Prof. Dr. Konstantinos Konstantinidis Chairman of General, Bariatric, Laparoscopic & Robotic Surgery, Athens Medical Center, Professor of Surgery, Ohio State University, USA, Scientific Director of Athens Medical Center

Chairs: Anastasios Karandreas, Andreas Karapashis

#### 18:40 - 19:05 KEYNOTE SPEAKER



"Modern Translational Research on Ultra-Low Temperatures in Biomedical Science" Prof. Dr. Nikolai Korpan Chairman, International Institute of Cryosurgery; Rudolfinerhaus Clinic, Vienna, Austria; 1st

Department of Surgery, National Medical University Kyiv, Ukraine

Chairs: Anastasios Karandreas, Andreas Karapashis

#### A word out of a life-threatening experience: from a famous recovered patient

#### 19:05 - 19:30 INTERACTIVE SESSION



#### "The Patients Perspective: Why (not) Me"

Encounter with the Famous goalkeeper **Carl Ikeme**, recovered patient of blood cancer Coordinator: Manolis Nikolousis

| 19:30 - 20:00 | Clinical Faculty Inauguration Ceremony<br>- Prof. Elizabeth Johnson, Dean<br>- Prof. Ioannis Patrikios, Deputy Dean |
|---------------|---|
| 20.00 - 21.00 | Cheese & Wine   |

**End of Sessions** 



10th International Multithematic Scientific Bio-Medical Congress (IMBMC) "Bio-medical Scientific Cyprus"

SATURDAY, 05 NOVEMBER 2022

## Program

- 8:45 8:50 EUC School of Medicine
- **8:50 9:30** (10 min each

## SELECTED ABSTRACTS

(10 min each **Oral Presentations** presentation) (The Presenting Authors are underlined)



"Externally Controllable Reprogramming Of Glioblastoma Multiforme by Radiofrequency - Responsive Genetically Engineered Neural Stem Cells" <u>Kyriacos Agathangelou</u><sup>1</sup>, Abdul Quddious, Nikolaos Dietis, Niovi Nicolaou<sup>1</sup>, Ina Meiser, Stavros Iezekiel, Costas Pitris and Andreani Odysseos<sup>1</sup> 1. Translational Nanomedicine and Nanobiotechnology Lab, EPOS-lasis Research & Development



"Repurposing Chemical Chaperones to the Rescue of Mouse Models of Alport Syndrome"

<u>C. Odiatis<sup>1</sup></u>, P. Ioannou<sup>1</sup>, K. Antoniadou<sup>1</sup>, M. Samiotaki, A. Malatras<sup>1</sup>, M. Pieri,

- G. Papagregoriou<sup>1</sup>, D. Ljubanović, K. Stylianou, C. Deltas<sup>1</sup>
- 1. Center of Excellence in Biobanking and Biomedical Research, Molecular Medicine Research Center, and University of Cyprus Medical School, Nicosia, Cyprus



"Epigenetic Enzymes As Potent Regulators Of Lipid Metabolism" <u>Evelina Charidemou</u>, Volker Behrends, Roberta Noberini, Tiziana Bonaldi, Julian L. Griffin, Antonis Kirmizis, Marie Curie Fellow, University of Cyprus



**"Automated Machine Learning-Based Prediction of Mortality and Survival Analysis in ICU Patients With Stroke"** Vasiliki Danilatou, Dimitrios Dimopoulos, Theodoros Kostoulas European University Cyprus, University of the Aegean Samos, GreeceEunomia Ltd, Ireland

Chairs: George Loukaides, Antonia Sophocleous

## SESSION XIII DIABETES The Magnitude of an unresolved Problem **Advances and New Treatment Approaches**

#### 9:30 - 9:50



## "Advances in Glucose Monitoring in Type 1 Diabetes" Assoc. Prof. Dr. Evangelos Rizos

Internal Medicine, European University Cyprus School of Medicine. Head of the outpatient Diabetes clinic, University hospital of Ioannina, Greece Chairs: Panagiotis Economides, Stelia Kadi Ioannidou





#### "Recent Developments in Automated Insulin Delivery Through Smart Pump Technology. Is it an Artificial Pancreas on the Way?" **Dr. Stavros Liatis**

NHS Director, Senior Consultant in Internal Medicine and Diabetology; Laiko General Hospital Chairs: Panagiotis Economides, Stelia Kadi Ioannidou

#### 10:10 - 10:30 "Preventing and Treating Diabetic Chronic Kidney Disease"



#### Dr. Ilias Migdalis Director in 2nd Medical Department and the Diabetes Centre at the NIMTS Hospital in Athens, Greece; core Member in the Scientific Advisory Group (SAG) in the field of diabetes/

endocrinology of the European Medicines Agency (EMA)

Chairs: Anastasios Mpagourdis, Zoi Dorothea Pana

#### 10:30 - 10:50 "Individualized Antithrombotic Therapy in Diabetics"



## **Prof. Dr. Christos Savopoulos**

Internal Medicine, Aristotle University of Thessaloniki, Director of 1st Medical Propedeutic Dept of Internal Medicine & Stroke Unit, Excellence Center of Hypertension, AHEPA University Hospital Chairs: Anastasios Mpagourdis, Zoi Dorothea Pana

10:50 - 11:10 "Management of Hyperglycemia in Type 2 Diabetes, 2022 Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)"



## **Prof. Dr. Apostolos Tsapas**

Prof. of Medicine and Diabetes; Director of the Second Medical Department; Director of MSc in Medical Research Methodology, Aristotle University Thessaloniki: Cruddas Link Fellow: Harris Manchester College; University of Oxford

Chairs: Andreas Ioannou, Christina Kousparou

#### "Multifactorial Aspects in Diabetes Management: New Perspectives" 11:10 - 11:30 Prof. Dr. Erifili Hatziagelaki



Prof. of Internal Medicine & Metabolic Diseases, 2nd Dept. of Internal Medicine, Research Institute & Diabetes Center University Hospital "Attikon" Medical School, National and Kapodistrian University of Athens, Greece

Chairs: Andreas Ioannou, Christina Kousparou

### **WORKSHOP I**

#### 11:30 - 12:45 CARDIOLOGY INTERACTIVE - SPORTS CARDIOLOGY In Greek Language. With physical presence



Organized & Sponsored By: Cyprus Sports Organization (CSO) Pre-Athletic Medical & Cardiological Testing for the Prevention of Sudden Cardiac Death in Young Athletes: Meet the experts

Σεμινάριο ενημέρωσης για το Προ-Αθλητικό Ιατρικό & τον Καρδιολογικό Έλεγχο στη Πρόληψη του Αιφνίδιου Καρδιακού Θανάτου στους Νέους, Αθλουμένους και Αθλητές ΚΥΠΡΙΑΚΟΣ ΟΡΓΑΝΙΣΜΟΣ ΑΘΛΗΤΙΣΜΟΥ



## ΚΥΠΡΙΑΚΟΣ ΟΡΓΑΝΙΣΜΟΣ ΑΘΛΗΤΙΣΜΟΥ ΑΝΩΤΑΤΟ ΣΥΜΒΟΥΛΙΟ ΥΓΕΙΑΣ ΑΘΛΗΤΩΝ ΚΥΠΡΙΑΚΟ ΙΝΣΤΙΤΟΥΤΟ ΚΑΡΔΙΟΛΟΓΙΑΣ

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Συνιστάται έγκαιρη δήλωση συμμετοχής στο lantonio@cytanet.com.cy



Οργάνωση Επιστημονικής Εκδήλωσης: Κυπριακό Ινστιτούτο Καρδιολογίας - Έρευνας και Μελέτης Μυοκαρδιοπαθειών και λοιπών Κληρονομικών Καρδιαγγειακών Νοσημάτων (ΚΙΚΕΜΜ)

Συντονιστής Εκδήλωσης: Δρ. Λοΐζος Αντωνιάδης MD, PhD, FESC, FACC, Καρδιολόγος, Πρόεδρος ΚΙΚΕΜΜ

Προεδρείο: Πέτρος Αγαθαγγέλου, Πρόεδρος Παγκύπριου Ιατρικού Συλλόγου και Γεωργία Δανιήλ, Καρδιολόγος, Γραμματέας Καρδιολογικής Εταιρείας Κύπρου Θέμα:



- Παρουσίαση Επιδημιολογικών δεδομένων για τον Αιφνίδιο Θάνατο των Νέων στον Κυπριακό πληθυσμό. Δρ. Ήρα Μούστρα Ηρακλέους, Πρόεδρος Καρδιολογικής Εταιρείας Κύπρου
- Παρουσίαση και Συζήτηση ενδιαφερόντων Ηλεκτροκαρδιογραφημάτων από την αξιολόγηση των Δελτίων Υγείας στις Ιατρικές Επιτροπές Αξιολόγησης των Δελτίων Υγείας του ΚΟΑ Παρουσίαση: Λοϊζος Αντωνιάδης, Καρδιολόγος, Πρόεδρος ΚΙΚΕΜΜ



Σχολιαστές:

- Άρης Αναστασάκης, Καρδιολόγος, Συντονιστής Εθνικού Δικτύου Ιατρικής Ακριβείας στην Καρδιολογία Επιστημονικός Υπεύθυνος Μονάδας Κληρονομικών και Σπανίων Νοσημάτων, Ωνάσειο Κέντρο
- Γιώργος Κ. Ανδρικόπουλος, Καρδιολόγος, Πρόεδρος του Ελληνικού Ινστιτούτου Αρρυθμίας, Διευθυντής Καρδιολογίας και του τμήματος Ηλεκτροφυσιολογίας και Βηματοδότησης του Νοσοκομείου Ερρίκος Ντυνάν



- **Σπύρος Παπαϊωάννου**, Καρδιολόγος, Επεμβατικός Καρδιολόγος, Διευθυντής Β΄ Καρδιολογικής Κλινικής, Ναυτικό Νοσοκομείο Αθηνών, πρόεδρος της Ελληνικής Αθλητικής Καρδιολογικής Εταιρείας

12:45 -13:30

Lunch Buffet

## **POSTER SESSION**

#### 13:30 - 13:55 KEYNOTE SPEAKER (HYBRID)

#### "Prediction and prevention of preeclampsia"

Special Quest (Hybrid Lecture)

#### **Prof. Dr. Kypros Nicolaides**

Professor in Fetal Medicine at King's College Hospital, London. One of the pioneers of fetal medicine, with seminal contributions to prenatal diagnosis and every major obstetrical disorder. Founder and chairman of the Fetal Medicine Foundation (FMF), UK

Chairs: Christos Liasides, Christina Stylianou

## **SESSION XIV**

CARDIOLOGY TODAY AND WHERE THE FUTURE TAKES US Blood Pressure: is it the tip of the spear? A note by the specialists

#### 13:55 - 14:15 "Noise Exposure and Hypertension: Connecting the Dots"



### Dr Dimitris Chatzis

Consultant Cardiologist, Clinical Hypertension Specialist (ESH) and Adj Assistant Professor European University Cyprus

Chairs: Bambis Nikolaides, Philippos Stylianou

#### 14:15 - 14:35 "Strategies to Improve Adherence and Persistence in the Treatment of Hypertension"



## Adj. Prof. Dr. Charalambos Grassos General Hospital of Attica "KAT" and Adjunct Professor, School of Medicine, European University Cyprus Chairs: Bambis Nikolaides, Philippos Stylianou

#### 14:35 - 14:55 "The Survival of the Fittest in the Cardiovascular Disease Continuum"



## Assoc. Prof. Dr. Andreas Pittaras Clinical Hypertension Specialist ESH, George Washington University, Washington DC, USA Chairs: Daniel Georgia, Era Moustra Heracleous

14:55 - 15:15 "Current Guidelines for the Prevention and Treatment of Cancer Associated Thrombosis"



#### Assoc. Prof. Dr. Gregoris Gerotziafas

Leader of the Thrombosis and Haemostasis Department in the Service d'Hématologie Biologique of Tenon University Hospital in Paris, France and the research group "Cancer Hemostasis and Angio- genesis" at the Faculté de Médecine, Sorbonne Université

Chairs: Daniel Georgia, Era Moustra Heracleous



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## SESSION XV

Arrhythmias – Electrophysiology and Cardiomyopathies- Atrial Fibrillation-Hypertrophic cardiomyopathy, Brugada syndrome-Heart Failure; Ways of Treatment for Proper Therapy: Is there such a thing?

#### **MEET THE EXPERTS**

### 15:15 - 15:35 "Myocarditis: Which Role For Genetics?"



**Dr. Aris Anastasakis** Consultant Cardiologist, Scientific Director, Unit of Inherited and Rare Cardiovascular Diseases **Onassis Cardiac Surgery Center** Chairs: Pantelis Kourtellaris, Elias Papasavvas

15:35 - 15:55 "Arrhythmia Induced Cardiomyopathy: From Bench to Bedside"



Prof. Dr. Stathis Iliodromitis Prof. of Cardiology, National and Kapodistrian University of Athens Chairs: Pantelis Kourtellaris, Elias Papasavvas

15:55 - 16:10 Coffee Break

Bayer X NOVAGEM



16:10 - 16:30 "Atrial Fibrillation: Is there any Room Left for the Good-Old Electrocardiogram (ECG)?" Prof. Dr. Vasilis Vasilikos Aristotle University of Thessaloniki, Director of Cardiology Department Chairs: Pantelis Kourtellaris, Elias Papasavvas

16:30 - 16:50 "Advances in Catheter Ablation of Arrhythmias" Is It Prime Time for Wider Application of Innovations and How the Patients Will Benefit from It?



Dr. George K. Andrikopoulos President of the Hellenic Arrhythmia Institute, Director of Cardiology and the department of Electrophysiology and Pacing, Henry Dunant Hospital

Chairs: Evagoras Economides, Giorgos P. Georgiou

16:50 - 17:10 "Artificial Intelligence for the Clinical Cardiologist"



Prof. Dr. Filippos Triposkiadis Form. Director of the Department of Cardiology of the Larissa University Hospital; School of Medicine, Larissa, Greece

Chairs: Evagoras Economides, Giorgos P. Georgiou

17:10 - 17:30 "Heart Failure Management: Update 2022"



**Prof. Dr. Gerasimos Filippatos** Professor and Chairman of the Department of Cardiology and Director of the Heart Failure and Cardioncology Unit at the Attikon University Hospital, Athens, Greece.

Chairs: Theodoros Christodoulides, Phivos Symeonides

#### 17:30 - 17:55 KEYNOTE SPEAKER



## "The Ultimate Goal: Is Gene Therapy in Hypertopic Cardiomyopathies Yet Possible?" Prof. Dr. Amanda Varnava

Head of cardiology, Imperial College NHS Trust, Consultant cardiologist at Welbeck, Expert advisor to the UK Football Association. Provides cardiac services to professional football teams, such as Arsenal, West Ham, Stoke City, Watford and Fulham

Chairs: Theodoros Christodoulides, Phivos Symeonides

#### 17:55 - 18:20 KEYNOTE SPEAKER



"Using Cells From Veins to Mend Broken Hearts: Where Do We Stand?" Prof. Dr. Paolo R Madeddu Chair of Experimental Cardiovascular Medicine, Bristol Heart Institute, Bristol, UK Chairs: Petros Agathaggelou, Anastasis Stephanou

18:20 - 18:30 Break

#### 18:30 - 19:30 CEREMONY: HONORARY PROFESSORSHIP



Professor Dr. Gregory Winter (Nobel 2018)



Professor Dr. Sir Martin Evans (Nobel 2007)

#### 19:30 - 19:35 **POSTER AWARDS**

**BY THE POSTER AWARD COMMITTEE** 

Congress Chair, Prof. Dr Ioannis Patrikios Award of a Honorary plaque from the Congress

#### **CLOSING REMARKS**

**Congress Chair, Prof. Dr Ioannis Patrikios** 

19:35- 20:45 Cheese & Wine

WORKSHOP I - FRIDAY, 04 NOVEMBER 2022, 14:00 - 17:00

## WORKSHOP II - SATURDAY, 05 NOVEMBER 2022, 14:00 - 17:00

"Rescue a Life, Yes You can" (In Both Greek and English Languages)

Workshop on Life Support By the Cyprus Resuscitation Council Parallel Sessions (Medical School, Amphitheater A for the introduction lecture and amphitheaters on 3rd floor for hands-on)

## Program

Moderators: Dr. Marios Georgiou, Dr. Aggeliki Mouzarou

- 14:00 14:30 Approach of the Deteriorating Patient (Airway, Breathing, Circulation, Disability, Exposure) Dr. Marios Georgiou, Dr. Nikos Savva
- 14:30 15:00 Basic Life Support (BLS) Defibrillation Dr. Aggeliki Mouzarou, Dr. Maria Georgiou

#### 15:10 - 17:00 Cardiac Arrest Simulation Teaching Sessions

Trainers will be separated into 3 teams of 5 persons each. Firstly, all participants will be trained in approaching the deteriorating patients. Then the program will be continued with a 30 minute session of Basic Life Support and Defibrillation, followed by a short lecture of Advanced Life Support. Finally, all participants will have the opportunity to handle three in-hospital cardiac arrest scenarios with the use of manikins and heart rhythm simulators.

## WORKSHOP III - FRIDAY, 04 NOVEMBER 2022, 14:00 - 17:00 WORKSHOP IV - SATURDAY, 05 NOVEMBER 2022, 14:00 - 17:00

Parallel Session (Amphitheatre Delta for the lecture and Ward on 3rd floor and Omega for hands on)

Workshop on Life Support-Airways By the Anesthesiology Society

14:00 - 14:30 Lecture

## 14:30 - 15:00 Approach the Patient and Life Support

#### 15:00 - 17:00 Simulation Teaching Sessions

Trainers will be separated into 3 teams of 5 persons each. Firstly, all participants will be trained in approaching the deteriorating patients. Then the program will be continued with a 30 minute session of Basic Life Support and Defibrillation, followed by a short lecture of Advanced Life Support. Finally, all participants will have the opportunity to handle three in-hospital cardiac arrest scenarios with the use of manikins and heart rhythm simulators.





## WORKSHOP V - FRIDAY, 04 NOVEMBER 2022, 10:00 - 12:00 "Thinking of working in the NHS, United Kingdom?"

**Parallel Session (Auditorium Beta)** 

## Program

 10:00 - 11:00 "Thinking of Working in the NHS, United Kingdom?" - An EUC alumnus experience
 Dr. Anthony Lisacek-Kiosoglous University College London Hospital NHS, Foundation Trust, United Kingdom; European University Cyprus, School of Medicine Author email: ANTHONY@LKIOSOGLOUS.COM
 11:00 - 12:00 "Does on Call Simulation Training have a Place in Medical Education?" Dr. Anthony Lisacek-Kiosoglous University College London Hospital NHS, Foundation Trust, United Kingdom; European University Cyprus, School of Medicine Dr. Ryan Reese (Primary co-author) would present this paper, as he will also attend. Bronglais General Hospital, Aberystwyth Wales; United Kingdom

Author email: RYAN\_REES@HOTMAIL.CO.UK

# WORKSHOP VI (Interactive) - SATURDAY, 05 NOVEMBER 2022, 14:30 - 16:30 "Beyond White Coats"

Cymsa, (E) IFMSA

Parallel Session (Auditorium Beta) Organized by (CyMSA/IFMSA)

## Program

14:30 - 15:10 "Community Outreach, International Networking opportunities for Medical Students"

CyMSA/IFMSA

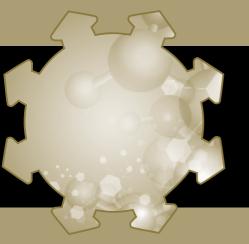
- 15:10 15:50 "Health Entrepreneurship Initiatives" Kyriakos Masonou, Junior Achievement Cyprus
- 15:50 16:30 "The Humanitarian Aspect of Being a Doctor Around the World" Dr. Apostolos Veizis

#### **Dr. I.Patrikios**

Founder and Chairman, Congress Scientific committee

| CLINICAL FACULTY        | Clinical Faculty Inauguration  |
|-------------------------|--|
| Avraam Elia             | CLINICAL PROFESSOR, PEDIATRICS - ARCHBISHOP MAKARIOS III<br>HOSPITAL   |
| Agathaggelou Petros     | CLINICAL ASSOCIATE PROFESSOR, CARDIOLOGY - C.Y.M.A PRESIDENT   |
| Alexandrou Maria        | CLINICAL ASSOCIATE PROFESSOR, MICROBIOLOGY – BIOPATHOLOGY<br>- LARNACA GENERAL HOSPITAL                                    |
| Amalia Hatzigianni      | CLINICAL ASSOCIATE PROFESSOR, CARDIOLOGY – AMMOCHOSTOS<br>GENERAL HOSPITAL   |
| Anagnostopoulos George  | CLINICAL ASSISTANT PROFESSOR, MEDICAL PHYSICS - GERMAN<br>ONCOLOGY CENTER  |
| Artemiou Omeros         | CLINICAL ASSISTANT PROFESSOR, CARDIOTHORACIC SURGERY -<br>GERMAN ONCOLOGY CENTER   |
| Benoit Marconi          | CLINICAL LECTURER, GENERAL PRACTICE – CARE MEDICAL CENTER  |
| Charis Armeftis         | CLINICAL ASSISTANT PROFESSOR, RESPIRATORY – LUNG CENTER,<br>LIMASSOL   |
| Christodoulou Sophia    | CLINICAL LECTURER, INTERNAL MEDICINE - GERMAN ONCOLOGY<br>CENTER   |
| Christos Mina           | CLINICAL PROFESSOR, PEDIATRIC SURGEON, ARCH. MAKARIOS III<br>HOSPITAL  |
| Christou Soteroulla     | CLINICAL ASSISTANT PROFESSOR, GENERAL MEDICINE, THAL-<br>ASSEMIA - THALASSEMIA CENTER, ARCHBISHOP MAKARIOS III<br>HOSPITAL |
| Constantinos Economides | CLINICAL ASSISTANT PROFESSOR, CARDIOLOGY – APOLLONION<br>HOSPITAL  |
| Constantinos Pougiouros | CLINICAL ASSISTANT PROFESSOR, NEUROLOGY – APOLLONION<br>HOSPITAL/AGIA SKEPI  |
| Doros Polydorou         | CLINICAL LECTURER, ENDOCRINOLOGY – PRIVATE PRACTICE  |
| Elias Tsougos           | CLINICAL ASSISTANT PROFESSOR, CARDIOLOGY - HYGEIA HOSPITAL<br>ATHENS   |
| Ferentinos Constantinos | CLINICAL ASSISTANT PROFESSOR, RADIATION ONCOLOGY - GERMAN<br>ONCOLOGY CENTER   |
| Fountzila Elena         | CLINICAL ASSOCIATE PROFESSOR, MEDICAL ONCOLOGY - GERMAN<br>ONCOLOGY CENTER   |

| George Astras          | CLINICAL ASSSOCIATE PROFESSOR, ONCOLOGY – AMERICAL MEDI-<br>CAL CENTER/AMERICAN CANCER CENTER PLATONAS |
|------------------------|--|
| George M. Georgiou     | CLINICAL ASSOCIATE PROFESSOR, CARDIOLOGY – APOLLONION<br>HOSPITAL                                      |
| Ioannides Kleanthis    | CLINICAL ASSISTANT PROFESSOR, RADIATION ONCOLOGY - GERMAN ONCOLOGY CENTER                              |
| Ioannis Stephanou      | CLINICAL LECTURER, CARDIOLOGY – APOLLONION HOSPITAL  |
| Karagiannis Efstratios | CLINICAL LECTURER, RADIATION ONCOLOGY - GERMAN ONCOLOGY<br>CENTER                                      |
| Kouriefs Chrysanthos   | CLINICAL ASSISTANT PROFESSOR, UROLOGY - GERMAN ONCOLOGY<br>CENTER                                      |
| Kyriakos Kakoullis     | CLINICAL ASSISTANT PROFESSOR, OB/GYN – APOLLONION HOSPITAL   |
| Michaelides Michalis   | CLINICAL LECTURER, DIAGNOSTIC AND INTERVENTIONAL RADIOLO-<br>GY - GERMAN ONCOLOGY CENTER               |
| Michalis Picolos       | CLINICAL ASSOCIATE PROFESSOR, ENDOCRINOLOGY – PRIVATE<br>PRACTICE                                      |
| Neophytou Andreas      | CLINICAL PROFESSOR, PEDIATRIC SURGERY -ARCHBISHOP MAKARI-<br>OS III HOSPITAL                           |
| Nicolas Polydorou      | CLINICAL ASSISTANT PROFESSOR, THORASIC SURGEON – APOLLON-<br>ION HOSPITAL                              |
| Nikolaou Annet         | CLINICAL LECTURER, MEDICAL ONCOLOGY - GERMAN ONCOLOGY<br>CENTER  |
| Pantziara Maria        | CLINICAL LECTURER, DIAGNOSTIC RADIOLOGY - GERMAN ONCOLO-<br>GY CENTER                                  |
| Petrou Athanasios      | CLINICAL ASSOCIATE PROFESSOR, SURGERY - GERMAN ONCOLOGY<br>CENTER                                      |
| Prokopi Marianna       | CLINICAL ASSOCIATE PROFESSOR, RESEARCH IN ONCOLOGY - GER-<br>MAN ONCOLOGY CENTER                       |
| Strouthos Iosif        | CLINICAL LECTURER, RADIATION ONCOLOGY - GERMAN ONCOLOGY<br>CENTER                                      |
| Thrasivoulou Yiannis   | CLINICAL ASSOCIATE PROFESSOR, ENT - GERMAN ONCOLOGY<br>CENTER  |
| Vrahimis Alexis        | CLINICAL PROFESSOR, NUCLEAR MEDICINE - GERMAN ONCOLOGY<br>CENTER                                       |



# Bio-medical Scientific Cyprus

# Speakers CVs



#### Professor Dr. Gregg L. Semenza, Nobel Prize in Medicine (2019)

Director, Vascular Program, Institute for Cell Engineering, Professor of Genetic Medicine, Johns Hopkins

Dr. Semenza is the C. Michael Armstrong professor of genetic medicine, with joint appointments in pediatrics, radiation oncology, biological chemistry, medicine, and oncology at the Johns Hopkins University School of Medicine. He serves as the founding director of the Vascular Program at the Johns Hopkins Institute for Cell Engineering and the founding director of the Armstrong Oxygen Biology Research Center.

Dr. Semenza received an A.B. (in Biology) from Harvard University and M.D. and Ph.D. (in Genetics) degrees from the University of Pennsylvania. He completed pediatrics residency training at Duke University Medical Center and postdoctoral training in medical genetics at Johns Hopkins. He has been a member of the Johns Hopkins faculty since 1990.

Dr. Semenza's lab discovered hypoxia-inducible factor 1 (HIF-1), a transcription factor that controls the expression of thousands of genes in response to changes in oxygen availability, for which he was awarded the 2019 Nobel Prize in Physiology or Medicine. His current research interests include investigating the molecular mechanisms of oxygen homeostasis and the role of HIF-1 in cancer progression. He has authored more than 450 research articles and book chapters, and his work has been cited by other scientists more than 175,000 times. Dr. Semenza is co-founder of HIF Therapeutics Inc., which is focused on the development of HIF inhibitors for the treatment of cancer and blinding eye diseases.

In addition to the Nobel Prize, Dr. Semenza has received the Albert Lasker Basic Medical Research Award (2016), Wiley Prize in Biomedical Sciences (2014), Lefoulon-Delalande Grand Prize from the Institut de France (2012), and the Canada Gairdner International Award (2010).





#### Professor Sir Gregory Winter, Nobel Prize in Chemistry (2018)

Laboratory of Molecular Biology, Medical Research Council; Master, Trinity College, Cambridge University, Cambridge, UK

Sir Gregory Winter is a member of the Medical Research Council Laboratory of Molecular Biology (LMB) in Cambridge and until recently, served as its Deputy Director. He is now the Master of Trinity College, Cambridge. Sir Gregory Winter graduated from Cambridge University in 1973, specializing in chemistry and biochemistry. He continued his studies with Cambridge University, receiving his PhD in 1976, specializing in protein and nucleic acid sequencing. Sir Gregory Winter is a pioneer in the science of protein engineering, focusing first on enzymes and then antibodies. At the LMB, he invented techniques to humanize rodent antibodies for use as therapeutics (1986), and later to make fully human antibodies (1989) using combinatorial gene repertoires. His inventions are used in about half of the antibody products on the market, including the humanized antibodies Campath-1H, Herceptin, Avastin, Synagis, and the first human antibody (Humira) to be approved by the U.S. Food and Drug Administration. Sir Winter is also an entrepreneur. He is a founder of Cambridge Antibody Technology (1989) and Domantis (2000). Both of these companies pioneered the use of antibody repertoire technologies to make fully human antibody therapeutics. In 2006, Cambridge Antibody Technology Ltd. was acquired by AstraZeneca PLC and Domantis Ltd. by GlaxoSmithKline PLC in 2006. Most recently, Sir Gregory Winter founded Bicycle Therapeutics Ltd., a biotechnology company dedicated to the development of a new generation of biotherapeutics.



#### Professor Sir Martin Evans, Nobel Prize in Medicine (2007)

Cardiff University

Professor Sir Martin Evans was the first scientist to identify embryonic stem cells, which can be adapted for a wide variety of medical purposes. His discoveries are now being applied in virtually all areas of biomedicine – from basic research to the development of new therapies.

In 2007, he was awarded the Nobel Prize for Medicine, the most prestigious honour in world science, for these "ground-breaking discoveries concerning embryonic stem cells and DNA recombination in mammals."

Sir Martin gained his BA in Biochemistry from Christ College, University of Cambridge in 1963. He received an MA in 1966 and a DSc in 1966. In 1969 he was awarded a PhD from University College, London. He joined the Cardiff University School of Biosciences in 1999.

Sir Martin has published more than 120 scientific papers. He was elected a Fellow of the Royal Society in 1993 and is a founder Fellow of the Academy of Medical Sciences. He was awarded the Walter Cottman Fellowship and the William Bate Hardy Prizes in 2003 and in 2001 was awarded the Albert Lasker Medal for Basic Medical Research in the US. In 2002 he was awarded an honorary doctorate from Mount Sinai School of Medicine in New York, regarded as one of the world's foremost centres for medical and scientific training. He has also received honorary doctorate awards from the University of Bath, University of Buckinghamshire, University College London, University of Wales and the University of Athens.

He was knighted in 2004 for his services to medical science and in 2009 was awarded the Gold Medal of the Royal Society of Medicine in recognition of his valuable contribution to medicine. In 2009 he also received the Baly Medal from the Royal College of Physicians and the Copley Medal, the Royal Society's oldest award, joining an eminent list of previous recipients including Albert Einstein.



#### **Professor Dr Kypros Herodotou Nicolaides**

Professor in Fetal Medicine at King's College Hospital, London. One of the pioneers of fetal medicine, with seminal contributions to prenatal diagnosis and every major obstetrical disorder. Founder and chairman of the Fetal Medicine Foundation (FMF), UK.

Kypros Herodotou Nicolaides was born on April 9th,1953, in Paphos, Cyprus. He studied Biochemistry and Physiology BSc (1st class honours), King's College (1974); Medicine, King's College Hospital, London University (1978) and Obstetrics and Gynaecology, MRCOG (1984). Since 1992 until now he is Professor of Fetal Medicine, King's College, London University. Director Harris Birthright Research Centre for Fetal Medicine, King's College Hospita.

#### Awards:

Highest awards of excellence from many professional bodies, e.g. International Society Ultrasound in Obstetrics & Gynecology, World Association of Perinatal Medicine, American Institute of Ultrasound in Medicine, International Academy of Perinatal Medicine, European Association of Perinatal Medicine, Intenational Society for the study of hypertension in pregnancy.

Eardley Holland Gold Medal for outstanding contribution to the science, practice and/or teaching of Obstetrics and Gynaecology, Royal College of Obstetricians and Gynaecologists.

Excellence in Letters, Culture and Science, Government of Cyprus, Medal of exceptional services to the Republic of Cyprus, Grand Cross of the Order of Makarios III from the Republic of Cyprus, Gold Cross of The Order of the Phoenix from the Republic of Greece.

Honorary Doctorates in Medicine from 14 Universities across the World

Scientific Activities:

Published 1,603 peer-review papers in Scientific Journals. His h-index is 184 (highest of all obstetricians and gyaecologists in the world) and his work has been cited more than 135 thousant times.

Supervised 66 doctors to undertake research leading to postgraduate qualifications and has provided training in Fetal Medicine to 600 doctors from 50 countries.

**Professional Activities:** 

Director of the Research Centre for Fetal Medicine, King's College Hospital

This centre, which was opened in 1984 by Princess Diana, was the first Fetal Medicine Centre in Britain and is the biggest one in the world. More than 10,000 patients are examined each year and many of these patients are referred from other hospitals in Britain and other countries because of serious complications of pregnancy. In addition, more than 200 doctors from all over the world visit the centre to observe and receive training.



#### Founder and Chairman of the Fetal Medicine Foundation

This charity was set up in 1995. The main source of income is a private clinic which donates all its profits to the charity. The aims are to promote research and training in Fetal Medicine throughout the World. More than £45,000,000 have been donated to finance the training of many doctors from all over the world and to carry out major multicentre studies.

#### Areas of research:

Developed new methods for screening for chromosomal defects and fetal abnormalities, screening and prevention of preterm birth and preeclampsia, fetal therapy.



#### **Professor Dr Stylianos E. Antonarakis**

Professor of Genetic Medicine at the University of Geneva Medical School, Switzerland.

Stylianos E. Antonarakis is currently Emeritus Professor (active) at the University of Geneva. He was previously Professor and founding Chairman of Genetic Medicine at the University of Geneva Medical School, and the founding director of iGE3 (institute of Genetics and Genomics of Geneva). He is a medical, molecular, human geneticist, physician-scientist, who studied extensively the relationship between genomic and phenotypic variation. He received his MD (1975) and DSc (1982) from the University of Athens Medical School, and after a specialization in Pediatrics in the University Hospital, Athens Greece, he moved to Baltimore, Maryland to the program of Medical Genetics at the Johns Hopkins University School of Medicine with Haig H. Kazazian and Victor McKusick (1980-1983). He joined the faculty of the Johns Hopkins University in 1983 and rose to full professor of Pediatric Genetics, Biology and Medicine in 1990. In 1992 he moved to Geneva. Switzerland to chair Genetic Medicine in the University of Geneva. His research work includes the structural and functional analysis of the genome, molecular bases of monogenic disorders and complex genetic disorders including the beta-thalassemias, hemophilias, and trisomy 21. His laboratory participated in the human genome sequence and functional analysis, particularly on chromosome 21. He is an international expert on disorders of chromosome 21, identifying genes for genetic disorders, development of diagnostic tests, genome structure and function, studies of the genome variability, and conserved non-coding sequences in human DNA. He has published extensively (more than 750 well-cited papers and reviews) in the scientific literature and is co-editor of the current edition of the classic textbook "Genetics in Medicine"; he is listed as one of the highly cited scientists by the ISI institute (ISI h-index 125, GoogleScholar index 156). He was the President of the European Society of Human Genetics (2001-2002), the President of HUGO (2013-2017), foreign member of the Academy of Athens (2003), member of EMBO (2006), honorary member of the Swiss Academy of Medical Sciences (2017). He holds Honoris Causa degrees from the University of Thrace (2016) and Athens (2018). He was the co-organizer of the European School of Genetic Medicine, and in the last 42 years taught in the Bar Harbor Genetics Course, Maine. He was awarded the Society of Pediatric Research Young Investigator Award (1984), International Jerome Lejeune Prize (2004), the European Society of Human Genetics Award (2005), the M.Trueta award 2019 for his contributions to trisomy 21, the Roscoe Awards for excellence in teaching, and the William Allan 2019 Award which is internationally the highest distinction in genetics. for his lifetime contributions to genomic medicine. Part of the work that led to the 2019 Nobel Prize on Medicine to Gregg Semenza was performed in his laboratory when Semenza was a postdoctoral fellow. He was elected to the Society of Scholars of the Johns Hopkins University (2006), the American Academy of Physicians (2010). He was awarded the Commander of the Order of Phoenix medal from the Hellenic Democracy (2007). More than 110 talented young scientists were trained in his laboratory (graduate students and postdoctoral fellows); in addition, more than 30 young physicians were trained in the Medical Genetics Clinic of his department. With Haig Kazazian he has established one of the first molecular diagnostic laboratories in USA as early as 1982. He was a member of the Swiss National Science Foundation Research Council for 8 years, and the Chair of the Genetics Review Panel of the EU ERC for 8 years. His research laboratory was/is supported by grants from the National Institutes of Health, the European Union (including the European Research Council), and the Swiss National Science

Foundation and numerous other Foundations including the Gebert, Lejeune, and ChildCare Foundations. His is the originator of the World Down Syndrome Day (http://en.wikipedia.org/ wiki/World\_Down\_Syndrome\_Day) celebrated yearly on March 21. His current interests and research projects are the functional analysis of the genome, the effect of human genetic variation to phenotypic variation, the discovery of genes and variation for mendelian disorders, the molecular pathogenesis of trisomy 21 and polygenic phenotypes, the functional characterization of the conserved fraction of the genome, the genomics of single cells, diagnostics and prevention of genetic disorders, and the societal implications of genetics and genome research. He has created a pioneer "Genome Clinic" at the University Hospitals of Geneva in 2014 to provide diagnostics based on the individual genetic variation. He founded in 2017 "Medigenome, The Swiss Institute of Genomic Medicine" and he serves as CEO and Chief Medical Officer.



#### Professor Dr Philippe Menasché

Clinical cardiac surgeon at the Hospital Européan Georges Pompidou, Professor (Emeritus) of Thoracic and Cardiovascular Surgery at the University of Paris Cité

Philippe Menasché is a clinical cardiac surgeon at the Hospital Européan Georges Pompidou, Professor (Emeritus) of Thoracic and Cardiovascular Surgery at the University of Paris Cité, and co-leader of an INSERM (National Institute of Health and Medical Research) team devoted to cell therapy of cardiovascular diseases. He also has a part-time affiliation with the Department of Biomedical Engineering of the University of Alabama in Birmingham. His group has a long-standing experience in basic, translational and clinical research, exemplified by two firstin-man surgical procedures (first myocardial transplantation of autologous skeletal myoblasts in 2000 and first transplantation of human embryonic stem cell-derived cardiac progenitor cells embedded into a fibrin patch delivered onto the epicardium of the diseased area in 2014). More recently, the group has refocused its interest towards leveraging the paracrine effect of cells to generate a cellular secretome, which might help streamlining the clinical applications.



#### **Professor Dr Paul Moss**

Prof. of Haematology and Deputy Head of the College of Medicine at the University of Birmingham, UK. Chief Investigator of the UK Coronavirus Immunology Consortium

Paul Moss is Professor of Haematology and Deputy Head of the College of Medicine at the University of Birmingham, UK. He runs a specialist clinical service in chronic lymphoid leukaemia and was Co-Author of Essential Haematology, one of the bestselling haematology textbooks. He runs an immunology research group with a focus on viral, cancer and transplant immunology and is Chief Investigator of the UK Coronavirus Immunology Consortium (UK-CIC), a consortium of 20 Universities which leads the UK immunology response to the pandemic. He holds Programme grant funding from the Medical Research Council and Cancer Research UK and several of his discoveries have been translated into clinical trials including a novel form of antigen-specific cell therapy. He has published over 230 publications with over 28,000 citations. Professor Moss was awarded an OBE in the Queens Honours List of 2022.



#### **Professor Dr Kostantinos Kstantinidis**

Professor of Surgery, Ohio State University, USA Chairman of General, Bariatric, Laparoscopic & Robotic Surgery, Athens Medical Center, Scientific Director of Athens Medical Center

is a World leader in robotic surgery. He was the first surgeon in Greece and Southeast Europe to perform robotic surgery in 2006. At the same time, he was a pioneer and opened up the way when, at the invitation of Intuitive Surgical, he performed the world's first single-incision robotic surgery, which was later followed by many more firsts in the field of robotic surgery.

After 15 years as a robotic surgeon, he has performed more than 3.500 operations. Add to this another 16.500 laparoscopic surgeries and his experience in minimally invasive surgery exceeds the landmark of 20.000 operations.

In his 30-year career in Greece, the prominent robotic-assisted general surgeon at the Athens Medical Center has been a mentor of hundreds of Greek and foreign surgeons, who follow in his footsteps with their achievements in the hospitals of Europe and the US. Intuitive Surgical awarded this important distinction to Dr. Konstantinidis, also considering the fact that the surgical operations he has performed extend to the whole spectrum of general surgery. In particular, his vast experience in surgery covers a number of procedures performed in the esophagus – stomach, pancreas, liver – bile duct, small and large intestine, as well as obesity and metabolic surgery, abdominal wall hernias, sports hernias, adrenal surgery, spleen and internal genital organs surgery and retroperitoneal tumors.

The US company, based in California, USA, is the manufacturer of the Da Vinci surgical robotic systems that have revolutionized the field of minimally invasive surgery recognised the Greek general surgeon in the world's leading position in the field of General Surgery.



#### Professor Dr Wolfgang F. Graier

Medical University of Graz, Austria Head of the Nikon-Center of Excellence for Super-Resolution Microscopy CEO and Owner, of Next Generation Fluorescence Imaging, Graz, Austria

Dr. Wolfgang F. Graier is Full Professor of Molecular Biology at the Medical University of Graz, Austria. Initially he studied pharmacy and did his Ph.D. in pharmacology at the Karl Franzens University of Graz (Graz, Austria). Thereafter, he joined the Dalton Cardiovascular Research Center at the University of Missouri (Columbia, USA). Afterwards, he became Assistant Professor and finally, in 2009, Full Professor and chair of the Institute of Molecular Biology and Biochemistry at the Medical University of Graz (Graz, Austria), and finally head of the Gottfried-Schatz-Research-Center in 2018. Prof. Graier is an expert in the regulation of mitochondrial ion homeostasis and organelle functions, and the contribution of mitochondria in diabetes mellitus, cancer and aging. His main research focus is on the molecular mechanisms, regulation and functions of cellular and mitochondrial Ca2+ homeostasis and their impact on physiological and pathophysiological processes. Recently he focused on the potential of mitochondria-endoplasmic reticulum interaction as potential target against aging, cancer and neuro-degenerative disease and designs test-compounds for such applications. To follow cellular changes in real time and in super-resolution, his laboratory specializes in cutting-edge microscopy like structured illumination microscopy (SIM). Since 2015 he is head of the Nikon-Center of Excellence for Super-Resolution Microscopy where his team continuously pushes the limits of light microscopic techniques. Moreover, his group creates, characterizes and employs organelle-targeted genetically encoded biosensors to follow, for instance, changes in spatial Ca2+, organelle ATP and sub-cellular NO• or K+ levels. This intensive focus led Prof. Graier to co-find a spin-off company, Next Generation Fluorescence Imaging (NGFI, www.ngfi.eu), that intends to develop affordable microscopic analyzers for molecular/cell biologists to help to establish high-content single cell analyses in more laboratories worldwide.



#### Professor Dr Nikolai N. Korpan

Chairman, International Institute of Cryosurgery; Rudolfinerhaus Clinic, Vienna, Austria; 1st Department of Surgery, National Medical University: Kviv, Ukraine

Nikolai N. KORPAN is born in Husiiv, Ukraine and he got his MD from the Kyiv National Medical University. In 1994 he was assigned as a Professor of Surgery in the State University Uzhgorod, Ukraine and in 1995 as an Assistant Medical Director, Vienna, Austria. Prof. KORPAN is the founder and Chairman of the International Institute of Cryosurgery, Vienna, Austria and is known worldwide both as a doctor and as a scientist and enjoys an excellent reputation among colleagues internationally. Dr. Korpan predominantly developed clinical implications that are used at extremely low temperatures, including an organ preservation technique. He presented his unique longstanding clinical experiences with ultra-low temperatures in treating patients with severe primary and secondary malignant diseases worldwide. To date, Prof. Korpan has made more than 300 scientific publications in every prestigious journal in the world and published 12 scientific monographs, including "Bible of CRYO". Yet he is not only an outstanding scientist, researcher and discoverer, but also a practical inventor. His innovative ideas have led to 57 national, European and international patents, including in the USA, Japan and China. He is awarded many honors including the Gold Medal of Hippocrates. Science, Technology, Society and International Nobel Movement. Tambov, Russia in 2017.



#### Professor Dr Paolo Madeddu

Chair of Experimental Cardiovascular Medicine (Cardiovascular regenerative medicine, Tissue engineering, Therapeutic angiogenesis, and Gene therapy), Bristol Heart Institute, Bristol, UK

Prof. Paolo Madeddu is an Italian – British born in Sassari, Italy. He got the degree in Medicine from the University of Sassari, Italy in 1976 with the title of "Doctor in Medicine and Surgery". He completed his specialty in Cardiology from the University of Sassari in 1980. Currently he has the post of full Professor. From the year 1980 to 2005 he served as a Senior Researcher with clinical appointment of Consultant at Institute of Internal Medicine, University of Sassari, Italy and in 2005 he was qualified as an Associate Professor in the same University. From 1999 to 2005 he was the director of Experimental Medicine and Gene Therapy INBB Interuniversity Consortium, Osilo and Alghero Technological Park, Italy. From 2012 to 2015 he served as the Head of Regenerative Medicine Section in the School of Clinical Sciences, Faculty of Medicine and Dentistry, University of Bristol. For the last 10 years in research, he granted more than 10M Pounds and he is an author of 327 publications in PUBMED with a Citation index of 64. His main Interests are: Cardiovascular regenerative medicine, Tissue engineering, Therapeutic angiogenesis, and Gene therapy.



#### Dr Amanda Varnava

Head of cardiology, Imperial College NHS Trust, Consultant cardiologist at Welbeck,

Expert advisor to the UK Football Association. Provides cardiac services to professional football teams, such as Arsenal, West Ham, Stoke City, Watford and Fulham.

Amanda Varnava is a Consultant Cardiologist, and Head of Service for cardiac services at Imperial College Healthcare Trust. Dr Varnava undertook her medical training at Oxford University and St Bartholomew's Hospital and completed with Honours. She went on to train in cardiology at The Royal Brompton Hospital & St George's Hospital, where she undertook an MRC research fellowship. She is a consultant cardiologist and honorary senior lecturer at Imperial College and the lead for Inherited Cardiac Conditions where she runs a busy service seeing over 2000 adult and paediatric patients a year.

She also has a specialist interest in sports cardiology, and is on the Football Association expert advisory panel and cardiologist to many premiership football teams including Arsenal and Watford football clubs.

Dr Varnava is the Trust lead for cardiac sarcoid disease and runs a multi-disciplinary service.

Dr Varnava has an interest in cardiology in pregnancy and runs a specialist pregnancy and heart disease service. She has extensive experience in managing patients with heart failure. Her research interests are in the non-invasive risk stratification of the sudden death syndromes, especially Hypertrophic cardiomyopathy and Brugada syndrome. She is council member for the Association of Inherited Cardiac Conditions, and expert advisor to Cardiomyopathy UK. She regularly lectures at international meetings and has published widely in leading medical journals.



#### **Professor Dr Vassilios Vassilikos**

Director of the 3rd Cardiology University Department at Hippokrateio General Hospital, Thessaloniki, Greece

Vassilios Vassilikos completed his medical education (1983) and obtained his Doctoral Thesis (1989) at the Aristotle University of Thessaloniki, Greece.

He was trained in Cardiology in Thessaloniki and UK, where he further specialized in Invasive Cardiology and Electrophysiology at St Bartholomew's Hospital London. He practiced as consultant Cardiologist for several years at the Onassis Cardiothoracic Centre, Athens. In 2014 he was elected Professor in Cardiology and Director of the 3rd Cardiology University Department, Thessaloniki. Since 2019 he is an Adjunct Professor at the European University of Cyprus.

He is the past President of the Hellenic Working Group on Pacing and Electrophysiology, and Treasurer of the Hellenic Cardiac Society. He is a committee member of the Working Groups for training in undergraduate and post-graduate Medicine, the National Guidelines for training in Cardiology, drug prescription on arrhythmias, Specialty Boards in Cardiology in Greece, and the new English-speaking Undergraduate Program in Medicine at the Aristotle University of Thessaloniki. Recently he was elected President-Elect of ISHNE (International Society for Holter and Non-Invasive Electrocardiology).

He is the founder and the PI of the National Registry of Ablations and CRM Devices in Greece. Has been working on the field of signal processing related to the prediction of atrial fibrillation occurrence and in digital Cardiology (development of smartphone apps for patients with various cardiac problems).

He participated in numerous international trials as Primary Investigator, published extensively, and actively participates in local, regional and international scientific meetings.

He is a Fellow of the American College of Cardiology, the European Society of Cardiology, and member of numerous National and International scientific societies.



#### **Professor Dr Filippos K. Triposkiadis**

Director of the Department of Cardiology of the Larissa University Hospital, Larissa, Thessaly, Greece

Filippos Triposkiadis was born in Athens, Greece in 1955. He graduated from the Medical School of the University of Athens in July 1979 and from October 1979 to December 1981 he did his military service in the Hellenic Navy. From October 1983 to October 1984, he did his provincial service in the Division of Cardiology, Cephalonia General Hospital, Cephalonia, Greece and thereafter he trained for one year in Internal Medicine in the Medizinische Klinik, Abteilung III, Universitaet Tuebingen, Germany. From January 1985 to January 1988, he did his Cardiology training in the Division of Cardiology, 251 Hellenic Air force General Hospital. He did postgraduate training in Cardiology for a total of two years in the Division of Cardiology, The Ohio State University, Columbus, Ohio, USA under the guidance of Prof. Harisios Boudoulas MD and Assistant Prof. Randall C. Starling MD. From March 1990 to October 1999, he served as an attending cardiologist in the Department of Cardiovascular Surgery, Hippokration General Hospital, Athens, Greece.

Dr Triposkiadis became Assistant Professor of Cardiology at the Faculty of Health Sciences of the University of Thessaly in September 1997, Associate Professor of Cardiology in May 2003, and Professor of Cardiology in October 2007. He was appointed adjunct Professor of Cardiology of the European University of Cyprus in June 2019. Dr Triposkiadis was the Director of the Department of Cardiology of the Larissa University Hospital for more than 20 years (2000 to 2021). He also served as Director of the Internal Medicine Sector of the Faculty of Health Sciences of the University of Thessaly for three mandates (2006-2007, 2008-2009 and 2009-2010) and as Chief Medical Officer of the Larissa University Hospital for one mandate (2011-2015).

Dr. Triposkiadis is currently a member of several international scientific societies including the European Society of Cardiology (Fellow), the American College of Cardiology (Fellow), and the Heart Failure Association (HFA) of the European Society of Cardiology (Fellow). He is also President-elect of the Hellenic College of Cardiology and Vice President of the Hellenic Society for the Study and Research of Heart Failure.

The clinical activities of Dr Triposkiadis have included invasive cardiology, heart failure, and intensive care. Moreover, he has done extensive research work on the physiology and pathophysiology of the left atrium, the significance of coexisting morbidities in heart failure, the pathophysiology and management of heart failure, the sympathetic nervous system, and the physiology and pathophysiology of the left ventricular ejection fraction.

Dr Triposkiadis has been a member of Steering Committee/National Coordinator and/or Principal Investigator of more than 25 international RCTs, and an author/co-author of about 300 publications in extenso. Additionally, he is the editor of one Textbook of Cardiology (two editions, Athens 2003, and Athens 2016) which has been adopted by several Hellenic Medical Schools and co-editor of one Textbook on Diabetes-Heart-Vessels (Athens 2010).



Dr Triposkiadis has organized several cardiology meetings including the Cardiology Congress of Central Greece (annual international meeting, 1998 to date) and Hellenic-Cypriot Seminar on Cardiovascular Diseases (annual international meeting, 2010 to 2019).



#### Dr George K. Andrikopoulos

Director of the 1st department of Cardiology and the department of Electrophysiology and Pacing, Henry Dunant Hospital, Athens, Greece

Dr George Andrikopoulos obtained his medical diploma from the Medical School of Athens University (1990) and his basic training as a Cardiologist at Hippokration Hospital in Athens (1999). As a research fellow of the European Society of Cardiology he was trained on cardiovascular genetics at the Department of Biological Sciences, University of Warwick, UK (2000) and as a Clinical Research Fellow at Walsgrave Hospital, Coventry, UK (1999). He received his PhD at Cardiovascular genetics from the University of Athens (2004).

He is president of the Hellenic Arrhythmia Institute (2018-2021), past-president of the Institute for the Study and Education on Thrombosis and Antithrombotic Therapy (2016-2018), founding member of the Hellenic Cardiovascular Research society (2007) and special scientific advisor of the board of the Hellenic Heart Foundation. Regarding his research activities he has published 132 manuscripts cited at Pubmed and a total of more than 300 papers. He was National coordinator of the EuroHeart project and member of the board for WP5 (2007-2009), National coordinator of the CHOB project of the European Heart Network (2004-2006), Principal investigator of the GEMIG, HELIOS, RHYTHMOS, TARGET, MANAGE-AF, PHAETHON, and other studies and co-principal investigator of the multicentre, international, SPICE study.

He works at Henry Dunant Hospital as a director of the 1st department of Cardiology and the department of Electrophysiology and Pacing.



#### **Professor Dr Gerasimos Filippatos**

Professor and Chairman of the Department of Cardiology and Director of the Heart Failure and Cardioncology Unit at the Attikon University Hospital, Athens, Greece.

Dr Filippatos is Professor and Chairman of the Department of Cardiology and Director of the Heart Failure and Cardioncology Unit at the Attikon University Hospital, Athens, GR. He was Dean of the School of Medicine, University of Cyprus. He studied Medicine at the University of Patras, GR, and earned his doctorate Cum Laude from the University of Athens. He completed his clinical training in Chicago, USA, and Cambridge, UK. He is past President of the Heart Failure Association of the ESC. He has served in the ESC Practice Guidelines Committee and the ACC/AHA Heart Failure Guidelines Writing Committee and as International Governor of the ACCP. He was Associate Editor of the European Heart Journal, and he is Senior Consulting Editor of JACC-HF. He has published over 500 articles in peerreviewed journals and authored more than 30 book chapters including the ESC Textbook of Acute and Intensive Cardiac Care, Highly Commended in the British Medical Association Medical Book Awards, and the books "Heart Failure: The Expert's Approach" and "Treatment Algorithms in Heart Failure". Prof. Filippatos is in the Thomson Reuters list of Highly Cited Researchers. He is Honorary Member of many Cardiac Societies.



#### Associate Professor Dr Grigoris Gerotziafas

Associate Professor of Hematology, Faculty of Medicine Sorbonne University, Paris, Head of the Thrombosis Department, Tenon Hospital, Paris & Director of the cancer and thrombosis research group

Grigoris Gerotziafas is Co-director of the research group "Cancer, Biology and Therapeutics" and leads the research team "Cancer-Haemostasis-Angiogenesis" INSERM UMRS-938. In his clinical activity he leads the Clinical Haemostasis Group at Tenon-Saint Antoine Hospital AP-HP.6 and is Associate Professor of Hematology at the Faculty de Medicine, Sorbonne University in Paris. The Research Group "Cancer-Haemostasis-Angiogenesis" is specialized in the interactions of cancer cells with blood coagulation and vasculature in tumor microenvironment and the development of new therapeutic strategies and risk assessment models.The Clinical Haemostasis Group, using personalized medicine approaches and artificial intelligence methodology, is expertized center on cancer associated thrombosis, thrombophilia, platelet disorders, antithrombotic treatment, vascular complications of pregnancy, subfertility and failure of assisted reproductive techniques related with vascular alterations. Prof Gerotziafas leads the post-graduated Master programme "Thrombosis and Haemostasis in Haematology" at the Faculty de Medicine, Sorbonne University in Paris. He animates an international group of experts which developed the COMPASS-CAT score for the risk evaluation of cancer associated thrombosis in ambulatory patients, the COMPASS-COVID-19 score for the evaluation of the risk of disease worsening in patients with COVID-19 and the COMPASS-COVID-19-ICU score for the risk of intubation of patients with severe COVID-19. He leads the ROADMAP-Thrombosis project which investigates for clinically relevant biomarkers of cellular hypercoagulability in patients with solid cancers, haematological malignancies, COVID-19. And vascular complications of pregnancy and infertility. On behalf of the Borad of the VAS European Foundation on Angiology and Vascular Medicine, Prof. Gerotziafas leads the International Project for Guidance on the management of vascular patients with COVID-19. He also leads the International Group for Integrated and Equitable Strategy Against COVID-19 Pandemic. Prof. Gerotziafas has leaded or contributed as an expert to the development of several international and national guidelines for the prevention and treatment of venous thromboembolic disease and arterial thrombosis. He is also member of the International Society on Thrombosis and Hemostasis (ISTH) Scientific and Standardization Committee for Haemostasis and Malignancy and for Control of Anticoagulation, the International Conference on Thrombosis and Hemostasis Issues in Cancer (ICTHIC) and the European Thrombosis and Haemostasis Alliance (ETHA). He chairs the Scientific committee of the Vascular Independent Organisation (VAS) and he is member of the Board of Trustees of the European and Mediterranean League against Thromboembolic Disease Foundation and Society. Professor Gerotziafas is Visiting Professor in Loyola Faculty of Medicine (Department of Molecular Pharmacology and Therapeutics), Chicago and at the School of Medicine at Hofstra/Northwell (Department of Medicine, Anticoagulation and Clinical Thrombosis Services) New York USA and Faculty of Medicine at the European University of Cyprus. Professor Gerotziafas has published extensively in peer-reviewed international journals and has authored several book chapters. He sits on the review boards of several international journals and is member of several professional societies.



#### Associate Professor Dr Emmanouil Nikolousis

Associate Professor of Hematology,

#### Chairman, School of Medicine, European University Cyprus

Emmanouil Nikolousis graduated from Aristotle University Medical School, Thessalonika, Greece in 1997. Following his graduation with 'suma cum laude' he has completed 3 years of General Medical Training in Greece. He was committed into research from his early days in Medicine and following General Medical Training he was successfully granted the PhD title in June 2002. He was trained as a Specialist Registrar in Haematology in the West Midlands region and completed his training at the end of March 2011 with sub specialisation in haematological malignancies ,stem cell transplants and cellular therapies when he was appointed as a Consultant Haematologist at Birmingham Heartlands Hospital on the 1st of April 2011.During his Consultant job he has published his clinical research in peer review journals and became a member of the national working party for AML and the systemic and intrathecal chemotherapy lead for Heart of England NHS Trust. He became the Clinical Director for Haematology in December 2014 after successfully finished his MBA health with distinction and ward 19 under his leadership won the team of the year award in 2019 and the innovative care award for the chemotherapy at home project in 2018.

In May 2019 he was appointed as the Deputy Divisional Director for University Hospital Birmingham Division 5 for Haematology and Stem cell transplantation, Oncology, Neurology, Neurosurgery and Plastic Surgery. He was the peer review inspector for Haematology since 2017 ensuring quality standards are maintained within Haematology Departments across the U.K.

Since September 2021 he is the Clinical Director for Haematology at Athens Medical Centre and the Associate Professor of Haematology at European University of Cyprus Medical School. He has published a significant number of high impact peer review papers and was invited as a guest speaker in numerous international meetings. During his free time, he enjoys sports and travelling.



#### **Professor Dr Vasso Apostolopoulos**

Pro Vice-Chancellor, Research Partnerships at Victoria University, Australia Expertise with development of drugs and vaccines

Vasso Apostolopoulos was born in Melbourne Australia in 1970. Her parents migrated to Australia from Amaliada Greece in 1966. She received her PhD in 1995 from the University of Melbourne and Advanced certificate in Protein Crystallography University of London. She has undertaken research at the Austin Research Institute Australia, Burnet Institute Australia, Sir William Dunn School of Pathology Oxford University, Scripps Research Institute USA, Mater Medical Research Institute (sabbatical) and was a visiting researcher at numerous Universities around the world. Her expertise is in the areas of immunology, crystallography, cellular biology, translational research and development of drugs and vaccines. Vasso has lead/Directed a number of research programs at the Austin Research Institute, the Burnet Institute, Centre for Chronic Disease at Victoria University, and, at the Institute for Health and Sport. She was the Vice President Research, Deputy Vice-Chancellor Research, Associate Provost (Research Partnerships) and is currently the Pro Vice-Chancellor (Research Partnerships) at Victoria University, Australia. Vasso has received >100 awards, published >500 research papers and books, is an inventor on 20 patents and her current interests are treating chronic diseases with an immunological focus, in particular in the areas of cancer, autoimmune disorders, mental health and infectious diseases.



#### Assistant Professor Dr Demetris Papamichael

Director of Medical Oncology at the Bank of Cyprus Oncology Centre, Nicosia.

Assist. Professor at St. George's Hospital-Medical School, University of London / UNIC Campus

Demetris Papamichael is Director of Medical Oncology at the Bank of Cyprus Oncology Centre in Nicosia, a post he has held since 1999. He is also an Assistant Professor at St. George's Hospital-Medical School, University of London / UNIC Campus. He obtained his medical degree from Charing Cross and Westminster Medical School, University of London in 1988. Dr Papamichael trained in internal medicine and obtained his Membership of the Royal Colleges of Physicians (MRCP) in 1992. His subsequent training in Medical Oncology was completed at the Royal Marsden and St Bartholomew's Hospitals in London. He is an American Society of Clinical Oncology (ASCO) Merit Award winner and is an active researcher having participated in Industry sponsored studies as well as clinical trials coordinated by the European Organisation for Research and Treatment of Cancer (EORTC) and the UK Medical Research Council/National Cancer Research Institute.

Dr Papamichael's main clinical interests include gastrointestinal cancer, and cancer in the elderly. He has published his work in peer-reviewed international journals. He is a member of ASCO, the European Society for Medical Oncology (ESMO), and the International Society of Geriatric Oncology (SIOG). Recently he headed a Task Force responsible for developing recommendations for the management of colorectal cancer in the elderly under the auspices of SIOG. He is a member of the ESMO Gastrointestinal Tumour Faculty and co-chairman of an ESMO/SIOG Cancer in the Elderly Working Group. Dr Papamichael is actively involved in the organisation and teaching for courses run by the European School of Oncology (ESO) and is a member of the Scientific Committee of the School.



#### Professor Dr Erifili Hatziagelaki

Research Institute & Diabetes Center, 2nd Dept. of Internal Medicine, University Hospital "Attikon"; Medical School, National and Kapodistrian University of Athens, Greece

Erifili Hatziagelaki is Professor of Internal Medicine & Metabolic Diseases at Medical School of National and Kapodistrian University of Athens, Greece, and Head of the Diabetes Center in the 2nd Dept. of Internal Medicine, Research Institute & Diabetes Center at the University Hospital"Attikon". She graduated from the Cologne University Medical School, Germany (1983) and then she completed her training in Internal Medicine and Diabetology at "Evangelismos" Hospital, Athens, Greece (1994). She holds a doctor's license in Germany and Greece. Her scientific interests comprise clinical and experimental research on the pathophysiology of diabetes mellitus (Pathogenesis, Genetic, Insulin Resistance, Immunology). During her time at the 2nd Dept. of Internal Medicine of Athens University, she focused on the clinical research field of Pharmacokinetics of human insulin as well as of oral antidiabetic drugs. Furthermore, she completed, with a scholarship by "NATO", a two-years (1995-1997) Postdoctoral Honorary Research Fellow at the Division of Immunology of Diabetes and Islet-Transplantation in the 3rd Medical Clinic and Policlinic of Justus-Liebig University of Giessen, Germany, which was a highly regarded Medical Center as International Registry of Pancreatic Islet Transplantation. She was engaged there in clinical and basic research in the field of immunology in diabetes and pancreatic islet transplantation. In addition, she extended her scientific focus as a Visiting Professor in the IV. Medical Clinik und Policlinic, Tübingen University, Germany, (Invitation from Professor H.U.Häring which was authorized by the Athens Medical School) for 5 years (2010-2015). During her stay in that department, she has been involved not only in research protocols but also in the daily monitoring of diabetic patients in the outpatient clinic as well as in hospitalized diabetic patients. Since November 2015 she works as a visiting professor at the University of Düsseldorf, Germany, German Diabetes Center (DDZ), Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf and she is involved in the research in the field of diabetes and fatty liver disorders. Over the years, she contributed to different fields of metabolic research, such as clinical trials on diabetes treatment, the role of islet autoantibodies for diabetes diagnosis, studies on diabetes genes and more recently fatty liver disease, an emerging field in metabolic research. Some of these activities attracted international funding by DAAD, Germany, NIDDK - the National Institutes of Health and the JDRF Juvenile Diabetes Research Foundation, USA. Her research is recognized by her serving as a reviewer in 21 International journals. In addition she is the Vice President of CEDA (Central European Diabetes Association) and Member of the European Type 1 Diabetes Genetics Consortium (ET1DGC), reflecting her international recognition in the field of diabetes. Furthermore, she serves as President of the Diabetes Committee of the Central Health Council of the Ministry of Health (KESY), as President of the Examination Committee for the Diploma of Specialty in Diabetes in Greece, as General Secretary of the Greek Association for the Study of Risk Factors for Vascular Diseases, as Vice President of the Greek Association "Diabetes Academy", as Member of the Secondary Scientific Advisory Board of the National Organization for Medicines (EOF) and as Member of the Secondary Scientific Advisory Board of the Hellenic Association of Pharmaceutical Companies (SFEE).



### **Dr. Dimitrios Kyparissopoulos**

Honorary Consultant Thoracic Surgeon at Royal Brompton & Harefield NHS Foundation Trust; Robotic & Minimal Invasive Thoracic Surgeon; Ygia Polyclinic, Limassol, Cyprus. Associate Clin. Professor, University of Nicosia, Medical School

Dimitrios Kyparissopoulos was Born on May 19th 1972 at Chania, Crete, Greece. Raised in Volos city, Greece, where he graduated from primary, secondary and high school having been graduated with countless golden academic medals and scholarships at school. Graduated from Pharmaucetical School, Aristotle University Thessaloniki with scholarship for 2 years, then passed with "Excellent" degree 1st in Medical School, University of Ioannina, Greece.

Graduated from Medical School of University of Thessaly, Larissa, Greece after total 6 years in the Medical School, where he had the honor to study and work under the guidance of famous late Professor Panayotis Spyrou.

Started his fellowship in Cardiothoracic Surgery at the University Hospital of Larissa, Greece, under Prof. Spyrou and then he was Resident of General Surgery for 3 years in total, at General Hospital of Lamia and Volos, Greece. Then 2 more years of Cardiothoracic Surgery at the University Hospital of Larissa, Greece with extra training of Cardiothoracic ITU at Onassis Cardiothoracic Centre, Athens, Greece.

In 2007, after being nominated twice with the Golden Medal in EACTS courses in Bergamo, Italy, he decided to continue his Residency abroad, starting in MST Spectrum Twente, Enscede, Netherlands. In 2008 he applied for a Residency Post in Cardiothoracic Surgery in the UK, and he was succesfully interviewed by a panel which was chaired Professor Magdi Yacoob, at notorious Harefield Hospital.

He finished his training as Cardiothoracic Surgeon at St. Thomas's Hospital, London, UK, and succesfully passed his specialty exams and becomes Cardiothoracic Surgeon. He was employed as Consultant Thoracic Surgeon at Harefield hospital where he worked for 3 years, where he performed more than 1.000 thoracic procedures, with excellent outcomes. He was trained and established VATS Lobectomies as standard practice for Curative Lung Resections and delivered more Cryotherapy treatment than anyone else in the UK.

In September 2014 he works as a Consultant Thoracic Surgeon at the John Radcliffe University Hospital of Oxford, which is the centre with the highest rate of VATS Lobectomies in the UK. On top of that, he operates on Sarcoma patients, as Oxford University Hospital is the bigest Sarcoma Centre in the UK and on of the biggest in the world. In February 2016 he moves to Cyprus where he has already performed the whole spectrum of Thoracic procedures for first time ever, either thoracoscopic or robotic.

He remains Honorary Consultant Thoracic Surgeon at Harefield Hospital (Royal Brompton and Harefield NHS Foundation Trust, London, UK. The highest honor and worldwide recognition come in February 2020 when the world-renowned medical journal CTSnet publishes an innovative robotic surgery performed last summer and presented for the first time in medical journals.

You can watch the video on CTS net webpage here

And that was only the beginning. Until now, four innovative (three of them are Robotic) and exceptionally difficult procedures have already been published by CTSnet magazine. That is a unique achievement, and speaks volumes about his medical experience and surgical efficiency.

Mr Dimitrios Kyparissopoulos is currently a Honorary Consultant Thoracic Surgeon at Harefield Hospital, Royal Brompton and Harefield NHS Foundation Trust, London, UK, the only Robotic and Thoracoscopic Minimal Invasive Consultant Thoracic Surgeon in Cyprus and one of the few around the world. He is an Associate Clinical Professor at University of Nicosia, Medical School



# Associate Professor Dr Athanasios S. Petrou

Associated Professor in Surgery, European University CY, School of Medicine; Director of the Advanced Laparoscopic Hepatobiliary-Pancreas and Surgical Oncology Center at Mediterranean Hospital, EU, Cy; Director of the Hepato-Pancreatico-Biliary (HPB) Department at, American Institute of Minimal Invasive Surgery (AIMIS), EU, Cy; Director of the Liver and Pancreatic Surgery Unit at, Athens Medical Center - Athens Medical Group

Athanasios Petrou completed his Higher Surgical Training in the First Department of Surgery, University of Athens Medical School, LAIKO Teaching Hospital, Athens, Greece in 2009. He completed his Higher Surgical Training in the First Department of Surgery, University of Athens Medical School, LAIKO Teaching Hospital, Greece in 2009, with Internship Training as a Honorary Clinical Fellow in HPB Surgery at the Department of HPB Surgery, Hammersmith Hospital, London, UK Clinical Fellow at the Hammersmith Hospital London - Department of HPB Surgery. During his Higher Surgical Training, he trained extensively in HPB Surgery along with Surgical Oncology.

His expertise in HPB and Surgical Oncology was further enhanced during his Fellowships in The Royal Marsden Hospital NHS Trust - Department of Academic Surgery (HPB & Surgical Oncology), and, in the Churchill Hospital, University of Oxford - HPB & Transplant Centre (Upper GI/HPB, and, Transplant surgery).

He gained a Master of Science (MSc in Hepato-Pacreatico-Biliary/HPB Surgery), in 2009 from the Democritus University of Thrace Medical School, and a PhD in Medicine (Liver Surgery), in 2010 from the National and Kapodestrian University of Athens, Medical School.

Dr Petrou deals with Surgical Treatments and Management for the whole spectrum of HPB diseases. These includes gallstone, biliary and pancreatic diseases. Surgery for cancer of the liver, biliary system and the pancreas also fall within his expertise. He also has a special interest in the Surgical Oncology.

The treatment of the Upper Gastrointestinal Tract malignancies (Oesophageal & Gastric Cancer), as well as, the Abdominal Retroperitoneal Sarcomas, Colorectal Surgery, and, the Adrenal surgery are integrated in his proficiency.

He is formally trained in minimal invasive surgery (Laparoscopic and Robotic surgery) and he established the first program of the Advanced Laparoscopic HPB Surgery in Cyprus.

Main topic of his clinical interest is the treatment of non-resectable Pancreatic and Liver malignancies with the IRE - Irreversible Electroporation method (Nanoknife).

From 2014 until 2020 he was leading the Nanoknife Program for the treatment of unresectable Liver and Pancreatic tumors at the American Medical Center, Nicosia, CY (www.amc.com.cy)

He is currently the Head of Hepato-Pancreato-Biliary & Surgical Oncology Department at Mediterranean Hospital of Cyprus and at the Athens Medical Center in Greece. On 2017, the European-African Hepato-Pancreato-Biliary Association (E-AHPBA) (http://www. eahpba.org/) has assigned him as Member of Committee on Educational Activities.

Dr Petrou is Associated Professor in Surgery at the European University - School of Medicine and a member of the Association of Upper GI Surgeons and the Association of Surgeons of Great Britain and Ireland. He is also Member of the International Hepato – Pancreato - Billiary Association (IHPBA), of the European Hepato – Pancreato - Billiary Association (EHPBA), and, the European Society of Surgical Oncology (ESSO).

He has more than 100 publications (https://athanasiospetrou.academia.edu/) (scientific original papers and abstracts) in international peer reviewed journals and decades of studies presented in international surgical meetings and conferences.



### Professor Dr Leonidas A. Phylactou

CEO and Medical Director, The Cyprus Institute of Neurology & Genetics, Nicosia, Cyprus.

Leonidas Phylactou studied in UK and USA and then did a postdoc at the University of Oxford, where he set up a team working on gene therapy for Myotonic Dystrophy. In 1998, he established a research group at the Cyprus Institute of Neurology and Genetics (CING) working on the gene function and gene therapy. In 2005, he was appointed Head of the Department of Molecular Genetics, Function and Therapy. His research interests focus on the gene therapy for muscular dystrophy, the identification of biomarkers in Myotonic Dystrophy and the investigation of molecular causes for inherited diseases. Since November 2015, he is also the Chief Executive Officer and Medical Director of CING and the Provost of the Cyprus School of Molecular Medicine at CING.



### Professor Dr George M. Spyrou

Chair of the Bioinformatics European Research Area and the Head of the Bioinformatics Group at the Cyprus Institute of Neurology and Genetics

George M. Spyrou is the Bioinformatics European Research Area Chair Holder and the Head of the Bioinformatics Department at the Cyprus Institute of Neurology and Genetics (CING). He holds a BSc on Physics, an MSc on Medical Physics and an MSc on Bioinformatics. Dr. Spyrou is the Bioinformatics Course Coordinator at the Postgraduate School of CING where he has been elected as full Professor in 2019. He is also a visiting instructor on Systems Bioinformatics and Network Analysis in other postgraduate courses. Dr. Spyrou is a Senior IEEE Member and a Member of the Steering Committee for the creation of the European Bioinformatics Infrastructure ELIXIR-Cyprus Node. Up to now, he has served as Editorial Board Member, Reviewer and Invited Speaker or Chairman in scientific sessions related to Biomedical Informatics topics while he has authored/co-authored a significant number of scientific publications in peer reviewed journals and in international conference proceedings. His work is focusing on Network-based Computational Diagnostics and Therapeutics.



### **Professor Dr Konstantinos Toutouzas**

Director of the cardio-oncology and structural valve disease outpatient clinic of First Department of Cardiology, Athens School of Medicine.

Dr Konstantinos Toutouzas completed his medical studies at University of Athens Medical School, his residency at the First Department of Cardiology of the University of Athens in Hippokration Hospital and an interventional cardiology fellowship in Centro Cuore Columbus, Milan, Italy. At present he is a Professor of Cardiology, Director Cardio-oncology outpatient clinic, Director of the valvular heart disease outpatient clinic at the First Department of Cardiology, Athens Medical School, Hippokration Hospital, Board member of the Onassis Cardiac Surgery Center and a Board member of the Athens Medical School Faculty

He is a member of several Greek and international scientific societies, including the Hellenic Society of Cardiology, the European Society of Cardiology (FESC), the European Association of Percutaneous Cardiovascular Intervention (EAPCI) and the Society for Cardiac Angiography and Interventions (SCAI). He has also served as Chairman of the Greek Working Group of Interventional Cardiology. His main clinical interest focuses on the area of Interventional Cardiology. He performs the full range of interventions in coronary circulation including coronary angiography, percutaneous angioplasty and intracoronary imaging techniques (intravascular ultrasound and optical coherence tomography). He also successfully deals with the interventional treatment of structural heart diseases.

He has rich scientific work with more than 290 publications in peer-reviewed journals and more than 5700 citations. At present, Prof. Toutouzas is Chairman of the Postgraduate Program 'Interventional Cadiology' at Athens School of Medicine. Prof. Toutouzas has just been elected (OCtober -21-2022) as the next president of the Hellenic Society of Cardiology.



### **Dr Dimitri Richter**

Head of Cardiac Department, Euroclinic Hospital, Athens, Greece

Dimitris Richter MD, FESC, FAHA is the Head of Cardiac Dept, Euroclinic Hospital, Athens, Greece since 2002. He has a Special interest in Lipids treatment, Coronary Artery Disease Prevention and Treatment and thrombosis management.

He was elected as President of Hellenic Lipidology Society 2013-2017, President of Institute of thrombosis research 2018-20, member of the board of Hellenic Heart Foundation since 2009, President WG epidemiology and Prevention - Hellenic Heart Society 2008-9, President of the Council of Clinical Practice of ESC 2018-20, and Member of Committee of Practice Guidelines of the ESC 2016-2020.

He is Editor in chief of "Heart and Vessels", the official publication of the Hellenic Heart Foundation since 2010, an ESC Fellow since 2005, AHA Fellow since 2006. He is author of various papers in international peer-reviewed journals with an IF of > 400 and Co-author of various ESC guidelines on: CVD prevention in clinical practice (2016) and revascularization (2014 and 2018), Dyslipidemia (2019).



### **Associate Professor Dr Andreas Pittaras**

Cardiologist, Clinical Hypertension Specialist ESH George Washington University, Washington DC, USA

Andreas Pittaras was born in Athens, Greece in 1959. He is currently Ass. Professor in the Faculty of medicine at the George Washington University, Washington DC, Director at MEDITON Medical Center Athens Greece, Head Consultant Cardiologist and Hypertension Specialist at Hypertension & Cardiovascular Prevention Clinic, Cardiology Department, Asklepeion Hospital, Athens, Greece, and President of Hellenic Society of Cardiovascular Prevention. He graduated (1984) from Medical School of National and Kapodistrian University, Athens, Greece. He then completed his clinical training in Cardiology (1992) at "Alexandra" Therapeutic University clinic, Athens, Greece. He has worked for 4 years (1993-1997) as cardiology research fellow in Hypertension and Atherosclerosis Institute at Veterans Hospital, Washington DC (Georgetown University educational program), and then currently cardiovascular research associate at the same department (George Washington University educational program). His research focuses on cardiovascular system, hypertension, coronary artery disease, arrhythmias, heart failure, lipids and exercise. He has published 40 papers in peer-reviewed journals (NEJM, Hypertension, Circulation, JACC etc), and 5 book chapters. He has given more than 100 lectures in international meetings, more than 400 lectures in national meetings, with several awards for best and top scoring abstracts in international meetings (AHA, ACC, ESC, ESH, ASH).



## **Dr Spyridon Papaioannou**

Commander Director of Cardiology Department of Athens Naval Hospital, scientific head of the nuclear cardiology department of the hospital, scientific director of the interventional cardiology department of the Central Clinic of Athens, Greece

Spyridon Papaioannou completed his medical studies at the Aristotle University of Thessaloniki in 1990. He graduated from the Military Medical School and then studied at the Mayo Clinic in Jacksonville, Florida, USA. He finalized his specialty at the Onassis Cardiac Surgery Center. After three years of education, he was declared Doctor in Aristotle University of Thessaloniki in hypertension subjects. Then he specialized in interventional cardiology at Walsgrave Hospital in England with a scholarship from the Hellenc heart Society. All these years actively involved in organizational committee's conferences in Greece and abroad and he has over 45 research publications in the field of cardiology.

Currently he is the Commander Director of Cardiology Department of Athens Naval Hospital, scientific head of the nuclear cardiology department of the hospital, scientific director of the interventional cardiology department of the Central Clinic of Athens, member of European and American Heart Association, In parallel is while practices cardiology in private sector. He is also founder of Biomedgene Molecular Genetics Laboratory



### Professor Dr Miltiadis (Miltos) Matsagkas

Vascular Surgeon, School of Medicine, University of Thessaly, Greece

Miltiadis Matsagkas was born in Ioannina, Greece in 1963. He is currently a Professor of Vascular Surgery in the Faculty of Medicine at the University of Thessaly, working as a Vascular Surgeon at the Vascular Surgery Department of the University Hospital of Larissa based in Larissa, Greece. He is the Associate Secretary of the European Society for Cardio Vascular and Endovascular Surgery (ESCVS), (May 2017-present) and the Greek Councilor of the European Society for Vascular Surgery (ESVS), (September 2018-present). He is a founding member and currently the Secretary General of the Institute for the Study and Education on Thrombosis and Antithrombotic Therapy, Greece (ISETAT), (September 2018-present) and the Director of the M.Sc. Course "Thrombosis and Antithrombotic Treatment" of the Faculty of Medicine of the University of Thessaly, (October 2018-present). Furthermore, he is the founder and current Editor in Chief of the Hellenic Journal of Vascular and Endovascular Surgery (HJVES), (April 2018-present), as well as a founding member and Vice President of the Institute of Vascular Diseases (IVD), (2010-present). He received his M.D. in 1987 and his Ph.D. with distinction in 1998 by the Medical School of Athens University, Greece. He was gualified as a Vascular Surgeon in 1998 after the end of the clinical training in surgery (3 years) and vascular surgery (4 years). Additionally, named member of the European Union of Medical Specialists (UEMS) Division and European Board of Vascular Surgery, in September 2002, and became Fellow of the European Board of Vascular Surgery (FEBVS).



#### **Professor Dr Vangelis G. Manolopoulos**

Director at the department of Pharmacology of Democritus University of Thrace Medical School in Alexandroupolis, Greece and at the Clinical Pharmacology Unit of the Academic General Hospital of Alexandroupolis

Dr Vangelis G. Manolopoulos is a full professor of Pharmacology, Pharmacogenomics, and Precision Medicine, and director at the department of Pharmacology of Democritus University of Thrace Medical School in Alexandroupolis, Greece and at the Clinical Pharmacology Unit of the Academic General Hospital of Alexandroupolis. He obtained a PhD from the Medical School of Patras University in 1991. Between 1992 and 1995 he did postdoctoral research at the Milwaukee Clinical Campus of the University of Wisconsin. Then he took a post as senior research scientist at the Medical School of the Katholic University in Leuven, Belgium, between 1995 and 1998. Since 1998 Dr Manolopoulos has been in a faculty member teaching basic and clinical pharmacology to medical students at his university and since 2001 he has developed and teaches a course in Pharmacogenetics, one of the first to be introduced to the Medical School undergraduate curriculum worldwide. He has authored more than 110 indexed publications that have received more than 2800 citations (H# 30), including one in New England Journal of Medicine as senior corresponding author (NEJM 369:2304, 2013). His current interests include research and clinical applications of pharmacogenomics and epigenetics in drugs used for cardiovascular diseases, diabetes, anticoagulant therapy, and psychiatric diseases. In addition he has a long-standing interest in endothelial cell physiology and atherosclerosis. He directs a Masters course in Clinical Pharmacology and Therapeutics and heads the Research Committee of his Medical School. He is a regular evaluator of EU Grants (FP6, FP7, HORIZON). He is the president of the Greek Society for Basic and Clinical Pharmacology. He is also President-elect of the European Society for Pharmacogenomics and Personalized Therapy (ESPT), and he is co-opted in the Executive Committee of the European Association for Clinical Pharmacology (EACPT).



### Professor Dr Kyriakos E. Kypreos

Chairman of the Pharmacology laboratory of the Department of Medicine at the University of Patras School of Health Sciences, Patra, Greece

Professor Kyriakos E. Kypreos received his Ph.D. in Biochemistry in 1998 from Boston University Medical School Division of Graduate Medical Sciences (Boston, MA. U.S.A). Following his graduation, Prof. Kypreos did his post-doctoral training at the Whitaker Cardiovascular Institute at Boston University Medical Center in the U.S.A (1998-2002) and at Leiden University Medical Center, Department of Human Genetics (2002-2004) in the Netherlands. In 2004 he returned to the USA where he became Instructor and in 2006 Research Assistant Professor in Medicine at Boston University School of Medicine. From 2001 to 2007 Prof. Kypreos served on the scientific advisory board of KOS Pharmaceuticals during which time he was introduced to the world of Pharmacology. In 2008, he was appointed as Associate Professor of Pharmacology at The University of Patras School of Health Sciences. Department of Medicine, in Greece. where in December 2013, he was promoted to the rank of full Professor of Pharmacology. Since September 2014, he is the Chairman of the Pharmacology laboratory of the Department of Medicine at the University of Patras School of Health Sciences. At this capacity, he established the service unit "Center for Clinical Pharmacology and Toxicology" of the laboratory aiming at facilitating precision medicine decisions. In addition to his main appointment, since September 2019 he also holds a secondary academic appointment as Adjunct Professor of Pharmacology and Metabolic Disorders at the European University Cyprus, School of Sciences, Department of Life Sciences.

Prof. Kypreos' research interests focus on the pharmacology of metabolic syndrome. In particular his team research the mechanisms underlying the development of the pathological conditions associated with metabolic syndrome with emphasis placed on the lipoprotein transport system. Ultimate goal of their studies is the identification of novel pharmacological targets and the development of lead compounds for the treatment of these conditions.Prof. Kypreos' previous research works have been featured in high profile international media including ASBMBToday.

Prof. Kypreos has been an EMBO Fellow, a Marie-Curie Fellow , and the winner of "Irvine H. Page" Atherosclerosis Research Award, offered by the ATVB council of the American Heart Association. His research activities have been funded by competitive research grants from the General Secretariat for Research and Technology, the Hellenic Foundation for Research and Innovation, the Hellenic State Scholarship Foundation, the European Community and the industry.

Prof. Kypreos is member of the editorial board of the American Journal of Physiology-Endocrinology and Metabolism, the Journal of Biomedical Research and the journal Androgens. As of Dec 1 2018, Prof. Kypreos is an elected member of the Executive Committee of the Hellenic Atherosclerosis Society (HAS), an affiliate of the European Atherosclerosis Society (EAS). Since 2016, Prof. Kypreos is the vice chairman of the National Pharmacovigilance Committee (EFAR), the committee responsible for the safety of medicines and vaccines for human use. Prof. Kypreos also served in the past as member of the Health Technology Assessment (HTA) committe (EAAΦAX) of the Hellenic Ministry of Health, the committee responsible for evaluating all new drug applications for being reimbursed by the public health system. At present he is aso a vice editor of the high impart peer revewed journal "pharmacology".

In addition, Prof. Kypreos has extensive teaching duties. Currently, he co-coordinates and teaches various Pharmacology courses for medical and graduate students at the University of Patras Medical School and other Institutions in Greece and abroad.



# Professor Dr Maria Konstandi

Professor and Chair in the Department of Pharmacology in the Faculty of Medicine at the University of Ioannina, Greece

Maria Konstandi was born in Thesprotiko -Preveza, Greece 1957. Currently she is a Professor and Chair in the Department of Pharmacology in the Faculty of Medicine at the University of Ioannina, Greece. She studied Pharmacy at the Aristotle University of Thessaloniki and received her PhD in Neuropharmacology at the National and Kapodistrian University of Athens. Her predominant research interests focus on the regulation of drug metabolizing enzyme systems emphasizing on the role of stress. She also investigates the potential anticancer properties of antipsychotics using in vitro and in vivo models. In the framework of her sabbatical leave, she worked as a visiting research scientist in the Department of Enzymology and Toxicology at the International Agency for Research on Cancer (IARC/WHO), Lyon, France for one and a half year (1992-1993 and 1996) and in the Laboratory of Metabolism at NCI/NIH, Bethesda, Maryland, USA for two years (2007-2009). During her 35-year academic career she has established collaborations with prestigious research institutes including the LM/NCI/NIH, Bethesda, USA, the University of Uppsala, School of Pharmacy, Uppsala, Sweden, the Karolinska Institute, School of Medicine, Stockholm, Sweden and the University of Queensland, National Research Centre for Environmental Toxicology (Entox), Australia.



### **Associate Professor Dr Evangelos C Rizos**

Diabetologist, Head of the outpatient Diabetes clinic, University hospital of Ioannina, Greece; Associate Professor, School of Medicine, European University Cyprus (EUC), Nicosia, Cyprus.

Evangelos C Rizos is a consultant in Internal Medicine, Diabetologist, University Hospital of Ioannina, Greece; Diabetologist, Head of the outpatient Diabetes clinic, University hospital of Ioannina, Greece; Associate Professor, School of Medicine, European University Cyprus (EUC), Nicosia, Cyprus.

He is former visiting Assistant Professor in Internal Medicine in the University of Cyprus Medical School, Professor of MSc in the Hellenic Open University, Patras, Greece, Honorary Clinical Research Fellow in the Molecular Pathology - Clinical Biochemistry Department of the Royal Free Hospital in London, National Expert on Secondment for the Scientific Advice and Orphan Drugs Sector in the EMA, London. He is Member of the European Commission Joint Research Center (JRC) expert panels in the field of Medical Devices related to Endocrinology & Diabetes. He is Principal or Co-investigator for 36 protocols/randomized clinical trials, 10 funded (mainly EU and UN) research projects.

Dr Rizos is author of 85 PubMed scientific articles (3282 citations, h-index 26) and 83 abstracts/ presentations in international and national conferences. He is Expert for ECDC and member of D&CVD EASD study group. His research interest is focused on diabetes mellitus, lipid disorders, hypertension, primary and secondary prevention of cardiovascular disease.



### **Professor Dr Christos Savopoulos**

Professor of Internal Medicine, Director of 1st Medical Propedeutic Dept of Internal Medicine & Stroke Unit, Aristotle University of Thessaloniki, AHEPA University Hospital, Thessaloniki, Greece

#### chrisavopoulos@gmail.com; csavvopo@auth.gr

Christos Savopoulos was born in 1965 at Thessaloniki, is married and father of 2 boys. He is Professor of Internal Medicine of Aristotle University of Thessaloniki and operates in the 1st Medical Propedeutic Department of Internal Medicine at AHEPA University Hospital. He has graduated from the Medical School of Aristotle University of Thessaloniki in 1989, specialized in Internal Medicine and he continued to serve the Medical School as an Affiliated Clinical and Research Associate in the 1st Propedeutic Dept of Internal Medicine of AHEPA Hospital until his election as Clinical Lecturer in Internal Medicine in 2002. In 2001 he received the European Hypertension Specialist degree from European Society of Hypertension, and in 2002 he received his PhD, from the Medical School, Aristotle University of Thessaloniki on "Sodium-lithium countertransport activity in healthy, dyslipidemic, and hypertensive individuals", with distinction. Since October 2010 he was offered a postgraduate appointment as Honorary Visiting Professor in the established and world-famous International Centre for Circulatory Health in Imperial College of London at St Mary's Hospital, actively participating in all Clinical and Research activities (Head: Prof Neil Poulter). During the same period, he was exposed to the Stroke Unit Clinical and Research activities in the Charing Cross Hospital and St Mary's Hospital under the instruction of Dr Diane Ames (for 6 month). In 2011 he was one of the principal establishers of a Stroke Unit in the University Hospital of AHEPA, Thessaloniki Greece and appointed as the Head of this Stroke Unit. During this period the Unit begun to offer thrombolysis treatment for the first time in this hospital. He continues collaborating with the International Centre for Circulatory Health in Imperial College of London as an Honorary Visiting Professor.

At present he is the Director of 1st Propedeutic Medical Dept of Internal Medicine & Stroke Unit and Clinical Director in the Outpatient Clinic of Internal Medicine, Excellence Center of Hypertension (recognized by ESH/ESC), Dyslipidaemia and Obesity-COM (recognized by European Society of Obesity).

He is collaborating with the University of Varna, Bulgaria, and he was awarded HONORARY DIPLOMA from Varna Rector, Prof Aneliya Klissarova. He participated in 37 research programs/ projects/protocols/studies -single or multicenter trials. He is a member of 23-member adviso-ry committee for doctoral theses, and he participated in 12 PhD Examination Committees. He is a member of 17 Greek or International Medical Scientific Societies, Associations or Working Groups.

Professor Savopoulos is a co-author in 321 full paper publications and he has an H- index of 31 and 3.400 citations. He is an author of 31 books or book chapters or editorial support in Greek translated chapters of foreign language publications and he gave 203 lectures or oral presentations or posters in Greek and international conferences. He is a reviewer in more than 29 Greek and/or international journals and Managing Editor of the Official Journal of Internal Medicine Society of Greece.



#### **Professor Dr Apostolos G. Tsapas**

Professor of Medicine and Diabetes, Aristotle University of Thessaloniki, Greece

Professor Apostolos Tsapas, MD PhD MSc (Oxon), is Chair of the Second Medical Department and the Diabetes Centre at Ippokratio Hospital Thessaloniki, founding Lead Investigator of the Clinical Research and Evidence-Based Medicine Unit at Aristotle University of Thessaloniki and Senior Research Fellow at Harris Manchester College at the University of Oxford. He earned his medical degree and PhD from Aristotle University of Thessaloniki, and subsequently qualified an MSc in Evidence-based healthcare from the University of Oxford in UK. Professor Tsapas completed a two-year fellowship at the Oxford Centre for Diabetes Endocrinology and Metabolism and worked for six months as visiting scientist in the Knowledge and Evaluation Research Unit at Mayo Clinic, Rochester MN USA. His main research interests include research methodology, knowledge synthesis (systematic reviews and meta-analyses), evidence-based practice, patient-centred care and clinical decision-making in medicine and diabetes. Professor Tsapas is a coauthor of three book chapters and has published over 100 peer-reviewed articles in journals including Annals of Internal Medicine, BMJ, Diabetes Care and Diabetologia.



### **Dr Ilias Migdalis**

Director of Diabetes Centre of Lefkos Stavros Hospital, Athens, Greece

Ilias Migdalis is director of Diabetes Centre of Lefkos Stavros Hospital, Athens, Greece. He was director of 2nd Medical Department and Diabetes Centre of NIMTS Hospital, Athens (1997-2021). Dr Migdalis graduated from the Medical School Aristotle University of Thessaloniki in 1976. He subsequently did his training in Indernal Medicine at NIMTS Hospital (Athens, Greece) and in Diabetes in the Diabetic Department of King's College Hospital (London, UK). Medical Thesis (PhD) was performed in the Medical School of University of Athens (1984).

His research and other areas of interest include on diabetes and chronic complications and the prevention of diabetes. He has 65 publications in Greek Medical Journals, 90 in International Medical Journals and contribution in 88 chapters in books.

Dr Migdalis is a member of professional societies, including Hellenic Diabetes Association (twice president), Hellenic Association of the Internal Medicine (Member of the executive board, twice) Mediterranean Group for the study of Diabetes (Member of the executive board for 9 years), Diabetic Neuropathy Study Group of the EASD, European Association for the study of Diabetes (EASD). He was Lead Guest Editor in seven International Medical Journals, and he had contribution in the position statement of the Hellenic Diabetes Association and the relative position of the ADA and EASD. He was core member in the Scientific Advisory Group for diabetes and endocrinology in the European Medicines Agency (2011-2021). He is core member in Multidisciplinary Joint Committee-Wound Healing in UEMS (European Union of Medical Specialists), 2019-2022.



### Dr Stavros Liatis, MD, PhD

NHS Director, Senior Consultant in Internal Medicine and Diabetology;

Laiko University Hospital.

Dr. Stavros Liatis graduated from the Athens University Medical School in 1989. He received board certification in Internal Medicine in 1999 and completed his thesis at the University of Athens Medical School in 2004. He completed his training in Diabetology at Laiko University Hospital in Athens in 2001.

Currently, Dr Liatis is NHS Director and Consultant in Internal Medicine and Diabetology at the First Department of Propaedeutic Internal Medicine and the Diabetes Center at Laiko University Hospital in Athens, Greece.

Apart from his clinical work in the diabetes outpatient clinic, Dr Liatis participates in the clinical training of 4th and 6th year medical undergraduates and Senior House Officers in Internal Medicine, Endocrinology and Diabetology.

In his carrier, Dr Liatis participated as principal investigator and co-investigator in several epidemiological and clinical studies and his main interest focuses on clinical Diabetes Epidemiology. He has published more than 110 papers in peer reviewed journals (citations: 3800, h-index: 27) and has authored several chapters in scientific textbooks dealing with diabetes, obesity and metabolism. He is member of the writing committee of the Greek guidelines for diabetes management since 2014.

Dr Liatis is a reviewer in several peer review journals and section editor in Epidemiology in Frontiers in Clinical Diabetes & Healthcare since 2020.

Dr Liatis served as chair of the steering committee of the European Diabetes Epidemiology Study group of the European Association for the Study of Diabetes (EASD) from 2016-2018 and also as member of the steering committee of the Hellenic Diabetes Society from 2013-2015 and from 2018-2021. He is a member of the EASD since 2004.



# Professor Dr Jeroen J. Bax

Director of Noninvasive Imaging, Department of Cardiology; Leiden University Medical Centre (LUMC), Leiden, The Netherlands. Immediate Past-President, European Society of Cardiology (ESC) 2018-2020

European Society of Cardiology (ESC) Immediate Past-President (2018 – 2020), Jeroen Bax is Director of non-invasive imaging and Director of the echo-lab at the Leiden University Medical Center, The Netherlands. His main interests include clinical cardiology, heart valve disease, heart failure, cardiac resynchronization therapy and the application of all different imaging modalities to these clinical fields. Professor Bax has authored numerous papers and holds several positions in national and international scientific organizations, as well as serving on the editorial boards of many different journals.



### Professor Dr Loizos G. Loizou

Clinical Professor of Pediatrics, Pediatric Oncology – Hematology, Medical School, University of Nicosia Fmr. Director of the Pediatric Oncology - Hematology Clinic, Archbishop Makarios III Hospital, Nicosia President of the ELPIDA Foundation for children and adolescents affected by

#### cancer or leukemia.

Loizos G. Loizou, after his studies in Medicine in Brussels, Belgium and his specialization in Pediatrics, and Pediatric Oncology - Hematology in Strasburg and Nancy in France, was invited by the Minister of Health of Cyprus in 1989 to return to Cyprus and undertake the establishment and operation of the Pediatric Oncology - Hematology Department at the Archbishop Makarios III Hospital, which he runs till today.

He is the founder of Pediatric Oncology-Hematology in Cyprus. He undertook the training of the medical nursing, in order to create the entire necessary infrastructure to provide the best possible care for the cancerous and leukemic children. In November 1996 he was in charge of the team of doctors who carried out the first bone marrow transplantation in Cyprus, writing a new chapter of historical importance for medicine in Cyprus. Additionally, this team created the first modern leukemia diagnostics laboratory and the first cryopreservation facility in the country for storing pluripotent umbilical cord and bone marrow stem cells at the Archbishop Makarios III Hospital in Nicosia. Since 1990 he established the first ever cancer registry in Cyprus, the Pediatric Oncology Registry of Cyprus (PORCY), which was initially and till 1998 a hospital-based registry. After the creation of the Cyprus National Cancer Registry in 1998, the PORCY was further developed and became a population-based childhood and adolescent cancer registry.

In 1990 he created and is the President of the ELPIDA Foundation for Children with Cancer and Leukemia (a nongovernmental charity organization) to strengthen and support the medical and social efforts to create the modern infrastructure for the care of children, adolescents and young adults affected by cancer and offer them the best possible therapies and overall management.

Prof. Loizou, with his unique experience of 37 years of exclusive clinical occupation with childhood cancer and leukemia, continues his clinical and research work in descriptive epidemiology, survivorship issues, cancer predisposition syndromes and trials including new anticancer agents, with innovative and pioneering actions for improving the survival rates and quality of life of children and adolescents with cancer or leukemia, as well as in general, to fight the scourge of cancer.



# **Dr Charalampos (Haris) Kartsios**

Consultant Haematologist, Royal Derby Hospital, University Hospitals of Derby and Burton, NHS Foundation Trust, UK

Charalampos (Haris) Kartsios was born in Thessaloniki, Greece in 1971. He graduated from the Medical School of the Aristotle University of Thessaloniki in 1995 and he finished his specialty training in Haematology in 2005.

In 2007 hel was awarded the Hellenic Society of Haematology Scholarship and he went to the Haematological Malignancy Diagnostic Service (HMDS) Leeds, UK where he excelled his clinical and lab skills under Prof. Peter Hillmen and Andy Rawstron. Subsequently he returned to Greece where he worked until 2011 as a Consultant Haematologist at Papageorgiou Hospital in Thessaloniki.

He was appointed as a Haematology Consultant at the Heart of England (now part of University Hospitals Birmingham) NHS Foundation Trust in 2011 where he worked until 2021. He was the VTE lead of the Trust and the Anticoagulant Service Lead (2019-2021), and the Clinical Service lead for Laboratory Haematology (2015-2018). Currently he is the Anticoagulant Service and VTE Lead for University Hospitals of Derby and Burton (2022).

His main scientific interests are thrombosis/anticoagulation, obstetric and diagnostic haematology. He has 30 publications in peer reviewed journals and a strong interest in clinical trials in both malignant haematology and thrombosis. He has been a local principal investigator in VTE real life studies of rivaroxaban, edoxaban and dabigatran. I am passionate about offering the 'right anticoagulant to the right patient at the right dose'.



#### **Professor Dr Nikolaos Grigoriadis**

Head of the of the B' Dept of Neurology, AHEPA University Hospital, the MS Centre and the Laboratory of Experimental Neurology and Neuroimmunology

Nikolaos Grigoriadis graduated from the Faculty of Medicine of the Aristotle University of Thessaloniki. He did his PhD thesis and residency in Neurology in the same institution. He has been specialized in clinical and experimental Neuroimmunology and CNS immunopathology in a number of research centers and institutions abroad.

He is now Professor of Neurology at the Aristotle University of Thessaloniki and Head of the of the B' Dept of Neurology, AHEPA University Hospital, the MS Centre (www.ms-center.gr) and the Laboratory of Experimental Neurology and Neuroimmunology (www.neuroimmunology. gr). He is also Affiliated Researcher at the Institute of Applied Bioscience, Centre for Research and Technology Hellas (CERTH, www.certh.gr).

Professor Grigoriadis is member of various international scientific committees such as the European School of Neuroimmunology, ParadigMS, the subcommittee of ENS for Multiple Sclerosis, the ECTRIMS committee, Co-founder and General Secretary of the Hellenic Academy of Neuroimmunology (www.helani.gr). He is Ex-President and nowadays General Secretary of the Hellenic Neurological Society. He is Ad Hoc reviewer in more than 40 international scientific journals, co-ordinator in more than 50 multicenter clinical trials for MS and principal investigator in collaborative research projects for experimental cell therapies in CNS autoimmune demyelination.

His field of interests are: Neuroimmunology; Multiple sclerosis; experimental models of autoimmune diseases (EAE etc); neurodegeneration; immunomodulation; cell therapies. He has published more than 225 papers in peer reviewed journals. He has been awarded several times for his scientific work.



## **Professor Dr Kevin Harrington**

Honorary Consultant Clinical Oncologist at The Royal Marsden NHS Foundation Trust and at St George's Hospital. Head of the Division of Radiotherapy, The Institute of Cancer Research. Specialist in head and neck cancer and in melanoma.

Kevin Harrington completed medical training at the University of London and gained his PhD from Imperial College, London. He is an NIHR Senior Investigator and Head of the Division of Radiotherapy and Imaging at The Institute of Cancer Research (ICR)/Royal Marsden Hospital (RMH). He is the RMH/ICR NIHR Biomedical Research Centre lead for the Targeted Physical Therapies theme, Director for the ICR/RM CRUK RadNet Centre of Excellence, Chair of the CRUK Advanced Radiotherapy Network (ART-NET) Network Accelerator, Chair of the ICR Well-come Trust Clinical Training Programme and an Executive Board member for the CRUK ICR/Imperial Major Centre for Convergence Science. His clinical duties are undertaken as an Honorary Consultant Clinical Oncologist at The Royal Marsden NHS Foundation Trust and at St George's Hospital, specialising in developing new treatments with a specific focus on head and neck cancer, in which subject he has led multiple phase I, II and III clinical trials. He has published >570 peer-reviewed publications and >50 book chapters.



## **Professor Dr Achilleas Gravanis**

Professor of Pharmacology, School of Medicine University of Crete

Researcher IMBB-FORTH; Affiliated Research Professor, Center of Drug Discovery, Northeastern University

Achilleas Gravanis is Professor of Pharmacology Medical School University of Crete and Researcher at the Institute of Molecular Biology & Biotechnology-FORTH. He served a member of the Biomedical Research Program Committee of European Commission, member of the Council of the Higher Education Quality Assurance Authority (ADIP) and President of the Sectional Committee of Life Sciences Hellenic National Research & Technology Council. He was also Member of the Scientific Council of the Hellenic Research & Innovation Foundation (ELIDEK), responsible for Life Sciences. Associate Research Professor at the Center for Drug Development, Northeastern University, Boston. Co-founder and scientific partner of the biotechnology spinoff companies Bionature and ReNeuroCell. Chair of International Scientific Advisory Board Athens LifeTech Park. Venture partner of BigPi Ventures. His research group is developing synthetic compounds, agonists of neurotrophin receptors, with neuroprotective and neurogenic properties and potential applications in therapeutics of neurodegenerative diseases. Additionally, his group is focusing on 3D microscaffold bioengineering and neural stem cell technologies to develop neuroimplants for spinal cord injury and neurobiosensors for drug discovery.



### **Professor Dr Charalampos Grassos**

Director of Cardiology Dept in General Hospital in Athens "KAT"

He serves as Director of Cardiology Department in General Hospital in Athens "KAT". He is a Head of Hypertension unit in the same Hospital -Excellent Center of European Society of Hypertension. After graduating from the Medical Faculty of University of Patras in1986, he continued his postgraduate studies in Bolton University where he completed PhD course in 2011 and in 2014 elected as Visiting Professor in the University of Bolton. In 2006, he completed successfully the European Master in Hypertension in the University of Brescia Italy and the Hellenic Society of Hypertension. He attended the Hypertension Summer Schools in Brescia (2004). Also, he serves as President of Hellenic Society of cardiovascular Protection and elected member of the board of Hellenic society of Cardiology. His main research interest focuses on Hypertension and preventive cardiology and stroke prognosis. He participates in observational studies and randomized controlled trials of hypertension as National coordinator or Principal Investigator. He is author of >100 articles in peer-reviewed journals like Hypertension, BMJ, Blood Pressure, Circulation, Atherosclerosis. He is currently assigned as a member of the examination committee for the diploma of specialty in cardiology in Greece. Dr Charalampos Grassos is an Adjunct Professor of the School of Medicine, European University Cyprus since 2018. Furthermore, he has been assigned as a member of the cardiology specialists selection committee for the national Health system in Greece - $E\Sigma Y$ , for the period 2022-2223.



### **Professor Dr Constantinos Deltas**

Professor of Genetics, Director, Molecular Medicine Research Center, University of Cyprus Deltas@ucy.ac.cy

Constantinos Deltas studied Pharmacy at the National Kapodistrian University of Athens. He received his PhD in Biochemistry and Biomedical Sciences at Rutgers University, the State University of New Jersey, USA. In 1991, while at the Duke University Medical Center, NC, USA, he was invited by Dr Lefkos Middleton to return to Cyprus and be amongst the first nucleus of scientists who established and developed the Cyprus Institute of Neurology and Genetics.

He is Professor of Genetics at the University of Cyprus since 2002, first at the Department of Biological Sciences where he was the first faculty and Chairman and then at the Medical School. He is directing a research lab with special interest in inherited disorders, developing molecular genetics, cell biology and animal model projects. With external competitive funding he was the first to establish a Biobank for genetic disorders in Cyprus, in 2011. More recently, with EU and national funding, he is founder and Director of biobank.cy, a Research and Innovation Center of Excellence, focusing on Biobanking and Biomedical Research, at the University of Cyprus. Amongst others he is leading the Cyprus Human Genome project, aimed to 1000 Cypriot genomes, at first phase. He published more than 150 papers and presented his work in multiple international conferences as invited speaker. In 2014 he was honoured with the Cyprus Research Award-Distinguished Researcher 2014, which is awarded to researchers with long standing experience in Cyprus and who have demonstrated outstanding research achievements with local and international impact, honouring Cyprus.

Amongst others, Prof. Deltas is appointed Member of the International Society of Nephrology (ISN) Eastern and Central Europe Regional Board, appointed by the Government Cabinet as member of the Cyprus National Bioethics Committee, elected Vice-Chair of the Cyprus Atherosclerosis Society and a member of the Scientific Committee of the Cyprus Anticancer Society.



# Assistant Prof. Dr Zoi Pana

Pediatrics, Epidemiology and Infectious Diseases; School of Medicine, European University Cyprus, Nicosia Cyprus

Zoi is a Specialist in Pediatrics, Faculty Member at the European University and Member of the CERIDES EUC innovation center. Zoi specialized in Epidemiology, Infection Control and Antimicrobial Stewardship at the Johns Hopkins Hospital USA (HEIC Department, JHH). Zoi has worked with the Armstrong Institute at JHH in projects related to patient safety and quality improvement in health. She holds two MSc (Masters), one in Medical Research Methodology (AUTH, GR), and one in Nanotechnology (AUTH, GR) and a PhD in infectious diseases in immunocompromised children with leukemia. She has received the European Infectious Diseases Society Fellowship Award in 2017 and she is currently active member of several European Committees and Expert Guideline Groups in infectious Diseases (ECMM, ECIL8, ESPID, IPFN, ESCMID, C4C). She is reviewer in several peer review international journals, and she has more than 60 publications in international Journals.

Zoi is a Scientific member of the COVID-19 National Committee tant at the Ministry of Health in Cyprus and Scientific Consultant of the Minister of Health. Last year she became Member of the European Confederation of Medical Mycology (ECMM) and Member of the Steering Board of the European Hematology Association. The EUC team together with Greek collaborators will coordinate the advanced module for Infection Control and Stewardship for the period 2022-2024 for ESCMID (European Society of Microbiology and Infectious Diseases). Zoi is representing Cyprus at the EU scientific advice platform on COVID-19 under the auspices of the European Commission. Zoi is participating in several EU COVID-19 projects, and she is the National Coordinator and Work Package Lead for the COVID-19 EU Horizon program VACCEL-ERATE, the pan European Vaccine Trial Network that aims to provide a single-entry point for vaccine clinical research in Europe under the HERA initiative.



### Professor Dr Eleni Arnaoutoglou

University Hospital of Larissa and Professor of Anaesthesiology in the Medical Department of School of Sciences, University of Thessaly

Professor Eleni Arnaoutoglou is Director of the Department of Anaesthesiology in University Hospital of Larissa and Professor of Anaesthesiology in the Medical Department of School of Sciences of University of Thessaly. She received her Doctor of Medicine degree at the University of Patras and completed her residency in Anaesthesiology at the University of Ioannina.

Professor Arnaoutoglou's research interests include perioperative antithrombotic management, postoperative cognitive dysfunction, and inflammatory response after procedures and minimal opioid anaesthesia.

She has 82 Publications in PubMed, 1098 citations with an h-index of 15, 77 presentations in International Congresses, 45 abstracts in International Journals and 4 Chapters in International Scientific Books. She also has been an Invited Speaker in 138 Greek Congresses and in 53 International ones, and as a Chair in 75 Scientific Sessions.

She is Secretary for the ISETAT (Institute for the Study and Education on Thrombosis and Antithrombotic Therapy) and a member of the working group of the IVD (Institute of Vascular Diseases).



## Associate Professor Dr Yiorgos Apidianakis

#### Biology Department, University of Cyprus

Yiorgos Apidianakis has been trained for 10 years at Harvard Medical School in Biomedical Research, 6 years as a postdoctoral fellow and 4 years as a Harvard Instructor in Medicine in the field of human infectious diseases and carcinogenesis, practicing his research at the Massachusetts General Hospital and the Shriners Hospitals for Children in Boston, USA. He is a Faculty Opinions member since January 2020 at the division of Cellular Death and Stress Responses (https://facultyopinions.com/) and an editor in Frontiers in Cellular and Infection Microbiology and ad hoc editor in Metabolites. He has published papers in peer-reviewed journals, such as Proceedings of the National Academy of Sciences USA, Nature Communications, Nature Protocols, Cell Host & Microbe, PLoS Pathogens, The Lancet Infectious Diseases and EMBO Reports. Many of his main author papers in the field of microbial infection and intestinal stem cell research have more than 100 citations each.

As an instructor at Harvard Medical School (2008-2011) he attracted competitive funding from various agencies including the Department of Defense (USA) and the Shriners Hospitals for Children. As a Professor at the University of Cyprus (2012-present) he has been awarded personal competitive funding from the Marie Curie Career Integration program, the Fondation Sante Biomedical Research Grants program and the Research & Innovation Foundation in Cyprus.

Prof. Apidianakis' supervisor responsibilities since 2012 include: postdoctoral researchers, 9 PhD thesis students, 12 MSc. thesis students, and 30 undergraduate thesis students. He is an expert in modelling Microbe-Metabolite-Host interactions leading to dysplasia and tumorigenesis using primarily Drosophila genetics and intestinal histopathology assays. He also runs the Cyprus Intestinal Health Study as the Coordinator of a clinical study on Colon Cancer prevention (http://cihs.cs.ucy.ac.cy/).



#### **Dr. Aristides Anastasakis**

Scientific Director in the Unit of Inherited and Rare Cardiovascular Diseases, Onassis Cardiac Surgery Centre

Dr. Aristides Anastasakis, MD, PhD, is a consultant cardiologist specialized in Inherited and Rare Cardiovascular Diseases. He was trained in Athens and London. He holds a Degree in Medicine and his PhD thesis was in the field of cardiomyopathies. Since 1997, is dynamically involved in the area of inherited cardiovascular diseases ("Pheidippides" program 1997 – 2004, EKKAN 2004 – 2017) and now holds the position of Scientific Director in the Unit of Inherited and Rare Cardiovascular Diseases, Onassis Cardiac Surgery Centre. He has been a member of ESC Task Force in Sports Cardiology (2004 – 2008) and an elected nucleus member of ESC Working Group on Myocardial and Pericardial Diseases (2012 – 2016). He represented Greece (2015 – 2017) in EUCERD (European Union Committee of Experts on Rare Diseases) and is an elected President (2018 – 2020) on Cardiomyopathy and Inherited cardiovascular diseases working group of the Hellenic Cardiac Society, as well as the President (2017 – 2020) of the National Council of Rare Diseases in Greece. He has been awarded with several grants and actively involved in international research projects (such as HCM Investigator Outcomes). Dr. Anastasakis has a significant volume of publications in international scientific journals, chapters in medical books and is the editor of the textbook "Heart diseases in adolescence". He is also a Board member for various scientific journals such as Hellenic Cardiac Society Journal, Cardiogenetics and Echo Research. Currently, he is the coordinator of National Network in Precision Medicine in Cardiology.



## Associate Prof. Dr Carsten Werner Lederen

Laboratory Scientific Officer, Molecular Genetics Thalassaemia Department The Cyprus Institute of Neurology and Genetics

Dr Lederer received his PhD from the University of East Anglia, Norwich, UK. He now holds the position of Scientist at the Molecular Genetics Thalassaemia Department of the Cyprus Institute of Neurology and Genetics (CING), where he heads the MGTD Gene Editing and Therapy unit. Dr Lederer is Associate Professor and course coordinator at the Cyprus School of Molecular Medicine, associate editor of Frontiers in Genome Editing and MDPI Genes, executive board member of the Global Globin Network, member of the core-development team of the ITHANET Portal, member of the ClinGen-recognised Haemoglobinopathies Variant Curation Expert Panel, board member of the Hellenic Society of Gene Therapy and Regenerative Medicine, and president of the Cyprus Society of Human Genetics. His current research focus is model development for haematopoietic disorders, investigating the role of miRNAs in erythropoiesis, and gene therapy of  $\beta$ -haemoglobinopathies and particularly of  $\beta$ -thalassaemia by three different approaches: (i) mutation-specific RNAi-supplementation of gene addition, (ii) genome editing of disease modifiers, and (iii) homology-independent gene repair.



### **Dr Konstantinos Zamboglou**

Radiation Oncology, Vice Medical Director, German Oncology Center

Konstantinos Zamboglou studied medicine in Freiburg, Germany until 2013. In this period, he completed his doctoral thesis at the laboratory of Prof. Aktories with the grade summa cum laude. He was resident in the Department of Radiation Oncology at the University of Freiburg in Germany under the supervision of the renowned oncologist Prof. Grosu. His main area of interest are Interventional Radiotherapy, Translational Oncology and implementation of novel imaging techniques in radiotherapy planning. In 2019 he obtained his board licence and in 2020 his postdoctoral lecture qualification. From 2019-2020 he worked as senior consultant, where he was responsible for the treatment of prostate cancer patients. In 2021 he became also the section head of the department of interventional radiotherapy. He published over 70 research articles in renown and peer-reviewed journals and in 2020 he received the "Herman-Holthusen" Award of the German Society of Radiation Oncology. Since 2021 he is an invited member of the German prostate cancer expert panel and member of the ESTRO-ACROP guideline committee for prostate cancer. Since 2021 he is the deputy medical director at the German Oncology Center in Limassol.



### Ran Nir-Paz

Professor of Medicine, Chair Executive committee ESGNTA – ESCMID study group for Non-Traditional Antimicrobial agents, Department of Clinical Microbiology and Infectious Diseases Hadassah-Hebrew University Medical Center, Jerusalem, Israel

Ran Nir-Paz has graduated his medical studies from the Hadassah-Hebrew University in 1996. He then completed a residency In Internal Medicine in 2000 at the Hadassah Medical center followed by sub-specialty in Infectious diseases in the same institution. From 2004-2007 he had performed a Postdoc period at the department of molecular and cell biology at UC Berkeley in California. Since 2007 he is a senior physician at the department of Clinical Microbiology and Infectious Diseases at the Hadassah Medical center, and since 2001 he is the clinical lead the Israeli center for Phage therapy, and the head of the service for innovative antimicrobial therapy. Additionally, he is appointed with tenure at the Hebrew-University faculty of medicine since 2007, and a full professor since 2021. His main area of research includes Mycoplasma associated diseases and was also the leader of the ESCMID study group on those topics from 2017-2021, and the chairman of the lates conference of the international Organization for mycoplasmology that was held in November last year. In the recent years he initiated the introduction of phage therapy for resistant and persistent infections in Israel. In Israel he was responsible for more than 15 compassionate uses of phages for unresolving infections as well as the PI in a study by TECHNOPHAGE for the use of phages for diabetic foot. As part of his international role on the use of phages he was invited to several conferences and initialed the ESCMID study group for Non-Traditional Antibacterial study group (ESGNTA) which he chairs since 2022.



### **Professor Dr Peter Karayiannis**

*Ex Associate Dean for Faculty & Research and ex Co-Chair of the Department of Basic & Clinical Sciences, University of Nicosia Medical School* 

is Professor of Microbiology/Molecular Virology at the University of Nicosia Medical School, Ex Associate Dean for Faculty & Research and ex Co-Chair of the Department of Basic & Clinical Sciences.

Professor Karayiannis holds a BSc Degree in Microbiology obtained at Liverpool University and a PhD in Medical Microbiology (Chlamydiology) from the same University. He has worked at the University of Liverpool for 4 years, 7 years at the Royal Free Hospital Medical School, and 24 years at St Mary's Hospital, Imperial College School of Medicine. He has served on a number of editorial boards and is currently European Editor of the Journal of Viral Hepatitis.

His research interests are concerned with the hepatitis viruses, predominantly B and C (HBV, HCV) and include the study of the mechanisms that favour viral persistence and evasion of the immune response during chronic infection, the effect of HBV variants arising during the natural history of the infection on long term disease outcome and those arising as a result of human intervention, through vaccination or antiviral treatment, as well as new approaches to treatment. Other research interests include studies on the basic molecular biology of both HBV and HCV, the role of various viral proteins in the replication of the viruses, possible interference with cellular biosynthetic or defense pathways, as well as their role in hepatocarcinogenesis. More recently, his research work has concentrated on the role of genomic HCV mutations that have been identified in isolates from immune privileged sites such as peripheral blood mononuclear cells and brain tissue, and the effect of such mutations on the replication capacity of infectious clones of the virus. He has co-authored 228 original papers in peer reviewed journals and chapters in books.

He is currently a member of the Advisory Committee for the Covid-19 pandemic to the Minister of Health.

## Speakers CVs



### Associate Professor Dr Konstantinos Voskarides

#### Assoc. Prof. Genetics and Molecular Biology, University of Nicosia Medical School

Dr Voskarides holds a BSc in Biology from Aristotle University of Thessaloniki and a PhD in Molecular Biology and Genetics from University of Cyprus. He is currently a Senior Editor at the Springer journals "BMC Medical Genomics" and "Journal of Molecular Evolution". His research and academic teaching experience counts more than 20 years. Dr Voskarides has authored until today 62 peer-review articles in high impact journals. Among others, he has published innovative research related with new genes in familial renal diseases, population genetics, genetics of psychiatric and autoimmune diseases, and cancer evolution.



#### Associate Professor Argyris Tzouvelekis

Associate Professor of Internal and Respiratory Medicine and Head of the Department of Respiratory Medicine at the University Hospital of Patras, Greece and Adjunct Associate Professor of Pulmonary Critical Care and Sleep Medicine Department, Yale School of Medicine, USA

Argyris Tzouvelekis graduated from the School of Medicine, University of Crete, Greece in 2003. From 2004-2008, he successfully completed his PhD studies in Medical School. Democritus University of Thrace. In 2004, he was granted with the European Respiratory Society Long Term Research Fellowship at Imperial College, Royal Brompton and Harefield Hospital, London. From 2007 to 2012, Dr. Tzouvelekis successfully completed his fellowship in Respiratory Medicine at the Department of Respiratory Medicine, Democritus University of Thrace, Greece. In October of 2013 he was awarded a fully-funded post-doctoral position at the Department of Pulmonary and Critical Care and Sleep Medicine, at Yale University. From 2016-2020 Dr. Tzouvelekis was Consultant Respiratory Physician at the Department of Respiratory Medicine in SOTIRIA General Hospital and a Marie Curie Respiratory Fellow. From May 2020 until now he is an Associate Professor of Internal and Respiratory Medicine at the University of Patras, Greece and Head of the Department of Respiratory Medicine at the University Hospital of Patras, Greece as well as an Adjunct Associate Professor of Pulmonary Critical Care and Sleep Medicine Department, Yale School of Medicine, USA. Dr. Tzouvelekis is an Executive Officer-Internal Auditor of European Respiratory Society, member of the European Respiratory Society (ERS) College of Experts, official reviewer of ERS fellowships and Awards, mentor of ERS young scientists (ERS mentoring scheme), Associate Editor of Respiratory Research and Frontiers in Medicine.

He is currently enumerate 189 Publications in peer-reviewed scientific journals in Pubmed, (with more than 4500 citations and a total H-index=37-Scopus, and H-Index: 38, i-index: 61-Google Scholar), more than 100 presentations and lectures in national and international conferences and 30 grants and honors, including a) the European Respiratory Society Long Term Research Fellowship and b) the European Respiratory Society-Young Scientist Sponsorship, c) the American Lung Association Senior Research Training Fellowship, and d) a European Respiratory Society/Marie Skłodowska-Curie Postdoctoral Research Fellowship.

## Speakers CVs



### **Dr Dimitris Chatzis**

Adj Assistant Professor European University Cyprus Consultant Cardiologist, Clinical Hypertension Specialist (ESH)

Dimitris Chatzis graduated from the Medical School of the National and Kapodistrian University of Athens in 1999. Thereafter, he specialized in Cardiology and during his specialization he has been an active member of the Hypertension unit of the 1st Cardiology clinic of the University of Athens (Hippokration hospital, Athens, GR, Director: Prof. K. Tsioufis) which is recognized as a center of excellence by the European Society of Hypertension.

He has been involved in several research protocols regarding the diagnosis and management of hypertensive heart disease and he completed his PhD in 2009 (Med School of Athens, GR). In addition, in the year 2015 he was awarded the title of "Clinical Hypertension Specialist" by the European Society of Hypertension. During the period 2014-2018 he has been working as Senior Medical Advisor at Pfizer Ltd where he was responsible for Hypertension and Atrial fibrillation related products and research for Greece, Cyprus and Malta.

Dr. Chatzis is a member of numerous national and international scientific organizations and he has participated in several national and international medical congresses both as speaker and as chair/moderator. He has also published scientific papers in numerous peer reviewed journals. Moreover, Dr. Chatzis is an Adjunct Assistant Professor in Cardiology at Med School of the European University Cyprus.



### **Apostolos Veizis**

#### Executive Director of INTERSOS in Greece

Veizis worked at the HQ of Medecins Sans Frontieres-Greece as Director of Medical Operational Support Unit(SOMA), Programs and Institutional relations Director and Medical Director. Prior to that worked as Head of Mission and Medical Coordinator for Medecins Sans Frontieres and Medecins Du Monde in Afghanistan, Azerbaijan, Russian Federation, Albania, Egypt, Georgia, Greece, Turkey. Participated in assessment, emergency assignments and evaluations in Kyrgyzstan, Morocco, Armenia, Lebanon, Syria, Ukraine, Turkmenistan, Zambia, Malawi, Uzbekistan, North Macedonia, Cyprus, Moldova, Poland and Tajikistan. He is an Advisory board member of the Lancet Migration European Regional Hub and Migrant Health Dermatology Working Group (MHDWG) of the IFD member. Participated and had announcements in international and national congresses and contributed to publications of relevant articles.

## Speakers CVs



### **Kyriakos Masonou**

#### Junio Achievement Cyprus

Kyriacos graduated from the University of Sussex, UK, with a degree in mechanical engineering. In the past few years, he discovered a passion for entrepreneurship and education; leading him to turn his career in those directions, by developing his own businesses and then by being employed at Junior Achievement (JA) Cyprus, where he currently works as a project manager. JA Cyprus is a member of JA Worldwide, an NGO which educates more than 10 million students every year across the globe, on topics surrounding entrepreneurship, financial literacy, and work readiness. Kyriacos believes that every individual has unlimited potential to what they can achieve, and he considers that engaging in entrepreneurial activities is one of the most effective ways for young people to realize their own potential, guide them towards recognizing real world challenges and back them with the necessary skills to bring solutions.

Cyprus Medical Students' Association (CyMSA) is an independent, non-profit, and non- governmental organization. It is the only approved association of medical students by the InstituC



#### **Professor Dr Reuven Zimlichman**

Head of Cardiovascular Research Institute, Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel E-mail: zimlich@post.tau.ac.il

Reuven Zimlichman, a full professor of internal Medicine, M.D. is presently the Director of The Brunner Cardiovascular Research Institute, Tel-Aviv University. He was Chief of Medicine and Head of Hypertension Institute at the E. Wolfson Medical Center, Israel, during the years 1991-2018: He is past Vice Dean and Head of School of Continuing Education. Tel Aviv University. Prof Zimlichman acted also as Director of the Institute for Quality in Medicine, Israeli Medical Association. He did his fellowship in Hypertension at the Hypertension Endocrine Branch and the Clinical Neurocardiology section, NIH, NHLBI in Bethesda, Maryland, USA. He is currently a member, board of directors, The Israeli Society for prevention of Acute Myocardial Infarction, Ministry of Health, a member, Steering Committee, the Israeli Study of Congestive Heart Failure. He is the past Chairman of the Supreme Court, Israeli Medical Association, and the past President of the Israeli Society of Hypertension. Prof. Zimlichman published more than 200 original research scientific publications, 6 books and multiple chapters in books. His publications are in the fields of basic research, cell cultures, animal research and clinical research. The majority of his publications are in the field of hypertension, cardiovascular disease, metabolic syndrome, end organ damage and evaluation of arterial properties. Prof Reuven Zimlichman is a well-known worldwide expert in Hypertension, Cardiovascular disease and the metabolic syndrome. He is a popular speaker invited to present in congresses all over the world and is chairperson of congresses in the fields of his expertise.



### **Associate Professor Dr Konstantinos Lampropoulos**

School of Medicine, European University Cyprus

Konstantinos Lampropoulos finished Bachelor's in Medicine (MD Degree) from Athens University of Medicine, Greece in 1999. He competed his MD Obligatory Practice, in Chania, Greece (1999-2001) and he was an Internal Medicine Resident at 251 General Air force Hospital, (2001-2002) and at 1st IKA Hospital, HIV Unit, Athens, Greece (2002-2004). He completed his Cardiology Residecy at 1st Cardiology Department, Athens University Medical School, Hippokration General Hospital, Greece and at 251 General Air force Hospital, Athens, Greece (2004-2008). Dr. Lampropoulos completed his PhD in Cardiology at the, Laboratory of Biomechanics, Center for Experimental Surgery of the Biomedical Research Foundation of the Academy of Athens (BRFAA), Greece in 2007 with Honors.

Dr. Lampropoulos Specialized in Interventional Cardiology at 251 General Air force Hospital, Athens, Greece and at the Department of Congenital and Structural Cardiology, Catholic University of Leuven, Belgium (2008-2010). Presently he is a Consultant Interventional Cardiologist at Evangelismos General Hospital of Athens, Greece.

He was an honorary Invited Researcher in multiple TAVI implantation procedures and Mitra clip in Catholic University of Leuven (KU Leuven), Belgium 2018-2019.

Dr. Lampropoulos is a MD Proctor in training Portico and Navitor transcatheter aortic valve implantation (Abbott) since 2020 and a Researcher at the Laboratory of Biomechanics, Center for Experimental Surgery, Foundation of Biomedical Research, Academy of Athens, Greece (2002-onwards). Between 2020-2022 Dr. Lampropoulos was elected as a Vice-Chair of Valvular Heart Disease, Adult Congenital Heart disease, Pulmonary Hypertension at the Hellenic Cardiological Society and He is now the Chair of Working group of Valvular Heart Disease at the Hellenic Cardiological Society.

Dr. Lampropoulos is the Vice-Chairman at the School of Medicine at European University of Cyprus since 2022 and he is an Associate Professor of Pathophysiology in the same Institution since 2021 and Fellow of European Cardiological Society (FESC) since 2011.



### **Dr Theodoros Christodoulides**

#### Consultant Cardiologis

Theodoros Christodoulides completed his medical education at University of Patras Greece, and he was then trained in Cardiology at Nicosia General Hospital, Cyprus. He has also studied Health Units Administration at Open University of Cyprus earning a master's degree. He specialized in heart failure after completing a two-year training program organized by the Heart Failure Association of European Society of Cardiology and the University of Zurich.

He is the Past President of Cyprus Society of Cardiology. He is actively involved in several activities of Cyprus Society of Cardiology and European Society of Cardiology such as co-ordinating registries, reviewing guidelines, and participating in Task Forces. He also serves as a reviewer for the ESC Heart Failure Journal.



Cyprus Medical Students' Association (CyMSA) is an independent, non-profit, and non-governmental organization. It is the only approved association of medical students by the Institutional bodies of the Republic of Cyprus and it was founded in 2014. The Association represents the medical students who study in all the medical schools in Cyprus and are recognized by the Ministry of Education of the Republic of Cyprus. The association, as a Pan-Cyprian family of medical students, aims to empower the voice of the medical students, protect their rights, and increase their activity in the community. In addition, the goal of the association is to promote opportunities for medical students through trainings, workshops, conferences, exchanges, educational programs, and activities. The trainers are certified by the International Medical Students' Association and trained in order to acquire the basic skills and be able to deliver trainings based on a peer to peer system. The themes of the workshops are inspired by the International and Regional priorities of IFMSA and contemporary issues in the sector of Health. The material of the trainings is provided by WHO and other scientific sources. Regardless of the fact that the association started just nine years ago, since the establishment of CyMSA we have organized many activities that supported the efforts of our Ministry of Health, our Universities, the Cyprus Medical Association, the Oncology Centre of the Bank of Cyprus, the Karaiskakio Foundation and other scientific companies and health institutions to improve the care provided to our citizens. In addition, the Association has recently been awarded by the Karaiskakio Foundation at a ceremony under the auspices of the President of the Republic of Cyprus for the contribution of our Association to the Foundation's work towards the registration of new Bone Marrow Donors. At the same time, the Association gives the opportunity to our students-members to take part in international conferences and trainings such as the UNESCO World Bioethics Conference in which members of CyMSA presented their projects. In August 2017, our Association became a full member of the International Federation of Medical Students' Associations (IFMSA) and it represents now officially Cyprus in the international community.



#### **Carl Ikeme**

#### Former football Player (Wolves keeper)

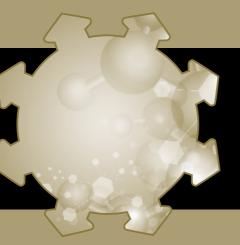
Cancer is still one of the leading causes of death in developed and underdeveloped countries. There are massive steps forward in terms of treating cancers as molecular biology has opened new ways of treating patients

I am thrilled to read all these amazing achievements in the newspapers

This time though it was myself-through a simple blood test.... suddenly the world has changed.... when my wife was expecting my second daughter I had the awful news being diagnosed with Acute lymphoblastic leukaemia a very aggressive form of blood cancer that really never crossed my mind while I was so focused on my professional career as a goalkeeper.

I was informed I will have to go through these achievements I was reading in the newspapers, and I was informed it is unlikely to be present while my wife delivers my daughter?

Why (not) me? One of the main things these awful cancers do for sure is that they do not discriminate, and we are all vulnerable



# Bio-medical Scientific Cyprus

## Abstracts

- Invited Abstracts
- Selected Abstracts
- Poster Abstracts

### IA01 Antibodies and Antibody Mimics as Pharmaceutical Drugs

#### **Professor Sir Gregory Winter**

Fellow, Trinity College, Cambridge CB2 1TQ

During the last century the conjunction of chemistry, structural biology and a molecular understanding of disease processes, has been responsible for driving the widespread development of chemicals as pharmaceutical drugs. The development of biologicals (manufactured by cell fermentation) was much slower and had to await the advent of recombinant DNA technology, and in the case of antibodies, of hybridoma technology. Antibodies have since become established as the paramount biological drug, particularly for the treatment of cancer and autoimmune disease, and are now making inroads into other areas poorly served by chemical drugs. Even as the application of antibodies expands, Darwinian selection technologies are leading to new drug platforms capable of creating tiny antibody mimics based on cyclic peptides. Will such developments spark

### IA02 Hypoxia-Inducible Factors in Physiology and Medicine

#### Professor Dr Gregg L. Semenza

Johns Hopkins University School of Medicine, Baltimore, Maryland USA.

Each of the fifty trillion cells in the adult human body require a continuous supply of O2. Hypoxia-inducible factors (HIFs) maintain O2 homeostasis by modulating the expression of thousands of genes in order to match O2 supply and demand.

### IA03 Human Genomes and the Evolution of Medicine.

#### **Professor Dr Stylianos Antonarakis**

Prof. of Genetic Medicine at the University of Geneva Medical School in Switzerland.

The human genome sequence and variation is a fundamental component in health and disease. The practice of Medicine is gradually changing because of the evolving knowledge of the individual genomic variation and the discovery of the impact of each genomic variant to the phenotypic variation. Diagnosis, prevention, and therapy are all evolving as the mysteries of the genome are elucidated. Genomic Medicine takes a center stage regarding the etiology of the myriad of constitutional and somatic disorders and provides hope for the development of rationalistic and intelligent therapeutic modalities.

#### IA04 How to Make an External Ear: The Story of FOXI3

#### **Professor Dr Stylianos Antonarakis**

#### Prof. of Genetic Medicine at the University of Geneva Medical School in Switzerland.

Craniofacial Microsomia (CFM) is a developmental disorder with multiple phenotypes including malformation of the external ear. The inheritance pattern of CFM is obscure and controversial. We have identified pathogenic variants in the transcription factor FOXI3 that cause one form of CFM. Human and mouse observations suggest a Recessive mode of inheritance in which the combination of rare (causative) and common (modifier) FOXI3 alleles are responsible for the phenotypic variation.

#### **IA05 Prediction and Prevention of Preeclampsia**

#### **Professor Dr Kypros Herodotou Nicolaides**

Professor in Fetal Medicine at King's College Hospital, London. One of the pioneers of fetal medicine, with seminal contributions to prenatal diagnosis and every major obstetrical disorder. Founder and chairman of the Fetal Medicine Foundation (FMF), UK.

Preeclampsia (PE) is a leading cause of maternal mortality and severe morbidity and is associated with increased perinatal risks. The condition is broadly divided into preterm and term PE with delivery at <37 and  $\geq$ 37 weeks' gestation, respectively. Extensive research in the last 30 years has led to the development of a method for identification of women destined to develop preterm PE at 11-13 weeks' gestation. A combination of maternal characteristics with blood pressure, uterine artery Doppler and serum placental growth factor can identify about 90% of women that develop PE <34 weeks, 75% of PE <37 weeks and 40% of PE at term. Subsequently we found that use of aspirin (150 mg per day from 12 to 36 weeks can reduce the rate of PE <32 weeks by 90%, PE <37 weeks by 60% but has no effect on term PE.

We also developed a method of screening for term PE at 36 weeks' gestation. A combination of maternal characteristics with blood pressure, serum placental growth factor and serum sFIt-1 can identify about 70% of women that develop term PE. We subsequently carried out a major multicentre study to screen about 30 thousand women and the high-risk group was randomised to receive either pravastatin or placebo. Unfortunately, this trial showed that pravastatin was not useful in reducing the rate of term PE.

We have now developed a new approach for prevent term PE. Essentially, we do screening at 36 weeks and on the basis of individual results we stratify the population into planned delivery at 37, or 38 or 39 or 40 weeks. We anticipate that this approach will reduce the rate of term PE by more than 50%.

## IA06 The role of miRNAs in signalling and use as biomarkers in Myotonic Dystrophy type I

#### Professor Dr Leonidas A. Phylactou

CEO and Medical Director, The Cyprus Institute of Neurology & Genetics, Nicosia, Cyprus. E-mail: laphylac@cing.ac.cy

Myotonic dystrophy type 1 (DM1) is the most common form of adult-onset muscular dystrophy characterised by progressive muscle wasting. Our group identified miRNAs, the levels of which were found to be altered in the serum of DM1 patients, compared to healthy individuals. Moreover, some of these miRNAs were elevated in the serum of progressive muscle wasting DM1 patients, compared to disease-stable patients. In-depth characterization of the ontology of the four muscle-specific miRNAs in the serum of DM1 patients revealed that these miRNAs are encapsulated within extracellular vesicles, isolated from the patients. Furthermore, we looked further into the mechanism of the release of miRNAs from muscle. We showed that intact skeletal muscle tissues secrete exosomes encapsulating the four muscle-specific miR-NAs, which then travel and communicate with neighbouring skeletal muscles. Based on these results, we went a step further and identified miRNAs which could associate with the course of the disease in individual patients.

All these results contribute to our knowledge about the function of extracellular RNA molecules and their role in the pathogenesis of Myotonic Dystrophy which eventually could prove to be beneficial for patients, as biomarkers for the progression of the disease.

### IA07 Cells for Heart Failure: Replacement Therapy or Paracrine Signaling?

#### Professor Dr Philippe Menasché

### Department of Cardiovascular Surgery; University of Paris, PARCC, INSERM; Hôpital Européen Georges Pompidou 20, rue Leblanc 75015 Paris, France

Over the past years, there has been a major change in the hypothesis underlying the mechanism of action of transplanted cells in the dysfunctional myocardium. This started from the consistent observation of a functional benefit at a time where the cells were no longer physically present in the transplanted tissue and has led to shift from the initial concept of replacement therapy to paracrine signaling whereby the blend of biomolecules secreted by the cells and largely clustered in extracellular vesicles (EV) harness endogenous repair pathways. The strongest rationale for the use of EV is that they have been shown to recapitulate the benefits of the transplantation of their parental cells in several preclinical models of cardiac diseases. However, for a given level of functional equivalence, EV feature clinically appealing advantages

over cells, including a pharma-like manufacturing process more akin to that of a drug, the lack of immunogenicity, at least when the secreting cells are cardiovascular progenitor cells, and a minimal loss of bioactivity after cryopreservation compatible with an off-the-shelf availability.

However, several translational issues still need to be addressed. They primarily include (1) the choice of the optimal parental cells and there is increasing evidence that the best outcomes are achieved by early-differentiated cells belonging to the same lineage as those of the target tissue, which has led us to select pluripotent stem cell-derived cardiac-committed cells; (2) the extent of purification of the conditioned medium and attempts at selecting a highly purified exosomal fraction, while still technically challenging, might indeed be less efficacious that using the almost whole secretome which also includes proteins and other soluble molecules; (3) the thorough characterization of the composition of the EV-based product, which can now be achieved by omics; (4) the development of straightforward in vitro potency tests required for quality controls and (5) the optimization of delivery strategies, which is actually an issue shared by both cells and their secretome; depending on the clinical setting, therapeutics can be injected directly into the myocardium but this approach is fraught with a rapid washout that likely weakens the therapeutic benefits, hence the interest of incorporating cells or EV into slow-release hydrogels intended to lengthen their exposure to the myocardium; if no open-chest procedure is indicated, the most appealing route is intravenous, primarily because of its lack of invasiveness and thus the possibility of repeated administrations likely critical for a sustained therapeutic benefit. Biodistribution and fate-tracking studies suggest that intravenously delivered cells or their secreted products are trapped in remote organs (lung, liver, spleen) with very limited cardiac homing even though using EV from cardiac-committed cells may improve their targeting at same-tissue recipient cells; the bridge between this remote sequestration and a cardiac benefit might be a shift of the phenotype of locally present endogenous immune cells towards a reparative pattern (M2 macrophages, regulatory T cells), thereby making these cells the conveyors of the cell- or secretome-induced protective effects. Thus, while the initial hypothesis underlying the use of cells for treating heart failure was that they could act as a replacement therapy, the current trend is to rather consider them as inducers of paracrine signaling. In the case of heart failure, but also for other conditions, the major effect of this signaling seems to be a modulation of systemic inflammation whose benefits then translate at the level of the diseased organ.

### IA08 Modern Translational Research on Ultra-Low Temperature in Biomedical Science

#### Professor Dr Nikolai N. Korpan

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Modern cryosurgery is to define as a surgical technique using deep freezing to destroy pathological tissue in situ, especially malignant tumor. Interdisciplinary development and the practical meaning of modern cryosurgery are increasing in the field of modern era of medicine worldwide. Modern cryosurgery is used more and more in practice, particularly in surgical oncology. Malignant tumor cell dissemination and mobilization of tumor cells forming metastases or local recurrence is improbable or even impossible under deep freezing process.

Numerous theoretical and experimental studies in vitro and in vivo have been carried out to understand the action of low temperatures on tissue. It has been determined that the processes of ice crystallization are here of primary importance. Current opinion holds that one of the most important elements contributing to the action of subzero cold is intracellular ice formation, which damages the delicate cell structures. Also important in cryoactivity is the formation of extracellular ice, which is followed by cell and tissue dehydration as well as protein denaturation and rupture of the cell membranes. But the major effect on cell damage and cell destruction in cryoactivity is exerted by the speed of freezing and of thawing of the tissue.

The main points of the anticancer concept using modern cryosurgery are: radical and palliative cryosurgical operations: cryoablation and cryoresection, minimal conventional tumor cryosurgery, processing and production of new cryosurgical technology as well as an international teaching and training.

The most important application medical fields are as follows: general and abdominal cryosurgical oncology, cryosurgical cancer urology, cryosurgical cancer gynecology, cryosurgical dermatology, cryosurgical orthopedics, cryoneurosurgery, cryosurgical pulmonology, etc.

Contraindications are not known at this point in time. The several advantages in modern cryosurgery are used in cancer treatment. The most important advantage of cryosurgery is the impediment of the metastatic spread during tumor removal - since no "cutting" takes place. Other advantages are: short trauma after both operation and general anesthesia, good cosmetic result: no scar formation, a vaccination effect, no local complications deriving from the operating table, quick and technically simple tumor removal process, good removal of both benign and malignant tumors. Finally, the substantial subjective facilitation with cancer patients is to achieve through cryosurgical palliative procedures with a pain reduction (painlessness or pain reduction) and fetor ex ore as well as improvement of the general condition through getting

the tumor growth under control.

The modern day of cryosurgery of the present consists of attain efficiency and effective modality through good, uncomplicated surgical results and a high curative rate (treatment rate) as well as high life quality of the operated patients.

Which theoretical, experimental and clinical visions and new innovative areas of cryoscience and cryosurgery can be developed in the near future worldwide?

The cryosurgical oncology could consists of the immobilisation tumor cryodiagnosis, nano-cryoscience, nano-cryomedicine, nano-cryosurgery, nano-cryoequipment, endoscopic cryosurgery, especially colon and stomach, navigation cryoscience and cryosurgery, anticancer cryovaccine, preventive cryomedicine in people with high-risk tumor, thyroid-cryosurgery, etc.

Therefore, a new standard for oncological diagnosis and surgery will establish a new level in the future of modern science and modern medicine in the short term. In medical practice, these theoretical steps will become a reality in the near future.

#### IA09 Metabolic Rewiring: Instigator or Consequence of Cellular Dysfunction?

#### Professor Dr Wolfgang F. Graier

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Most human diseases are either accompanied or even instigated by metabolic changes on the cellular level. The current understanding builds on the concept that, in most cases, an operational malfunction in cells secondary yields prepared adaptive changes in the cellular metabolism that accompanies cellular dysfunction. However, recently another process of changes in cellular metabolism has been introduced: metabolic rewiring. The phenomenon of metabolic rewiring describes a fast and reversible switch of main metabolic paths to address sudden environmental stress to preserve cell functionality. Perhaps the best-known metabolic rewiring is anaerobic glycolysis, compensating for the lack of oxygen by regenerating NADH++H+ to NAD+, thus maintaining the glycolysis and ATP production under hypoxia. In recent work, we could demonstrate that just lowering the Ca2+ levels within the junction between the endoplasmic reticulum (ER) and the mitochondria instantly evokes a reversible status of "pseudohyoxia" induced by the lack of citrine activity (PMID: 35058562) and reduced basal mitochondrial Ca2+ uptake (PMID: 30790505). Notably, the latter is a highly spatial (PMID: 31427612) and directed process (PMID: 35778442). Intriguingly, if such metabolic rewiring persists, it may yield cellular "metabolic reprogramming" as an advantageous survival strategy in e.g. cancer cells (PMID: 33614647; 35740887; 27642082). Besides such profitable metabolic switching, metabolic rewiring may yield reprogramming of the cell, causing de-/transdifferentiation of specialist cells and, subsequently, the manifestation of organ dysfunction and disease. Currently, we explore the basic molecular mechanisms of metabolic rewiring and the cellular consequences thereof as promising druggable targets against the development or progression of human diseases.

### IA10TheUltimateGoal: isGeneTherapy in HypertrophicCardiomyopathyYetPossible?

#### Dr Amanda Varnava

#### Head of Cardiology, Imperial College Healthcare Trust

Hypertrophic cardiomyopathy is the most common genetic heart condition, affecting 1 in 500 of the population and is an important cause of sudden cardiac death in young people. The underlying genetic basis is now well understood and involves mutations in genes encoding the cardiac sarcomere. Genetic variants in these genes lead to either a degraded protein, which causes an insufficiency of that protein, or a non-functioning protein that disrupts sarcomeric function. The altered sarcomeric energetics in turn lead to myocyte hypertrophy and myocardial fibrosis. To date there have been no available therapeutic options that correct either the underlying genetic mutation or the abnormal sarcomeric mechanics. This talk will review current and potential therapies that address these molecular targets and describes the road to targeted therapy for avoiding the complications of this sudden death syndrome.

#### IA11 Pseudomonas Aeruginosa: An Opportunist With a Cause

#### Izel Ungor1 and Yiorgos Apidianakis1\*

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Pseudomonas aeruginosa is a Gram-negative, rod-shaped, aerobic, human opportunistic bacterial pathogen able to infect plants and animals. While a regular inhabitant of soil and water, it is frequently isolated from hospital environments and hospitalized patients. P. aeruginosa requires a significant breach in the host's immune system to cause infection. To become life-threatening, it requires a local and eventually systemic compromise in the host defense. While its resistance to antibiotics and its vast array of virulence factors are well-known, the tropism of P. aeruginosa cannot be explained only by its interaction with the host. Why are P. aeruginosa infections so rare in the intestine, compared to the lung and the skin? We aim to explain P. aeruginosa virulence based on its ability to interact synergistically with bacteria found in the human skin and lung, while antagonistically with bacteria usually found in the human intestine. To do this we consider the polymicrobial setting in which P. aeruginosa interacts with its host. By responding to Gram-positive bacteria peptidoglycan, P. aeruginosa induces factors able to modify the composition of the microbial community, while boosting its damaging capacity towards to the host. However, Proteobacteria able to ferment sugar and fat to lactic and acetic acid may decrease P. aeruginosa growth and virulence. Therefore, bacterial composition at the infection site can change host conduciveness to P. aeruginosa infection, a feature that provides clues towards clinically applicable treatments.

#### IA12 Vaccines in The New Era: What Have We Learnt in The Last 30 Years?

#### **Professor Dr Vasso Apostolopoulos**

*Pro Vice-Chancellor, Research Partnerships at Victoria University, Australia Expertise with development of drugs and vaccines* 

The basis of T cell stimulation is via the specific interaction of an immunogenic peptide in complex with MHC by a T cell receptor. Other co-stimulatory molecules such as CD80, CD86 on antigen presenting cells, are recognised by T cells via CD28 and CTLA-4 which results in T cell activation. In recent years the identification of checkpoint markers such as PD-L1, PD-L2 on antigen presenting cells, epithelial cells etc and their interaction with PD-1 on activated T cells results in apoptosis of T cells and immune escape mechanisms, in the case of cancer. The role of checkpoint markers in a range of disorders including autoimmune disorders, inflammatory disorders and cancer are being studied with a plethora of information being published in the last 5 years. In addition, peptide alterations of T cell epitopes with 1-2 amino acid mutations can have drastic effects on the outcome of this recognition. Such peptides are termed, altered peptide ligands that can act as modulators of immune responses as they have the ability to downregulate or upregulate responses. Over the last 25 years, there has also been an emphasis on carriers, adjuvants and delivery systems to modulate immunity in vitro, in vivo in animal models of disease and in human clinical trials. With this information we are well placed to develop novel immune modulators / therapeutics / vaccines for diseases and we have been successful in developing novel immune modulators for cancer, autoimmune disorders and infectious diseases, all of which will be discussed in the presentation.

## IA13 Coronary Artery Disease (CAD) is The Leading Cause of Death in the Western World.

#### Professor Dr Jeroen J. Bax

Director of Noninvasive Imaging, Department of Cardiology; Leiden University Medical Centre (LUMC), Leiden, The Netherlands. Immediate Past-President, European Society of Cardiology (ESC) 2018-2020

The non-invasive assessment of CAD is crucial for early diagnosis of coronary atherosclerosis – which is predominantly done by (multi-slice) computed tomography (CT): both the coronary artery calcium score and CT coronary angiography are used.

#### Coronary calcium score

Nowadays, the calcium score is used as a marker of the presence/severity of coronary (calcified) atherosclerosis; this biomarker is mostly used for risk stratification in large populations: a low calcium score is associated with good outcomes, while coronary events increase in parallel to increasing calcium scores. Important, coronary artery calcium score does not provide any information on non-calcified coronary atherosclerosis, and therefore a calcium score of zero does not exclude "non-calcified coronary atherosclerosis".

#### CT coronary angiography

Over the last decade, CT coronary angiography has gained significant attention – and is used increasingly in clinical cardiology (mostly "outpatient clinics"). It provides the number of coronary artery lesions in the entire coronary artery tree (using mostly a "17-segment model"). For each of the 17 segments, the "obstructivity" of the stenosis can be defined (<50% is non-obstructive) and the plaque composition (non-calcified, calcified or mixed). Based on these segmental scores, a score for the entire coronary artery tree can be calculated.

#### Ischemia imaging

For assessment of myocardial ischemia (as a surrogate marker for obstructive CAD) is obtained by imaging the patient post-stress and in the resting situation. Comparison of the 2 images can discriminate between stress-inducible ischemia and previous infarction (scar formation).

Different stress-rest imaging modalities are used: echocardiography, scintigraphy (PET and SPECT), cardiovascular magnetic resonance imaging (CMR). Both pharmacological stress (adenosine, dobutamine) and physical exercise are used as "stressors". In some of these tests, wall motion imaging is used, whereas in other tests perfusion is used. Also, simple exercise test (bicycle or treadmill) can be used, looking at ischemia detected on the ECG (ST-T segment depression). CT can also be used to assess stress and rest left ventricular perfusion to assess ischemia.

Lastly, CT FFR (fractional flow reserve) is also available to assess the hemodynamic significance of the coronary artery stenosis.

### When to use which imaging technique?

In Europe, coronary calcium score is not used often in the (outpatient) clinical setting. However, in the United States, the score is often used for initial risk stratification of (asymptomatic) low-risk individuals. CT coronary angiography is used for the lower risk patients (to assess/ exclude coronary atherosclerosis), whereas "ischemia assessment" is used in the higher risk patients.

### IA14 Effectiveness and Safety of Direct Oral Anticoagulants (DOACs) in the Treatment of Venous Thromboembolism (VTE)

#### Professor Dr Miltos Matsagkas

#### Vascular Surgeon, School of Medicine, University of Thessaly, Greece

DOACs have emerged as a new treatment modality for Venous Thrombo-Embolism (VTE) a decade ago and during the last 2-3 years have been established as the first line treatment according to various Guidelines published recently. DOACs have been proved at least equal in efficacy (if not better) to the conventional therapy with LMWHs and coumadins, while at the same time they were safer in terms of major bleedings (especially intracranial hemorrhage). Additionally, the field where DOACs changed dramatically the so far clinical practice is the extended anticoagulation, using half-dose policies, which proved efficacious and extremely safe and thus giving the capability to substantially reduce the recurrence of VTE.

#### IA15 Noise Exposure and Hypertension: Connecting the Dots

#### **Dr Dimitris Chatzis**

Adj Assistant Professor European University Cyprus Consultant Cardiologist, Clinical Hypertension Specialist (ESH)

Hypertension is an established risk factor for cardiovascular disease and there is emerging evidence supporting a causative link between noise pollution and the development of hypertension in the general population.

It seems that exposure to both traffic and occupational noise - mainly via the stimulation of sympathetic nervous system and also various other related pathophysiologic mechanisms, such as increased levels of inflammation and oxidative stress – is associated with an increased risk of several aspects of cardiovascular disease. More specifically, it is well known that acute noise exposure – both in laboratory settings where traffic noise is simulated and in real-life working environments – can cause increases in blood pressure, heart rate and cardiac output. Most importantly, there is evidence supporting the fact that the most damaging type of noise exposure is during nighttime and this may be related among others to sleep disturbance and impaired circadian rhythm.

The magnitude, as well as the impact of this problematic situation have been recognized by World Health Organization (WHO) and other national and international scientific societies and various measures have been proposed so far, with mixed results.

## IA16 How a Mendelian Monogenic Disease Behaves as a Multifactorial Phenotypic Chameleon: Inherited Hematurias

#### **Professor Dr Constantinos Deltas**

Medical and Molecular Genetics, University of Cyprus School of Medicine Director, biobank.cy Center of Excellence in Biobanking and Biomedical Research Tel. 22-892815; E-mail: Deltas@ucy.ac.cy

Inherited hematuric syndromes comprise a genetically and clinically heterogeneous group of conditions. Mutations in several genes cause leaking of red blood cells into the urine and increase the predisposition for further development to proteinuria and chronic kidney disease, even end-stage renal disease (ESRD) and the need for dialysis or kidney transplantation. Most frequently mutated genes are those encoding the alpha3, alpha4 and alpha5 chains of trimeric collagen IV (COL4A3, COL4A4, COL4A5), which is the most abundant component of

basement membranes. Mutations in the X-linked gene COL4A5, result in the typical X-linked Algort syndrome, where most untreated males reach ESRD by the age of 30-yrs. While homozygous mutations in the COL4A3 or the COL4A4 gene cause the autosomal recessive form of Alport syndrome, affecting equally frequently both genders, heterozygous carriers present with microscopic hematuria during childhood, and they have a variable course of disease on long follow-up. In a genetic phenomenon that we name Unilocus Mutational and Phenotypic Diversity (UMPD), these mutation carriers may be subsequently diagnosed with thin basement membrane nephropathy, familial benign hematuria, autosomal dominant Alport syndrome, focal segmental glomerular sclerosis, or cystic kidneys. To some extent, this variability may be attributed to the broad allelic heterogeneity as more severe mutations predispose to more severe phenotypes. More recently we hypothesized that additional DNA variants in kidney function related genes might modify the phenotype. Whole exome sequencing of 115 patients heterozygous for a COL4A3 or COL4A4 mutation, classified as SEVERE (94) or MILD (21) based on clinical criteria was revealing. Nearly all patients co-inherited a variable number of DNA variants of potential functional significance, out of a total of 645 variants in 305 genes. After evaluating every variant and deriving a polygenic risk score (PRS) for each patient, it turned out that MILD patients had on average a statistically significantly lower PRS compared to SEVERE patients. The average PRS amongst SEVERE and MILD patients was 24,17 (range of 7-48) and 18,9 (range of 10-32), respective.

In conclusion, these findings indicate that the full spectrum of the phenotype of patients heterozygous for COL4A3 or COL4A4 mutations, behaves as a multifactorial condition, implicating primary genes, modifier genes and environmental factors.

#### **IA17 Heart Failure Update**

#### **Professor Dr Gerasimos Filippatos**

National and Kapodistrian University of Athens, School of Medicine, Attikon University Hospital, Athens, Greece

Over the past few years, there have dramatic advances in the management of patients with heart failure (HF). Sodium glucose cotransporter 2 inhibitors (SGLT2i) have been shown to improve HF outcomes and slow renal function decline across the spectrum of left ventricular ejection fraction (LVEF), with a notable safety and with a unique robustness and consistency of evidence across different HF trials; the mechanisms of benefit of these drugs in HF remains to be elucidated. The oral soluble guanylate cyclase stimulator vericiguat has been shown to improve HF outcomes in patients deteriorating on optimal background therapy, thus providing a second-line agent for patients with reduced LVEF (HFrEF). In the field of inotropes, the my-osin activator omecaptiv mecarbil improves HF outcomes in more advanced HFrEF patients,

while istaroxime, that combines Na+/K+-ATPase inhibition with sarcoendoplasmic reticulum Ca2+ ATPase activation, thus inotropy with lucitropy, is under investigation. The interest on diuretics have been revived with the positive results of ADVOR trial, having showed that intravenous acetazolamide, used on top of intravenous loop diuretics, improved diuretic response and decongestion in hospitalized HF patients. The non-steroidal mineralocorticoid receptor antagonist finerenone, that combines the potency of spironolactone and the selectivity of eplerenone, has been shown to provide cardiovascular and renal benefits in patients with diabetes and chronic kidney disease, including a reduced risk of incident HF, and is further being studied in HF patients. In the field of ventricular assist devices, the new frontier is transdermal charging without the need for an external lead, thus allowing lower risk of infections and better quality of life.

#### IA18 Strategies for Adherence and Persistence in the Treatment of Hypertension.

### **Professor Dr Charalampos Grassos**

Director of Cardiology Dept in General Hospital in Athens "KAT"

The global epidemic of hypertension is largely uncontrolled, and hypertension remains the leading cause of noncommunicable disease deaths worldwide. Suboptimal adherence, which includes failure to initiate pharmacotherapy, to take medications as often as prescribed, and to persist on therapy long-term, is a well-recognized factor contributing to the poor control of blood pressure in hypertension. Several categories of factors including demographic, socio-economic, concomitant medical-behavioral conditions, therapy-related, healthcare team and system-related factors, and patient factors are associated with nonadherence. Understanding the categories of factors contributing to nonadherence is useful in managing nonadherence.

In patients at high risk for major adverse cardiovascular outcomes, electronic and biochemical monitoring are useful for detecting nonadherence and for improving adherence.

Increasing the availability and affordability of these more precise measures of adherence represent a future opportunity to realize more of the proven benefits of evidence-based medications.

In the absence of new antihypertensive drugs, it is important that healthcare providers focus their attention on how to do better with the drugs they have. This is the reason why recent guidelines have emphasized the important need to address drug adherence as a major issue in hypertension management.

## IA19 Designing Brain-on-Chip Platforms to Simulate Human Brain Function and Malfunction

#### **Professor Dr Achilleas Gravanis**

Professor of Pharmacology, School of Medicine University of Crete

Researcher IMBB-FORTH; Affiliated Research Professor, Center of Drug Discovery, Northeastern University

One of the challenges in developing new therapies for diseases of human brain is the lack of reliable animal models which effectively simulate human brain function. The recent significant advances in human stem cell technologies, polymer and material sciences, and nanobioengineering were an impetus to develop ex vivo microdevices and human cell-on-a-chip platforms, populated with human neuronal and glia cells, as experimental models of human brain pathologies. These microdevices are reliable platforms to study the pathophysiology (cell to cell interactions, cellular and molecular dynamics, proteomic and genomic analysis) of human brain diseases and use them for screening of drugs on a biological system of human origin. We are developing human brain-on-a-chip platforms to study neuroinflammation, blood brain barrier permeability, spinal cord or optic nerve injury. Additionally, we use these platforms to test our proprietary compounds, neurotrophin receptor agonists, with neuroprotective, anti-neuroinflammatory and neurogenic properties and potential therapeutic applications in the above brain pathologies.

(Kourgiantaki et al Nature Reg Med 2020, Varone et al Biomaterials 2021, Pediaditakis et al iScience 2022)

### IA20 Multifactorial Aspects in Diabetes Management: New Perspectives

#### Professor Dr Erifili Hatziagelaki

Research Institute & Diabetes Center, 2nd Dept. of Internal Medicine, University Hospital "Attikon"; Medical School, National and Kapodistrian University of Athens, Greece

The global prevalence of diabetes is predicted to increase in the coming decades as the population grows and ages, in parallel with the rising burden of overweight and obesity. IDF projections show that by 2040 600 million adults will be living with diabetes. T2D is associated with an increased risk of micro- and macrovascular complications, which are major causes of reduced quality of life and morbidity. Glucose-lowering therapy remains a mainstay of diabetes management, in conjunction with a healthy lifestyle and with other medications specifi-

cally addressing the prevention or therapy of diabetes-related complications. Approximately one out of three adults with T2D have cardiovascular disease, which is the leading cause of death. The mortality risk is twofold higher in patients with both diabetes and cardiovascular disease than in patients with diabetes alone. Along with glycemic control, several risk factors (hypertension, dyslipidemia, smoking and obesity) must be managed to prevent cardiovascular disease. Recently, two antidiabetic drug classes have been shown to reduce cardiovascular disease and clinical guidelines have been changed to encourage the use of such drugs. Guidelines and consensus statements to date have acknowledged the practice-changing evidence surrounding GLP1-ra and SGLT2-i and are actively recommending their use in appropriate patients (those with CVD, at high risk of CVD, with chronic kidney disease or heart failure). In conclusion, strategies that reduce CV outcomes must be prioritized in the management of diabetes. To achieve this, a multifactorial approach is required.

## IA21 Effectiveness and Safety of DOACs for the Prevention of Recurrent Venus Thromboembolism (VTE)

#### Dr Charalampos (Haris) Kartsios

Consultant Haematologist, Royal Derby Hospital, University Hospitals of Derby and Burton, NHS Foundation Trust, UK

Several direct oral anticoagulants (DOACs) are now available that dose-dependently inhibit thrombin or activated factor X and offer potential advantages over vitamin K antagonists. such as rapid onset and offset of action, absence of an effect of dietary vitamin K intake on their activity, and fewer drug interactions. Since their introduction, DOACs have gained in popularity for the treatment and prevention of recurrence of venous thromboembolism (VTE) and they currently represent the standard of care. A wealth of clinical evidence over the last 10 years, supports the use of DOACs in challenging populations like the frail and elderly, chronic kidney disease, unusual site thrombosis and also cancer-associated VTE. At the same time we have learned more about managing DOAC-related bleeding and also DOAC-thromboprophylaxis failures.

### IA22 Is There a Rationale for Combining Radiotherapy and Immunotherapy in Patients With Head and Neck Cancer?

#### **Professor Dr Kevin Harrington**

#### Professor in Biological Cancer Therapies, NIHR Senior Investigator

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In the last decade, immune checkpoint inhibitors (ICPIs) have emerged as new standard-ofcare therapies across a range of tumour types and histologies. For patients with relapsed/ metastatic SCCHN, we have delivered studies that have led to approvals of nivolumab [Check-Mate-141]1 and pembrolizumab [KEYNOTE-040]2 in the second-line setting, and single-agent pembrolizumab and pembrolizumab-chemotherapy combination therapies in the first-line setting [KEYNOTE-048]3. Regrettably, we have also seen negative randomised phase II and III studies testing the addition of anti-CTLA4 antibodies (ipilimumab, tremelimumab) and ICOS-ligand agonist (feladilumab) in the first-line setting [CheckMate-651, CheckMate-714, KESTREL, Induce-3]. In addition, in ongoing studies, we are currently testing anti-vascular endothelial growth factor-targeting with lenvatinib and anti-CD47 blockade with ALX-148/evorpacept in randomised phase II/III studies in first- and second-line settings alongside the anti-PD1 ICPI, pembrolizumab [LEAP-009, LEAP-010, ASPEN-03 and ASPEN-04].

The positive outcomes from the CheckMate-141 and KEYNOTE-040 and -048 studies fed the assumption that these agents would also be effective in combination with radiotherapy, including in the contexts of palliative treatment of relapsed/metastatic disease and curative-intent treatment with radiotherapy/chemoradiotherapy. Gold-standard CRT regimens for locally-advanced SCCHN, 70 Gy in 35 fractions over 7 weeks plus concomitant cisplatin on days 1, 22 and 43, can be combined safely with anti-PD1/-PD-L1 ICPI and trials have been conducted with the goal of delivering improvements in progression-free/event-free and overall survival outcomes. Preclinical studies suggested that ICPI therapy should be given concomitantly with RT and this was extrapolated into trial designs based on anti-PD1/-PD-L1 therapy given 1 week before, concomitantly during and adjuvantly for one year after CRT. The resultant JAVELIN-100 Head and Neck study of avelumab (anti-PD-L1) was negative at the primary (progression-free survival) and secondary (overall survival) endpoints4. The KEYNOTE-412 study of pembrolizumab adopted a very similar design and a recent press-release has confirmed that it too has failed to meet its primary endpoint of event-free survival5. Of further concern, other studies, notably Pembro-Rad [RT-pembrolizumab vs RT-cetuximab] and REACH [RT-cetuximab-avelumab vs RT-cetuximab (platin-ineligible) or RT-platinum (platin-eligible)] have also delivered negative outcomes at primary/secondary endpoints.

As a counterpoint to these negative studies in patients with HNSCC, the PACIFIC trial of adjuvant anti-PD-L1 (durvalumab) therapy following curative-intent chemoradiotherapy for stage III non-small-cell lung cancer was impressively positive (hazard ratios of 0.526 and 0.687 for progression-free and overall survival, respectively). Post hoc analysis of the data showed that the greatest benefit accrued to patients who started adjuvant immunotherapy within 2 weeks of the end of CRT, raising the possibility that RT/CRT-induced conditioning of the tumour-immune microenvironment persists for a short period of time and serves as a substrate for subsequent immunomodulatory therapy.

In addition to a detailed review of the mechanistic basis of RT-immunotherapy combinations, this presentation will outline potential novel strategies to maximise opportunities to develop effective combination regimens for patients with locally-advanced head and neck cancers. Specific reference will be made to concomitant addition of DNA damage response inhibition during RT/CRT and to adjuvant addition of innate immune activators after completion of RT/CRT.

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### IA23 Evolution of SARS-CoV2 Since the Start of the Pandemic

#### **Professor Dr Peter Karayiannis**

*Ex Associate Dean for Faculty & Research and ex Co-Chair of the Department of Basic & Clinical Sciences, University of Nicosia Medical School* 

SARS-CoV2 and its spread around the globe from November 2019 onwards has been the cause of the first major pandemic of the 21st century. Nearly three years after the first cases were detected in Wuhan City in China, it is still ongoing, having caused so far 6 waves of infection, with 586 million notified cases and 6.5 million deaths worldwide. Each one of these waves has been caused by a different variant arising in different countries such as the UK, South Africa and India, apart from the original SARS-CoV2 which arose in China. The appearance of these variants has been the result of the high mutation rate of the virus during its replication and their emergence and dominance of some of them under local selection pressures. Surveillance programs for the detection of emerging variants in different parts of the world has proven invaluable in alerting countries to so called variants of concern, operating as an early warning system. The successful development of vaccines and vaccination drives by many countries around the world has ameliorated the pressure on the health systems by reducing hospitalisations and the number of recorded deaths. Thus, the development of immunity has had its beneficial effects leading to relaxation of restrictive measures, but at the same time, exerted pressure on the virus to adapt and evolve. This has led to the emergence of variants which appear increasingly more easily transmissible and more capable in evading the immune response. Thankfully, the increased number of mutations has rendered the virus less pathogenic leading to less severe disease in immunized individuals. It remains to be seen what the future holds and whether this is the beginning of the entry into the endemic phase of the infection.

#### IA24 Tachycardiomyopathy: From Bench to Bedside

### **Professor Dr Efstathios Iliodromitis**

Emeritus Professor of Cardiology National & Kapodistrian University of Athens

Tachycardiomyopathy is a clinical condition in which atrial or ventricular ectopy result in worsening of left ventricular (LV) function and finally in the development of heart failure. There are two forms of this entity, the pure one and the impure. The pure form is referred as arrhythmia induced cardiomyopathy, in which the arrhythmia is the sole reason for left LV dysfunction/ failure and the impure form is referred as arrhythmia mediated cardiomyopathy, in which the arrhythmia may exacerbate ventricular dysfunction, or it worsens the heart failure in existed heart disease. Numerous supraventricular or ventricular arrhythmias result in microstructural, histologic or anatomic gross changes of the heart. The increased heart rate, the irregular cardiac rhythm, desynchrony and the duration of arrythmia, are the main factors which contribute to the development of heart failure. All these clinical conditions cause ATP depletion, increase the oxidative stress, provoke myocardial ischemia and facilitate alterations in the molecular mechanism, all having critical role for the deterioration of LV functioning. Experimental studies have described three phases regarding the progress of left tachycardiomypathy: the compensatory period lasting in one week, the LV dysfunction phase, which ranges in duration between one and three weeks, and the LV failure phase which appear after a three-week period. Significant intracellular changes in sarcoplasmic reticulum and cytosolic Ca2+ handling as well as cellular remodeling and extracellular matrix remodeling, occur during these three phases. More sustained arrhythmias such as atrial fibrillation, junctional reciprocal tachycardia, very frequent ventricular extrasystoles, sustained or non-sustained ventricular tachycardias or permanent pacing result in deterioration of LV function. However, brief periods of atrioventricular reentry tachycardias and rare atrial or ventricular extrasystoles are not implicated in the development of arrhythmia induced tachycardiomyopathy. Of note, the development of cardiomyopathy in response to arrhythmia may take months to years to appear whilst, recurrent arrhythmia can result in rapid LV function decline, suggesting residual ultrastructural abnormalities. The diagnosis in suspected tachycardiomyopathy includes clinical examination, family history, continuous ECG recordings, echocardiography and/or MRI imaging for structural diseases, catheterization if it is indicated and even genetic counseling if needed. The arrhythmic burden and the patient's symptoms are critical for the therapeutic decisions. The minimization of arrhythmias includes the treatment of the underline heart disease, such as coronary artery or valves disease, optimization of the medical treatment for LV heart failure, interruption of the cascade of events with drugs, or with ablation for the eradication of arrhythmias and thus, for prevention of LV worsening by the elimination of the triggers. Several open questions remain, regarding the differential diagnosis, patient's symptoms, risks for sudden death, longterm outcomes and existed experience in the proposed therapeutic interventions. Finally detailed information to the patient for potential complications from the treatment approaches, their advantages or disadvantages as well as explanation for the natural history of the disease is necessary.

### IA25 From Diagnostics to Therapeutics; Antibodies Take Centre Stage in COVID-19

#### **Professor Dr Paul Moss**

*Prof. of Haematology and Deputy Head of the College of Medicine at the University of Birmingham, UK. Chief Investigator of the UK Coronavirus Immunology Consortium* 

The COVID-19 pandemic has led to the death of over 20 million people to date and remains a major global health concern. Effective control of primary infection is mediated by the innate and adaptive immune systems and leads to partial protection against reinfection. The introduction of effective SARS-CoV-2 vaccines in November 2020 helped to contain the pandemic and spike-specific antibody and cellular immune responses underpin clinical efficacy.

Spike-specific antibodies are the major 'correlate of protection' following vaccination and individual responses depend on a range of factors such as age, gender and co-morbidity. Detailed information is now available on the molecular and physical features of antibody binding and how these relate to protection. However, immune pressure is driving the development of viral variants such as Omicron and the immunogenic landscape of the virus is evolving rapidly

Unlike many acute viral infections, coronaviruses cause repeated re-infections and it is increasingly clear that current vaccines are not able to provide long term 'sterilizing' immunity. This may relate to the fact that coronavirus-specific antibodies 'wane' after infection although the biological basis for this is uncertain and will require study of memory B cells and plasma cells.

Antibodies have also emerged as powerful therapeutic agents, both for the treatment of acute infection and for prophylactic protection for immune suppressed patients who are unable to develop adequate humoral immunity. The success of this approach has depended on advances in fundamental understanding of the regulation of antibody degradation in vivo but will necessitate continuing update of appropriate reagents to overcome viral mutation.

Antibodies have been centre stage in the control, prevention and policy management of the COVID-19 pandemic. The information that has been derived from this challenge can now be applied effectively to a range of other medical conditions.

### IA26 Robotic Thoracic Surgery: From Science Fiction to Everyday Practice

#### Associate Clin. Prof. Dimitrios Kyparissopoulos

Robotic, Cardiothoracic surgeon, IASO Medical center; Harefield Hospital, Royal Brompton and Harefield NHS Foundation Trust, London, UK

Hippocrates of Kos (c. 460 - c. 370 BC), was a Greek physician who is traditionally referred to as the "Father of Medicine". He is also considered to be the first Thoracic Surgeon, as he described how to treat an empyema on a wounded soldier!

Medicine has been practiced since prehistoric times, during most of which it was an art (an area of skill and knowledge) frequently having connections to the religious and philosophical beliefs of local culture.

The modern era really began with the discovery of the smallpox vaccine at the end of the 18th century. A true medical revolution was the discovery of antibiotics around 1900.

Thoracic surgery followed these innovations. The first anatomical resection ever recorded was in 1912 by Hugh Morriston Davies. Until recently, the (only) surgical approach was the thoracotomy, which involves cutting the muscles and breaking the ribs in order to have good access to the tumor.

Within the next century, thoracic surgery speeded up by introducing minimal invasive techniques (VATS), however, since 2000 seems to be traveling with the speed of light, as the first robotic Da Vinci surgical system was launched.

Today, almost the whole spectrum of thoracic procedures can be performed using the robot and has been recommended by the international guidelines (NCCN/ESMO) as the golden standard of treatment. Who could have imagined that the same procedure, under the same principles, could be achieved faster, safer, with no scars or pain?

The introduction of Robotic DaVinci system is the revolution of our times. Amazing accuracy, 3600 3D vision, small scars are some of the unprecedented advantages that make it the Ferrari of surgical treatment.

Primary lung cancer, one of the leading causes of death around the globe (WHO, Research-Gate), if diagnosed early and treated properly, appears to be curable.

The outcomes after resection of mediastinal lesions is beyond any expectation. Thus, the robotic thymectomy is a game changer.

The decision of what treatment is best should be the outcome of an MDT where the experienced thoracic surgeon has a leading role.

In this presentation, the advantages and the disadvantages of the use of robot in thoracic surgery will be explained, videos will demonstrate the superiority against the old techniques and finally our personal experience with our outcomes will be presented.

## IA27 Advances in Catheter Ablation of Arrhythmias: Is It Prime Time for Wider Application of Innovations and How the Patients Will Benefit from It?

#### Dr George K. Andrikopoulos

Director of the 1st department of Cardiology and the department of Electrophysiology and Pacing, Henry Dunant Hospital, Athens, Greece

Catheter ablation of arrhythmias has advanced significantly during the last 3 decades. Its improved efficacy and safety have changed dramatically the treatment of common arrhythmias and most importantly, catheter-based therapies have been expanded in new indications including atrial fibrillation. Notably, the prevalence of atrial fibrillation in the general population may exceed 10% over the age of seventy years and its overall incidence in the population is still increasing due to demographic changes and the sedentary way of life.

The most important reason for the progress of electrophysiology is the remarkable advances in technology, data analysis and imaging in cardiology, which enabled the development of new therapies.

Accurate and reliable electroanatomical mapping, merging of CT/MRI anatomy with electroanatomical models, balloon ablation systems, multielectrode catheters, catheters with contact force sensors, intraprocedural echo-guided cardiac imaging, remote navigation systems, high power catheters, radiation free MRI-guided catheter ablations and use of pulsed electric fields in catheter ablation are possibly the most important innovations in catheter ablation of arrhythmias.

Although it is difficult to foretell which of these advances will have the most important effect on catheter ablation of arrhythmias, I would choose the latter. The use of pulsed electric fields known as pulsed fields ablation (PFA) is the technology that may have the most important influence in clinical practice. The first published data from studies on atrial fibrillation ablation are very promising and our clinical experience is in symphony with the currently published data.

What can the patients expect from PFA? Tissue selectivity, improved safety and efficacy and shorter duration of electrophysiological procedures are the most obvious benefits of wider use of PFA. Is it prime time for its wider application? There are at least 6 PFA novel systems waiting

for FDA and CE approval. The prime time for PFA is now but the most promising evolution for catheter ablation of arrhythmias soon would be the incorporation of PFA in MRI-guided, radiation-free catheter ablation.

#### **IA28 Viruses in Multiple Sclerosis**

#### **Professor Dr Nikolaos Grigoriadis**

Head of the of the B' Dept of Neurology, AHEPA University Hospital, the MS Centre and the Laboratory of Experimental Neurology and Neuroimmunology

Multiple sclerosis is an immune-mediated disease where both genetic background environmental factors are implicated. Already at the end of the 19th century, a plausible though yet unproven hypothesis that viruses are either directly or indirectly implicated in Multiple Sclerosis (MS) pathogenesis, had been established. Indeed, a number of viruses or viral elements predominantly Epstein-Barr virus (EBV), human endogenous retroviruses (HERVs) and human herpesvirus 6 (HHV-6), John Cunningham virus, cytomegalovirus and human endogenous retroviruses and others had been associated with MS. These viruses can establish lifelong infections with periods of reactivation, which might be linked to the relapsing course of MS. Moreover, anti-viral antibodies against mumps, measles, varicella-zoster, and EBV are often present in MS but their relevance is unclear. Importantly enough, it has recently been reported that EBV is the leading cause of MS. Anti-EBV antibody titters in over 99% of MS patients provide evidence for an epidemiological link between MS and EBV. Symptomatic infectious mononucleosis during EBV infection increases risk for MS. Molecular mimicry between virus and self-antigens is a potential mechanism that might explain this association. Antibodies against certain EBV nuclear antigen 1 (EBNA1) regions have been found in MS patients, including the region AA365-4265, indicating molecular mimicry between EBNA1 and the glial cellular adhesion molecule GlialCAM. Whether a vaccine against EBV might protect against MS or antivirals that target EBV might provide effective therapy, especially when given early in the course of disease, is a matter of future investigation.

## IA29 High Density Lipoprotein: Guardian Angel or Indifferent Bystander?

### Professor Dr Kyriakos E. Kypreos

University of Patras, School of Medicine, Department of Pharmacology, Rio Achaias, TK. 26500, Greece; European University Cyprus, Nicosia, Cyprus

The latest epidemiological data indicate that a relation between high density lipoprotein cholesterol (HDL-C) levels and the risk for cardiovascular disease (CVD) does exist but follows rather a "U-shaped" relationship rather than a linear one, as once believed. Optimal range of HDL-C concentration is set at 0-70 mg/dl for men and 50-70 mg/dl for women. Moreover, as research in the field of lipoproteins progresses it becomes increasingly apparent that HDL particles possess different attributes and depending on their structural and functional characteristics, they may be "antiatherogenic" or "proatherogenic". Considering this information, it is highly doubtful that the choice of experimental drugs and the design of respective clinical trials that put the HDL-C raising hypothesis at test, were appropriate. Key data from the biochemistry, epidemiology and pharmacology of HDL, including data from new clinical trials, strongly suggest that HDL remains a valuable target for the treatment of cardiovascular disease and the clinical pharmacology of HDL-C modulation must be revisited with properly designed agents and clinical trials.

## IA30 Novel Tools and Approaches for Translational Research in Haematopoietic Cells and Beyond

### Associate Professor Carsten Werner Lederer

Molecular Genetics Thalassaemia Department, The Cyprus Institute of Neurology & Genetics | Cyprus School of Molecular Medicine

A growing molecular tool kit comprising viral vectors for overexpression, RNA interference for gene knockdown, classical genome editors based on DNA double-strand breaks, and most recently DSB-independent DNA editors, is revolutionising therapy development and functional dissection of gene function. This is particularly true for research of readily accessible and therapeutically relevant hematopoietic stem cells and related cell lines, which often serve as the showcase for new technologies.

The present talk highlights recent technology development of wider relevance for mechanistic and therapeutic insights in health and disease. In the process, I will touch on corresponding translational research results of our group in hematopoietic cells, based on the above tools individually or in combination. Our findings cover the combination of RNApolII-driven protein and shRNA expression for therapy, high-efficiency homology-independent DNA editing for mutation-specific gene repair and for functional analysis of protein isoforms, homology-indepen-

dent editing for endogene activation, precision editing for disease model development, and employment of small-RNA transcriptomics to inform tag-activated miRNA-mediated endogene deactivation for lineage-specific functional studies.

IA31 Cancer in Children and Adolescents in Cyprus: Incidence Rates Among the Highest in the World, Cancer Type Distribution Differences, Temporal Trends and the Search for the Causes.

### Clinical Professor Dr Loizos G. Loizou

President "Elpida" Foundation for children and adolescents with cancer and leukemia Clinical Professor, Medical School, Nicosia University Consultant Pediatric Oncologist/ Hematologist; Fmr. Director, Pediatric Oncology/ Hematology Clinic Archbishop Makarios III Hospital, Nicosia, Cyprus.

Childhood cancer represents 1-2% of all cancer cases but is globally underreported, because of diagnosis and registration issues. Creating a population based pediatric oncology registry in every country is a fundamental prerequisite for solving this problem. The incidence rates and temporal trends constitute important information for improving the management of patients and resources attribution; furthermore, regional variations could generate hypotheses regarding aetiology. In Cyprus, we studied comprehensively the incidence and trends of childhood cancer using the newly established population-based pediatric oncology registry. Our findings demonstrate that the combined incidence rate for all the 12 diagnostic groups of the International Childhood Cancer Classification 3 is among the highest globally. The temporal trends did not show significant variation, except for thyroid cancer in adolescents. The distribution of the four most frequent childhood cancers was found to be different than what is reported globally. Our research revealed these interesting and perplexing questions which merit answers. A cancer registration issue, overdiagnosis or environmental and genetic factors specific to Cyprus may all contribute to the particularities found in the epidemiology of childhood cancer in Cyprus. Further exploring these issues is mandatory in order to shed light about the aetiologies causing the differences of the situation in Cyprus in comparison with what is described internationally. We are currently exploring the genetic (cancer predisposition syndromes), nutritional and other environmental factors.

### IA32 Recent Developments in Automated Insulin Delivery Through Smart Pump Technology. Is it an Artificial Pancreas on the Way?

### **Dr Stavros Liatis**

### First Department of Propaedeutic Internal Medicine & Diabetes Center, Laiko General Hospital, Medical School, National & Kapodistrian University of Athens, Greece

The discovery of insulin 100 years ago was initially thought to signal the cure of type 1 diabetes, a disease caused by the complete absence of insulin, leading to death shortly after presentation. It was soon, however, realized that despite insulin replacement, devastating complications became apparent a few years following diagnosis due to chronic hyperglycaemia. At the same time, hypoglycaemia, a common side effect of insulin therapy further contributed to excess morbidity and mortality. Today, it is well established that optimal glycemic control is the cornerstone of type 1 diabetes management, increasing life expectancy and minimising complications.

Modern insulin replacement therapy in type 1 diabetes aims to euglycaemia by struggling to mimic the physiologic insulin secretion pattern. This can be achieved either through multiple daily insulin injections or by continuous subcutaneous insulin delivery via highly advanced devices called insulin pumps. The latter involve the connection of a subcutaneously placed insulin delivering catheter to a high-tech apparatus (the pump), that is programmed to continuously supply the body's insulin needs. Pump therapy is a complicated treatment scheme, demanding special education and skills. The recent advent of glucose-responsive automated insulin pumps, which involve the generation of a closed-loop between the pump, a continuous glucose sensor and a feedback dose-calculating algorithm, has revolutionised the management of type 1 diabetes, succeeding to maintain time spent in euglycaemic range over 70-75%, while minimizing hypoglycaemia. Evolution of these so-called hybrid closed-loop systems from research to clinical practice has been considered as a major step towards the artificial pancreas, the holy grail of type 1 diabetes therapy. Nevertheless, important challenges to this direction still remain: full automation (current systems need patient interference for meal dose calculation), size reduction, improvement of subcutaneous catheters and, most importantly, portal circulation access are near-future targets of intense scientific research.

#### IA33 Using Pericytes to Mend Broken Hearts: Where do we Stand?

### Professor Dr Paolo Madeddu

Chair of Experimental Cardiovascular Medicine (Cardiovascular regenerative medicine, Tissue engineering, Therapeutic angiogenesis, and Gene therapy), Bristol Heart Institute, Bristol, UK

Pericytes are a heterogeneous population of cells located in the blood vessel wall and surrounding capillaries. They were first identified in the 19th century by Rouget, however their biological role and potential for drug targeting have taken time to be recognised. Isolation of pericytes from several different tissues has allowed a better phenotypic and functional characterization. These findings revealed a tissue-specific, multi-functional group of cells with multilineage potential. Given this emerging evidence, pericytes have acquired specific roles in pathobiological events in vascular diseases. In this lecture, I will provide a compelling overview of the therapeutic potential of pericytes for the treatment of ischemic disease. These specific aspects will be discussed: (i) Pericytes' potential to drive heart regeneration / repair after a myocardial infarct (angiogenesis, scar stabilisation etc). (ii) Regenerative medicine approaches involving pericytes: cell and molecular therapy – benefits and limitations. (iii) Pharmacological modulation of resident cardiac pericytes' phenotype - benefits and limitations of systemic drug administration. (iv) The future of regenerative medicine: pericyte-engineered synthetic coronary vessels.

## IA34 Implementing Pharmacogenomic Testing in Fluoropyrimidine-Treated Cancer Patients to Prevent Toxicity

### **Professor Dr Vangelis G Manolopoulos**

Laboratory of Pharmacology, Medical School, Democritus University of Thrace, Alexandroupolis 68100, Greece; Individualised Medicine & Pharmacological Research Solutions Center (IM-PReS), Alexandroupolis, Greece; Clinical Pharmacology Unit, Academic General Hospital of Alexandroupolis, Greece

Fluoropyrimidines are widely used for the treatment of solid tumors. Approximately 10-30% of fluoropyrimidine-treated patients develop early-onset severe or life-threatening toxicity. Dihydropyrimidine dehydrogenase (DPD), encoded by DPYD gene, is the rate-limiting enzyme responsible for fluoropyrimidine catabolism. DPYD gene variants seriously affect DPD activity and are well validated predictors of fluoropyrimidine-associated toxicity. DPYD variants rs3918290, rs55886062, rs67376798 and rs75017182 are currently included in genetic-based dosing recommendations for fluoropyrimidines developed by the Clinical Pharmacogenetics Implementation Consortium. On March 2020, European Medicines Agency has recommended that patients receiving fluoropyrimidine therapy should be tested at least for these four DPYD

variants before treatment initiation. Furthermore, polymorphisms in several other genes have been suggested to play a role in this effect but evidence is still not conclusive. I will present data from a clinical study in Greek cancer patients confirming the clinical validity of DPYD variations as predictive risk factors for development of fluoropyrimidine-associated toxicities. I will also discuss the current state-of-affairs on fluoropyrimidine pharmacogenomics testing all over Europe.

Funding: Financial support for the project IMPReS (MIS 5047189) was provided by the Program "Competitiveness, Entrepreneurship and Innovation" (NSRF 2014–2020) co-financed by Greece and the European Union (European Regional Development Fund).

### **IA35 Stress Impact on Hepatic Drug Metabolism**

### Professor Dr Maria Konstanti

## Department of Pharmacology, Faculty of Medicine, School of Health Sciences, University of Ioannina, Ioannina, Greece

The majority of prescribed drugs and pre-carcinogens are metabolized in the liver by cytochromes P450 (CYPs). The available experimental data suggest that psychophysiological stress can modify various factors with a high impact in CYP regulation, thus altering a drug's pharmacokinetic profile. Accumulating evidence indicates a gene-, stress-, age- and species-specific interference in the stress-mediated regulation of genes that encode the most important drug-metabolizing CYP isozymes. Preclinical studies demonstrated that stress induced several CYPs including those of CYP3A and CYP2C subfamilies, thus accelerating the metabolism of their drug-substrates, a condition that usually results in sub-therapeutic drug levels and failure of pharmacotherapy. In contrast, the stress-mediated down-regulation of CYP2E1 and CY-P2B1/2 that is followed by reduced metabolism of their drug-substrates, and the consequent rise of their levels in the blood could lead to toxic manifestations. The main stress effectors, glucocorticoids and the adrenergic receptor (AR)-linked pathways hold primary and distinct roles in the stress-mediated regulation of CYPs. It appears that stress and AR-systems have a significant impact on some of the major drug and pre-carcinogen-metabolizing enzymes. Although, most of the available data come from preclinical studies, and the findings can not be directly extrapolated to the human condition, they support the notion that stress should be eliminated and AR-agonists or antagonists should be considered in order to assure the optimal efficacy and minimize the adverse effects of prescribed drugs and in particular, when multiple drugs of vital importance to the patient are used, or they display small therapeutic windows and significant adverse effects.

### IA36 Effectiveness and Safety of Direct Oral Anticoagulants (DOACs) in the Treatment of Venous Thrombo-Embolism (VTE)

### Professor Dr Miltiadis (Miltos) Matsagkas

Vascular Surgery; School of Medicine, University of Thessaly

DOACs have emerged as a new treatment modality for Venous Thrombo-Embolism (VTE) a decade ago and during the last 2-3 years have been established as the first line treatment according to various Guidelines published recently. DOACs have been proved at least equal in efficacy (if not better) to the conventional therapy with LMWHs and coumadins, while at the same time they were safer in terms of major bleedings (especially intracranial hemorrhage). Additionally, the field where DOACs changed dramatically the so far clinical practice is the extended anticoagulation, using half-dose policies, which proved efficacious and extremely safe and thus giving the capability to substantially reduce the recurrence of VTE.

### IA37 Preventing and Treating Diabetic Chronic Kidney Disease

#### Dr Ilias N. Migdalisc

#### Director, Diabetic Centre, Lefkos Stavros Hospital; Papadiamantopoulou 16, Athens, Greece

Worldwide studies show that chronic kidney disease (CKD) is a leading cause of end-stage renal disease (ESRD) in type 2 diabetes mellitus (T2DM), which also increases cardiovascular mortality. Various studies have estimated a 27.9-63.9% diabetic chronic kidney disease (DCKD) prevalence among adults with T2DM. In Greece, we previously reported a 45% prevalence of CKD (mild, moderate and severe) on a hospital-based T2DM population. Pharmacological treatment of DCKD is primarily targeted towards lowering HbA1c and blood pressure. Glycemic control may delay progression of DCKD, with most guidelines recommending a goal HbA1c around or below 7.0%. First line antiglycemic medications are metformin and SGLT2 inhibitor. For the hypertension, treatment with angiotensin-converting enzyme inhibitors and angiotensin-II receptor blockers showed the greatest efficacy for the prevention of CKD. People with DCKD typically have significant hypertriglyceridemia, high LDL and low HDL cholesterol. The role for dyslipidemia in the development and progression of DCKD is unclear. But, mainly, because of cardiovascular risks, hypolipidemic treatment with statins should be considered for all patients with DCKD, stages 3-5. Proper diet and education with smoking cessation should also be encouraged. In all the cases, a better understanding of the therapeutic strategies offers educational benefits to primary care physicians, which can result in an overall more successful and efficient management of T2DM with DCKD.

### IA38 CAR-T Cells in Haematological Malignancies -a Key to Success?

#### Associate Professor Dr Emmanouil Nikolousis

Associate Professor of Hematology, Chairman, School of Medicine, European University Cyprus

CAR T-cell therapies have been used to treat relapsed and refractory patients with Diffuse large B cell lymphomas and Acute lymphoblastic leukaemia over the past five years. This new cellular intervention undoubtedly revolutionized the treatment of these highly aggressive diseases which were previously treated with conventional chemotherapy with very little efficacy and increased toxicity especially considering these patients have received multiple lines of treatment. Therefore, therapies represent a valuable new treatment option however their role in the sequence of treatment needs to be well established by clinical trials and real-world data but currently they are yielding impressive complete remission rates and improving survival. Grade 3 or higher cytokine release syndrome and neurotoxicity occurred in 10% and 16% patients, respectively. Best objective and complete response rates were 73 to 80% and 40%, to 50% respectively in different trials and median overall survival has not been reached in some trials. Treatment in SoC setting with CD19 CAR T-cell therapies for R/R LBCL and ALL showed a manageable safety profile and high objective response rate and CR rates while the OS conveys a promising future for a curative option. These promising cellular therapies have now been expanded to include other haematological malignancies at later lines of treatment like mantle cell lymphoma, follicular NHL and multiple myeloma.

However, in other haematological malignancies like the myeloid malignancies there isn't the same progress within cellular therapies and allo genetic stem cell transplantation still remains the golden standard as the curative treatment.

### IA39 The Role of the Robotic Surgery in the Evolution of the Minimal Invasive Surgical Oncology: Where we stand.

### Associate Professor Dr Athanasios S. Petrou

European University CY, School of Medicine; Director of the Advanced Laparoscopic Hepatobiliary-Pancreas and Surgical Oncology Center at Mediterranean Hospital, EU, Cy; Director of the Hepato-Pancreatico-Biliary (HPB) Department at, American Institute of Minimal Invasive Surgery (AIMIS), EU, Cy; Director of the Liver and Pancreatic Surgery Unit at, Athens Medical Center - Athens Medical Group

In our era surgeon is frequently exposed to new technologies and instrumentation. Robotic surgery has the potential to alleviate the fundamental limitations of laparoscopic surgery such

as two-dimensional imaging, limited instrument movement and intrinsic human tremor. It helps the surgeons in operating inaccessible areas of human body with ease, in comparison to traditional open surgical techniques and laparoscopy. Patients are being benefitted by minimal scar, reduced blood loss, early recovery, minimum wound-related complications, and reduced hospital stay.

Unlike the use of robotics in benign conditions, the use in cancer surgery is different. Probably there are some disadvantages in robotic surgery, such as anaesthetic challenges because of the extreme positions, lack of haptic feedback which may result in cutting through the tumour, increased duration of the surgery, and the increased cost incurred.

Despite that recent studies resulted that Robotic surgeries in cancer have shown promising early results regarding feasibility, oncological safety, and learning curve. However, long-term oncological outcome in patients who have undergone robotic surgery is not well studied. Comprehensive view to identify all technical, ethical, and legal issues should be considered in each patient for a favourable outcome.

For this reason, the establishment of set criteria for adequate and standardized training and credentialing of surgical residents, fellows and those trained surgeons wishing to perform RS has become a priority. In this rapidly evolving field, we herein review the past, present and future of robotic technologies and its penetration into different surgical specialties.

### IA40 The Survival of the Fittest in the Cardiovascular Disease Continuum

### Associate Professor Dr Andreas Pittaras

Cardiologist, Clinical Hypertension Specialist ESH George Washington University Washington DC USA

The evidence supports the critical role of physical activity (PA), exercise training, and cardiorespiratory fitness (CRF) in the primary and secondary prevention of cardiovascular disease (CVD). The measurement of CRF reflects the complex system of O2 transport and utility and is dependent on cardiac function (systolic and diastolic), pulmonary ventilation, and the ability of the vascular system to deliver and unload O2. During exercise, these systems work in concert to help meet the O2 demand of contracting muscles. A practical clinical evaluation of CRF is by estimated METs, which is commonly determined by speed and incline on a treadmill using standardized algorithms, and most studies have expressed CRF in the context of survival benefit per MET. Generally, METs are categorized based on fitness levels, with <5, 5-8 and >8 METs corresponding with least fit, moderately fit, and highly fit groups, respectively. More than a decade ago, Kodama et al performed a meta-analysis of 33 studies with more than 100,000 participants, demonstrating that for every increase of 1 MET in CRF, mortality and CVD or coronary heart disease events were reduced by 13% and 15%, respectively. These results were recently updated by Laukkanen et al in a meta-analysis of 37 studies of nearly 2.3 million participants, showing that every increase of 1 MET in CRF was associated with an 11% reduction in mortality. The top tertile of estimated CRF had a 45% lower mortality compared with the lowest tertile of estimated CRF. Clearly, considerable evidence supports the importance of CRF. In fact, in many studies, patients with higher fitness and a major CVD risk factor, such as diabetes, obesity, hypertension, or dyslipidemia, generally had a better prognosis than those without these risk factors but with low fitness.

In the last issue (August 1, 2022) of the Journal of the American College of Cardiology, our research group extended this important information in an analysis of more than 750,000 U.S. veterans, which included large numbers of septuagenarians, octogenarians, African Americans, Hispanics, Native Americans, and women. During a median follow-up period of 10.2 years and more than 7.8 million person-years of observation, adjusted associations of CRF and mortality risk were inverse and strongly graded across the age spectrum, sex, and race. The lowest mortality risk in both men and women was in those who achieved at least 14 estimated METs (76% and 77% reductions in risk, respectively, compared with the least fit). Men and women in the ≥98th percentile of peak exercise capacities of approximately 14.0 METs lived 6.0 and 6.7 years longer, respectively, compared with those in the <20th percentile of CRF. We concluded that being unfit carried a greater risk than any other CVD risk factor. Our study not only supports the large body of evidence on the importance of CRF for CVD risk but also provides considerable data from a substantial cohort of U.S. veterans and a very diverse population regardless of age, sex, race, and ethnicity, supporting the importance of CRF across various U.S. populations, with no increased risk at very high CRF. Although some studies have suggested a threshold of harm or at least loss of benefit at very high levels of PA and exercise, whereas others have not, in our study does not seem to be any loss of benefit or harm at very high CRF. Finally, being fit is key to longevity. Certainly, at least moderate to high CRF (eg, >8 METs) is known to reduce major CVD events and all-cause mortality. Although the main way to achieve high CRF is with regular PA or exercise training, a large segment of the world's population remains physically inactive, with considerable sedentary behavior. Additionally, some evidence suggests that CRF is a better predictor of survival than is PA. Our study demonstrates that CRF may be a good and independent predictor of CVD-related mortality for men and women, across the spectrum of age and race, even superior to accepted CVD risk scores and risk factors, which makes CRF a valuable tool in the armamentarium for the prevention of CVD U.S. and European guidelines should include CRF as a CVD predictor and health marker at all ages, independently of both sex and race. Improving CRF should be considered a target in CVD prevention, similar to improving lipids, glucose, blood pressure, and weight. Although clinical graded exercise testing is frequently used for diagnostic purposes, clinicians, especially specialists in CVD, are encouraged to consider incorporating this highly prognostic tool in their

patient evaluations. Objectively quantifying one's CRF may eliminate any false impressions of a patient's self-reported PA level, which is often misrepresented by recall error. Identifying those in the least fit categories for their age and sex can help prompt referrals to clinical exercise physiologists and/or other exercise programs aimed at supporting the adoption of a physically active lifestyle at levels that have been demonstrated to improve CRF, as the evidence supports that fit is it for healthy living and longevity across populations.

## IA41 The Enemy of Your Enemy is Your Friend - The Reintroduction of Bacteriophages for Resistant and Persistent Infections.

### Professor Dr Ran Nir-Paz

The Hadassah-Hebrew university medical center and the faculty of Medicine the Hebrew University, Jerusalem, Israel; The ESCMID study group for non-traditional antibacterial agents ES-GNTA

Bacterial antimicrobial resistance and non-resolving infections are a global problem and efforts to achieve alternative therapeutic approaches are in need. While phages were introduced almost 100 years ago, it was abounded for many years. Bacteriophages are re-emerging today as a potential treatment option, as a personalized therapeutic option with minimal collateral damage of antimicrobial resistance for persistent and non-resolving infections.

In the last few years we have established, a collaboration Center of Hadassah and the Hebrew University. The center termed the Israeli Phage Therapy Center (IPTC) in which we offer all the stages needed to achieve treatment with phages. This includes a wide phage bank of over 500 characterized phages, characterizing the bacterial isolate, finding the best lytic phage and developing treatment schemes. From January 2019 until August 2022, a total of more than 130 requests from Israel and abroad, were reviewed in IPTC. Out of those 15 Israeli patients received compassionate intravenous bacteriophage therapy. 50% of requests were of MDR bacteria and respiratory, skin and soft tissue infections were among the most common types, accounting for 52.2% of requests. In all cases bacteriophage treatment was administered as an adjuvant to standard of care antibiotic therapy. Additionally, early stage 2 clinical trials were performed as well.

In this talk the topics of clinical trials outcome, and status of phage therapy around the globe and in Europe in particular will be discussed

# IA42 Lipid Management in 2022. Is There a Reasonable Gap Between Guidelines and Clinical Practice?

### **Dr Dimitris Richter**

### Head of Cardiac Department, Euroclinic Hospital, Athens, Greece Past-Chair of CCP-ESC; General Secretary of Hellenic Heart Foundation

In 2019, the newest guidelines for the treatment of dyslipidemia were announced, with major changes in daily clinical practice. These guidelines directly affect daily clinical practice as they are directly adopted by the cardiology societies of all European countries as well as by many other specialty societies. Their creation together with the European Atherosclerosis Society significantly increases their adoption in the various countries and specialties.

There are several types of dyslipidemia, the most common of which is elevated total cholesterol and LDL, which is the main target of pharmaceutical treatment. The incidence of metabolic syndrome, i.e., abdominal obesity, with low (<40 mg/dl for men and <50 mg/dl for women) HDL-cholesterol and high (>150 mg/dl) triglycerides. There are also other forms, with pathological only HDL cholesterol or particularly elevated triglycerides only.

Cholesterol is obtained from food, but it is also produced in the body in a ratio of about 1 to 2. Increased intake of saturated fatty acids, found mainly in animal fats, such as red meat and fatty cheeses, and obesity are often causes of hypercholesterolemia related to lifestyle. Unfortunately, the importance of high cholesterol is particularly important in the younger age groups (30-60 years) and gradually recedes to give the second place (first is smoking), as a risk factor, to hypertension. In Greece, in the last 20 years, coronary heart disease has consistently been the first cause of death, with a constant difference from the second, which is tumors. Since 2001, we have around 20.000 deaths from coronary artery disease in Greece and about 25.000 from strokes.

Analysis of several studies showed that for every 10% reduction in LDL, the incidence of coronary heart disease was reduced by 22% in the next 2 to 5 years and by 25% after 5 years. The intervention had to be of at least two years to produce a clinically meaningful benefit. This means that an occasional diet or use of medication, which will improve cholesterol values, is not enough if it is not long-lasting. And this duration is usually life-long.

We should keep in mind that only permanent and systematic treatment of dyslipidemia produces results (which are often impressive) in reducing heart attacks and other forms of coronary heart disease. Although the main goal of hypolipidemic treatment is always LDL with all other indicators being secondary, we have a significant change in its goals with currently the high-risk patients to have a target of < 55 mg/dl.

Lipoprotein a is recommended to be measured in the whole population once in a lifetime, its levels are heritably determined, and high levels increase cardiovascular risk and although we do not have a specific drug for it we can reduce the overall risk of these patients with further LDL reduction. The risk increases from Lp(a) levels of 30 mg/dl.

If a patient's triglycerides exceed 150 mg/dl they are considered elevated and if they exceed 200 mg/dl they are candidates for drug therapy depending on patient's overall risk. The drug of first choice to reduce them, is again statins.

As in America, the amount of calcium in CT coronary angiography is introduced as an indicator of atherosclerosis in addition to the carotid or lower limb arteries ultrasound. When an atheromatic plaque is found in the us, or significant amount of calcium in the CT, the patient changes risk category and is ranked higher risk.

In very high-risk patients, whether they already have coronary heart disease or are in primary prevention (a division that narrows further in these guidelines and patients are divided based on their risk alone), the LDL goal drops from 70 mg/dl to 55 mg/dl. In patients who have had two acute episodes within two years (e.g., two heart attacks or one heart attack and one stroke) the target drops to < 40 mg/dl.

High-risk patients have a new target of 70 mg/dl instead of 100 mg/dl, and moderate-risk patients 100 mg/dl instead of 115 mg/dl. The scientific data we have obtained in recent years have shown that there is no lower safety limit for low LDL, but at the same time the benefit from the reduction of cardiovascular events increases as LDL drops lower.

At the pharmaceutical level, the use of ezetimibe has been strongly upgraded and is now increasingly recommended in combination with a high-potency statin at a high dose.

Another big upgrade in the recommendation for PCSK9 in off-target patients which after their last successful studies these drugs were entitled to. The arrival of inclisiran with a one every six months administration should improve compliance.

The limits are constantly falling, and many are protesting if this is normal and correct. The scientific reality evolving through large, randomized studies documents where the benefit ends from the reduction of a risk factor, and in terms of LDL it has not yet reached the lowest point. The lower the better is systematically confirmed in each new study.

There is a significant time gap between guidelines publication and implementation in clinical practice. Doctors' inertia is major cause for this phenomenon.

Anyway, in order to succeed in such a project that changes established views of the last decades, it needs support from two valuable allies. First of all, pharmacists who usually have significantly more time with their patient than the doctor and confirming or raising doubts about the treatment recommended by the doctor plays a crucial role in his future compliance. And mainly the biochemists-microbiologists who, through the normal values and the separation of normal and pathological values, create the first strong feeling of security for the patient as to whether he should seek further therapeutic advice. No such venture will really succeed unless there is synergy and alliance between the various parties

### IA43 Advances in Glucose Monitoring in Type 1 Diabetes

### Associate Professor Dr Evangelos Rizos

Diabetologist, Head of the outpatient Diabetes clinic, University hospital of Ioannina, Greece; Associate Professor, School of Medicine, European University Cyprus (EUC), Nicosia, Cyprus.

Background and aims: Continuous glucose monitoring (CGM) and continuous subcutaneous insulin infusion (also known as insulin pumps) are widely used in type 1 diabetic patients.

Materials and methods: We assessed the literature on current and future perspectives of CGM for type 1 diabetes.

Discussion: Different types of CGM, including their mode of function, calibration, applicability, and accuracy will be presented. Summary results of CGM and explanation of their metrics and graphical appearance will be discussed. Cases of summary reports from CGM will be presented.

### IA44 Individualized Antithrombotic Therapy in Diabetics

### **Professor Dr Christos G. Savopoulos**

Director of 1st Medical Propedeutic Dept of Internal Medicine; Excellence Center of Hypertension & Stroke Unit, Aristotle University of Thessaloniki, AHEPA University Hospital

Individualized therapy in Internal Medicine is a common procedure for most chronic diseases since there are 2 axioms in this specialty: the holistic approach and the individualization. On the other hand, we are facing a dramatic increase in Diabetes Mellitus (DM) worldwide; subsequently, DM seems to be a major problem for Public Health, especially considering the cost of direct and indirect complications of this chronic condition.

Atherosclerosis in DM is more aggressive and characterized by extensive and diffuse macrovascular involvement. Unstable atherosclerotic plaques continue to challenge our ability to prevent acute events. There is a very complex and still poorly understood pathogenetic process which is at least at present partly explained by insulin resistance, oxidative stress (in-

creased production of reactive oxygen species- ROS), chronic inflammatory state, endothelial dysfunction (NO reduction - increase of ET-1), stimulation of SNS and RAS (catecholamines increase, AngII), vascular hyperplasia smooth muscle cells and increase of TGF- $\beta$ : fibrosis/sclerosis. In addition, glycoxidation of basal membrane proteins: increased ROS and production/ deposition of advanced glycation endproducts -AGEs.

The increased thrombotic predisposition in DM is based on increased coagulation, endothelial dysfunction, disorders of fibrinolysis and increased platelet activity.

Platelets play a" key" role in the formation, development, and stabilization of the thrombus and subsequently in the occurrence of thrombotic complications.

They are characterized by dysregulation of multiple pathways and demonstrate increased adhesion, activation, and aggregation. Cellular adhesion molecules are expressed at an increased rate on their surface with an increased expression of activation markers (CD31, CD49b, CD62P, and CD63) associated with the same groups of non-diabetic individuals. Such a "hyperactive" platelet phenotype may be responsible for most diabetic patients with a reduced response to antiplatelet agents.

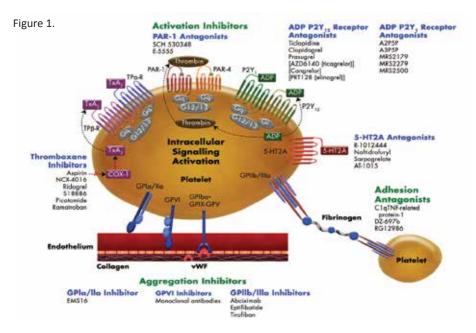


Figure 1 includes all available antiplatelet agents (Aspirin, Clopidogrel, Ticagrelor, and Prasugrel). Furthermore, intravenous antiplatelet agents are available such as GP IIb/IIIa inhibitors (abciximab, eptifibatide, tirofiban).

Antiplatelet drug fails to inhibit its specific target (e.g., aspirin-COX1, clopidogrel-P2Y12 receptors). It should not be confused with "treatment failure, "which means the occurrence of ischemic events despite therapy. They play a possible role in the occurrence of adverse cardiovascular events. In addition, Diabetic patients demonstrate an increased "resistance" compared to non-diabetics. Individualized therapy aims to implement the individual's genetic profile to determine the most appropriate drug and its dose. The overall approach should include the effect of various non-genetic factors, such as the patient's clinical condition, environmental factors, diet, and drug-drug interactions.

The assessment of thromboembolic risk is based on CHA2DS2-VASc (Figure 2). According to that, in some people with diabetes, there is an indication for anticoagulation therapy (mainly in Atrial Fibrillation): vitamin K antagonists (acenocoumarol, warfarin) targeting INR 2-3 or novel oral anticoagulants - NOACs (Figure 3).

| CHADS <sub>2</sub> -> | CHA2DS2VASc |
|-----------------------|-------------|
|-----------------------|-------------|

| CHADS2 Risk   | Score | CHA2DS2-VASc<br>Risk            |  |
|---------------|-------|---------------------------------|--|
| OF            | 1     | CHF or LVEF ≤ 40%               |  |
| Hypertension  | 1     | Hypertension                    |  |
| Age > 75      | 1     | Age ≥75                         |  |
|               |       | Diabetes                        |  |
| Diabetes      | 1     | Stroke/TIA/<br>Thio mboembolism |  |
| Sticke or TIA | 2     | Vascular<br>Disease             |  |

| TA/ 2<br>embolism |               |
|-------------------|---------------|
| 1                 |               |
| -74 1             | and a         |
| 1                 | enth/         |
| -74               | eye/<br>ents/ |

Score

1

4

2

1

| Score                     | Risk     | Anticoagulation<br>Therapy<br>No anticoagulant<br>therapy |  |
|---------------------------|----------|---|--|
| 0 (male) or<br>1 (female) | Low      |   |  |
| 1(male)                   | Moderate | Oral anticoagulant should be considered                   |  |
| 2 or greater              | High     | Oral anticoagulant is<br>recommended                      |  |

From ESC AF Quidelines http://econtlo.org/puidelines-econe sec-guidelines/Quidelines/Occurre guidelines-atto-FT.pdf

Figure 2.

|                                  | Apixaban<br>(Eliquis* 2,5 & 5)<br>Direct Anti- Xa-Inhibitor | Riveroxaban<br>(Xarelto* 15 & 20) Direct<br>Anti- Xa-Inhibitor | Dabigatran<br>(Pradaxa* 110 & 150)<br>Direct IIa- (thrombin)<br>Inhibitors | Edoxaban<br>(Lixiana* 15, 30 & 60)<br>Direct Anti- Xa-Inhibitor |
|----------------------------------|---|--|--|---|
| Cmax : 2 - 4 h<br>T ½ : 7 - 15 h |   |  |  |   |
| Elimination                      | 27% renal<br>73% hepat                                      | 36% renal<br>64% hepat   | 80% renal<br>20% hepat   | 35% renal<br>65% hepat  |
| Dosing                           | 2x/d  | 1x/d   | 1x/d, 2x/d   | 1x/d  |
| Monitoring                       | No  | No   | No   | No  |
| Antidote                         | Yes   | Yes  | Yes  | No  |

Figure 3.

The incidence of thrombotic events among COVID-19 Diabetic patients varies and depends on the severity of the infection, the hospitalization of diabetics, the comorbidities of each person with diabetes, and several other factors. Low-Molecular-Weight-Heparin (LMWH) should be administered in these patients since it improves the outcome of COVID-19 and its thrombotic complications.

In conclusion, DM is rapidly reshaping the risk of CVD, AF, and CV mortality.

We are still lacking what would be considered appropriate for everybody in need, an antithrombotic strategy to reduce CVD risk in DM at an acceptable level. DM is very complex and quite resistant to different therapeutic interventions, perhaps because it is a group of diseases even when we address it as Type 2 DM. Aspirin and clopidogrel resistance is surprisingly common in this population. New anti- thrombotic treatments and combination therapies are our great expectation to overcome antiplatelet resistance in DM patients and reduce morbidity and mortality attributed to CVD.

## IA45 Bioinformatics Insights to Post-analysis of Computational Drug Repurposing Results

### Professor Dr George M. Spyrou

Bioinformatics ERA Chair and Senior Scientist, Head of the Bioinformatics Department, Professor, The Postgraduate School of the Cyprus Institute of Neurology & Genetics

The classical computational drug repurposing efforts have given a significant boost in the drug discovery efforts around several diseases. Nevertheless, the lists of candidate repurposed drugs need further analysis, filtering and re-ranking in order to provide short lists of drugs that would be prioritized candidates to be tested against another disease. In this talk I will present several bioinformatics methods and tools that we have developed in the Bioinformatics Department at the Cyprus Institute of Neurology and Genetics that take into account a priori knowledge related to existing drug discovery efforts as well as mathematical formulations of scoring schemes that facilitate the production of both primary and re-ranked lists of candidate repurposed drugs.

#### **Professor Dr Philippos Triposkiadis**

### Department of Cardiology, Larissa University Hospital Larissa, Thessaly, Greece

The scale and complexity that medical data are collected require innovative approaches to statistics and computer science that draw on the rapid advances in artificial intelligence (AI) for efficiently identifying insights into disease processes. In this regard, AI refers to a collection of computational concepts that can be summarised as a machine's ability to generalise learning in order to efficiently achieve complex tasks autonomously. Machine learning (ML) achieves this target by employing algorithms to improve task performance without needing to be explicitly programmed and can be broadly divided into supervised and unsupervised approaches. In supervised learning, paired input and output variables are iteratively optimized for use in regression and classification tasks. In unsupervised learning, only input data are available, and algorithms are used to find inherent clusters or associations. In recent years, ML has become dominated by deep learning (DL), which uses multilayer neural networks to progressively obtain more abstract representations of complex data.

### IA47 Management of Hyperglycemia in Type 2 Diabetes, 2022 Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

### **Professor Dr Apostolos G. Tsapas**

#### Professor of Medicine and Diabetes, Aristotle University of Thessaloniki, Greece

The American Diabetes Association and the European Association for the Study of Diabetes convened a panel to update the previous consensus statements on the management of hyperglycaemia in type 2 diabetes in adults, published since 2006 and last updated in 2019. The target audience is the full spectrum of the professional healthcare team providing diabetes care in the USA and Europe. A systematic examination of publications since 2018 informed new recommendations. These include additional focus on social determinants of health, the healthcare system and physical activity behaviours including sleep. There is a greater emphasis on weight management as part of the holistic approach to diabetes management. The results of cardiovascular and kidney outcomes trials involving sodium-glucose cotransporter-2 inhibitors and glucagon-like peptide-1 receptor agonists, including assessment of subgroups, inform broader recommendations for cardiorenal protection in people with diabetes at high risk of cardiorenal disease. With regards to medication management, for patients with clinical cardiovascular disease, a sodium-glucose cotransporter 2 (SGLT2) inhibitor or a glucagon-like peptide 1 (GLP-1) receptor agonist with proven cardiovascular benefit is recommended. For patients with chronic kidney disease or clinical heart failure, an SGLT2 inhibitor with proven

benefit is recommended. GLP-1 receptor agonists are generally recommended as the first injectable medication. After a summary listing of consensus recommendations, practical tips for implementation are provided.

### IA48 Lung Cancer And Fibrosis – Distinct Horn of the Same Devil

### Associate Professor Argyris Tzouvelekis

Associate Professor of Internal and Respiratory Medicine and Head of the Department of Respiratory Medicine at the University Hospital of Patras, Greece and Adjunct Associate Professor of Pulmonary Critical Care and Sleep Medicine Department, Yale School of Medicine, USA

Pulmonary fibrosis (PF) constitutes the end stage of a broad range of heterogeneous fibrotic interstitial lung diseases characterized by progressive scarring of the lung. Patients with PF are at high-risk of developing lung cancer, with a nearly 5-fold increased risk compared with general population. Lung cancer has a negative impact on patients' quality of life. Despite abundant mechanistic links between pulmonary fibrosis and lung cancer, there is considerable lack of knowledge on the diagnostic and therapeutic management of patients diagnosed with both clinical entities. Importantly the identification of a solitary nodule on HRCT in patients with IPF represents a major pitfall for practicing clinicians due to challenging diagnostic approaches. Interventions including procedures such as bronchoscopy, CT-guided transthoracic needle biopsy or surgery are quite often limited by the patients' performance status and the presence of comorbidities such as emphysema and could be proven detrimental in ILD progression. Most recent evidence suggests safety and efficacy of platinum-doublets and immune-check point inhibitors in patients with fibrotic ILD and lung cancer; yet, studies are severely underpowered and rigid conclusions cannot be drawn. So far, the only European effort to address this major issue is a recently published study, by our study group, which collected data from 3178 patients with IPF and 324 with concomitant lung cancer from 18 European centers of excellence for ILD. This study demonstrated that use of anti-fibrotics and surgical resection of lung cancer lesion significantly reduced the risk of mortality underlining the necessity for early diagnosis and optimal management

### IA49 Adaptation and Cancer Genes: From Cells to Populations

### Associate Professor Konstantinos Voskarides

### University of Nicosia Medical School, Nicosia, Cyprus

Mutations in Tumor Suppressor Genes can cause several types of cancer. TP53 gene is mutated in at least 50% of tumors. However, evidence is increasing that these mutations can be adap-

tive, in human or animal populations, and at the somatic level as well.

Germline TP53 carcinogenic mutations have been associated with increased longevity in mouse, drosophila, C. elegans and humans, and with higher fertilization rates in mice. Additionally, p53 amino-acid residues that cause cancer in humans, are part of the normal p53 protein sequence in some mammals, reducing apoptosis potential of their cells. It is assumed that this is the way that their cells resist under extreme cold and high altitude (hypoxia). Laboratory experiments gave evidence that carcinogenic TP53 mutations could be adaptive for zebrafish larvae, contributing to higher survival rate under extreme starvation conditions.

Similar evidence exists for humans. Extreme starvation exposure has been associated with some cancer types in humans. Additionally, genetic variants in or close to tumor suppressor genes are under selection in people living in extreme cold and high-altitude environments. These human populations exhibit very high incidence of cancer. Another study showed that BRCA1/2 mutations are related with increased fertility in Utah women.

At the somatic level, NOTCH1 and TP53 carcinogenic mutations were found under selection in a large percentage of somatic cells in healthy humans. It seems that carcinogenic mutations may protect our cells under harmful micro-environments. "Mutator" bacteria use the same mechanism to survive under antibiotic stress or other stressful conditions. This selection procedure may also explain why excessive antibiotic use predisposes humans for colorectal cancer.

These data show that evolution, adaptation, and selection can explain multiple phenomena related with cancer.

### IA50 From Radiomics to Clinical Trial to Clinical Practice: Novel and Pioneer

### **Strategies for Treating Patients**

### **Dr Konstantinos Zamboglou**

### Radiation Oncology, Vice Medical Director, German Oncology Center

The development of precise medical imaging procedures simultaneously to improvements in big data analysis has led to the establishment of radiomics - a computer-based method of extracting and analyzing image features quantitatively. This approach bears the potential to assess and improve cancer detection, tissue characterization and clinical outcome prediction. This talk gives an overview on the current aspects of methodology and summarizes available literature on radiomics in cancer patients, showing its potential for personalized therapy approaches.

### **IA51 Management of Colorectal Cancer in Elderly Patients**

### Assistant Professor Dr Demetris Papamichael

Director of Medical Oncology at the Bank of Cyprus Oncology Centre, Nicosia. Assist. Professor at St. George's Hospital-Medical School, University of London / UNIC Campus

As global life expectancy is increasing in most countries, there is a rising percentage of patients over 65 years old being diagnosed with colorectal cancer. Despite an increase in the incidence and prevalence of colorectal cancer in older individuals, this cohort receives adjuvant therapy at a decreased rate due to anticipated intolerance. The presumed limitations seem to be based on chronologic age, competing co-morbidities, and the paucity of data for this patient population in major clinical trials. This review explores the evidence regarding disparities in the treatment of older patients with colorectal cancer, safety and efficacy of adjuvant therapy, and some newer tools to make decisions based on the biologic age, rather than chronologic age, of the patient.

### IA52 Robotic General Surgery 16 Years of Experience at Athens Medical Centre

### Prof. Dr. Konstantinos Konstantinidis

Professor of Surgery, Ohio State University, USA; Chairman of General, Bariatric, Laparoscopic & Robotic Surgery, Athens Medical Center, Scientific Director of Athens Medical Center

Robotic Surgery is the revolution of the 21st century, opening up new horizons in the field of Medicine. Robotic assistance has made possible the removal of many constraints regarding operations in some difficult fields of surgery.

The precision of the robot's surgical arms has made it easy for surgeons to perform difficult operations, accessing the most difficult to reach and tiny parts of the human body.

In 2006, the first robotic surgery that was carried out in SE Europe, at Athens Medical Center, inaugurated a new era for Medicine in the region, with significant scientific results and benefits for patients. Athens Medical Group's robotic departments have been acknowledged as international Centers of Reference and Excellence, partnering with Universities in Greece and abroad, such as Strasburg's Medical School IRCAD/EITS and Clinique Saint-Augustin in France

Currently our team is performing the vast majority of the indicated operations robotically which has enabled faster patient recovery and discharge from hospital with minimal complications

Robotic surgery treats both benign and malignant diseases of the esophagus, stomach, small

intestine, colon, pancreas, spleen, and adrenal glands.

Particular emphasis is given to the fact that in cases of rectal cancer, robotic surgery largely avoids the need for colostomy.

### IA53 How new Technologies can benefit Public Health - The Role of Harm Reduction in the Area of Smoking

### Prof. Reuven Zimlichman

### Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel

The benefits of tobacco control strategies and education efforts to date are undoubted and have significantly decreased the smoking prevalence in Europe and worldwide. However, there still remains a significant number of smokers that do not quit, even in the face of serious disease.

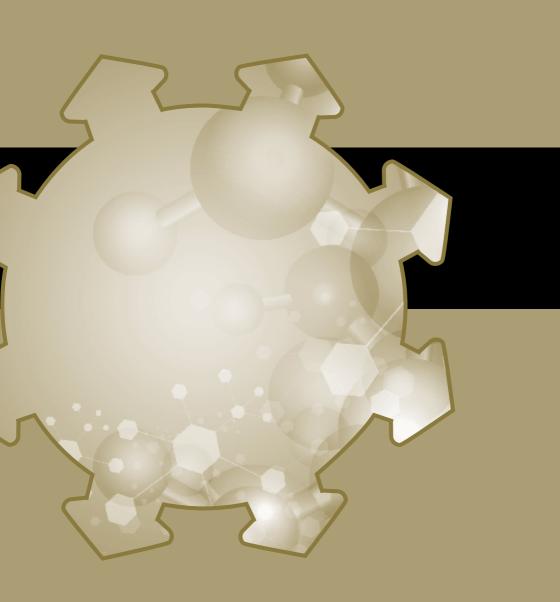
How are we to help this group?

We know that for a proportion of the population quitting as the only approach is clearly not working. In addition to the existing tobacco control strategies, such as smoking cessation or preventing initiation, we need to explore and adopt new innovative approaches such as harm reduction, which is a tool to reduce the burden of poor lifestyle choices and unhealthy or addictive behavior.

The development of innovative new technologies that deliver nicotine in a less harmful way than through cigarette smoke may not only offer a less harmful way of nicotine intake for continuing smokers but also an opportunity to improve public health at large.

### Tobacco Harm Reduction

There is growing evidence that new innovative smoke-free products (such as snus, vaping devices, and heated tobacco products) are less harmful than cigarettes because they expose users to much lower levels of harmful chemicals. This opens up a new avenue to apply the harm reduction principle to continuing smokers. While the currently existing data around innovative smoke-free products is very promising, we must continue to critically assess the emerging science around smoke-free products to fully understand the long-term public health benefit of switching to such products.





# Photos from





# 2021 Events











# Selected Abstracts

## SA01 Vitamin D – Hormone of the Modern Age as Adjuvant Therapy in Skin Diseases

### Andrija Stanimirović 1,2, Tea Štrbac3, Josip Rešetar 4

1Dermatology & Venereology, University of Applied Health Sciences, Mlinarska cesta 138, 10000 Zagreb, Croatia; 2School of Medicine, European University Cyprus, Diogenis Str 6 Nicosia, 2404, Cipar; <sup>3</sup>Department of Emergency Medicine of Zagreb County, Zagreb, Croatia; 4Faculty of Pharmacy and Biochemistry, University of Zagreb, UI. Ante Kovačića 1, 10000 Zagreb, Croatia

Background: During the last few years, investigations of the role of vitamin D in certain skin conditions have significantly increased. Numerous laboratory studies have demonstrated the dose-dependent molecular effects of vitamin D and its analogs on cell proliferation, differentiation, and apoptosis. Vitamin D administration was also associated with immunomodulatory, antioxidative, and cytoprotective effects why is considered as a new hormone.

Objective: We provide an overview of the pivotal information about the effect of systemic treatment with vitamin D along with other therapy in patients with skin diseases.

Results: A clinical amelioration, after systemic administration of vitamin D, was observed in patients with psoriasis, vitiligo, and congenital ichthyosis. Some studies proved that combination treatment with oral vitamin D and topical tacrolimus is more effective in reaching repigmentation than topical tacrolimus alone in patients with vitiligo. Currently, there is insufficient evidence of treatment outcome in patients with scleroderma and alopecia areata. Vitamin D may reduce clinical features in atopic dermatitis, especially in pediatric population with a severe AD in combination with topical corticosteroid. Vitamin D deficiency is correlated with the severity of acne vulgaris, as well as hidradenitis suppurativa, so the use of peroral D3 vitamin as an adjuvant therapy is considered useful in forms with inflammatory lesions. Oral administration of vitamin D may improve the clinical presentation of skin tumors, but does not affect the survival rate. Finally, chronic use of systemic corticosteroids in many skin diseases increases risk for osteoporosis which additionally confirms the value of treatment with vitamin D, regardless of the direct impact on the skin disease.

Conclusion: An increasing number of studies demonstrate positive effects of vitamin D or its analogues in a variety of skin diseases, but further clinical studies are needed to determine the efficacy, optimal dosing, and adverse effects of vitamin D in combination with the baseline therapy.

### SA02 Epigenetic Enzymes as Potent Regulators of Lipid Metabolism

### Evelina Charidemou\*, Volker Behrends, Roberta Noberini, Tiziana Bonaldi, Julian L. Griffin, Antonis Kirmizis

Marie Curie Fellow, University of Cyprus

Background: Accumulating evidence in recent years has highlighted strong regulatory interactions between epigenetic mechanisms and metabolic transformations, mainly through transcriptional control of key metabolic genes. However, what has been overlooked is the direct effect of histone modifying enzymes on cellular metabolism as they are large consumers of sentinel metabolites. Therefore, we hypothesize that histone modifying enzymes and their mediated post-translation modifications (PTMs) on histones directly drive metabolic rewiring which subsequently impacts the cellular metabolic status.

Methods: Specifically, we focus on the use of different acetyl-CoA consumption-capacity histone acetyltransferases (HATs) to determine whether our hypothesis is a general mechanism for HATs (and not a HAT-specific or PTM-specific effect) to control metabolism and whether the consumption level will have different impacts on the phenotype. Using interdisciplinary, state-of-the-art approaches that integrate subcellular stable isotope metabolomics, lipidomics and high-throughput epiproteomic techniques we interrogate how the activity of a very high (NAA10), high (NAA40), medium (GCN5) and low (MYST) acetyltransferase controls the abundance of acetyl-CoA and, in turn, defines the metabolic status of a cell.

Results: We show that the higher the consumption of acetyl-CoA by the aforementioned modifiers the more neutral lipids, specifically monoglycerides, diglycerides and triglycerides, accumulate upon the specific HAT depletion in hepatocytes. Consistently, the increase in these lipid species coincide with the accumulation of cytoplasmic lipid droplets and lipid droplet forming protein, perilipin-1, impairing insulin signalling indicated by decreased glucose uptake. Using 13C-tracing, we show in HAT-deficient hepatocytes, acetate-derived acetyl-CoA that comes from protein deacetylation is the primary substrate for lipid accumulation. We also show that the expression of these acetyltransferases decreases in aged mice, suggesting their involvement in age related insulin resistance.

Conclusions: This study reveals a novel path through which modifying enzymes influence cellular metabolism with potential implications in metabolic disorders. Specifically, epigenetic alternations and metabolic deterioration are crucial hallmarks observed during ageing. Therefore, the above novel path might underlie aged related metabolic diseases.

# Selected Abstracts

### SA03 Amygdalin as a Chemoprotective Agent in Co-Treatment with Cisplatin

### Panayiota Christodoulou1,3, Panagiotis Boutsikos1, Christiana M. Neophytou2, Theodora-Christina Kyriakou1,2, Maria-Ioanna Christodoulou3, Panagiotis Papageorgis2, Anastasis Stephanou1, Ioannis Patrikios1

1 School of Medicine, European University Cyprus, Nicosia, 2404, Cyprus; 2 Tumor Microenvironment, Metastasis and Experimental Therapeutics Laboratory, Basic and Translational Cancer Research Center, Department of Life Sciences, European University Cyprus, Nicosia 2404, Cyprus; 3 Tumor Immunology and Biomarkers Laboratory, Basic and Translational Cancer Research Center, Department of Life Sciences, European University Cyprus, Nicosia 2404, Cyprus

Background: Amygdalin, a naturally occurring glycoside of traditional Chinese medicine, is known for its anti-cancer properties. However, its effect on normal cells has not been investigated. Aim: To explore possible chemo-protective roles of Amygdalin against the cytotoxic effects of the chemotherapeutic drug Cisplatin. Methods/Results: Human non-tumorigenic MCF12F epithelial cells, fibroblasts, breast cancer MCF7 and MDA-MB-231 cells were treated with Cisplatin in the absence or presence of Amygdalin. When MCF12F cells and fibroblasts underwent pre-treatment with Amygdalin (24 hours) followed by Cisplatin treatment (24 hours), cell viability was increased (22%, p<0.001) as indicated using MTT assay. As attested by flow cytometry, combination treatment was associated with decreased percentage of late apoptotic cells compared with monotherapy (fold-change =1.6 and 4.5 for  $15\mu$ M and 20µM, respectively). Also, expression of PUMA, p53, phospho-p53 and Bax decreased, in the combination treatment. Moreover, the mRNA levels of the pro-apoptotic genes PUMA, p53 and BAX were significantly downregulated (~83%, ~66% and ~44%, respectively), and those of the anti-apoptotic genes BCI-2 and BcI-XL were upregulated (~44.5% and ~51%, respectively). Combination index (CI) assay indicated that Amygdalin could be possibly considered as an antagonist to Cisplatin for MCF12F and fibroblast cells (2.2 and 2.3, respectively). In contrast, for breast cancer MCF7 and MDA-MB-231 cells, Amygdalin and Cisplatin indicated a synergistic effect (0.8 and 0.65, respectively). Discussion/Conclusion: Our findings suggest that Amygdalin in combination with Cisplatin, can protect normal breast cells as well as fibroblasts during chemotherapy treatment, indicating a strong selective chemoprotective ability and may contribute to a better quality of life for cancer patients.

## SA04 Repurposing Chemical Chaperones to the Rescue of Mouse Models of Alport Syndrome

## C Odiatis1\*, P Ioannou1\*, K Antoniadou1, M Samiotaki 2, A Malatras1, M Pieri3, G Papagregoriou1, D Ljubanović4, K Stylianou 5, C Deltas1

1Center of Excellence in Biobanking and Biomedical Research, Molecular Medicine Research Center, and University of Cyprus Medical School, Nicosia, Cyprus; 2Institute for Bio-Innovation, Biomedical Sciences Research Centre "Alexander Fleming", Vari, Greece; 3Department of Life and Health Sciences, School of Sciences and Engineering, University of Nicosia; 4Department for Nephropathology and Electron microscopy, University of Zagreb, Croatia; 5Department of Nephrology, University of Crete Medical School

\*These authors had equal contribution

Alport Syndrome (AS) is a severe inherited glomerulopathy caused by mutations in the genes encoding the  $\alpha$ -chains of type IV collagen, the most abundant component of the glomerular basement membrane (GBM). Alport patients lack effective therapies beyond blockade of the renin-angiotensin system. This work describes the repurposing of two FDA-approved chemical chaperones (4-PBA and TUDCA) to the rescue of two mouse models of AS, both bearing the Col4a3-p.Gly1332Glu mutation (the most common mutation found in Cypriot patients).

After a long-term treatment, with these two chaperones, we found that the GBM morphology and structure of the 4-PBA treated mice showed a considerable improvement compared with the control (placebo treated) group. Based on EM measurements there is a 43% reduction of lesions and a significant decline of the lesion's severity in the GBM of 4-PBA treated Alport mice. However, the measurements from TUDCA-treated AS mice did not differ from the placebo group. Additionally, the 4-PBA treatment could inhibit proteinuria and hematuria and fibrosis in AS mice when compared with control mice. Probably, the administration of 4-PBA can effectively stabilize the conformation of the mutated Col4a3, improve its folding, alleviating with this way the glomerular filtration barrier in the Alport mice.

Grants: Funded by the Alport Syndrome Foundation, Inc. (ASF), Pedersen Family and the Kidney Foundation of Canada (KFOC) and by the Cyprus Research and Innovation Foundation programme POST-DOC/0916/0190.

# Selected Abstracts

### SA05 A Personalized Risk Assessment Tool for Colorectal Cancer Prevention Through 3'mRNA Sequencing of Normal-Appearing Mucosa in the Cypriot Population (MoCo Project)

### Katsaounou Kyriaki

University of Cyprus, Department of Biological Sciences, Infection and Cancer Laboratory

Colorectal cancer (CRC) is the 3rd most prevalent cancer worldwide with an inextricably complex genetic and environmental etiology. Sporadic CRC is hard to foresee, as no molecular biomarker for clinical use has been evidenced yet. To deal with this intricacy, we intend to improve the practice of conventional colonoscopy, to include specific molecular biomarkers, as a basis for the development of a non-invasive risk assessment tool for CRC and its subsequent involvement in the clinical practice, as a cutting edge, new-generation molecular colonoscopy. To achieve the aforementioned, we target in a thorough understanding and characterization of the Cypriot Gut Microbiota utilizing multi-omics technologies in order to exploit the transcriptional, inflammatory, metabolomic and microbiota signatures that could predict more precisely the likelihood of a cancer prone patient to become a CRC-bearing host.

In this context, 316 individuals have been recruited in our clinical study. Using Lieberman's et al. criteria, 36 of them have been diagnosed as cancer prone patients. A first 16s rRNA Seq analysis of faecal microbiota revealed a clear up-regulated expression of commensal bacteria along GI tract of 113 healthy individuals, while in 17 cancer prone patients, greater abundance of inflammatory microbial communities and significant lower diversity of commensal bacteria were recorded. Through Volatolomics feces analysis, we ended up with dozens of metabolites identified and quantified. A non-parametric test of Spearman Correlation in both analyses notably resulted in the statistically significant increase of 2-Pentanone, simultaneously with the decrease of Fusicatenibacter in the samples.

# SA06 Externally Controllable Reprogramming of Glioblastoma Multiforme by Radiofrequency-Responsive Genetically Engineered Neural Stem Cells

## *Kyriacos Agathangelou1, Abdul Quddious2, Nikolaos Dietis3, Niovi Nicolaou1, Ina Meiser4, Stavros Iezekiel2, Costas Pitris2 and Andreani Odysseos1.*

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Major challenges in glioblastoma multiforme (GBM) management are mainly attributed to high tumor heterogeneity and inefficient drug delivery. Reprogrammable neural stem cells (NSC) have emerged as a promising intervention in autologous cell-based therapies, due to their tumoricidal potential and in vivo generation of molecular therapies epitomized by micro-RNAs. The Mir34 family targets multiple oncogenic pathways including NOTCH and EGFR, being delivered as exosome cargo. Modulation of gene expression through radiofrequencies (RF), is emerging as an externally controllable approach towards nano-communication-mediated cancer therapeutics.

We have aimed to (i) reprogram GBM cells through multi-targeting miRNA34a exosome cargos generated by genetically engineered iNSCs, (ii) generate RF interfaces with rationally designed plasmid constructs of RF-responsive promoters and (iii) optimize the therapeutic efficacy under modulated RF control.

NSCs were generated with differentiation of human induced pluripotent stem cells (hiPSCs) and chemically transfected with the Egr1-hMiR34a-mKate2 gene construct, sub-minimally expressed under normal culture conditions and conferring tumor targeting and red fluorescence attributes. Exosomes released from iNSCs have undergone morphological and optical characterization. Intracerebral injection of iNSCs in tumour-bearing immunosuppressed mice has led to statistically significant prolongation of survival. RF-mediated over-transcription of therapeutic miR signatures was documented with spectrophotometric analysis and quantification of fluorescence and RT-PCR in a nano-communication system.

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# Selected Abstracts

## SA07 Chemical Characterization and Biological Evaluation of Nasturtium Officinale (watercress) in an Experimental Model of Human Malignant Melanoma

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Malignant melanoma is the most lethal type of skin cancer. On the other hand, Nasturtium officinale (watercress) plant is a rich source of glucosinolates, isothiocyanates and polyphenols which have been associated with significant anti-cancer activity against various tumour types. The aim of the present study was (i) the extraction and content characterization of the various phytochemicals from the aerial parts (i.e., flowers, leaves and stems) of watercress and (ii) the characterisation of the antioxidant capacity of the isolated extract(s) in a cell-free system as well as a cell-based platform of human malignant melanoma. A series of extractions were performed by utilizing solvents of various polarities. The content determination of all phytochemicals was performed via spectrophotometric assays and UPLC-MS/MS analytical instrumentation. Moreover, induction of oxidative stress was assessed via fluorometric assays according to which the content of superoxide and peroxide anions was determined. Finally, extract(s) of watercress were biologically evaluated for their capacity to induce an antioxidant and/or apoptotic response (determined as extrinsic and/or intrinsic apoptosis) using a colorimetric assay. Our data reveal that watercress flowers posse the highest content of all phytochemicals tested when compared to those of leaves and stems. In particular, it was noticed that watercress flowers contain the highest concentration of quercetin-3-O-rutinoside (1459.3  $\pm$  12.9 ng of analyte/g of dry extract), protocatechuic acid ( $134.7 \pm 1.2$  ng of analyte/g of dry extract), gluconasturtiin ( $82.1 \pm 0.6$  ng of analyte/g of dry extract) and phenethyl isothiocyanate (273.9  $\pm$  0.9 ng of analyte/g of dry extract). To these ends, our data support evidence for a potential role of watercress as a preventive (through its antioxidant capacity) and/or therapeutic (through its apoptotic induction capacity) means on malignant melanoma development.

# SA08 Investigation of the Aetiology of Community Acquired Pneumonia in Cyprus and Characterization of Host Factors in Viral/Bacterial Co-Infections

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Introduction: Community-acquired pneumonia remains the leading cause of hospitalisation for infectious disease in Europe and a major cause of morbidity and mortality. Severe pneumonia can result in sepsis and acute respiratory distress syndrome (ARDS). Its causes include bacteria, viruses and fungi. According to the World Health Organization pneumonia accounts for 17% of all deaths of children under the age of five worldwide.

Scope: The rapid diagnosis of the etiologic agent of CAP is the hallmark of appropriate management of the disease along the rational use of antivirals and antibiotics. Published data on aetiology and frequency of CAP causative agents for the Cypriot population does not exist. Therefore, we have designed a prospective observational study in collaboration with the Nicosia General Hospital, which aims to determine and characterize for the first time the aetiology of CAP in hospitalized adults in Cyprus as well as to assess genetic host factors associated with CAP severity and progression.

Methodology: Respiratory and blood samples were collected from patients admitted to the Nicosia general hospital with signs of acute respiratory tract infection that progressed to pneumonia. Real-time and RT-PCR were employed for the detection of bacterial and viral pathogens respectively. Next generation using the respiratory pathogen ID/AMR enrichment panel (RPIP) analysis was used to elaborate on the presence of respiratory pathogens as well as to investigate the antibiotic resistance genes of bacterial pathogens. Multiplex real-time PCR was employed for probe based allelic discrimination in order to investigate host factors associated with CAP.

Results: The age median of patients was 62.5 years old, with 33 patients being female and 67 being male. The majority (94%) of admitted patient had some form of comorbid condition. A causative pathogen was detected in 84% of patients. Viral infections accounted for 25% of cases the with the most prevalent being Influenza A, human Rhinovirus and Sars-COV-2. Bacterial infections accounted for 17% of cases with the most prevalent being Streptococcus pneumoniae, Staphylococcus aureus and Haemophilus influenzae. Viral-bacterial co-infections accounted for 41% of cases the most prevalent co-infections being between Sars-COV-2 and Acinetobacter baumani. Antibiotic resistance genes were detected in 20% of the samples for six pathogens S.pneumoniae, S.aureus, E.coli, M.tuberculosis and A.baumani with macrolides and penicillins being the most resisted drug class. For host factors we detected a positive correlation between bacterial infections and the NOS3 G allele (rs1799983) and the FCGR2A G allele (rs1801274). A positive correlation was also detected with the ACE insertion genotype (rs1799752) and severity of pneumonia.

# Selected Abstracts

Conclusions: The most common detected pathogens are in accordance with other similar studies. We detected a high frequency of bacterial pathogens that are common in both community and nosocomial pneumonia such as S.aureus, E.coli and A.baumani and all these pathogens were characterize by the presence of antibiotic resistance genes. For host factors our results for the TNF-A (rs1800629) allele and the ACE insertion genotype (rs1799752) are in accordance with other studies. For the NOS3 G allele (rs1799983) and the FCGR2A G allele (rs1801274) studies report potential correlations with bacterial infections, but to our knowledge this is the first time these alleles have been correlated with bacterial infections in patients with community acquired pneumonia.

# SA09 Automated Machine Learning-Based Prediction of Mortality and Survival Analysis in ICU Patients With Stroke

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#### Introduction

Ischemic stroke is a leading cause of death worldwide. Treatment requires occasionally specialized care at the Intensive Care Unit (ICU). Unfortunately, progress in preventing stroke mortality has declined over the years, so improving quality of care and more specialized prognostic tools are urgently needed. Mortality prediction and prompt identification of risk factors could impact clinical practices and allow efficient allocation of health resources. Machine learning (ML) algorithms are taking advantage of the vast amount of information available in the ICUs and are becoming popular in predictive medical analytics. This study aims to predict mortality in critically-ill patients with stroke, and stratify them into distinct prognostic groups.

### Methods

All data were derived from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database [1]. 3,646 unique patients admitted for the first time in the ICU with a primary diagnosis of stroke, based on ICD9 codes, were selected (mean age 68.14). A vast variety of clinical and laboratory information were pre-processed to consider the temporal characteristics of a patient's stay. More specifically, every 8-hour time-period, for the first 72 hours of admission, min, max, mean and standard deviation values of laboratory measurements were added in the training model. The dataset was split into 70/30 training/test sets. The automated ML platform JADBio [2] was used, which employs a 10-fold cross validation performance protocol. Mortality prediction was performed using classification supervised ML algorithms, whereas

survival analysis was performed to predict the time to event using ridge cox regression and survival Random Forests (RF). Feature selection was performed using least absolute shrinkage and selection operation (LASSO) and Test-Budgeted Statistically Equivalent Signature (SES) algorithms.

### Results

Preliminary analysis indicates sufficient ability to predict mortality at the end of a given day during the patient's stay (AUC 0.81, CI 0.75-0.84, day 1, 0.84, CI 0.81-0.88, day 2 and 0.85, CI 0.82-0.89, day 3). A group of features such as age, ethnicity, Glasgow coma scale, hypoxia, metabolic acidosis, red cell distribution width (RDW) and Braden scale, were identified as important risk predictors. Survival analysis during the first 8 hours of admission classified patients into three prognostic groups with a concordance index 0.79 [CI 0.756, 0.822] (Figure 1).

### Conclusion

The main contribution of this work is the exploration of an extended number of features stored in the health record in a timely manner to assist clinicians. The idea behind this was that during the various ICU shifts, a health practitioner does not have an accurate estimate of fluctuations in the laboratory measurements of the patient. Applying an automated recording of these changes and using ML algorithms to predict mortality would possibly identify new dynamic markers that will improve the quality of care. Our results are promising but independent validation is further needed in prospective cohorts.

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https://jadbio.com

# Selected Abstracts

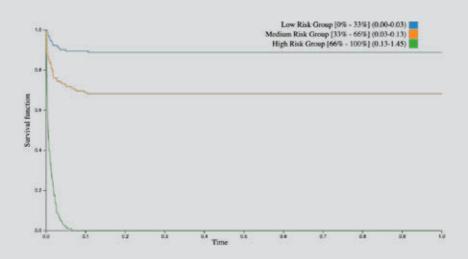


Figure 1. Kaplan Meier curves for low, medium and high-risk patients with stroke admitted in the ICU.

## SA10 Effective Bedside Prognostic Tools for Septic and Septic Shock patients – A Necessity

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Background: Proper management of sepsis poses a challenge even today, with early diagnosis and targeted treatment being the most important steps. Easy, cost effective bedside tools are needed in order to pinpoint towards the outcome of sepsis or septic shock.

This study aims to find a correlation between Sequential Organ Failure Assessment (SOFA), Acute Physiology and Chronic Health Evaluation II (APACHE II) and Simplified Acute Physiology Score II (SAPS II) severity scores, the Neutrophil-Lymphocytes Ratio (NLR) and carboxyhemoglobin (COHb) levels in septic or septic shock patients with the scope of establishing a bed side cost effective prognostic tool.

Materials and methods: A pilot, prospective, observational, and ongoing study was conducted on 61 patients admitted with sepsis or septic shock according to the SEPSIS 3 Consensus definition. We followed clinical and paraclinical parameters on day 1 (D1) and day 5 (D5) after meeting the inclusion criteria.

Results: On D1 we found a statistically significant positive correlation between each severity score (p <0.0001), r = 0.7287 for SOFA vs. APACHE II with CI: 0.5841-0.8285, r = 0.6862 for SOFA vs. SAPS II with CI: 0.5251-0.7998 and r = 0.8534 for APACHE II vs. SAPS II with CI: 0.7663 to 0.9097. On D5 we observed similar results to D1: a significant positive correlation was found between each severity score (p <0.0001), with r = 0.7877 for SOFA vs. APACHE II with CI: 0.6283 to 0.8836, r = 0.8210 for SOFA vs. SAPS II with CI: 0.6822 to 0.9027 and r = 0.8880 for APACHE II vs. SAPS II., CI: 0.7952 to 0.9401. Nil correlation was found between the severity scores, NLR and COHb on D1 and D5.

Conclusion: Cost-effective bedside tools to pinpoint towards the outcome of sepsis are yet to be found, however the positive correlation between the severity scores point out to a combination of such tools for prognosis prediction of septic or septic shock patients.

Conflicts of Interest: The authors declare no conflict of interest.

This work was supported by the University of Medicine, Pharmacy, Sciences and Technology "George Emil Palade" of Târgu Mureş Research Grant number 10126/17.12.2020.

PA01 Direct Oral Anticoagulant-Related Bleeding in Atrial Fibrillation Patients Correlates with Demethylation of NOS3 and ADAMTS7

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Introduction: Direct Oral Anticoagulants (DOACs) consist the main therapy for the prevention of thrombus formation in Atrial Fibrillation (AF) patients. DOACs present high efficacy, but bleeding events may occur in DOACs-treated patients. We are conducting a prospective clinical study to uncover potential influences of DOACs at the epigenetic level. Here we present our findings regarding the effect of DOACs on DNA methylation patterns in newly diagnosed AF patients initiating DOAC treatment. The DNA promoter methylation of two genes was analyzed, one related to endothelium healing, the Endothelial Nitric Oxide Synthase (NOS3), and one associated with hemostasis, the ADAM Metallopeptidase with Thrombospondin Type 1 Motif 7 (ADAMTS7). In addition, we compared the methylation of these 2 genes promoters between AF patients and non-AF controls.

Methods: This is an ongoing study. So far, 44 AF patients treated with apixaban, dabigatran, or rivaroxaban and 18 non-AF controls have completed the study. gDNA from patients' blood was isolated at 3-time points: t0 for controls, and patients before DOAC initiation and, at 7 (t1) and 28 (t2) days of DOAC treatment. The gDNA was bisulfite converted and used as input to methylation analyses of promoters of genes of interest via qMSP-PCR.

Results: No significant bleeding or thrombosis events have been reported. Out of the 44 patients, 15 experienced minor bleeding events. NOS3 CRE and PRDI/II promoter elements were highly methylated, whereas ADAMTS7 promoter was lightly methylated, in both patients and controls. The percentage of DNA methylation of NOS3 and ADAMTS7 at t0 did not differ neither among AF patients and non-AF controls, nor from t0 to t2 for patients. When patients were categorized into experiencing bleeding events (cases) or not (controls), NOS3 CRE was demethylated from t1 to t2 in cases (-18.3% in cases vs. -2.8% in controls, p=0.023). No differences were found for NOS3 PRDI/II element methylation. In the case of ADAMTS7 promoter methylation, from t0 to t2, methylation was decreased in cases (-3.9% in cases vs. -1.9% in controls, p=0.017).

Conclusion: This is the first study of DOAC's effect on DNA methylation. Our preliminary results suggest that the NOS3 CRE promoter element and ADAMTS7 promoter are demethylated when DOAC-related bleeding occurs, increasing their expression levels, and subsequently promoting through different pathways hemostasis.

Conflict of interest statement: The authors declare they have no conflicting financial interests.

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# PA02 Symptoms of Post-COVID/Long-COVID Syndromes in the Population of Polish Patients Hospitalized Under the Comprehensive Rehabilitation Program After the COVID-19 Disease

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Background: Most patients who recover from COVID-19 continue to experience the following symptoms: fatigue, dyspnea, myalgia, and more even for several months after the acute phase of the disease, which qualifies as post-COVID/long-COVID syndrome. The present study aimed to assess the frequency of symptoms of post-COVID/long-COVID syndrome in the population of Polish COVID-19 convalescents, depending on gender.

Methods: The study group consisted of 543 patients with a history of SARS-CoV-2 infection (Caucasians, 232 men and 311 women, aged ≥18 years). A retrospective analysis was carried out based on patients' medical records participating in the rehabilitation program at the Cardiac Rehabilitation Department of the "Ustroń" Health Resort (Poland). The study was approved by the Ethical Committee of the Medical University of Silesia in Katowice (PCN/CBN/0022/KB1/68/21).

Results: Patients (mean age of  $63,51\pm10.23$  years) participated in the rehabilitation program in an average time of  $172.86\pm83.42$  days from the onset of COVID-19. Several symptoms of post-COVID/long-COVID syndrome were more common in women than in men, i.e. myalgia (in 98.39% of women and 94.40% of men, p=0.010), increased/unstable blood pressure (in 5.47% of women and 1.29% of men, p=0.006), palpitations (in 18.65% of women and 7.33% of men, p<0.001), concentration disorders/memory deterioration (in 57.88% of women and 48.71%

of men, p=0.034), depressed mood/sleep disturbances (in 36.33% of women and 25.00% of men, p=0.005), loss/impairment of smell (in 3.54% of women and 0.86% of men, p=0.032), hair loss (in 8.71% of women and 1.73% of men, p<0.001), and dizziness (in 22.51% of women and 11.21% of men, p<0.001). No differences were observed in the distribution of fatigue/ weakness, dyspnea, cough, chest pains, low-grade fever/fever, and deterioration of eyesight and hearing.

Conclusions: The present study indicated that women were more prone to have numerous post-COVID/long-COVID syndrome symptoms four months after the acute phase of COVID-19 compared to men.

### PA03 The Role of Tobacco and Alcohol in the Development of Pancreatic Cancer Compared to the Role of Genetics as a Risk Factor for Pancreatic Cancer

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Pancreatic cancer is the 2nd most common gastrointestinal cancer (after colorectal cancer). In this context, tobacco smoking is considered the most important risk factor, while alcohol consumption is the fourth most important one. Furthermore, given that smoking behavior is often associated with alcohol consumption, it is possible that there is effect modification due to the interaction of these two, in affecting the risk of the development of pancreatic cancer. However, it should be mentioned that cessation of smoking for 10 or more years returns the relative risk of pancreatic cancer to levels equivalent to non-smokers. So, as it seems, lifestyle factors significantly affect the development of pancreatic cancer, as it was found that many pancreatic cancer cases would have been prevented if the general population led a healthier lifestyle. Another factor that plays a vital role in the development of pancreatic cancer is genetics. DNA exists in every cell in our bodies and each DNA strand contains many different genes that are responsible for a specific function. All cancers begin when DNA mutations cause cells to divide and grow out of control. So, in the aftermath, pancreatic cancer is caused by inherited and acquired mutations in specific cancer-associated genes. About 10% of the pancreatic cancer cases are hereditary mutated DNA that passes from generation to generation (germline mutations) and lead to hereditary pancreatic cancer. Prevention is, at the moment, the only way to effectively reduce the risk of this disease, as early detection of pancreatic cancer in the general population is virtually impossible.

PA04 Identification of Novel Peripheral Blood Biomarkers Through the Use of 'Omics' Technologies for Liver Fibrosis in β-Thalassemia patients.

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Introduction: Beta-thalassaemia is a hereditary haemoglobinopathy caused by reduced or absent expression of beta-globin, which may lead to severe anaemia and related complications in major organs. Iron overload in the liver of the patients is one of the main causes of organ damage. If left untreated, initial liver fibrosis can progress to cirrhosis and hepatocellular carcinoma. Having a method to easily and reliably detect and stage liver fibrosis would allow personalised management of iron chelation in beta-thalassaemia patients and avoid further liver damage. Liver biopsy is the gold standard for the accurate evaluation of liver, although it is not a routine examination or screening technique for thalassaemia patients due to its invasive nature. Non-invasive alternatives such as the Fibroscan test and existing plasma biomarkers lack accuracy and specificity for detecting liver fibrosis in beta-thalassaemia. The aim of this project is to identify potential non-invasive, novel plasma diagnostic biomarkers for liver fibrosis in beta-thalassaemia patients using combined data from proteomics, metabolomics and transcriptomics studies. Materials and methods: Peripheral blood samples and clinical data for 140 β-thalassaemia patients staged for liver fibrosis based on Fibroscan tests and 40 healthy controls were collected. Plasma was extracted and stored until needed. Plasma samples from 10 β-thalassaemia patients without fibrosis, 11 thalassemia patients with severe fibrosis and 10 healthy controls (age and sex matched) were subjected to discovery proteomics (BGI), discovery metabolomics (NMR - National and Kapodistrian University of Athens), discovery metabolomics (MS - Utrecht Medical Centre), and short RNAseq (BRFAA). Results/Discussion: Discovery proteomics data are currently available and have been analysed, however, targeted proteomics verification is pending. All samples passed QC. Using data Independent Acquisition (DIA) mode, 9777 peptide and 835 proteins were quantitated. A number of differentially expressed proteins (DEPs) were detected in comparisons between Healthy controls VS Fibrotic thalassaemia patients (118 proteins), Healthy controls VS Non-fibrotic thalassaemia patients (115) and Non-fibrotic patients VS Fibrotic patients (38). DEPs for the Non-fibrotic VS Fibrotic patients fall into a variety of pathway classes (transport and catabolism, signal transduction,

infectious diseases, immune system), while the histidine, biotin and beta-Alanine metabolic pathways are enriched. Before further analysis is warranted, targeted proteomics need to be performed for verification of the discovery proteomics results.

#### PA05 Functional Investigation of ANO10

#### Androniki Chrysanthou

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Anoctamin 10 (ANO10) is a transmembrane protein exhibiting phospholipid scrambling and ion transport activities. The existing literature data implicate ANO10 in many physiological processes, including endosomal sorting, spindle assembly, calcium signalling, and apoptosis. ANO10 is primarily localized to the endoplasmic reticulum (ER); however, a recent study also showed an association with acetylated tubulin of spindles in mouse macrophages. Its ortholog in Drosophila, Axs, is associated with microtubules during spindle assembly, while protein defects cause abnormal spindle formation and chromosome segregation. These findings suggest a possible ANO10 involvement in spindle assembly and cell division. ANO10 pathogenic variants have been associated with rare spinocerebellar ataxia, known as autosomal recessive spinocerebellar ataxia type 10 (SCAR10). Degeneration of Purkinje cells in the cerebellum, mediated by an abnormal ANO10 protein, is the proposed mechanism of SCAR10 pathogenesis; however, the exact role of ANO10 in disease pathology remains unclear.

Fluorescence microscopy was employed to detect ANO10 localization in SH-SY5Y and U2OS cells, using two different antibodies. In addition, we performed ANO10 silencing using RNA interference technology to resemble and study the effects of a pathogenic deletion (c.289del [p.Thr96\_Met97ins\*]) identified in three individuals of a Cypriot family exhibiting SCAR10 features. Gene knockdown was verified by RT-qPCR and Western-blot analysis.

ANO10 was found to localize at the centrosomes of U2OS and SH-SY5Y cells and the ER, in agreement with previous studies. Transfection of cells with siRNA targeting ANO10 mRNA, resulted in a significant reduction in both gene and protein expression levels.

Centrosomic localization of ANO10 suggests a potential role of the protein in cell division and cell cycle. Further ANO10 investigation is currently conducted by examining the effects of ANO10 knockdown in SHSY-5Y and U2OS cells.

### PA06 Can the distribution of substances in the tablets change depending on the storage conditions - the results of analysis of coated tablets containing nifuroxazide?

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Background:The effectiveness of pharmacotherapy depends on the quality of the medicinal product. Differences in the structure of a drug appear as a result of physical and chemical changes occurring during drug storage may result in a decrease in bioavailability and thus result in insufficient pharmacological activity, clinical effect, and safety profile. The aim of the present study was to evaluate the distribution of substances in the coated tablets containing nifuroxazide stored in different conditions.

Methods:The following coated tablets containing nifuroxazide were analyzed: unexpired (n=10; expiration date 11.2024), expired (n=10; expiration date 11.2019; stored at ambient conditions), and stressed (n=4; expiration date 11.2024; stored at 40oC). The measurements of homogeneity of distribution of substances were made using X-ray microtomography (Germany). To compare the inner of expired and unexpired tablets, the analysis of density was performed since the absorption of x-rays by a sample is proportional to its density. Since the brightness of the pixels in X-ray scans corresponds to the density of the analyzed area, the calibration phantom was scanned together with the analyzed tablets to establish the grayscale level of reference density of the standards (A:1.13 g/cm3, B:1.16 g/cm3, C:1.26 g/cm3, D:1.65 g/cm3, E:1.90 g/cm3). Based on the histograms obtained with the ImageJ software (ImageJ 1.53a; USA), a calibration curve was determined which in turn allows assessing the density of any area of the tablet's scan. The study was funded within the projects: PCN-1-097/N/1/F; PCN-1-058/K/2/O.

Results:We analyzed 20 random scans of each type of the analyzed tablets using image processing methods. The selected area of the tablet image was marked and the average brightness was read from the histograms. Stressed tablets have significantly lower density compared to unexpired tablets (1.180 g/cm3  $\pm$  0.003 vs 1.193 g/cm3  $\pm$  0.003; p< 0.001) as well as to expired tablets (1.180 g/cm3  $\pm$  0.003 vs 1.191 g/cm3  $\pm$  0.002; p< 0.001). In turn, there was no significant difference between unexpired tablets and expired tablets in terms of density.

Conclusions: The present study indicates that storage under stressful conditions may influence the density of the inner of the coated tablets with nifuroxazide.

# PA07 Country-specific calibration of Polygenic Risk Scores for breast cancer in European ancestry populations

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Background and Goals: Breast cancer is influenced by multiple genetic risk factors, including common low-risk variants mainly identified via genome-wide association studies. Polygenic Risk Scores (PRS) combine the weighted additive effect of multiple common susceptibility variants, and could stratify women based on their breast cancer risk. Recently, a 313 variants PRS (PRS313) has been developed for the prediction of breast cancer risk in European ancestry women, using data from the Breast Cancer Association Consortium (BCAC). However, specific calibration of the PRS313 across the different European populations has not been extensively performed, which may provide more accurate risk estimation. Here, we explored the distribution of the PRS313 across 17 countries of Europe, as well as in Australia, Canada, Israel and the USA, and explain what might be causing variation across the countries, using 111,814 female breast cancer cases and 94,718 female controls of European ancestry from studies participating in the BCAC.

Methods: PRS313 was calculated in each individual as described in Mavaddat et al (2019). Mean and standard deviation of PRS313 were calculated by country separately in cases and controls and a fixed-effect meta-analysis was performed for the calculation of the overall estimates across the countries. Determination of the extent to which the differences in the distribution of the PRS can be captured by the ancestry informative principal components (PCs) has also been explored. Alternatively, country-specific estimates were calculated using an Empirical Bayes (EB) approach, as described in Clayton and Kaldor (1987).

Results: Mean PRS313 differed significantly across the countries in the control population (heterogeneity: I2=72%, p-value<0.01), being highest in the Republic of North Macedonia and Greece, and lowest in Ireland. When the PRS313 was adjusted by the first 5 ancestry informative PCs, the difference in the distribution was eliminated (heterogeneity: I2=0%, p-value>0.5). Alternatively, when an EB approach was used for the calculation of the means, estimates for countries with smaller available sample size had higher shrinkage towards to the overall esti-

mates, compared to countries with large available sample size.

Conclusions: These results indicate that the genetic background influences the distribution of the PRS even within Europe. Therefore, the implementation of the PRS in risk-stratified prevention for European ancestry populations will require country-specific calibration. The PCs seems to explain most of the variability across the countries. Alternatively, an EB approach seems to provide more reliable estimates, as it takes account the uncertainty due to small available sample size.

Conflicts of interest: The authors declare no conflicts of interest.

Source of funding: Telethon

# PA08 SURGICAL MODEL FOR TYMPANOSTOMY TRAINING PRODUCED BY ADDITIVE MANUFACTURING

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#### Objective

Tympanostomy (myringotomy) is used in patients suffering from Eustachian tube dysfunction. During the procedure, a small grommet is inserted into an incision of eardrum (myringotomy). The inserted myringotomy tube provides drainage and aeration of tympanic cavity both of which are prerequisites for proper healing of the middle ear mucosa. The main goal of this study was to create a surgical model that would closely resemble real myringotomy tube insertion and provide otology trainees with possibility of performing the procedure without posing a risk to actual patients.

#### Material and methods

The model was created based on high-resolution computed tomography of a healthy ear of teenage girl. The DICOM files were uploaded to 3D slicer software. The threshold of desired anatomical structures was identified and 3D mesh was created. Sculpting software was used to slightly adjust the model (mainly smoothing and erasing of unwanted defects). The 3D mesh was then split into several parts to provide possibility of insertion of a latex membrane resembling an eardrum. The model was 3D printed using a conventional fused filament fabrication 3D printer and polylactic acid filament. The model was modified for use in OtoSkills trainer that provides possibility of improving microsurgical skills of otology trainees.

#### Results

Our model was assessed by 2 otology consultants both of whom identified all important anatomical structures and inserted a myringotomy tube into a myringotomy in the latex membrane representing a tympanic membrane. They confirmed that our model closely resembles real situation. The model was then provided to young physicians who also confirmed its suitability for training of the procedure.

#### Conclusion

The presented model shows the benefits of cooperation between experts in theoretical sciences and clinical practice. The model closely resembles real situation and provides the possibility of mastering the procedure without posing a risk to actual patients. Creating models for other procedures such as stapedoplasty will follow.

#### Acknowledgements

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#### Keywords

additive manufacturing; ventilation tube insertion, tympanostomy training; surgical mod

### PA09 Kaempferol derived flavonoids show promising in vitro anticancer activity against pancreatic adenocarcinoma

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Objective: Pancreatic cancer is one of the most lethal types of cancer worldwide. The purpose of this study was to investigate the in vitro anti-cancer activity of flavonoids of kaempferol in pancreatic ductal adenocarcinoma. Specifically, kaempferol and its glycosylated derivatives, tiliroside, and its semisynthetic derivative peracetylated Tiliroside (Tac) were tested for their in vitro anticancer effect against pancreatic cancer cells.

Materials & Methods: The cytotoxic activity of the congeners was tested against the human pancreatic adenocarcinoma cell line PANC-1. To determine the in vitro cytotoxicity the SRB method was implicated. The most active compound, Tac, was further studied for its ability to inhibit the formation of colonies using a colony-forming assay and the migratory ability of PANC-1. Additionally, after exposure of the cells to specific concentrations (10µM and 20µM)

and time intervals (6h / 12h / 24h), we examined its effect on the viability of PANC-1 cells via the trypan blue method. Finally, we examined whether Tac is involved in the MAPK pathway by inhibiting the function of p90RSK kinases. To this aim, western blot analysis was performed on these cells to study the expression levels and phosphorylation status of p90RSKs.

Results: Based on the results obtained from the above-described study, it was observed that the peracetylated derivative of Tiliroside, Tac, showed the strongest antiproliferative and cyto-toxic effect against the human pancreatic cancer cell line PANC-1. This action was apparently both dose-dependent and time-dependent and from the results of the immunoblotting it that Tac affects the function of p90RSK, by inhibiting some of the most important for the activation of these kinases phosphorylations.

Conclusions: The results indicate significant in vitro anti-cancer activity against the PANC-1 cancer cell line via a dose and time dependent mechanism involving the inhibition of p90RSKs. The mechanism of action of this compound is still under investigation in our laboratory.

#### PA10 Nanomechanical assessment of solid tumors

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A number of pathological conditions, including cancer, are thought to be closely related to alterations in the content, structure and mechanical properties of biological tissues. Fibrosis in general, and desmoplasia, a specific type of cancer fibrosis, poses a major barrier to effective drug delivery and has been associated with poor prognosis. Tissue stiffening can cause blood vessel inefficiency and hypo-perfusion, and as a result, it poses major physiological barriers to the systemic delivery of drugs. Consequently, there is an urgent need for the development of novel biomarkers that characterize the mechanical state of a particular pathological tissue so as to support the development of novel therapeutic strategies that target the tumor mechanical microenvironment. Atomic Force Microscopy (AFM) arises as a unique tool for assessing the nanomechanical properties of tissues. In this work we present our research results on using AFM and optical microscopy techniques (including polarized microscopy) for assessing the nanomechanical profile of highly demsoplastic tumors (i.e., breast, sarcoma and pancreatic cancers) during cancer progression. Also, AFM techniques were used for assessing specific treatment outcomes (i.e., anti-fibrotic treatments). Our results highlight that AFM is sensitive enough to assess small nanomechanical alteration during pathological conditions progression and during or after treatment. The identification of unique AFM-based nanomechanical fingerprints can lead to the development of novel mechanical biomarkers for treatment perdition and monitoring.

# PA11 Does 'On Call' simulation training have a place in medical education programs?

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Introduction: There is a growing body of evidence newly qualified doctors feel underprepared for working "on-call" shifts. The aim of this report is to make medical educators aware of the potential for On-Call Simulation training at a local and regional level. Our hope is that Medical Educators will be able to consider this as a teaching aid in undergraduate curricula.

Methods: 44 final year medical students completed a 1-2 hour on call simulation session at Bronglais General Hospital, Aberystwyth, Wales, UK, during their final year clinical placement.

Results: Our findings from our study showed that all students found the session useful. There was an overall improvement from an average of 3/10 to 7/10 in terms of their confidence for preparing for on call shifts as a day 1 Foundation Doctor in the UK. Accordingly, the students provided excellent feedback as none of them had had any training previously like this. Their comments give testament to the need for similar training in the undergraduate curricular.

Conclusion: This study gives testament to the growing body of literature that there may be a place for on call simulation training for undergraduate medical students that mimics the stressors of being on call.

Keywords: Simulation training, on call, foundation year 1 doctor, F1 doctor.

Study Type: Mixed, qualitative and quantitative

Each named author has substantially contributed to conducting the underlying research and drafting the manuscript. Additionally, to the best of our knowledge, the named authors have no conflict of interest, financially or otherwise. Informed consent was obtained for this paper to be written.

### PA12 Ras suppressor-1 (RSU1) long isoform inhibits apoptosis in invasive breast cancer cells

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Ras Suppressor-1 (RSU1) is a cell-extracellular matrix (ECM) adhesion protein implicated in

breast cancer (BC) cell metastasis. Nevertheless, its role in apoptosis is yet unknown. In the present study, we used bioinformatics tools to evaluate the association of RSU1 expression and BC patient survival, the expression of basic pro- and anti-apoptotic genes in metastatic BC samples and their relation with the expression of RSU1. Then, we specifically depleted RSU1 using a short hairpin RNA (shRNA) silencing approach in two BC cell lines, the non-invasive MCF-7 and the highly invasive MDA-MB-231-LM2 cells and assessed gene expression of pro-and anti-apoptotic genes, as well as cell survival and apoptosis. Our results showed that high RSU1 expression was correlated with poor survival and significant changes were found in the expression of apoptosis-related genes (PUMA, TP53, BCL-2 and BCL-XL) in metastatic BC. Moreover, RSU1 silencing resulted in the upregulation of PUMA and TP53 and concomitant downregulation of BCL-2 and BCL-XL, with the effect being more prominent in invasive MDA-MB-231-LM2 cells. Finally, RSU1 depletion leads to a dramatic increase in apoptosis of MDA-MB-231-LM2 cells, while no change was observed in the apoptotic rate of MCF-7 cells. This is the first study that links RSU1 with apoptosis and provides evidence for its differential role in cell lines of different invasive potential. This indicates that RSU1 represses apoptosis in aggressive cancer cells helping them evade cell death and survive.

#### PA13 Genetic epidemiology of Amyotrophic Lateral Sclerosis in Cyprus

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Amyotrophic Lateral Sclerosis (ALS) is a devastating, uniformly lethal neurodegenerative disease of motor neurons, characterized by degenerative changes in both upper (UMN) and lower motor neurons (LMN). These changes cause the selective loss of motor neurons, resulting in the inability of neuronal transmission from the brain and spinal cord to the muscles. The scientific landscape surrounding ALS continues to shift as the number of genes associated with the disease risk and pathogenesis, and the cellular processes involved, continues to grow. Even though over 50 potentially causative or disease-modifying genes identified, aetiology of ALS remains unexplained. This study aimed to conduct a detailed genetic epidemiological investigation of ALS in the Cypriot population. A total of 80 ALS patients were included and screened for disease-causing mutation in the most common genes; C9orf72, SOD1, TARDBP, FUS, SMN1 and ATXN2. Assessment of these genes revealed one patient with the c.800A>G (p.Asn267Ser) mutation in the TARDBP (1.25%) and 16 additional patients carrying a pathogenic hexanucleotide repeat expansion in the C9orf72 (20%) gene. No pathogenic variants were identified in the SOD1 or FUS genes. Additionally, patients did not harbouring intermediate-length polyglutamine (polyQ) repeat expansions in the ATXN2 gene, nether have an association with SMN1 gene duplications, which are both considered a genetic risk factors for sporadic ALS. These findings indicate that C9orf72 repeat expansions are indeed causative for ALS and agree with findings from other European countries. Genetic clusters of the remaining genes are not pres-

ent in the Cypriot population. However, further genetic investigations will be performed in order to identify genetic risk factors in both sporadic and familial ALS cases.

# PA14 Studying mechanism of action of hydrogen molecules on ROS production and NAD+/NADH ratio of cardiac muscle in vitro

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Number of studies on molecular hydrogen are evolving tremendously and has been growing exponentially during the last decade. Molecular hydrogen is claimed to support body's antioxidant system, has anti-inflammatory properties, can help balance the pH of the blood and attenuates radiation-induced nucleobase damage to DNA. Also, it was shown that H2 has evident therapeutic potential to cope with the top 7 fatality-causing diseases including cardioand cerebro-vascular diseases. In this work investigation of ROS production and NAD+/NADH ratio were carried on in the cell culture exposed to H2 rich DMEM medium at rest and under stimulation (electric and chemical). ROS were analysed by means of fluorescence probes selectively sensitive for hydroxyl radical by hydroxyphenyl fluorescein, and other species (e.g. superoxide anion) resulting in formation hydrogen peroxide by chloromethyl-dichlorofluorescein (CM-H2DCFD). Quantification of NAD+ and NADH from cell lysates were investigated by the enzymatic-fluorometric method (ab176723, ABCAM). To visualize functional changes in mitochondrial membrane potential and antioxidant capacity fluorescence confocal microscope Zeiss Observer Z1 was used. For that purpose, many of fundamental fluorescence probes, such as JC-1 and CM-H2DCFDA were used.

All authors declare that they have no conflicts of interest.

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#### PA15 Biological Pathways Underlying Multimorbidity

### Kristina Tomkova, Marius Roman, Adewale Adebayo, Melanie Gulston, Lathishia Joel-David, Florence Lai, Antonio Murgia, Bryony Eagle-Hemming, Sophia Sheikh, Tracy Kumar, Hardeep Aujla, Julian Griffin, Gavin Murphy, Marcin Wozniak

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Introduction: Multimorbidity is the presence of two or more chronic conditions and over twothirds of people over 65 suffer from multimorbidity. These patients are at increased risk of organ injury, hospitalisation and death. We aimed to identify multimorbidity mechanisms that can lead to organ injury regardless of composite chronic conditions. It will facilitate biomarker identification for patient stratification and help identify intervention targets.

Methods: We analysed a cohort of 144 cardiac surgery patients. Biopsies were collected from the right atrium before the cardiopulmonary bypass surgery. Blood samples were collected before and after the procedure. We performed metabolomic analysis in plasma and myocardial samples, and mRNA sequencing in cardiac biopsies. Mitochondrial function was examined using the Seahorse method in monocytes, and the ribosomal DNA (rDNA) copy numbers and the nucleolar structure were assessed in heart biopsies using qPCR and immunohistochemistry, respectively.

Results: The metabolomic analysis has shown that levels of energy substrates like glucose, pyruvate, glutamate, alpha-ketoglutarate or acylated carnitines directly correlate with the number of comorbidities. That is accompanied by decreasing levels of long-chain lipids in pre-operative plasma. Pre-operatively, lower respiratory reserve capacity and respiratory control ratio was observed in multimorbid patients. The changes were specific to mitochondrial ATP production, as there was no difference in glycolysis levels. That was also evident in the myocardial tissue from multimorbid patients with lower levels of ATP, a-ketoglutarate and long chain acyl-carnitines. Transcriptomics data has shown changes in the expression of genes involved in the mitochondrial electron transport chain, beta-oxidation, senescence, chromatin modification, translation, and polymerase I transcription. Transcripts involved in mitochondrial function and translation were downregulated in multimorbidity, whilst senescence transcripts were upregulated. Weighted correlation analysis identified a set of genes correlating with the number of comorbidities that enriched pathways involved in the regulation of rRNA expression, indicating nucleolar stress. This was also supported by higher copy numbers of 5.8S rDNA and altered morphology of nucleolin and fibrillarin.

Conclusions: Our results suggest that multimorbidity is specifically associated with the nucleolar imbalance and translational changes. We propose that this leads to nucleolus-dependent decreases in mitochondrial energy production which contribute to the widespread cellular dysregulation and result in the adverse events post-surgery observed in multimorbid patients.

### PA16 Study of the in vitro anticancer activity of the PDK-1 inhibitor GSK2334470 in pancreatic cancer

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Objective: This work aimed to study the in vitro anti-cancer activity of the small molecule GSK2334470 which is reported to be a PDK-1 inhibitor, in a human PDAC (pancreatic ductal adenocarcinoma) cancer cell line. PDK1 (Phosphoinositide-dependent kinase-1) is a constitutively Serine/threonine kinase that acts as a master kinase, phosphorylating and activating a subgroup of the AGC family of protein kinases, amongst them interacts with and controls the function of p90RSKs, important downstream kinases of the MAPK/ERK pathway.

Materials & Methods: The effects of GSK2334470 were studied against the PANC-01 cell line. Firstly, was performed an SRB cytotoxicity test of GSK2334470 to determine the in vitro anticancer features of this agent. Subsequently, a clonogenic assay and a wound healing assay were performed to check the inhibitor's antiproliferative ability in both single cells' capability to form colonies and against their migration capacity. Finally, flow cytometry was performed to identify the cell cycle phase in which GSK2334470 acts.

Results: The data obtained from the above experiments suggest that GSK2334470 exhibits good antiproliferative and cytotoxic effects on the pancreatic cancer cell line PACN-01 as its GI50 was found to be around 10 $\mu$ M. In addition, GSK2334470 was both able to inhibit colony formation at the concentration of 0,1 $\mu$ M and the migration capacity of pancreatic cancer in concentrations close to 1 $\mu$ M. Finally, GSK2334470 was observed to act in a phase-specific mechanism as it was found to arrest the cell cycle at the G0/1 to S transition phase.

Conclusions: GSK2334470 PDK-1 inhibitor was found, for the first time worldwide, to exhibit promising in vitro anticancer activity against the PANC-1 human pancreatic cancer cell line which was further found to be time and dose-dependent. This action was found to be also cell cycle phase-specific.

#### PA17 Effect of hydrogen molecules on cellular respiration

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H2 is the smallest molecule, hydrophobic, has the highest diffusivity of all gases, and therefore can be easily get through the cell membranes. It has been reported that the hydrogen molecule acts as an antioxidant, in particular as a selective scavenger of hydroxyl radicals and peroxynitrite. The major source of ROS under physiological and pathological conditions has been emerged the reactions related to mitochondrial oxidative phosphorylation. Therefore, our research was aimed at studying the effects of H2 on mitochondrial respiration in different culture cells (H9c2 and NIH 3T3). High-resolution respirometry revealed changes in mitochondrial oxygen consumption that were manifested by increased routine respiration, increased maximal capacity of the electron transport system and increased non-phosphorylating respiration. Cellular energy homeostasis is essential for the growth and survival of all living cells. Any compound that either directly or indirectly improves aerobic respiration and so maintains the production of cellular energy should be considered as an agent with the broad beneficial impact.

# PA18 The Effect of Hydrogen Molecules on Cellular Energetics of Cardiac Muscle in vitro

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Since 2007, there has been a significant focus on the role of hydrogen molecule (H2), in particular its anti-oxidative properties which may tackle some of the most fatality-causing diseases such as Alzheimer's disease, diabetes mellitus or cardio-/cerebro-vascular diseases. Additionally, recent studies also describe the possible effect of drinking the hydrogen rich water on muscle fatigue caused by physical exercise. Physical exercise is associased with glycolysis, which generates two ATP molecules per glucose molecule and produces lactate, the end product of anaerobic glycolysis in the cytosol. As the mechanism of how H2 acts on cellular levels is still not fully explained, the production/utilization of lactate in cardiomyoblasts exposed to H2 rich DMEM (dulbecco's modified eagle medium) was evaluated here to explain the role of H2 on mitochondrial processes and metabolic pathways. According to the results, the intake of hydrogen rich water may prevent the elevation of blood lactate during physical exercise. This study was carried on the H9C2 cell line (cardiomyoblasts), which was used to investigate the lactate and pyruvate production under H2 rich supplementation conditions. For this reason, cells were cultivated in various conditions including high glucose, normal glucose, high lactate, with insulin and without pyruvate at rest and under norepinephrine stimulation conditions. The quantification of lactate and pyruvate is determined by the enzymatic-colorimetric methods. The obtained results indicate that the exogenous H2 should be appraised as a possible biomedical agent that could affect a muscle fatigue caused by physical exercise.

All authors declare that they have no conflicts of interest.

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PA19 Watercress extract-contained major phytochemicals induce a cytotoxic response by regulating the expression of key apoptotic gene targets in an in vitro model of human malignant melanoma

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The increasing global incidence of malignant melanoma highlights the urgency for the development of innovative therapeutic approaches. To this end, Nasturtium officinale (watercress) is a cruciferous vegetable, enriched in various phytochemicals like phenethyl isothiocyanate (PEITC) which has been shown to exert an antioxidant and anti-carcinogenic capacity. This current study aims to characterize the underlying mechanism(s) by which watercress induces a cytotoxic action in an in vitro model of human malignant melanoma consisting of malignant melanoma (A375, COLO-679, COLO-800), non-melanoma epidermoid carcinoma (A431) and normal immortalized keratinocyte (HaCaT) cells. An initial chemical characterization of various watercress extracts was performed by utilizing methodologies based on UPLC MS/MS, HPLC and spectrophotometry for the determination of the content of various phytochemicals (e.g., glucosinolates, isothiocyanates, polyphenols, flavonoids, pigments, ascorbic acid, etc.,). In addition, cell viability was evaluated (by Alamar Blue assay) as an initial step towards the biological characterization of watercress extracts. Interestingly, we observed increased cytotoxicity in all malignant melanoma cell lines whereas in A431 and HaCaT cells the extract showed reduced or no cytotoxicity, respectively. To validate the levels of reduced cell viability, in the context of increased cytotoxicity, levels of apoptotic induction were determined by means of measuring the activation of caspases 3, -8 and -9 (by commercially available fluorescence kits). Finally, an RT-PCR based methodology was employed to identify major anti- and pro-apoptotic gene targets involved in inducing the extrinsic and/or intrinsic apoptotic pathways. To this end, we have revealed the expression of 14 genes (involved in both intrinsic and extrinsic apoptotic pathways) as potential key targets in regulating watercress-induced apoptosis. Overall, our data support a beneficial role of watercress (a rich source of PEITC) as an adjuvant therapeutic means for the pharmacological management of malignant melanoma patients.

PA20 Investigating the effect of different concentrations of two antibiotics (cefaclor and amoxicillin) on the growth of lentils (Lens culinaris) and beans (Phaseolus vulgaris).

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Although antibiotics constitute a major benefit for public human health, they can be hazardous for wildlife when used in an uncontrolled manner. The European Commission's "One Health" action plan promotes the integrated cooperation between different scientific fields to tackle the consequences of Antimicrobial Resistance (AMR). This shows the significance of increased research focus on antibiotics use. The aim of this exploration is to investigate the effect of different concentrations (500 mg dm-3, 750 mg dm-3 and 1000 mg dm-3) of antibiotic solutions (containing cefaclor and amoxicillin) on plant growth (in the species; Lens culinaris and Phaseolus vulgaris). Previous studies have investigated this effect with smaller concentrations of antibiotics (ranging from 5 to 10,000mg dm-3). The growth rate is measured by changes in the length of the stem (cm  $\pm$  0.1) every three days, for a period of 22 days. Seeds (placed in pots with cotton wool) are sprayed twice every day, with water from day 1-12 and with antibiotic solutions from day 13-22. Results indicating statistical significance have only been obtained for Cefaclor 1000 mg dm-3 (see Graph 1) for the species Lens culinaris, where a statistically significant negative effect on the growth rate of the shoot length was shown. However, no particular overall trend (deriving from statistically significant observations) is identified for neither species.

### PA21 Decitabine treatment induces a viral-mimicry response in cervical cancer and increases response to chemotherapy

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The development of effective therapeutic approaches for patients with cervical cancer (CC), the fourth most common cancer in females worldwide, comprise an urgent medical need. Chemoresistance to existing chemotherapeutic drugs is a significant unmet clinical obstacle. In addition, use of immune checkpoint therapy has proved to hold an exceptional promising anti-cancer potential, but only a minority of patients benefit. Epigenetic therapy using DNA methyltransferase (DNMT) inhibitors as anti-cancer agents in solid tumours has attracted great attention in the recent years, with particular interest in the potential of these drugs to modulate tumour immunogenicity and/or increase chemosensitivity in cancer. However, whether DNMT inhibitors could enhance cancer immunogenicity and/or induce chemosensitivity in CC is unknown. Herein, testing the anti-cancer, immunomodulatory and chemosensitizing potential of a DNMT inhibitor, 5-aza-2'-deoxycytidine (decitabine, DAC) in human papillomavirus (HPV)-associated CC or HPV-CC cells in vitro. To assess the anti-cancer potential of DAC treatment in CC cells, in vitro end-point assays were developed, and biomarkers of response were used. We have shown that low doses of DAC treatment activate an anti-viral pathway

characterized by long-term activation of double-stranded RNA (dsRNA), upregulation of the interferon-related gene 7 (IRF7) and the dsRNA-sensing molecule MDA5 whilst reducing cell viability and promoting robust G2/M phase cell cycle arrest. In addition, DAC treatment stimulated prolonged time-dependent induction of immune-associated molecules in CC cells in vitro and increased the levels of apoptotic cancer cells as indicated by flow cytometry analysis. Nanomolar doses of DAC treatment resulted in a greater response of CC cells to low doses of the chemotherapeutic drug, cisplatin, as indicated by the significantly reduced cell number in response to combination treatment compared to each agent alone. Increased response to cisplatin was associated with significantly higher gene expression levels of pluripotency-related factors suggesting a role of these factors in the response of CC cells to treatment. Our results showed that low doses of DAC treatment can exhibit both immunomodulating and chemosensitizing effects in CC, offering a variety of opportunities for novel therapeutic interventions in cancer management, providing solutions to current therapeutic challenges for the treatment of CC.

#### PA22 Appraising the causal role of risk factors in coronary artery disease and stroke: A systematic review of Mendelian Randomization studies

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Background: Mendelian randomization (MR) offers a powerful approach to study potential causal associations between exposures and health outcomes, by using genetic variants associated with an exposure as instrumental variables. In this systematic review, we aimed to summarize previous MR studies and to evaluate the evidence for causality for a broad range of exposures in relation to coronary artery disease (CAD) and stroke.

Methods: MR studies investigating the association of any genetically predicted exposure with CAD or stroke were identified in Pubmed. Studies were classified into four categories, namely robust, probable, suggestive and insufficient, built on the significance of the main MR analysis results and its concordance with sensitivity analyses (MR-Egger, weighed median

and MR-PRESSO). Associations that did not perform any sensitivity analysis were classified as non-evaluable.

Findings: We identified 2,718 associations eligible for evaluation, examining 535 distinct exposures. Of them, 138 were classified as robust, 347 as probable, 109 as suggestive and 886 had insufficient evidence. The most prominent robust associations were observed for anthropometric traits (i.e., body mass index, height, waist to hip ratio and birth weight) and lipids and lipoproteins (i.e., low- and high-density lipoproteins, triglycerides) and type 2 diabetes with CAD, clinical measurements (i.e., systolic and diastolic blood pressure) with CAD and stroke, and thrombotic factors (i.e., factors XI and VII, iron and vitamin K) with stroke.

Conclusion: Despite the large number of studies that have been conducted, only a limited number of associations were supported by robust evidence. About half of the associations presented a MR sensitivity analysis along with the main analysis which further supported the causality of associations. Future research should focus on more thorough assessment of sensitivity MR analyses and assessment of mediation effects and nonlinearity in associations.

# PA23 A novel adjuvant treatment protocol combining Tazemetostat with various synthetic isothiocyanates enhances apoptotic induction in an in vitro model of human malignant melanoma

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Malignant melanoma is one of the most aggressive types of human cancer, with a high fatality rate mainly due to its resistance to current therapeutic protocols. On the other hand, the extensive deregulation of normal epigenetic marks is associated with melanoma onset and progression. In this context, given the well-established association between epigenetic modifications and alterations in gene expression, together with the reversible nature of such modifications, it becomes apparent that they have attracted scientific interest as potential therapeutic targets. On the other hand, isothiocyanates (ITCs; the bioactive compounds found in various cruciferous vegetables) have been previously reported to possess significant anticancer activity against various types of cancers, including melanoma. In the present study, we aimed to characterize the therapeutic effect of the EZH2 inhibitor, Tazemetostat, alone or in combination with various synthetic ITCs (Sulforaphane; SFN,Iberin; IBN, Phenethyl isothiocyanate; PEITC and Benzyl isothiocyanate; BITC) in an in vitro model of human malignant melanoma (A375 and Colo-679) and non-tumorigenic immortalized keratinocyte (HaCaT) cells. Our results revealed, for the first time, that exposure to Tazemetostat significantly reduced cell viability, in a dose- and time-dependent manner, via activation of apoptosis in A375 and Colo-679

cells whereas HaCaT cells remained unaffected. In addition, combinatorial treatments with ITCs resulted in further reduction of cell viability an effect that was accompanied by higher apoptotic rates. Overall, we have developed an experimental therapeutic protocol based on novel combinatorial conditions with the aim to enhance the anticancer potential of clinically relevant epigenetic drugs thereby ensuring enhanced therapeutic potency, while we maintain safety, against human malignant melanoma cells.

# PA24 Title: Evaluation of two methodologies for the quantification of Neurofilament-Light, a biomarker of axonal damage.

### Pafiti A, Krashias G, Tzartos S, Tzartos J, Gaglia E, Smoleski E, Christodoulou C, Pantzaris M, Lambrianides A.

The Cyprus Institute of Neurology and Genetics

Introduction: Under physiological conditions, neurofilaments are highly stable in axons and are critical for radial growth and stability. Neurofilament-Light (NfL), is a biomarker of axonal damage in Multiple Sclerosis (MS). Extensive research has been done on the quantification in CSF samples. The aim is to evaluate the concentrations of NfL in serum using, Enzyme-Linked Immunosorbent Assay (ELISA) and Single Molecular Array (Simoa) advanced technology using samples from MS patients and healthy controls (HC). Verifying the most accurate technique for the quantification of NfL will be of huge benefit in clinical settings. To our knowledge, this is the first study comparing Simoa technology with the new commercially available ELISA kit for serum by Quanterix.

Methods: Blood samples were collected from 54 MS patients and 30 HCs. The protocols accompanying the kits were followed. The threshold for ELISA was set as 3 S.D above the mean of the HCs. Using Simoa technology, Z-scores which take into consideration the participant's BMI and age were calculated using the application created by Jens Kuhle group (with permission). Samples with a concentration above the threshold using ELISA or a z-score  $\geq$ 1.5 for Simoa were considered to have subclinical disease activity.

Results: To our knowledge, this is the first study to find a strong positive correlation between ELISA and Simoa advanced technology for the identification of NfL in serum, with an r-value of 0.919. Importantly, participants that had a concentration above the threshold using ELISA, were also found to have a z-score  $\geq$ 1.5.

Conclusion: Despite the strong correlation found in quantifying NfL in serum, Simoa has better analytical sensitivity and can detect small changes in longitudinal samples of MS patients making it valuable in clinical settings.

### PA25 A custom CRISPR knockout screen to identify novel $\gamma$ -globin repressors for the treatment of $\beta$ -haemoglobinopathies

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Reactivation of y-globin for the production of HbF can ameliorate  $\beta$ -thalassaemia and sickle cell disease. Although therapeutic strategies involving addition of a functional  $\beta$ -globin gene or genome editing for y-globin reactivation are promising, the high cost and limited availability together with safety and efficacy issues constrain such therapies to younger patients with access to sophisticated clinical care. The only FDA-approved HbF-inducing drug is hydroxyurea but its use in  $\beta$ -thalassaemia patients is restricted because of efficacy and toxicity reasons. Luspatercept, a recently FDA/EMA-approved medication that works through enhancing erythroid maturation, despite its benefits for  $\beta$ -thalassaemia patients, has a limited effectiveness in severely affected patients. Additionally, the multiple functions of BCL11A and LRF make their targeting with small molecules a real challenge. Hence, reactivation of y-globin with pharmacological means is still a useful and much needed avenue to explore. To identify novel y-globin repressors as potential druggable targets, we performed a custom CRISPR/Cas9 knockout screen targeting 293 genes selected from previously published literature. Their selection was based on the existence of evidence suggesting a possible y-globin regulatory role but absence of supporting functional data. Screening this library in the HUDEP-2 cell line resulted in the identification of several candidate y-globin repressors. The two most promising candidate genes (based on their ranking and known function) have been selected for further validation and functional studies. One gene encodes for a protein involved in ion transport and iron homeostasis whereas the other gene is a transcriptional regulator. These genes will be subjected to validation in HUDEP-2 and human primary erythroid progenitors to verify their role as y-globin repressors. Additionally, the mechanism of action of these genes will be investigated with regards to erythroid maturation and haemoglobin switching. Our work could potentially identify new HbF regulators, which may provide novel therapeutic targets for the treatment of  $\beta$ -haemoglobinopathies.

# PA26 Effects of Dietary Acrylamide on Gene Expression of Colon Tissue in BALB/c Mice

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partment of Life Sciences, European University Cyprus, Nicosia 2404, Cyprus

Background: Acrylamide (AA) has been linked to carcinogenicity, as suggested by animal studies and in vitro studies using human cells. When AA is taken orally, the gastrointestinal (GI) tract is exposed to considerable amounts of this substance. However, epidemiologic data on the association of AA intake with cancer risk are limited and contradicting. In addition, the potential cancer-inducing molecular pathways activated in the GI tract by dietary AA are not clear. Aim: To collect mechanistic information on the induction of colon carcinogenesis by dietary AA, using an established animal model. Methods: Male Balb/c mice were randomized to a mock-treated and an AA-treated group, which respectively received 0.1 mg/kg PBS or AA daily for 4 weeks through oral gavage. After treatment, colon tissue samples were excised, processed and total RNA extraction was performed, followed by RNA sequencing, FastQ files were processed for differential gene expression analysis between groups, using the following cut offs: false discovery rate (FDR) < 0.05 and fold-change > 2 or < 0.5. Gene-set enrichment analysis of differentially expressed genes was performed using freely available databases through the STRING-DB portal. We also evaluated the expression of specific genes in normal vs colon cancer patient samples using the Human Protein Atlas, UALCAN and Kaplan Meier plotter websites. Results: We identified a list of 213 genes that were differentially expressed in the AA-treated compared to mock-treated groups. We designed a protein-protein interaction network and determined certain genes (RPS9, RPS14, RPS15, RPS17, RPS24, RPS27A, RPL4, RPL11, RPL13A, RPL14, RPL18, RPL24, RPL36, RPL39, and EIF4A2) that take part mainly in RNA metabolism, ribosome structure and protein synthesis pathways (FDR < 0.02) and are also implicated in carcinogenesis as mentioned in the literature. These genes were found to be highly expressed in primary colon cancer samples compared to normal tissues (statistical significance < 0.05) in humans and are correlated with decreased overall survival of colon cancer patients. Conclusion: Our results provide insights to the molecular pathways affected by dietary AA in the GI tract and may be used in the future to fully characterized the mode of action of this chemical to the colon that ultimately leads to carcinogenesis.

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# PA27 Quercus alnifolia leaves as a source of phytochemical compounds with potential anticancer properties

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Quercus alnifolia is an endemic oak species of Cyprus, which grows on the ultrabasic rock formations of Troodos at an altitude range between 400 to 1800 meters. Q. alnifolia is morphologically and genetically distinct from other related species. Published studies focus on its morphological and genetic characteristics. Remarkably, there is no available research on this species regarding its phytochemical composition and the potential properties of its extracts. Aim: The aim of this study was to investigate the phytochemical composition of Q. alnifolia leaves, and how they differ in relation to the location (different altitudes) and the maturity stage of the leaves. In addition, it aimed to identify anti-cancer properties of the most promising extracts based on the phytochemical composition. Methods: Sampling took place in the period of August-September 2021 at different altitude locations of the island (Kionia 1300 m, Platres 1700 m, Tripilos 1200 m) and sampled plant individuals were selected based on environmental exposure factors. Young (gold abaxial) and mature (brown abaxial) leaves were harvested, and a series of phenotypical macroscopic observations and phytochemical analyses were conducted. The phytochemical composition was appraised by measuring the total content of phenolics, flavonoids, condensed tannins and the in vitro antioxidant activity. Moreover, a preliminary examination of their anti-cancer activity using the MTT assay on the MCF-7 breast cancer cell line was performed. For the anticancer properties were used young leaves extracts from the tree numbers 5 and 6 of Kionia area and the tree number 12 of Tripilos area. Results: The morphological characteristics of the leaves substantially varied among the harvested plants. Phytochemical analyses showed statistically significant differences between the mature and young leaves, while differences among harvest locations were limited. Young gold leaves showed higher levels of antioxidant activity and total phenolics compared with mature brown leaves. Flavonoids and tannins displayed similar trends with higher values recorded for the brown mature leaves of Platres and Tripilos. MTT assay preliminary results indicated that the three selected extracts (in the concentration of 2 mg/ml) can significantly reduce MCF-7 cell viability (by 38.17-54.45%). Conclusion: The results of this preliminary study contribute to unravelling the undiscover phytochemistry and potential anticancer properties of Quercus alnifolia leaf extracts.

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#### PA28 Fine-scale mapping analysis of risk regions associated with breast cancer

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Introduction To date more than 200 genomic regions have been associated with breast cancer that were identified by Genome Wide Association studies (GWAS). In order to identify the causal variant within these regions, fine-mapping frameworks are applied. We aim to implement state-of-the-art Bayesian fine-mapping tools (namely PolyFun, SuSiE, FINEMAP), which were proven to outperform traditional stepwise regression analyses in the identification of causal variants. Based on derived results we aim to define the best practice process in providing the most optimal list of credible causal variants (CCVs) associated with breast cancer. Ultimately, we aim to explain a larger fraction of disease heritability and improve breast cancer risk estimation. Subsequent phases will involve the identification of associated target genes, as well as networks and pathways implicated in disease aetiology and drug repurposing opportunities.

Methods Summary statistics data based on GWAS from 247,173 individuals with breast cancer and controls were used for the analyses of 150 previously fine-mapped regions and 32 unexplored loci. Functionally-informed fine-mapping was performed in association to overall breast cancer using prior causal probabilities calculated by PolyFun, that were used by SuSiE and FINEMAP for the identification of independently-associated CCV sets. Prior causal probabilities were calculated using variant functional annotations derived from ENCODE, Roadmap Epigenomics Project, Haploreg, Remap etc. In both approaches, a pre-computed LD matrix from the UK Biobank was used and a maximum of 10 causal variants were assumed per region.

Results Credible sets were identified across 182 regions, at a 95% posterior probability (PP) of causality. We identified smaller number of variants within each credible set, compared to earlier analyses and of hundreds of strong variant associations (33% and 28% of credible sets identified by SuSiE and FINEMAP respectively, contained a single CCV). The PolyFun + SuSiE framework has shown to be more conservative in the construction of credible sets compared to PolyFun + FINEMAP, with the latter identifying a considerable higher number of CCVs at a 95% PP.

Conclusions Combining PolyFun with the SuSiE and FINEMAP frameworks has efficiently resulted in the identification of independently-associated credible sets and potentially causal variants within them. The significant variant prioritization observed within credible sets, highlights the importance of using variant functional annotations in Bayesian fine-mapping and the capability of the above methods in identifying more associations to breast cancer.

PA29 Predicting vital sign deviations during surgery: developing and validating deep learning models.

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Background: Reliable real-time prediction models for the most frequently measured vital signs could assist surgeons and anaesthesiologists in their work and help prevent complications in perioperative patients.

Methods: We developed and validated deep-learning algorithms for predicting a wide range of intraoperative vital sign deviations by analysing vital sign data streams collected during surgery. First, the recurrent neural network models perform a regression task predicting the respective vital sign as a continuous value, then we compare the predicted value against upper and lower vital sign limits, so that the result of the algorithm indicates the corresponding vital sign value as too high or too low. Tackling the original problem as a regression task with a post-processing step to infer the too low and too high values makes the model training limit-agnostic, thus the overall approach is easy to adjust for different alarm settings. To test the robustness of our method, we resorted to a 10-fold cross-validation procedure for training and internal validation. To test the generalization of the approach, external validation was conducted with the publicly available eICU data set. This data comes from ICU from different countries instead of operation rooms and has lower resolution and poses a great generalization challenge which our models handle successfully.

Results: We used vital sign data streams of 37069 patients recorded with 1/60Hz and 1Hz resolution to train, validate and test the models. We considered 13 vital signs including Temperature (Temp), Heart rate (HR), Pulse rate (PR), ST-segment deviation (ST-segment), Invasive arterial blood pressure (IABP), Central venous pressure (CVP), Respiratory rate (RR), Tidal volume (TV), End-tidal CO2 concentration (etCO2), Train of four ratio (TOF%), Bispectral Index<sup>®</sup> (BIS), Oxygen saturation (SpO2), Non-invasive arterial blood pressure (NIABP). NIBP is only available for low resolution 1/60Hz data set. Internal and external validation showed good results of almost all models. Our models could predict vital sign deviations in both directions, i.e., too high and too low, 20 seconds in advance, for all 12 vital signs available in 1Hz resolution with a balanced accuracy of >0.8. Five minutes in advance, our models still predicted ten of the 13 vital signs in both directions with a balanced accuracy of >0.8. For the external data, our models predicted all eight available vital signs (Temp, SpO2, HR, RR, ST-segment, IABP, CVP, etCO2) in both directions 25 minutes in advance with a balanced accuracy >0.8.

Conclusions: This study is the first to provide deep learning models for a wide range of vital sign forecasts and alarm predictions, which may form the basis for a meaningful decision support tool that could assist surgeons and anaesthesiologists in everyday clinical practice. Such a tool would be ideally employed inside a patient monitor, where the required input data is constantly available.

### PA30 Elucidating the role of Klarsicht in Drosophila tracheal remodelling Elena Savvidou, Chloe Antoniou, Evi Yianni, Nikoletta Kizh, Chrysoula Pitsouli

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Sprouting angiogenesis and tracheogenesis are homologous branching morphogenesis processes of the vertebrate's vasculature and the Drosophila's tracheal system, respectively. During branching morphogenesis, specialized cells lumenize forming subcellular seamless tubes. Well-characterised examples include the terminal cell tubes of the Drosophila tracheal system (TTCs) and the seamless endothelial cell tubes of the vertebrate vascular system. The extension of extra branches from those tubes, is oxygen dependent, a process that is regulated by the conserved Hif1 signalling cascade. How these tubes are formed, shaped and maintained remains poorly understood. A Drosophila population genetics screen assessing TTC remodelling under hypoxia identified klarsicht (klar) as a regulator of branching. Tracheaand TTC- specific silencing of klar leads to increased TTC branching in the fly larva in normoxia. Interestingly, although TTCs induce their branching in response to hypoxia, klar-silenced TTCs do not respond further indicating that the gene might be linked to the conserved Hif-1a hypoxia response pathway. klar encodes a KASH-domain protein, which has been shown previously to coordinate microtubule-based transport in embryos, salivary glands, muscles and photoreceptors but its function has not yet correlated with trachea. We propose to use a combination of genetic, molecular and imaging approaches, to uncover a novel function of Klar in TTCs and seamless tube morphogenesis during physiological and low oxygen levels. The identification of the elaborated TTC behaviour during lumen formation and seamless tube outgrowth, which relies on topological constrains, in the comparatively simple Drosophila tracheogenesis model will contribute to a conceptual framework for elucidating similar processes in the more complex vertebrate system.

### PA31 SARS-CoV-2-specific antibody responses following BNT162b2 vaccination in individuals with Multiple Sclerosis receiving different disease- modifying treatments

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Background: The study aims to evaluate the concentration of IgG antibodies against the receptor-binding domain of the SARS-CoV-2 spike1 protein (S1RBD) in BNT162b2- vaccinated multiple sclerosis (MS) individuals receiving disease- modifying treatments (DMTs). Methods: Serum from one hundred and twenty-six MS volunteers was collected three months after the administration of the second dose of the Pfizer-BioNTech BNT162b2 vaccine. Additional samples were analysed after the administration of the booster dose in fingolimod- treated MS. Anti-S1RBD IgG antibody concentrations were quantified using the ABBOTT SARS-CoV-2 IgG II Quant assay. Findings: Anti-S1RBD IgG antibody concentrations in MS individuals receiving natalizumab, interferons, teriflunomide, and dimethyl fumarate showed no significant difference to those in healthy controls. However, fingolimod- treated MS individuals showed a marked inability to produce SARS-CoV-2- specific antibodies (p<0.0001). Furthermore, a booster dose was not able to elicit the production of IgG antibodies in a large portion of matched individuals. Interpretation: A possible explanation for the altered immune response in fingolimod- treated MS individuals could be due to the medication inhibiting the circulation of lymphocytes, and possibly in turn inhibiting antibody production. Overall, patients on DMTs are generally of no disadvantage towards mounting an immune response against the vaccine. Nevertheless, further studies require evaluating non-humoral immunity against SARS-CoV-2 following vaccination, as well as the suitability of such vaccinations on patients treated with fingolimod.

# PA32 Are zebrafish a good model organism to investigate the involvement of mechanical load in mediating osteoarthritis?

#### **Giorgos Marangos**

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Osteoarthritis (OA) is a chronic degenerative disease of the diarthrodial joint. Despite the plethora of animal models used to study OA, a "goldstandard" model which can effectively recapitulate human OA and allow communication between different tissues of the joint does not exist.

A systematic review was conducted using scientific databases such as Web of Science and PubMed. The extensive evaluation of peer-reviewed primary research articles evaluated the suitability of zebrafish (Danio rerio) for the study of OA, with a particular focus on whether is an appropriate model organism to investigate the involvement of mechanical load in mediating osteoarthritis.

In the last decade, zebrafish have been used to model human diseases as they show conservation of 70% of all genes with humans. In addition, genetic manipulation is more efficient compared to murine models. In terms of skeletal disorders, the zebrafish has been increasingly used to study bone homeostasis in osteogenesis imperfecta.

Recent studies have shown that similar to humans, its spine is anteroposteriorly loaded, and its jaw joint has synovial morphology. It is found that all putative OA genes are expressed in the development of the larvae and of the adult's skeleton. Furthermore, genetic manipulation of these genes in zebrafish alters cartilage morphology similar to that observed in humans. Cartilage deformation, changes in joint morphology, and localization of type II collagen which were successfully observed in col11a2 heterozygous mutant fish exhibit the same alterations that characterize the primary changes which increase OA risk in humans. Moreover, zebrafish have enabled the successful examination of age-related degenerative alterations in the spine and indicated that spinal curvatures' acuteness ameliorates with age.

It is concluded that the zebrafish is a valuable OA model in studying the pathogenesis and genetics of the disease. Investigations have used zebrafish to show that OA risk factors i.e., age and mechanical load can be successfully recapitulated. However, preventive OA therapies have yet to be discovered, hence there is a need to utilize zebrafish to evaluate how potential drugs can delay cartilage degradation, by combining high-throughput screenings and drug discovery approaches that have already been established in this animal model for other human diseases such as diabetes.

# PA33 Optimising adeno-associated viral vector mediated gene delivery to the central nervous system

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Objective: The aim of this study was to evaluate the transduction efficiency of two adeno-associated virus capsids, PHP.eB and AAV9 by examining the expression of an eGFP transgene under a modified CBh promoter in the CNS tissue of mice after intravenous injection and the possible enhancing effect of the shuttle peptide THR to facilitate the ability of the vector to cross the blood-brain-barrier (BBB).

Background: The AAV-PHP.eB capsid has as parental serotype the AAV9, an FDA-approved delivery vehicle for the treatment of SMA. Even though the former differs in a few amino acids of the capsid protein it demonstrates an enhanced BBB permeability facilitated by an endothelial receptor LY6A. The CBh is a strong ubiquitous CNS promoter modified for direct transgene expression in neuronal cells with stable long-term expression. Thus, AAV-PHP.eB is a promising capsid for intravenous administration of the viral vector reaching CNS cells for achieving transgene expression under the modified promoter in neuronal cell populations.

Design/Methods: 1x1012 viral copies of each viral vector construct were injected by lateral tail vein administration either conjugated with the THR-peptide or without in C57BL/6 mice. The outcome was examined at 4 weeks post-injection by immunostaining and VCN analysis of CNS tissue. In addition, liver tissue was evaluated as the main off-target organ.

Results: The AAV.PHP.eB vector construct exhibited CNS tissue wide and robust eGFP expression compared to the AAV9 vector demonstrating minimal eGFP expression at 4 weeks post-injection. Noteworthy, was the viral vector injection site gradient observation with relatively intense transgene expression in the lumbar area and lesser in the cervical. The THR-peptide failed to improve the uptake of either vector constructs through the BBB, while AAV9 showed higher liver uptake in comparison to AAV-PHP.eB.

Conclusions: Low doses of intravenously administered AAV-PHP.eB achieved robust and CNS cell targeted gene delivery offering thereby a significant delivery advantage and thus thera-

peutic benefit in mice expressing the specific receptor.

### PA34 Anticancer activity of σ2 agonist siramesine in pancreatic cancer *Giovanovits N.1, Koutsougianni F. 1, Alexopoulou D. 1, Dimas K. 1*

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Objective: Siramesine, is a  $\sigma^2$  agonist that is reported to show a promising antiproliferative and cytotoxic activity in tumor cells in vitro as well as in vivo. The aim of this study is the investigation of the in vitro activity of siramesine in the human pancreatic cancer cell line PANC-1.

Materials & Methods: We used the methods of SRB cytotoxicity test to determine the GI50, TGI, and LC50 of siramesine against PANC-1, the clonogenic assay, and the wound healing assay to investigate the cytotoxic activity of siramesine, the ability of single cells to make clones, and the ability of the specific cells to migrate when they were exposed to siramesine, respectively. Furthermore, through flow cytometry, we analyzed the viability of siramesine-treated cells and studied the effect of the compound on the cell cycle to investigate if the activity is cell cycle phase-specific.

Results: The data of this study, confirmed that siramesine has a strong antiproliferative and cytotoxic activity under the experimental conditions that have been tested. Moreover, siramesine was found to inhibit the ability of single cells to create colonies and to migrate in a time and dose-dependent manner. The flow cytometry data suggest that siramesine induces cell cycle arrest at the G0/1 phase of the cell cycle.

Conclusions: Siramesine, under the experimental conditions tested herein, exhibits strong anti-clonogenic and anti-migratory activity. Furthermore, we show that the activity of the compound is cell-cycle phase-specific against the PANC-1 cells. These data are reported for the first time worldwide for siramesine. Further studies on the mechanism by which the compound exhibits these effects are ongoing.

# PA35 Toll pathway regulates Drosophila intestinal stem cell mitosis and endoreplication

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The Drosophila midgut is maintained by pluripotent intestinal stem cells (ISCs) that self-renew and give rise to transient enteroblasts (EBs), which will terminally differentiate into polyploid enterocytes (ECs). A common property of differentiating Drosophila cells that need to cope with tissue development and homeostasis is endoreplicative cell growth. Endoreplication is a

recurrent evolutionary innovation for post-mitotic cell growth, which allows cells to replicate their genomes without segregating chromosomes and thereby become polyploid. Compensation for cell death is crucial for tissue maintenance and can occur via two different mechanisms: stem cells divide to produce more cells, and growing ECs increase in size via endoreplication to produce bigger cells. When stem cells are genetically forced to quiescence, by downregulating smvt or npc2c, we observed that spätzle, a ligand of Toll pathway, is induced in the Drosophila midgut. We also observed an increase in nucleus size upon stem cell quiescence. Therefore, we hypothesize that when unable to sufficiently induce stem cell mitosis, regenerative signals invest instead in compensatory endoreplication, with Toll pathway acting as a regulator of this compensatory interplay. We now find that genetic manipulation of Toll in the Drosophila midgut ISCs and EBs affects mitosis and endoreplication, respectively, supporting the role of Toll in the regenerative balance between cell renewal and cell growth.

#### PA36 IMPORTANCE OF BITE MARKS IN FORENSIC ODONTOLOGY

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Introduction: The analyzation of bite marks at crime scenes has been a crucial piece of evidence when it comes to finding a potential biter in criminal cases. A bite mark is the registration of the cutting edges of maxillary and mandibular teeth that can be found on skin, materials, objects, and food elements.2 The role of Forensic Odontology comes into play when investigations need to be conducted to identify individuals. The identification process using bite marks is very challenging, since many factors play a role on it and human dentition is unique between individuals.3 Thus, making the attention to detail essential to Forensic dentists in order to properly analyse the bites. The human bite mark analysis is by far the most demanding and complicated part of Forensic Dentistry. 1

Aim: To establish the importance of bite marks in various criminal scenarios such as sexual assaults, attacks, and crime scenes, as these are essential in the investigative analysis of dental morphology to pinpoint an individual offender.

Materials and Methods: We conducted a comprehensive electronic database search using various reliable data source: (PubMed, Google Scholar, NCBI, ScienceDirect, etc.) with the keywords: forensic odontology, forensic dentistry, bite marks, dental identification to establish a protocol into the subject.

Discussion-Conclusion: The importance of dental morphology is often overlooked, as many limit the human dentition to inside only the clinic cases walls. Dental morphology plays a larger and more important role outside the clinic as well, especially in solving violent crimes that drastically change the lives of individuals. Despite the challenging nature of bite marks in forensic dentistry, when evidence is analysed in a correct and extensive matter, it can be decisive to identify and give proofs for incrimination in various scenarios.

#### Citations

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(2) Hinchliffe, J. (2011). Forensic odontology, part 4. Human bite marks. British dental journal, 210(8), 363-368.

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### PA37 Kinetics and impact of the SARS-CoV-2 Omicron Variants BA.1 and BA.2 in Cyprus

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Over the past 2 years, the world has witnessed several waves of SARS-CoV-2 infection, usually associated with the emergence of new viral variants labelled 'variants of concern' (VOCs) many of them involve an unusually large number of defining mutations that impact critically their transmission, immune evasion or severity. By November 2021, the Delta VOC had outcompeted most pre-existing variants of SARS-CoV-2 being the predominant variant with more than 100 sub-lineages circulating, when the Omicron variant (B.1.1.529) appeared and rapidly advanced to replace Delta worldwide. Aim of this study was to investigate and obtain insight into the appearance, the spread and impact of the Omicron variant and their sub-lineages in Cyprus by analysing 611 high-coverage full genome sequences for the period from November 2021 until April 2022. All viruses sequenced were identified to belong to either Delta (B.1.617.2) or Omicron (lineage BA.1 and BA.2, respectively). Within the Delta lineage, 17 different sub-lineages were distinguished, with the AY.43, AY.122 and AY.4 being the most frequently encountered. The BA.1 and BA.2 lineages identified consisted of 14 and 6 sub-lineages, respectively, with BA.1.1, BA.1, BA.1.17.2 and BA.2, BA.2.9 being the most common sub-lineages encountered. The Omicron variant BA.1 emerged at the beginning of December 2021 in a background of high vaccination (81% of adult population) and pre-existing natural immunity giving rise to the largest wave of infections with daily numbers skyrocketing confirming its increased ability for immune evasion reflecting the selection pressure exerted by previous vaccination and natural infection. It was shortly followed by the BA.2 variant and its sub-lineages in a pattern that was observed in many countries around the world. Within a period of only five months the percentage of the Cypriot population with a confirmed infection increased from  $\sim$ 15% of total population to >57%. Despite unprecedented case numbers, a significant reduction of hospital burden and mortality was observed. Our findings highlight

the role of importation of new variants through travel towards the emergence of successive waves of incidence in Cyprus and demonstrate the importance of genomic surveillance in determining viral genetic diversity and the timely identification of new variants for guiding public health intervention measures.

# PA38 Extracts from near-endemic Onosma Fruticosa (Cyprus) show cytotoxic activity against human MCF-7 breast cancer cells: preliminary data

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Background: Emerging experimental data supports the ability of natural products to intervene in complicated molecular pathways associated with pathogenesis of certain human morbidities, including cancer. Indeed, numerous plant-derived compounds or their derivatives are now in the forefront of chemotherapeutics, showing beneficial effects for cancer patients. Assessment of newly discovered plant products are expected to significantly enrich the anticancer armamentarium. Among them, Onosma sp. have been shown to possess anti-cancer properties. Aim: To investigate the possible anti-cancer capacity of near-endemic Onosma fruticosa of Cyprus in human breast cancer cells. Methods: O. fruticosa plants were collected from different altitudes (Koilani, and Pera Oreinis ground herba) using water as extraction solvent. Their cytotoxic activity was tested using the MTT method on MCF-7 human breast cancer cells, in a range of concentrations (2.5-12.5 mg/ml) at 24 and 48 hours. Cisplatin (30µM) was used as positive control. Results: From all extracts tested, "stem extract from Pera Oreinis" showed cytotoxic activity against MCF-7 cells in a dose- and time dependent-manner (t-test vs untreated cells: p<0.005, linear correlation mg of extract vs % cell viability: Pearson r=-0.9385, p=0.06) and "stem extract from Koilani" significantly decreased cell viability (t-test vs untreated cells: p<0.05). Discussion/Conclusion: Our preliminary data indicated the possible anti-cancer properties of O. fruticosa (Cyprus). Further investigation is needed to evaluate the potential of these extracts to be incorporated in current anti-cancer treatments.

# PA39 Large-scale sequencing of 34 putative susceptibility genes in Cypriot female breast cancer cases

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Introduction: Germline pathogenic variants (PVs) in cancer-susceptibility genes have been associated with an elevated risk of breast cancer. Individuals carrying PVs can benefit from risk management strategies including closer surveillance at an earlier age, prophylactic surgery and targeted therapies. It is estimated that around 7 to 10% of women with breast cancer carry a PV in a cancer susceptibility gene. However, the prevalence of PVs and the associated risk estimates of breast cancer among the Cypriot population are currently unknown.

Aims: Herein, we aimed to investigate the prevalence of protein-truncating variants (PTVs) and rare missense variants in a large series of breast cancer cases and controls in Cyprus.

Methods: Using the BRIDGES panel, we performed targeted panel sequencing on 34 established and suspected breast cancer susceptibility genes on case-control samples from the MASTOS cohort, a population-based case-control study of breast cancer in Cyprus. The cohort includes 990 breast cancer cases unselected for family history of breast and/or ovarian cancer or age at disease diagnosis and 1,094 aged-matched healthy controls. Details on library preparation, sequencing, variant calling and classification are provided in the main BRIDGES paper.

Results: The prevalence of PTVs in established breast cancer risk genes was 3.6% among cases and 0.4% among controls. Among the patients, the highest prevalence of PTVs was observed for BRCA2 (1.8%), ATM (1.0%), PALB2 (0.5%) and BRCA1 (0.3%). We further detected 285 and 266 unique rare missense variants among cases and controls, respectively.

Discussion: Here, we report the prevalence of PTVs and rare missense variants in established breast cancer–predisposition genes among the Cypriot population. We further aim to explore the associated estimates of breast cancer risk.

### PA40 MUTATION-SPECIFIC CORRECTION OF HBBIVS1-110-THALASSEMIA USING HBBBAS3 GLOBE-BASED MIR30-SHRNA EXPRESSION VECTORS

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Ex vivo gene therapy based on autologous hematopoietic stem cells (HSCs) represents a promising the rapeutic approach for  $\beta$ -thalassemia patients. However, particularly for gene addition of  $\beta$ -globin transgenes by lentiviral vectors (LVs), treatment success is genotype-dependent. Addressing this shortcoming we have previously shown that for the aberrantly spliced HBBIV-SI-110(G>A) mRNA, mutation-specific shRNA expression can achieve substantial phenotype correction as monotherapy and enhanced therapeutic effect in combination with  $\beta$ -globin gene addition (Patsali et al. 2018). In the present study and toward clinical exploitation of this phenomenon, we thus express HBBIVSI-110(G>A)-specific miRNA30-embedded shRNAs (miR30shRNAs) from the  $\beta$ -globin promoter, either alone or from intron 2 of a same-vector anti-sickling HBBBAS3 transgene in derivatives of the clinically relevant GLOBE LV. Evaluation of the ability to restore  $\beta$ -globin expression in HBBIVSI-110(G>A)-transgenic cells shortlisted erythroid-specific RNApolII-driven miR30shRNA expression or single-vector, combined miR-30shRNA/HBBβAS3 expression strategies for analysis in primary patient-derived HSCs. This showed that erythroid-specific RNApolII-driven designs for isolated expression of HBBIV-SI-110(G>A)-specific miR30shRNAs only marginally increased  $\beta$ -globin levels compared to parental GLOBE LV. However, some LV designs for combined miR30shRNA/HBBBAS3-expression showed significant improvement of  $\beta$ -/ $\alpha$ -globin ratios in HBBIVSI-110(G>A)-transgenic cells. Our results highlight the therapeutic potential of mutation-specific synergistic strategies combining miR30shRNA and protein expression for HBBIVSI-110(G>A) β-thalassemia.

#### GLOBE AS32

miR30-shRNA expression cassette3which can be processed from small hairpin RNAs generated from an expression vector. In some recently described vectors, the siRNAs are expressed from synthetic stem-loop precursors of microRNAs (miRNAs

1.Patsali, P. et al. Short-hairpin rna against aberrant HBB IVSI-110(G>A) mRNA restores  $\beta$ -globin levels in a novel cell model and acts as mono-and combination therapy for  $\beta$ -thalassemia in primary hematopoietic stem cells. Haematologica vol. 103 e419–e423 (2018).

PA41 IL-37e levels associate with development of type-2 diabetes and metabolic syndrome: preliminary data

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Background: Type 2 diabetes mellitus (T2D) is a metabolic disorder with growing cardiovascular mortality, associated with chronic inflammation in pancreatic islets and insulin-sensitive tissues. T2D immune microenvironment is characterized by increased incidence of macrophages, B cells, Th1, Th2, Th17, and cytotoxic T cells and secretion of pro-inflammatory cytokines. IL-37 is a novel cytokine with regulatory properties expressed mainly by innate immune cells and B cells. Its implication in T2D-associated inflammation has not been explored. Aim: To investigate the expression pattern of IL-37 and its specific isoforms (a-e) in patients with T2D and pre-diabetic individuals. Methods: cDNA was reverse transcribed from RNA samples extracted from whole blood of 22 T2D patients and 18 controls. Specifically developed gPCR assays for each IL-37 isoform were applied. Results: Among all isoforms, IL-37e exhibited increased expression in patients (mean±SE: 10.11±4.018) versus controls (0.2186±0.1219: Mann-Whitney. p=0.039). More interestingly, there was a linear trend of increase in IL-37e levels following the order: controls without risk factors for the disease  $(0.1616\pm0.1577, n=8) \rightarrow$  controls with T2D risk factors (1.749 $\pm$ 1.051, n=10; Jonchkeere-Terpstra p=0.048)  $\rightarrow$  T2D patients. Discussion/Conclusion: Our preliminary data indicate the possible differential distribution of IL-37e in patients with T2D and pre-disposed individuals. Ongoing experiments in larger cohorts are expected to validate this observation, and also pinpoint the association of IL37e expression pattern with T2D-specific pro- and anti-inflammatory cytokine mRNA signatures as well as with clinicopathological features of the disease. Future studies may reveal the involvement of this cytokine in the regulation of T2D inflammatory responses and involvement in disease's pathophysiology.

### PA42 Impact of Adiposity on Serum Calcitonin in Patients with Thyroid Nodules

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Background: Thyroid nodules are extremely common in the general population. Calcitonin is a hormone produced by the parafollicular thyroid C-cells and is elevated in patients with medullary thyroid carcinoma (MTC). However, as elevated calcitonin can also be found in benign

conditions, its use as a screening tool for MTC in patients with thyroid nodules remains controversial. Obesity is also extremely common. The most widely used measure for measuring obesity is Body Mass Index (BMI). Studies that examined the relation between calcitonin and BMI reported conflicting results. Elevated levels of calcitonin may have an involvement in lipid and glucose metabolism regulation. There are no studies published so far, that specifically examined the association between BMI, thyroid nodules and elevated calcitonin.

Methods: A retrospective cohort study of 604 consecutive patients (138 males and 466 females) with thyroid nodules who underwent a comprehensive clinical evaluation and a thyroid ultrasound examination with a GE Logiq E9 system. Calcitonin levels were measured in all patients. The patients were categorized according to their BMI into two groups: normal (BMI < 25 kg/m2) and overweight with obese (BMI  $\geq 25 \text{ kg/m2}$ ). BMI was calculated for each patient by measuring the weight and height at the first evaluation appointment.

Results: The normal weight group (BMI < 25 kg/m2) included 264 patients, while the overweight and obese group (BMI  $\ge$  25 kg/m2) consisted of 340 patients. Overweight and obese patients had significantly higher levels of calcitonin compared to normal-weight patients.

Conclusion: In patients with thyroid nodules, adiposity is associated with elevated levels of calcitonin. Further studies are needed to examine this association and provide more insight into the possible mechanisms involved.

| Clinical characteristics   | BMI < 25 (n= 264) | BMI ≥ 25 (n=340) | P-value |
|----------------------------|-------------------|------------------|---------|
| Gender                     |                   |                  |         |
| Male (n, %)                | 27 (10.2%)        | 108 (31.8%)      | 0.00    |
| Female (n, %)              | 237 (89.8%)       | 232 (68.2%)      |         |
| Age (years, mean ± SD)     | 42.2 ±13.8        | 50.9 ±13.6       | 0.00    |
| Elevated Calcitonin levels | 7 (2.7%)          | 25 (7.4%)        | 0.01    |

# PA43 HBBIVSI-110(G>A)-SPECIFIC GENE EDITING AS ADVANCED THERAPY FOR $\beta$ -THALASSEMIA

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 $\beta$ -Thalassemia is brought about by defective  $\beta$ -globin (HBB) formation and in severe cases requires regular blood transfusion and iron chelation for survival. Genome editing allows cor-

rection of underlying mutations as therapy. As potentially safer alternatives to double-strand break (DSB)-based editors, base editors (BEs) catalyse base transitions (cytosine BEs: C>T, adenine BEs: A>G) for precision editing of DNA target sites. Four recently published BEs with relaxed protospacer adjacent motif (PAM) requirements are being evaluated for their ability to correct the common Cypriot HBB[IVSI-110(G>A)] splice mutation.

BEs were obtained from Addgene and the T7 promoter inserted to allow in vitro mRNA transcription. Editors were delivered into primary hematopoietic cells by nucleofection. Additionally, HBB-deficient cell models were created by DSB-based editing and plate-sorted on a BD FACSAria III for clonal isolation. DecodeR and EditR were used to assess DSB-based and base editing efficiencies, respectively, at the DNA level. HPLC and immunoblot analyses after erythroid differentiation were used for measurements at the protein level.

BEs were designed for three strategies, i.e. editing of (i) the mutated A, (ii) the G of the aberrant AG splice motif, or (iii) upstream sequence elements critical for aberrant splicing. In the process, efficiency of the ABEs for HBB[IVSI-110(G>A)] target sites was confirmed, including by correction of  $\beta$ -globin expression, and removal of the GFP reporter doubled on-target efficiency for the SPRY BE. Finally, to facilitate further analyses, DSB-based precision editing of HUDEP-2 cells was applied to create HBB[IVSI-110(G>A)]-homozygous cell models, displaying characteristically decreased HBB, and same-site deletion models.

PA44 New ethical challenges facing clinicians in the digital era: the paradigm of a clinical trial using AI-enabled tools for remote heart-failure patient monitoring and management.

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Introduction: Chronic Heart Failure (HF) is a major cause of disability and premature death throughout the world. Although the exploitation of e-health technological advancements might provide promising solutions regarding HF patient management -aimed at reducing mortality and hospitalisation rates and improving the quality of life of HF patients, more research needs to be conducted to validate these potentials. Motivated by a use case of an ongoing H2020 research project (RETENTION, GA965343) that will develop an Artificial Intelligence (AI)-driven platform to support outpatient monitoring and management of HF patients, this paper provides an overview of the ethical challenges associated with the conduction of relevant randomized controlled trials (RCTs), based on a literature review.

Method: Our perspective in conducting this review stems from an ethics-by-design approach, aimed at providing useful insights to both clinicians and developers designing and conducting said RCTs. The framework under which the selected ethical concerns were analysed included

the fundamental principles of bioethics and relevant sector-specific guidelines and regulations.

Results: The examined ethical challenges ranged from traditional medical ethics issues that needed to be revisited in the context of the trial's particularities to prevalent issues that derive from the data-driven nature of the supporting technology (concerning amongst other data privacy and security, training data integrity and quality). Of important relevance to the project were complex issues related to ensuring transparency and human oversight on the operation of the AI component, along with reflections on the potential negative effects of the introduction of AI in healthcare. Although the employment of such tools may empower patients through active participation in their care plan, it may disrupt processes of shared decision-making, in ways that could deeply affect the quality of life and influence the personal experience of health. Issues such as potential overreliance on the platform by patients and clinicians or imposition of burdensome routines were also considered, as issues that could result in harming the participating patients and/or compromise the results of the RCT. Wider socioethical concerns in the relevant literature further focused on equal access, non-discrimination, and fair data-sharing.

Conclusion: To develop trustworthy and patient-centered technological solutions in the healthcare sector, clinicians need to revise their traditional thinking regarding ethics appraisal, whereas interdisciplinary collaboration and awareness-raising discussions between law, bio-ethics, computer science and medical experts are urgently needed.

# PA45 Quercus alnifolia leaves as a source of phytochemical compounds with potential anticancer properties

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Quercus alnifolia is an endemic oak species of Cyprus, which grows on the ultrabasic rock formations of Troodos at an altitude range between 400 to 1800 meters. Q. alnifolia is morphologically and genetically distinct from other related species. Published studies focus on its morphological and genetic characteristics. Remarkably, there is no available research on this species regarding its phytochemical composition and the potential properties of its extracts. Aim: The aim of this study was to investigate the phytochemical composition of Q. alnifolia

leaves, and how they differ in relation to the location (different altitudes) and the maturity stage of the leaves. In addition, it aimed to identify anti-cancer properties of the most promising extracts based on the phytochemical composition. Methods: Sampling took place in the period of August-September 2021 at different altitude locations of the island (Kionia 1300 m, Platres 1700 m, Tripilos 1200 m) and sampled plant individuals were selected based on environmental exposure factors. Young (gold abaxial) and mature (brown abaxial) leaves were harvested, and a series of phenotypical macroscopic observations and phytochemical analyses were conducted. The phytochemical composition was appraised by measuring the total content of phenolics, flavonoids, condensed tannins and the in vitro antioxidant activity. Moreover, a preliminary examination of their anti-cancer activity using the MTT assay on the MCF-7 breast cancer cell line was performed. For the anticancer properties were used young leaves extracts from the tree numbers 5 and 6 of Kionia area and the tree number 12 of Tripilos area. Results: The morphological characteristics of the leaves substantially varied among the harvested plants. Phytochemical analyses showed statistically significant differences between the mature and young leaves, while differences among harvest locations were limited. Young gold leaves showed higher levels of antioxidant activity and total phenolics compared with mature brown leaves. Flavonoids and tannins displayed similar trends with higher values recorded for the brown mature leaves of Platres and Tripilos. MTT assay preliminary results indicated that the three selected extracts (in the concentration of 2 mg/ml) can significantly reduce MCF-7 cell viability (by 38.17-54.45%). Conclusion: The results of this preliminary study contribute to unravelling the undiscover phytochemistry and potential anticancer properties of Quercus alnifolia leaf extracts.

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### PA46 Genome Editing for Beta-Haemoglobinopathies Without Double-Strand DNA Cleavage

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Background/Objectives: Haemoglobinopathies, such as sickle-cell disease and  $\beta$ -thalassaemia, are the commonest monogenic diseases. Of these,  $\beta$ -thalassaemia has high prevalence in Cyprus and is marked by low adult haemoglobin ( $\alpha 2\beta 2$ , HbA), owing to defective  $\beta$ -globin (HBB) expression. Increased levels of foetal haemoglobin ( $\alpha 2\gamma 2$ , HbF) can ameliorate the severity of

the disorder and may be achieved by erythroid reduction of  $\gamma$ -globin repressors, such as the transcription factor BCL11A. While corresponding clinical trials are currently based on double-strand-break (DSB)-dependent CRISPR/Cas editors, DSB-independent base editors (BEs) may instead be employed as safer and likely more efficient tools for curative  $\gamma$ -globin induction. Mindful of the high clinical potential of BE technology, this study aims to adopt the newest generation of BEs for application to targets of relevance for  $\beta$ -haemoglobinopathies.

Methods: Based on in silico design of target- and platform-specific guide RNAs (gRNAs) and on mRNA/gRNA delivery of BE technology in HUDEP-2 and patient-derived CD34+ cells by nucleofection, this study modified therapeutic targets for  $\beta$ -haemoglobinopathies. In the process, editing efficiencies and functional parameters at the DNA, RNA and protein level were measured in comparisons of different BEs against one another and against ribonucleoprotein (RNP)-based delivery of CRISPR/Cas DSB-based technology targeting the well-known BCL11A erythroid enhancer. To achieve higher HbF levels, a duplex base editing strategy was established targeting both and trans-acting factors and cis-acting elements.

Results: Establishment of in vitro mRNA synthesis for mRNA/gRNA-based delivery of BEs allowed efficient, non-toxic BE delivery. Our data indicate differential same-target efficiency of different BEs for the clinically relevant BCL11A target, with peak precision editing of 86% bulk efficiency for the BE4-PpAPOBEC1 BE in HUDEP-2 cells. Duplex base editing in patient-derived CD34+ cells of both, trans-acting factors (BCL11A) and corresponding cis-regulatory elements (HBG), resulted in 1.8-fold elevated HbF induction compared to simplex edits and in up to 60% increase of HbF levels compared to baseline. Moreover, duplex BE application resulted in 70% contribution of HbF to total hemoglobin compared to 60% for DSB-based editing technology, at vastly decreased risk of genome recombination events.

Conclusions: The present study demonstrates high efficiency, low toxicity and superior editing outcomes of RNA-based delivery for base editing technology compared to the clinically applied RNP-based DSB-mediated editing standard. In particular duplex editing of BCL11A as therapeutic target resulted in superior editing outcomes compared to simplex BE and DSBbased editing application, and to superior, therapeutically relevant HbF induction.

# PA47 Evaluation of induction of fetal hemoglobin synthesis by genome editing of cis- and trans-acting components of the $\beta$ -globin locus

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The reactivation of y-globin can ameliorate the clinical phenotype of  $\beta$ -hemoglobinopathies by functional compensation of  $\beta$ -globin deficiency and anti-sickling action of fetal hemoglobin (HbF). Most importantly, it constitutes a universal therapy approach that can potentially be applied to all βhemoglobinopathy patients, irrespective of genotype. This work focuses on genetic modification of globin expression regulators and the  $\beta$ -globin locus as potential therapeutic approaches for  $\beta$  hemoglobinopathies by reactivation of y-globin. To this end, we employ the clustered regularly interspaced short palindromic repeat (CRISPR)/CRISPR-associated protein 9 (Cas9) system to abolish expression of two known y-globin gene repressors, BCL11A and ZBT-B7A (trans editing), and a dual targeting single RNA-guided CRISPR/Cas12a system to create a large (7.4-kb)  $\beta$ - $\delta$  intergenic deletion at the  $\beta$ -globin locus (cis editing). Tools are delivered as ribonucleoprotein (RNP) complexes by nucleofection of human umbilical cord blood-derived erythroid progenitor-2 (HUDEP-2) cells and primary thalassemic CD34+ cells. Edited cells are assessed for on-target editing efficiency and analysed for globin expression after induction of erythroid differentiation, by reversed-phase high performance liquid chromatography (RP-HPLC) and immunoblotting. Subpopulations of high and low HbF-expressing cells within each bulk population of edited cells are isolated by fluorescence activated cell sorting (FACS) and analyzed for differential editing levels by Inference of CRISPR Edits (ICE) and digital polymerase chain reaction (dPCR). Preliminary results of the study suggest that generation of the 7.4-kb cis deletion at the  $\beta$ -locus, relying on the highly efficient non-homologous end-joining (NHEJ) repair mechanism of double-strand breaks (DSBs), may lead to higher HbF levels than the disruption of trans-acting components also involved in other essential functions of hematopoiesis, as are the γ-globin repressors BCL11A and ZBTB7A. A direct comparison of tools in clones of edited cells is underway to confirm findings in bulk populations.

# PA48 High levels of IL-37 in patients with bladder urothelial cancer: a favorable prognostic factor for overall survival

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Background: Bladder cancer (BLCA) is a common malignancy in humans, accompanied by high mortality rates and management costs. Immune system plays pivotal role in the development

and progression of BLCA, while immunotherapy is considered as one of the most promising treatment approaches for the patients. Aim: To explore the potential of IL-37, a novel cytokine with immunoregulatory properties and its specific isoforms, as a biomarkers in human bladder cancer. Methods: We utilized a series of bioinformatics tools and -omics datasets to unravel possible associations of IL-37 expression levels, with tumor development, histopathological characteristics, and survival rates of patients. We also used specifically developed qPCR assays to investigate the expression profile of the five IL-37 isoforms (a-e) on human bladder cancer cell lines (T24 και RT4) and tumor biopsies. Results: TNMplot revealed that IL-37 mRNA levels are significantly higher in BLCA tumors (n=411), compared to non-BLCA bladder biopsies (n=30; fold-change=44, p=1.44x10-10) or adjacent normal tissues (n=19; fold-change=35, p=0.0023). Importantly, high IL-37 levels correlate with better overall survival (OS) of patients [HR=0.69 (0.51-0.94), p=0.0176] (Kaplan-Meier Plotter). Preliminary qPCR experiments on the T24 και RT4 cell lines and bladder cancer biopsies (n=3) detected the expression of IL-37c and e isoforms. Discussion/Conclusion: Our data indicate, for the first time, the BLCA-specific expression pattern of IL-37 and highlight the need for further study of its specific variants as potential biomarkers in large patient cohorts. They also suggest future research to fully elucidate the underlying pathogenetic implication of IL-37 in BLCA development and progression, as well as its value as a possible therapeutic target.

#### PA49 A Systematic Review Radar Based Human Vital Signs Detection Methods

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Continuous monitoring of vital sign parameters heart and respiration of the individuals health can be more beneficial if prior health status or information is available to avoid some major happening occur to the person. Sensing of vital sign can be done any of the two techniques available i.e. contact and other is noncontact based. Contact based technique is conventional method of detecting the vital signs which may not be convenient for long time use in all types of affected patients. Some patients due to their movement may be older or child for long time use skin irritation or allergy problem may occur and so unable to get connected continuously. On the other hand some patients may be COVID-19 infected disease and burn patients etc is not possible to connect as both case are unexpected for the required purpose. This paper presents a state-of-the-art review of recent monitoring methods and signal processing techniques for health monitoring in medical fields of operations. These methods and techniques are used as a tool to acquire, visualize and analyze the sampled data collected in any environment either indoor or outdoor.

Keywords: Healthcare, non contact, Doppler radar, continuous wave, techniques and methods, vital sign detection, biomedical, respiration and heart beat detection

# PA50 Increased L-dopa treatment efficacy by targeting Enterococcus faecalis in the gut

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The primary medication used to treat Parkinson's disease is levodopa. To be effective, levodopa must enter the brain where it is converted to the neurotransmitter dopamine by the human enzyme aromatic amino acid decarboxylase (AADC). However, levodopa decarboxylation also occurs in the periphery with the gastrointestinal tract being a major site for levodopa decarboxylation. Dopamine generated in the periphery cannot cross the blood-brain barrier and consequently a large proportion of levodopa does not reach the brain. Multiple lines of evidence suggest that gut microbial interactions with levodopa influences the outcome of treatment. A recent study identified the gut commensal Enterococcus faecalis as being involved in the metabolism of levodopa to dopamine via the enzyme tyrosine decarboxylase (TyrDC). The metabolic conversion by Enterococcus faecalis results in reduced bioavailability of levodopa. The goal of our study is to determine whether the targeted reduction of Enterococcus faecalis in the gut through the use of bacteriophages can lead to a decrease in peripheral levodopa decarboxylation and consequently an increase in bioavailable levodopa.

## PA51 Oct4 interactions and associated functions are modulated by the presence of HPV E7 in cervical cancer.

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Abstract: The stem cell-related transcription factor Oct4 has well-defined roles in embryonic development and has recently been implicated in the process of carcinogenesis. However, the postnatal function of Oct4 is poorly understood. We and others have shown that Oct4 is expressed in cervical cancer and its expression is elevated in HPV-associated cancers. The upregulation of Oct4, as well as its proliferation-associated phenotypes in cervical cancer, are in part linked to an interaction between Oct4 and the E7 oncoprotein of HPV. We hypothesised

that the diverse Oct4 mediated outcomes in HPV+ and HPV- cervical cancer cells are attributed to different Oct4-protein interactions. Hence, to identify Oct4 interactors we used proteomic and bioinformatic approaches. Mass spectrometry and bioinformatics data have revealed several members of the NuRD (Nucleosome Remodelling and Deacetylase) complex as potential interactors of Oct4 in cervical cancer cells. We have validated these protein-protein interactions using co-immunoprecipitation. Interestingly, we have found that different members of the NuRD complex interact with Oct4 in the presence and absence of E7. In HPV- cancer cells Oct4 interacts with the Mbd2-NuRD variant whereas in the context of E7 expression, Oct4 immunoprecipitated with the Mbd3-NuRD variant. To further investigate the role of Mbd2 and Mbd3 in Oct4-mediated transcriptional changes and phenotypes in cancer cells, we used knockdown strategies and a pharmacological inhibitor targeting the function of Mbd2. We found that by knocking down or chemically inhibiting the function of Mbd2 in cells where E7 is absent, cellular viability decreases. We thus propose that in the presence or absence of E7, Oct4 interacts with distinct NuRD variants and this might explain the diverse functions of Oct4 in different cellular contexts.

# PA52 Signatures of co-deregulated genes and their transcriptional regulators in kidney cancers

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There are several studies on the deregulated gene expression profiles in kidney cancer, with varying results, depending on the tumor histology and other parameters. None of these however, has identified the networks that the co-deregulated genes (co-DEGs) across different studies, create. Here we reanalyzed 10 GEO studies to detect and annotate co-deregulated signatures across different subtypes of kidney cancer, or in single-gene perturbation experiments in kidney cancer cells and/or tissue. We aimed at deciphering the networks that they form along with their upstream regulators, using a systems biology approach. Differential expression and upstream regulators, including transcription factors (MYC, CEBPD, RELA, ZMIZ1, NELFE and KLF4) and protein kinases (CSNK2A1, MAPK1, MAPK14, SIRT1, CDK1, CDK4, HIPK2 and ERK1/2), were computed using the Characteristic Direction as well as GEO2Enrichr and X2K, respectively, and further subjected to GO and KEGG pathways enrichment analyses. Furthermore, using CMap, DrugMatrix and the LINCS L1000 chemical perturbation databases. we highlight putative re-purposing drugs, including Etoposide, Haloperidol, BW B70C, Triamterene, Chlorphenesin, BRD-K79459005 and  $\beta$ -Estradiol 3-benzoate, among others, that may reverse the expression of the identified co-DEGs in kidney cancers. Overall, we identified critical co-DEGs across different subtypes in kidney cancer and our results provide an innovative

framework for their potential use in developing personalized therapeutic strategies.

### PA53 Distinct genomic features across cytolytic subgroups in skin melanoma. Roufas C 1, Georgakopoulos-Soares I 2, Zaravinos A 1,3.

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Skin melanoma is a highly immunogenic cancer. The intratumoral immune cytolytic activity (CYT) reflects the ability of cytotoxic T and NK cells to eliminate cancer cells, and is associated with improved patient survival. Despite the enthusiastic clinical results seen in advanced-stage metastatic melanoma patients treated with immune checkpoint inhibitors, a subgroup of them will later relapse and develop acquired resistance. We questioned whether CYT associates with different genomic profiles and thus, patient outcome, in skin melanoma. We explored the TCGA-SKCM dataset and stratified patients to distinct subgroups of cytolytic activity. The tumor immune contexture, somatic mutations and recurrent copy number aberrations were calculated using quanTIseq, MutSigCV and GISTIC2. Chromothriptic events were explored using CTLPScanner and cancer neoepitopes were predicted with antigen garnish. Each tumor's immunophenoscore was calculated using Immunophenogram. Mutational signatures and kataegis were explored using SigProfiler and compared to the known single or doublet base substitution signatures from COSMIC. Metastatic skin melanomas had significantly higher CYT levels compared to primary tumors. We assessed enrichment for immune-related gene sets within CYT-high tumors, whereas, CYT-low tumors were enriched for non-immune related gene sets. In addition, distinct mutational and neoantigen loads, primarily composed of C > T transitions, along with specific types of copy number aberrations, characterized each cytolytic subgroup. We found a broader pattern of chromothripsis across CYT-low tumors, where chromosomal regions harboring chromothriptic events, contained a higher number of cancer genes. SBS7a/b, SBS5 and SBS1 were the most prevalent mutational signatures across both cytolytic subgroups, but SBS1 differed significantly between them. SBS7a/b was mutually exclusive with SBS5 and SBS1 in both CYT subgroups. CYT-high patients had markedly higher immunophenoscore, suggesting that they should display a clinical benefit upon treatment with immune checkpoint inhibition therapy, compared to CYT-low patients. Overall, our data highlight the existence of distinct genomic features across cytolytic subgroups in skin melanoma, which might affect the patients' relapse rate or their acquisition of resistance to immune checkpoint inhibition therapies.

# PA54 Epigenetic regulation of Notch signaling in spontaneous intestinal dysplasia during aging

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Intestinal stem cells (ISCs), a shared feature of mammalian and insect intestine, are the tumor-initiating cells for most sporadic colorectal cancer cases. In the Drosophila midgut, Notch signaling loss inhibits stem cell differentiation and leads to tumorigenesis. Interestingly, tumor formation preferably occurs in the posterior regions of the midgut, while in anterior regions tumors are rarely detected. The distribution of hot and cold-spots of forming tumors within the same tissue is not genetically driven suggesting that ISCs have intrinsic properties that make them more prone to dysplasia under stress conditions. Previous work has focused on investigating the role of stem cell proliferation in carcinogenesis but failed to address the epigenetic impact of stem cell differentiation deregulation in dysplasia and tumor onset. We hypothesize that ISCs found in tumor hot-spots are epigenetically predisposed to cell fate reprogramming towards enteroendocrine (EE)-cell fate route and formation of dysplastic clusters of mixed cell type identity. This results in DNA damage and tumor formation upon aging. By using a combination of high-throughput genome-wide experiments and physiological studies, we show that components of the Notch signaling pathway and genes involved in DNA damage and repair present differences in expression between tumor hot- and cold-spot areas. Importantly, we find evidence for potential crosstalk between Notch-induced dysplasia and the level of DNA damage. Moreover, we are exploring the impact of chromatin-modifying proteins of Polycomb and Trithorax groups in shaping dysplasia in both sexes. Our work aims to provide novel insights into how normal stem cells are predisposed to dysplasia early in life, except for genetic predisposition, when others are resistant and how they transition into tumor phenotypes later in life. Hence, the exploitation of related regulatory pathways constitutes an attractive target

to prevent tumor onset in early stages of tumorigenesis.

PA55 Natural Bio-Molecules as Add-Ons in Cancer Chemotherapy Promoting Anti-Tumor Immunity

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Advancements in chemotherapy and tumor ablation, both principal treatments modality for cancer, have increased patient survival. However, cancer still remains one of the leading causes of morbidity and mortality, as some malignancies are either non-responsive to traditional chemotherapy or develop resistance. Thus, the development of novel treatment modalities with improved efficacy and side-effect profiles is imperative. In an ever-growing pharmacological world of design, nature and compounds resulting from billions of years of evolution can offer a source of inspiration. As plants are organisms of relatively restricted mobility, they develop complex protective mechanisms and phytochemical arsenals to deal with potential threats, whether those are predators or pathogens. That is perhaps why naturally occurring plant compounds have been used through the ages to treat illness, even before the emergence of modern medicine. Marine and land species have already been used to develop commonly used chemotherapeutics such as vincristine and paclitaxel. Today, they still offer a rich source for discovery of new therapies. In this review, we will discuss plant-derived biomolecules and examine their potential as an add-on therapy for cancer as well as anti-tumor immunity boosters, including their normal cell cytoprotective abilities. We will focus on molecules such as curcumin, epigallocatechin gallate (EGCG), resveratrol, quercetin, graviola, amygdalin, the coumarins and the flavonoids. We will analyse each of these compounds in terms of the in vitro and in vivo evidence of efficacy against cancer, as well as the proposed molecular targets and their effects on cancer hallmarks including, but not limited to, unrestricted proliferation, evasion of apoptosis, dysregulated metabolism, metastasis, including their capabilities as anti-tumor immunity boosters and normal cell cytoprotective agents during chemotherapy.

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# Medical Students Volunteers

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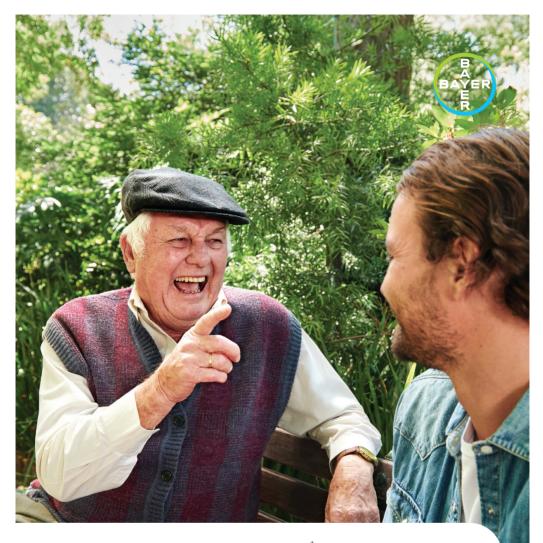
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