6th International Multithematic Scientific **Bio-Medical Congress** 

# **Bio-medical** Scientific Cyprus

15 - 17 November 2018,

Cultural Center, European University Cyprus

**18** Credits of Continued Medical Education (CME) will be awarded

**International Recognition by Nature Publishers:** cell Death & Disease Journal

The Congress is under the auspices of the Ministry of Health and the Cyprus Medical Association (CYMA)



Organized & Supervised by: Professor Dr Ioannis Patrikios



**European** School of University Cyprus Medicine



















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## Welcome Address

By the Rector Professor Kostas Gouliamos



Distinguished Guests and Honorable Participants,

It is with great pleasure that I welcome you to the European University Cyprus, and with honor that I address the 6th Multidisciplinary Scientific Bio-Medical Congress 2018, "Biomedical Scientific Cyprus".

European University Cyprus is an agile academic institution undergoing rapid growth while maintaining highest quality teaching and research; it has an exceptionally gifted student body, a world renowned faculty and innovative specialized disciplines; it is surrounded by first-rate research centers and laboratories and cutting-edge high tech infrastructures that open up a world of possibilities for multidisciplinary education and research.

European University Cyprus belongs to the largest European university organization, Galileo with French Government as a major stock holder.

European University Cyprus has secured a momentous distinction following the assessment by QS TOP UNIVERSITIES (QS StarsTM), the independent and most authoritative university-rating tool globally which places European University Cyprus among the top universities in the world with the highest distinction of 5-Stars in Teaching, Facilities, Inclusiveness, Social Responsibility and Internationalization. European University Cyprus is the only University in Cyprus to be rated by QS TOP UNIVERSITIES.

European University Cyprus promotes opportunities for long – term strategic partnerships with an impact on academics, the economy and society at large. Such a strategic Partnership was created when Microsoft s selected European University Cyprus to be its partner institution for the establishment of the only Microsoft Innovation Center in Cyprus and one of 100 that operate globally. The operation of The Microsoft Innovation Center (MIC) at European University Cyprus will have an enormous impact on students, faculty, IT professionals, researchers, the economy and society at large.

We are also more than pleased to say that European University Cyprus is now one of the 816 distinguished and historic universities that form the internationally recognized organization Observatory Magna Charta Universitatum.Moreover, the European Commission has awarded European University Cyprus (EUC) one of the most prestigious international awards, recognizing its contribution to research excellence, the "HR Excellence in Research Logo".

Dear Colleagues,

The European University Cyprus is becoming an Institution with high quality targets. Research, innovation, technology and excellence are our priorities and we are investing with emphasis on Biomedical-Sciences, with the latest, the launch of the Dentistry School since September 2017.

Exceptional events like this one have without any doubt our full support.

It is really an honor for us to have world known scientists and especially Nobel laureates participating and lecturing in our Institution.

Saying this, I salute and welcome you all and warmly congratulate Professor Dr Ioannis Patrikios, Chairman and Faculty member of the School of Medicine for his initiative and hard work to organize and give flesh and bones to his idea; and for giving us the opportunity to successfully be here today for a 6th time. It is now considered as a tradition.

I also acknowledge Bayer / Novagem Ltd, the diamond sponsor of the congress and all other sponsors and supporters for their contribution.

I wish you all a successful and productive congress.

Professor Kostas Gouliamos Rector, European University Cyprus

## Welcome Address

By the Acting Dean Dr Elizabeth O. Johnson



Dear Friends & Colleagues,

It is a sincere pleasure to welcome you to European University Cyprus and to the 6th International Multithematic Scientific Bio-Medical Congress.

The faculty, staff and administration at European University Cyprus, School of Medicine are fully committed to the quality dissemination of medical knowledge. We constantly strive towards providing an optimal learning environment by: 1) keeping current with our understanding of medical knowledge; 2) remaining innovative, both in our curriculum and teaching practices; and 3) inspiring our students to be passionate about providing their patients with the best possible care.

As we enter the Era of Bioinformatics, medical educators are challenged to seek innovative teaching methods that address the multitude and magnitude of scientific, technological and demographic factors that have converged to revolutionize today's approach to human health and well being. These advancements not only bring challenges and new demands to today's physicians, but also to today's medical educators. EUC's mission is to prepare our students to excel in the art of healing, but also to become inspired innovators for the advancement of knowledge and patient-centered healthcare.

EUC is stepping 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 created an excellent scientific program, which includes 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. The underlining themes, which highlight new basic, translational and clinical scientific findings feature:

Education & Research Advances in Cancer Advances in Cardiology Genetics as a Diagnostic Tool Obstetrics-Gynecology-Maternal Fetal Medicine Neurodegenerative Diseases

Distinguished scientists and clinicians have joined to take part in the plethora sessions, assuring that this event will not only remain one of the major scientific events in Cyprus, but will

continue to serve as a primary forum for global academic exchange. In addition to reviewing the latest scientific developments and best clinical practices across the basic, clinical, population and translational contents presented at the meeting, the rich social program provides many opportunities for scientists to network with colleagues from around the world in an exciting environment. The EUC Multi-thematic Congress will indubitably provide you the opportunity to interact with your colleagues and stimulate the creative and productive exchange of ideas for a personally and professionally rewarding experience.

Congratulations to Professor Patrikios, whose inspiration was the incentive for creating this meeting. A sincere word of gratitude to our sponsors, Bayer/Novagem Ltd (Diamond Sponsor), Energon Lab Equipemnt, Scientronics and Remedica (Gold Sponsors), Biotronics and bioMED-GENE lab (Silver Sponsors) and Amatheus Travel and C. Georgiou Lab Supplies (Supporters)

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,

Professor Elizabeth O. Johnson Acting Dean School of Medicine European University Cyprus

## Welcome Address

By Professor Dr Ioannis Patrikios



Dear Congress participants and guests

It is my great pleasure to welcome you to the 6th International Bio-Medical Scientific Cyprus Congress of the School of Medicine of the European University of Cyprus (EUC) that is taking place in Nicosia, Cyprus on the 15<sup>th</sup>, 16<sup>th</sup> and 17<sup>th</sup> of November 2018.

The School of Medicine of the EUC and Myself personally welcome all distinguished invited keynote and plenary speakers and the scientific community of Cyprus as well as the delegates from all over the world (Iran, Greece, Nigeria, Poland, UK, Israel, Lebanon, Egypt, Italy, Germany and other) that are attending this exceptionally high quality and high caliber Multidisciplinary Scientific Symposium. My warm regards and welcome extends to our very Special key note speaker the Distinguished Professor Dr Aaron Ciechanover, winner of The Nobel Prize in Chemistry 2004 – for: "the discovery of ubiquitin-mediated protein degradation".

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. Since last year our congress has been institutionalized by CYMA, something that happens for a first time ever; 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 the decision.

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 backing and trust in me and my abilities to organize this event at the highest possible level.

I thank all of my colleagues participating as chairmen/moderators of the session committees or the highly specialized round table workshop satellites; The Cyprus Society of Cardiology that is endorsing the workshop on cardiology, the poster participants from local higher Institutions as well as from abroad, but also my colleagues here at the School of Medicine for their genuine support and willingness to help making this an unforgettable date of our calendar through the years.

It was my strong desire to establish this congress: "Biomedical Scientific Cyprus, (BSC)" to become an annual event with global recognition. Here we are for a sixth consecutive year. The target has been accomplished. Now the only thing we have to do is just 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 and scientific excellence in Medical Science.. and that is the new promise.

Our congress is upgraded to three-days event with participation and submission of

more than 100 abstracts that are published in the ISBN referenced congress abstract book and 55 scientific papers for the "Poster Sessions"; 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 in the world. Our congress has been internationally recognized by one of the most trustable and reputable publishers in the world; through a Meeting Report in the Nature-Publisher-journal "Cell Death & Disease".

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

Finally, I would like to thank the sponsors of the congress, the diamond sponsor, Bayer and 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 many more. Our thanks extend to our Gold sponsors Energo lab equipment, Scientronics, Biotronics Analytical and Biometical solutions, Remedica Pharmaceuticals, BioMEDGENE analytical lab, and to the silver sponsors, Amatheus Travel and the supporters C. Georgiou Lab Supplies, Taverna Zanettos and Gallop Catering.

This year, IMBMC will continue providing a higher interactive platform for Research and Innovation, Drug Discovery, Diagnostics and Clinical Management.

The conference is being held in early 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 Acting Chair, Faculty of Medicine, School of Medicine, European University Cyprus Founder, Chairman and General Congress Supervisor



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## Chairmen / Speakers

### Chairmen

**Dr** loannis Patrikios Dr Kostas Tsioutis Dr Hadjigeorgiou George Dr Elias Nikas Dr Loizos Loizou Dr Elpida Nikolousi Dr Eirini Agapidakis **Dr Panayiotis Politis** Dr Marios Antoniades Dr Symeou Anastasia Dr Zachariades Andreas Dr Ntinioti Trisevaeni Dr Anastasis Stephanou, Dr Christou Soteroula Dr Andreas Neophytou Dr Argyrou Sotiroula Dr Spyros Papaioannou, Dr George Miltiadous Dr Stelios Hadjistyllis **Dr Evagoras Economides** Dr Myrianthefs Michael Dr George Georgiou Dr Christodoulos Kaisis Dr. Joannis Patrikios Dr Marios Loizou Dr Kyproula Christodoulou **Dr Panayiotis Politis** Dr Hadjigavriel Michalis Dr Hadjigeorgiou George Dr Michaelides Constantinos Dr Adonis Ioannides (Aretaieio) Dr Elias Avraam (Makario) Dr Fvis Christou Dr Chrysanthou Andreas Dr Adamos Hadiipanagis Dr Maria Tsiskari Dr Eftychiou Christos (Nicosia G) Dr Ioannides Marios(Nicosia G) **Dr Petros Agathaggelou** Dr Papaioannou Spyros

**Dr Michalis Neophytou Dr Komodromos Themis Dr Giorgos Andrikopoulos** Dr Kvriakos Ioannou Dr George Skordos Dr Yiangou Kyriakos **Dr Spyropoulos Alex** Dr Eirini Agapidaki Dr Michalis Petrou Dr Zachariades Andreas Dr Konstantinos Deltas Dr Panayiotou Panayiotis (Aretaieio) Dr Vasilis Vasiliades Dr Christos Demitriou **Dr Marios Pantziaris** Dr Aris Anaourides **Dr Kougialis Andreas** Dr Loucaidou Panayiota **Dr** Papanastassiou Vakis Dr Ziyad Milat Ibrahim **Dr Michaelides Costas Dr** Angelos Gregoriou Dr Demetris Ntourakis Dr Dia Voniatis **Dr** Constantinos Michaelides

### **Plenary Speakers**

Prof. Dr Theodoros Xanthos Prof. Dr Apostolos Papalois Prof. Dr Nikolaos Zamboglou Prof. Dr Anastasis Stephanou Ass. Prof. Dr Antonis Kirmizis Prof. Dr Loizos Loizou Assist. Prof. Dr Dimas Konstantinos Assist. Prof. Dr Giorgos Apidianakis Ass. Prof. Dr Konstantinos Evangelou Prof. Dr Wolfgang Graier Prof. Dr Nickolas Papadopoulos Adjunct Prof. Dr Charalambos Grassos Prof. Dr Tentes Ioannis Prof. Dr Kyriakos Kypreos Prof. Dr Vasilis Vasilikos Dr Giorgos Andrikopoulos Assist. Prof. Dr Marios Ioannides Assist, Prof. Dr Carsten Werner Lederer Prof. Dr Konstantinos Deltas Prof. Dr Kvriakos Kvriakou Prof. Dr. Panagiotis Politis Ass. Prof. Dr Violetta Anastasiadou Asst. Prof. Dr Trompoukis Pantelis Prof. Dr Apostolos P. Athanasiadis Prof. Dr Gerotziafas Grigoris Dr Christos Christou Prof. Dr Joannis Goudevenos Ass. Prof. Dr Konstantinos Toutouzas Prof. Dr Filippos Triposkiadis Prof. Dr Spyropoulos Alex Prof. Dr Aspasia Tsezou Assist, Prof. Dr. Fleni Zamba Prof. Dr Kleopas Kleopa Prof. Dr Savvas Papacostas Dr Tasos Georgiou Prof. Dr Theodoros Kyriakides Prof Dr Achilleas Gravanis Dr Periklis 7evridis Dr Silviu Brill Prof. Dr Leonidas Phylactou Prof. Dr AT Michael-titus Prof. Dr Massimo Philippe Ass. Prof. Dr Marios Pantzaris Prof. Dr Evangelia Ntzani Prof. Dr Nikos Grigoriadis Prof. Dr Philip Calder

### **Keynote Speakers**

Prof. Dr Aaron Ciechanover Prof. Dr Maddalena Lettino Prof. Dr Nickolas Papadopoulos Prof. Dr Wolfgang Graier Prof. Dr Spyropoulos Alex

### **Independent Poster Award Committee**

Professor Dr Wolfgang Graier, NIKON-Center of Excellence; Medical University of Graz, Austria Professor Dr Achilleas Gravanis, School of Medicine, University of Crete Associate Professor Panagiotis Politis, Center of Basic Research, Biomedical Research Foundation Academy of Athens



Program



## 6th International Multithematic Scientific Bio-Medical Congress

### **Bio-medical Scientific Cyprus**

Institutionalized by the Cyprus Medical Association, 18 C.M.E

**THURSDAY 15 NOVEMBER 2018** 

## Program

- 08:15 09:40 Registration / Coffee
- 09:40 09:45 EUC School of Medicine Video
- 09:45 09:50 Welcome
- 09:50 10:00 European Antibiotic Awareness Day "Antibiotic Resistance a Global Thread" Prof. Dr George Petrikkos, School of Medicine, European University Cyprus

### **EDUCATION AND RESEARCH**

- 10:05 10:25 "Is there a need for inter-porfessional training in healthcare education?" Prof. Dr Theodoros Xanthos, School of Medicine, European University Cyprus Chairs: Constantinos Tsioutis, Hadjigeorgiou George
- 10:25 10:45 "The Role of Modern Experimental Biomedical Translational Research in the Development of New Products with Clinical Applications. Ethical Justification, Implementation, Education and New Frontiers." Prof. Dr Apostolos Papalois, ELPEN research center Chairs: Hadjigeorgiou George, Elias Nikas

### ADVANCES IN CANCER Cancer genetics/Cancer Immunology /Radiotherapy/Aging and Pioneer New Therapies

- 10:45 11:10 "New perspectives in Oncology" Prof. Dr Nikolaos Zamboglou, German Oncology Center Chairs: Loizos Loizou, Elpida Nikolousi
- 11:10 11:30 Coffee and Snack

- 11:30 11:50 "Triptolide Promotes Cell Death in Cancer cells by Targeting Na+/K+ ATPase Pump" Prof. Dr Anastasis Stephanou, School of Medicine, European University Cyprus Chairs: Loizos Loizou, Aris Angouridis
- 11:50 12:10 "Epigenetic deregulation in cancer: the case of histone acetyltransferase Naa40" Ass. Prof. Antonis Kirmizis, University of Cyprus Chairs: Eirini Agapidaki, Panayiotis Politis
- 12:10 12:30 "How to improve the survival rates and quality of life of children and adolescents with cancer or leukemia: The role of the pediatrician and the family doctor" Prof. Dr Loizos Loizou, Pediatric Oncology-Hematology Clinic, Archbishop Makarios III Hospital Chairs: Marios Antoniades, Symeou Anastasia
- 12:30 12:50 "Targeting p90rsk for the development of novel anticancer therapies Ass. Prof. Dr Dimas Konstantinos, University of Thessaly, School of Medicine Chairs: Marios Antoniades, Symeou Anastasia
- 12:50 13:30 Lunch Buffet
- 13:30 13:50 "Diet-depended competition between Pseudomonas aeruginosa and Escherichea coli in the host intestine" Assist. Prof. Dr Giorgos Apidianakis, University of Cyprus Chairs: Zachariades Andreas, Ntinioti Trisevgeni
- 13:50 14:15 "Escaping from oncogene induced senescence: Role in cancer" Ass. Prof. Dr Konstantinos Evangelou, Substitute Prof. Dr Vasilis Gorgoulis National and Kapodistrian University of Athens Chairs: Zachariades Andreas, Ntinioti Trisevgeni

### 14:15 - 14:40 KEYNOTE SPEAKER

"Mitochondria – endoplasmic reticulum crosstalk as therapeutic target against aging, cancer and diabetes" Prof. Dr Wolfgang Graier, NIKON-Center of Excellence; Medical University of Graz, Austria Chairs: Anastasis Stephanou, Christou Soteroula

- 14:40 15:10
   KEYNOTE SPEAKER

   "Liquid Biopsy for the early detection of cancer: applications in screening and minimal residual disease."

   Prof. Dr Nickolas Papadopoulos, Oncology, Johns Hopkins, USA

   Chairs: Andreas Neophytou, Argyrou Sotiroula
- 15:10–15:30 Coffee Break

## ADVANCES IN CARDIOLOGY/CARDIOVASCULAR DISEASES/STROKES / DYSLIPIDEMIA / NEW TREATMENTS - PART 1

15:30 – 15:50	<b>"Air pollution and cardiovascular diseases"</b> Dr Charalambos Grassos , Director of Cardiology Dept. in General Hospital of Attica "KAT" Chairs: Spyros Papaioannou, George Miltiadous
15:50 – 16:15	"Cholesterol and phospholipid patterns of the erythrocyte membrane: a potential 'mirror' or a 'troyan horse' acting within the context of metabolic disease." Prof. Dr Tentes Ioannis, School of Medicine, University of Alexandroupoli Chairs: George Miltiadous, Spyros Papaioannou
16:15 – 16:40	"Is there such a thing as "good cholesterol"? Insights from HDL Biochemistry and Pharmacology." Prof. Dr Kyriakos KypreosSchool of Medicine, University of Patras Chairs: Stelios Hadjistyllis, Evagoras Economides
16:40 – 17:00	Coffee Break
17:00 – 17:25	"Evolution of invasive therapies for arrhythmias" Example, Reference in Greece: past, present and future Prof. Dr Vasilis Vasilikos , Aristotle University of Thessaloniki, Cardiology Department Director Chairs: Stelios Hadjistyllis, Evagoras Economides
17:25 – 17:50	New drugs, new tools for invasive treatment and new data from clinical trials on Atrial fibrillation. "Is there any hope for the treatment of the "incurable" arrhythmia?" Dr Giorgos Andrikopoulos, Henry Dunant Hospital, Cardiology and Department Director Chairs: Petros Agathaggelou, Georgios Georghiou
17:50 – 18:20	KEYNOTE SPEAKER Update in Acute Myocardial Infraction Treatment. "What is new in updated STEMI guidelines" Prof. Dr Maddalena Lettino Humanitas Research Hospital, Milan, Italy President of the European Society of Cardiology (ESC) Acute Cardiac Care Association, Europe. Chairs: Petros Agathaggelou, Georgios Georghiou
18:20 – 19:00	Coffee Break

### 19.00 – 19:30 Opening Ceremony

Greek Music- Violist Michalis Tserkezos

### Welcome Addresses

- Prof. Dr Ioannis Patrikios, Congress Chair and Chair of the School of Medicine, European University Cyprus
- Prof. Dr Elizabeth Johnson, Acting Dean, School of Medicine
- Prof. Kostas Gouliamos, Rector, European University Cyprus
- Mr Demetris Syllouris, President of the House of Representatives
- Other Representatives of Government
- Dr Petros Agathaggelou, President, Cyprus Medical Association

### 19:30 – 20:00 CONFERMENT CEREMONY Doctor Honoris Causa

### Prof. Dr Aaron Ciechanover, Nobel Laureate Chemistry, Nobel 2004

Prize motivation: "for the discovery of ubiquitin-mediated protein degradation." Technion - Israel Institute of Technology in Haifa, Israel.

Announcement of Professor Dr. Aaron Ciechanover as a Honorary Professor of the School of Medicine, European University Cyprus; By the Rector of the European University Cyprus, Prof. Kostas Gouliamos

### LECTURE OF EXCELLENCE

- 20:00 20:30 "Ubiquitin Proteolytic System From Basic Mechanisms thru Human Diseases and on to Drug Development". The Nobel Lecture Prof. Dr Aaron Ciechanover Chairs: Christodoulos Kaisis, Ioannis Patrikios, Marios Loizou
- 20:30 21:30 Wine and Cheese





## 6th International Multithematic Scientific Bio-Medical Congress

### **Bio-medical Scientific Cyprus**

Institutionalized by the Cyprus Medical Association, 18 C.M.E

FRIDAY, 16 NOVEMBER 2018

## Program

- 08:30 10:35 Registration / Coffee
- 10:15 10:20 Introduction to the EUC School of Medicine

### **GENETICS AS A DIAGNOSTIC TOOL AND NEW THERAPIES**

- 10:20 10:40 "A single NIPT for aneuploidies, microdeletions and point mutations" Assist. Prof. Dr Marios Ioannides, R&D Senior Manager at NIPD Genetics Chairs: Kyproula Christodoulou, Panayiotis Politis
- 10:40 11:00 "Gene therapy of β-hemoglobinopathies: trials and trends" Assist. Prof. Dr Carsten Werner Lederer, Cyprus School of Molecular Medicine at The Cyprus Institute of Neurology & Genetics Chairs: Christou Soteroula, Kyproula Christodoulou
- 11:00 11:20 "Oedipus Tyrannous: A lesson in genetics" Prof. Dr Konstantinos Deltas, Cyprus University Chairs: Kyproula Christodoulou, Panayiotis Politis
- 11:20 11:40 The Cyprus School of Molecular Medicine at The Cyprus Institute of Neurology & Genetics "The Contemporary Contribution of genetics in the diagnosis and treatment of Cancer" Prof. Dr Kyriakos Kyriakou Chairs: Hadjigevriel Michalis, Hadjigeorgiou George
- 11:40 12:00 "Gene regulation networks in nervous system development and cancer progression" Prof. Dr. Panagiotis Politis, Center of Basic Research, Biomedical Research Foundation, Academy of Athens Chairs: Hadjigavriel Michalis, Michaelides Constantinos`
- 12:00 12:20 Coffee Break

### 12:20 – 12:40 "Hereditary Cancer syndromes, genetic counseling and testing: the experience in Cyprus" Ass. Prof. Dr Violetta Anastasiadou, Archbishop Makarios III, Clinical genetics; The Cyprus School of Molecular Medicine at The Cyprus Institute of Neurology & Genetics Chairs: Adonis Ioannides, Pantelis Palaiologos

### **OBSTETRICS - GYNECOLOGY - MATERNAL FETAL MEDICINE**

- 12:40 13:00 "The value of laparoscopic and minimal access surgery in modern medical practice and education." Asst. Prof. Dr Trompoukis Pantelis, School of Medicine, European University Cyprus Chairs: Adonis Ioannides, Pantelis Palaiologos
- 13:00 13:20 "Metabolic signatures in pregnancy complications" Prof. Dr Apostolos P. Athanasiadis, Aristotle University of Thessaloniki, Greece Chairs: Maria Tsitskari, Adamos Hadjipanagis
- 13:20 13:45 KEYNOTE SPEAKER "Earlier Detection of Cancers Using Non-Plasma Non-Invasive Tests" Prof. Dr Nickolas Papadopoulos, Oncology, Johns Hopkins, USA Chairs: Maria Tsitskari, Adamos Hadjipanagis
- 13:45 14:25 Lunch Buffet POSTER SESSION

### ADVANCES IN CARDIOLOGY/CARDIOVASCULAR DISEASES/STROKES /DYSLIPIDEMIA/ NEW TREATMENTS - PART 2

- 14:25 14:45 "Clinical assessment of hemodynamics in heart failure" Dr Theodoros Christodoulides, CardioHealth Center, NicosiaCyprus Chairs: Marilia Loizou, Stavros Antoniou
- 14:45 15:05
   "Personalized management of cancer associated thrombosis: Actual status and perspectives"

   Prof. Dr Gerotziafas Grigoris, Thrombosis Consultation - Oncology, University Hospitals of Eastern Paris – APHP Chairs: Stavros Antoniou, Panagiotis Papageorgis
- 15:05 15:25 "New development in treating Aortic stenosis" Dr Christos Christou, American Heart Institute Chairs: Nikos Karpettas, Theodoros Christodoulides
- 15:25 15:45 "Perioperative management of anticoagulant and antiplatelet therapy" Prof. Dr Ioannis Goudevenos, School of Medicine, University of Ioannina, Greece, President of the Hellenic Society of Cardiology Chairs: Petros Agathaggelou, Theodoros Christodoulides

15:45 -	16:00	Coffee	Break
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16:00 – 16:20	<b>"When Cardiology meets Oncology"</b> Ass. Prof. Dr Konstantinos Toutouzas, National and Kapodistrian University of Athens Chairs: Papaioannou Spyros, Michalis Neophytou
16:20 – 16:40	<b>"Brain Heart Interactions in Heart Failure"</b> <b>Prof. Dr Filippos Triposkiadis, University of Thessaly and Director of the Department of</b> <b>Cardiology of the Larissa University Hospital</b> Chairs: Michalis Neophytou, Papaioannou Spyros

### 16:40 – 17:05 KEYNOTE SPEAKER

President of the European Society of Cardiology (ESC) Acute Cardiac Care Association, Europe. "From the European Society of Cardiology (ESC) guidelines to the everyday practice: how to fill the gap" Prof. Dr Maddalena Lettino, Humanitas Research Hospital, Milan, Italy Chairs: Giorgos Andrikopoulos, Economides Evagoras

### 17:05 – 17:30 KEYNOTE SPEAKER

"Thromboprophylaxis in Medically III" Prof. Dr Spyropoulos Alex, The Donald and Barbara Zucker School of Medicine at Hofstra/ Northwell in NY, USA Chairs: Giorgos Andrikopoulos, Economides Evagoras

### 17:30 – 17:55 KEYNOTE SPEAKER

"Personalized Medicine"

Honorary Prof. Dr Aaron Ciechanover, Nobel Laureate Chemistry, Nobel 2004 Technion - Israel Institute of Technology in Haifa, Israel. Chairs: Andreas Neophytou, Christodoulos Kaisis

17:55 – 18:05 Coffee Break

### IN PARALLEL TO THE PROGRAM Under The Auspices of the Cyprus Society of Cardiology

## 18:05 – 19:30 INTERACTIVE "SATELLITE" WORKSHOP: Room Omega Update on Thrombosis Therapeutic approach – Presentation and discussion of cases In Room Coffee "Heart failure; is there a need for antithrombotic drugs in the absence of Atrial fibrillation"

Filippos Triposkiadis; University of Thessaly and Director of the Department of Cardiology of the Larissa University Hospital

"Difficult decisions in thrombo-embolic risk prevention in Atrial fibrillation" Giorgos Andrikopoulos, Henry Dunant Hospital, Cardiology and Department Director

**"Optimal antithrombotic drugs in patients undergoing cardiology procedure"** Konstantinos Toutouzas, National and Kapodistrian University of Athens

### "Aborted sudden cardiac death. What is the cause?"

Vasilis Vasilikos; Aristotle University of Thessaloniki, Cardiology Department Director:

## "Acute Coronary Syndrome (ACS) Management in a Patient in Need of Noncardiac Surgery"

Ioannis Goudevenos; School of Medicine, University of Ioannina, Greece, President of the Hellenic Society of Cardiology

Chair/Moderation:

- Petros Agathaggelou, President of Cyprus Medical Association
- Yiangou Kyriakos, The Cardio Clinic Heart Center, President of the Cyprus society of Cardiology
- Spyropoulos Alex, School of Medicine at Hofstra USA

19:30 – 20:30 Wine and Cheese





## 6th International Multithematic Scientific Bio-Medical Congress

### **Bio-medical Scientific Cyprus**

Institutionalized by the Cyprus Medical Association, 18 C.M.E

SATURDAY, 17 NOVEMBER 2018

## Program

### **POLYTHEMATIC SESSIONS**

- Advances in Neurology, Neurodegenerative and Musculoskeletal Diseases Research and New Potential Treatment Approaches
- Pain
- Cardiovascular
- Ophthalmology

- 8:00 8:45 Coffee Break
- 8:45 9:05 "Functional genomics and epigenetics in osteoarthritis: evidence for metabolic deregulation" Prof. Dr Aspasia Tsezou, School of Medicine, University of Thessaly Chairs: Panaviotis Politis. Adonis Ioannides
- 9:05 9:25 "Epidemiology of Rare Diseases in Cyprus" Assist. Prof. Dr Eleni Zamba, Director of Clinic D (Neuromuscular, Neurogenetic diseases and Clinical Electromyography) at the Cyprus Institute of Neurology and Genetics (CING). Chairs: Adonis Ioannides, Eirini Agapidaki,
- 9:25 9:45 "Developing cell-targeted gene therapy for neuromuscular and neurological disorders" Prof. Dr Kleopas Kleopa, Head of Neurology Clinic E and Neuroscience Laboratory at the Cyprus Institute of Neurology and Genetics (CING) Chairs: Michalis Petrou, Zachariades Andreas
- 9:45 10:05 "The effect of seizures on quality of life" Prof. Dr Savvas Papacostas, Head of the Epilepsy and Behavioral Neurology Clinic of the Cyprus Institute of Neurology and Genetics (CING) Chairs: Zachariades Andreas, Giorgos Potamitis

- 10:05–10:25 "The role of Omega-3 Fatty Acids in Aging Retina" Dr Tasos Georgiou, Consultant Ophthalmologist at Ophthalmos Educational and Research Institute in Nicosia, Cyprus Chairs: Konstantinos Deltas, Elpida Nikolousi
- 10:25 10:45 Coffee Break
- 10:45 11:05 "The role of complement in the amyloidoses-a new therapeutic avenue?" Prof. Dr Theodoros Kyriakides, Senior Consultant at the Cyprus Institute of Neurology and Gene Chairs: Kyriakos Ioannou, Panayiotou Panayiotis
- 11:05 11:30 "Neurogenic compounds as inducers of brain self-repair" Prof. Dr Achilleas Gravanis, School of Medicine, University of Crete Chairs: Kyriakos Ioannou, Panayiotou Panayiotis
- 11:30 11:50 "Advance techniques for pain management" Dr Periklis Zavridis, Anaesthesiologist at the Apollonio Private Hospital and the American Medical Centre in Nicosia Chairs: Vasilis Vasiliades, Christos Demitriou
- 11:50 12:15 "The 'Green Revolution': the experience of Patients using Medical Cannabis" Dr. Silviu Brill, Director of the Institute of Pain Medicine, Tel Aviv Medical Centre in Israel Chairs: Christos Demitriou, Vasilis Vasiliades
- 12:15 12:40 KEYNOTE SPEAKER
- **"The Periprocedural Management of Patients with Atrial Fibrillation on Direct Oral Anticoagulants"** Prof. Dr Spyropoulos Alex, The Donald and Barbara Zucker School of Medicine at Hofstra/ Northwell in NY, USA Chairs: Christodoulos Kaisis, Andreas Neophytou
- 12:40 13:20 Lunch Buffet POSTER SESSION
- 13:20 13:40 "Oligonucleotide-based therapy for Muscular Dystrophy" Prof. Dr Leonidas Phylactou, Chief Executive Medical Director; The Cyprus Institute of Neurology and Genetics (CING) Chairs: Marios Pantziaris, Ntinioti Trisevgeni
- 13:40 14:05 "Neuroprotection and neurorepair in brain and spinal cord injury" Prof. Dr AT Michael-titus, Centre for Neuroscience and Trauma, Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London Chairs: Kougialis Andreas, Loucaidou Panayiota

14:05 – 14:45 The hurdles, the existing evidence and the promise" Prof. Dr Dimitris Karoussis, Chairman of the Neuroimmunology Unit and MS Center at Hadassah and the neuroimmunology laboratory Chairs: Kougialis Andreas, Loucaidou Panayiota

- 14:30 14:55 "Imaging brain networks in demyelinating and neurodegenerative diseases" Prof. Dr Massimo Filippi, Director of the Residency School in Neurology and President of the Bachelor's Degree in Physiotherapy, Vita-Salute San Raffaele University; Director, Neuroimaging Research Unit, INSPE, Division of Neuroscience, San Raffaele Scientific Institute, Milan, Italy Chairs: Papanastassiou Vakis, Ziad Milad Ibrahim
- 14:55 15:15 Coffee Break
- 15:15 15:35 "Inflammatory prothrombotic pathways in Multiple Sclerosis. The role of the antiphospholipid antibodies" Ass. Prof. Dr Marios Pantzaris, Senior Neurologist and Head of the Neurology Clinic C and the Neurovascular Department Chairs: Papanastassiou Vakis, Ziad Milad Ibrahim
- 15:35–15:55 "DHA, EPA and antioxidants for multiple sclerosis: where we stand" Prof. Dr Evangelia Ntzani, University of Ioannina School of Medicine, Ioannina, Greece & School of Public Health, Brown University, RI, USA Chairs: Vasilios Kimiskidis, Angelos Gregoriou
- 15:55 16:15 "CNS-Immune System Dynamic Dialogue in Neurology" Prof. Dr Nikos Grigoriadis, Aristotle University of Thessaloniki; Head of the of the B' Dept of Neurology, AHEPA University Hospital, the MS Centre and the Laboratory of Experimental Neurology and Neuroimmunology Chairs: Vasilios Kimiskidis, Angelos Gregoriou
- 16:15 16:35 "Omega-3 fatty acids have a role in prevention of coronary heart disease" Prof. Dr Philip Calder, Human Development and Health, Faculty of Medicine, University of Southampton, Southampton, United Kingdom Chairs: Dia Voniatis, George Hadjigeorgiou
- 16:35 16:45 Coffee Break

### **ORAL PRESENTATION (SELECTED ABSTRACTS)**

16:45 – 18:45 Heavy recreational cannabis use negatively impacts on bone health – A cross-sectional study Antonia Sophocleous, Roy Robertson, Nuno B. Ferreira, James McKenzie, Stuart H. Ralston.

European University of Cyprus, Nicosia, Cyprus

Therapeutic trial of an oral c5a agonist in a mouse model of Alzheimer's disease Elena Panayiotou, Rana Abu Manneh, Eleni Fella, Savanna Andreou, Revekka Papacharalambous, Petroula Gerasimou, Paul Costeas, Stella Angeli, Ioanna Kousiappa, Savvas Papacostas, Theodoros Kyriakides. The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus

## Transporters control intestinal homeostasis, infrction-induced regeneration and cancer in Drosophila

K. Neofytou and C. Pitsouli. University of Cyprus, Nicosia, Cyprus

### Activin A signaling regulates IL13Rα2 expression to promote breast cancer metastasis

Maria Kalli, Fotios Mpekris, Chen K. Wong, Myrofora Panagi, Arthur W. Lambert, Sait Ozturk, Sam Thiagalingam, Triantafyllos Stylianopoulos and Panagiotis Papageorgis. European University Cyprus, Nicosia, Cyprus

### Tissue-intrinsic Eiger/TNF as a dual switch of intestinal stem cell divisions

Vasilia Tamamouna, Myrofora Panagi, Andria Theophanous, Maria Demosthenous, Savvas Teloni, Maria Michael, Markella Papadopoulou, Chrysoula Pitsouli, Yiorgos Apidianakis. University of Cyprus, Nicosia, Cyprus

Normalization of tumor microenvironment in combination with cytotoxic nanomedicine reprograms macrophages, suppresses metastasis and improves overall survival Myrofora Panagi, Chrysovalantis Voutouri, Fotios Mpekris, Panagiotis Papageorgis, Margaret R Martin, John D Martin, Christiana Polydorou, Motohiro Kojima, Genichiro Ishii, Kazunori Kataoka, Horacio Cabral, Triantafyllos Stylianopoulos. University of Cyprus, Nicosia, Cyprus

Moderating effect of Psychosocial factors in the relation between Symptom Severity and Quality of Life in Irritable Bowel Syndrome (IBS) Hester Bowers, Nuno Ferreira, David Gillanders. University of Nicosia

### Proteomic analysis in mouse kidneys reveals novel lupus nephritis biomarkers Orthodoxia Nicolaou, Kleitos Sokratous, Anastasis Oulas, George M. Spyrou, Kyriaki Michailidou, Christiana Demetriou, Andreas Hadjisavvas, Bernard R. Lauwerys, Kyriacos Kyriacou.

Cyprus School of Molecular Medicine, Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus

### Mutational signatures and kataegis across distinct cytolytic subgroups of colorectal cancer

Apostolos Zaravinos, Konstantinos Roufas, Christos Dimopoulos. European University Cyprus, Nicosia, Cyprus

## Depletion of Ras Suppressor-1 (RSU-1) promotes cell invasion of breast cancer cells through a compensatory upregulation of a truncated isoform

Vasiliki Gkretsi, Maria Kalli, Christodoulos Efstathiades, Panagiotis Papageorgis, Vassilios Papanikolaou, Lefteris C. Zacharia, Aspasia Tsezou, Evangelos Athanassiou, Triantafyllos Stylianopoulos.

University of Cyprus, Nicosia, Cyprus; European University Cyprus, Nicosia, Cyprus

### Gene replacement therapy for CMT1X Neuropathy

Kagiava A, Richter J, Tryfonos C, Karaiskos C, Sargiannidou I, Christodoulou C, Kleopa K. The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus.

Analysis of polymorphism in the TLR3 gene of NK cells from Multiple Sclerosis patients Elie Deeba, George Krashias, Dana Koptides, Marios Pantzaris, Christina Christodoulou. The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus

## EPTRI - European Paediatric Translational Research Infrastructure: a bridge towards the future of paediatric medicine

Marios Phylactides, Marina Kleanthous, Anthi Demetriadou. The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus

## CRISPR/Cas9- and TALEN-mediated disruption of aberrant regulatory elements restores normal splicing and gene function

Petros Patsali, Giandomenico Turchiano, Panayiota Papasavva, Marianna Romito, Constantinos Loucari, Coralea Stephanou, Soteroulla Christou, Maria Sitarou, Claudio Mussolino, Tatjana I. Cornu, Michael N. Antoniou, Carsten W. Lederer, Toni Cathomen, and Marina Kleanthous.

The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus

Systemic sclerosis susceptibility in the Greek-Cypriot population: a replication study of HLA and non-HLA genetic variants Paraskevi Chairta, Savvas Psarelis, Kyriaki Michailidou, Christiana Demetriou, Paschalis Nicolaou, Kyproula Christodoulou. The Cyprus Institute of Neurology and Genetics, Nicosia, Cyprus

Chairs: Elizavet Johnson, George Hadjigeorgiou Chairs: Marios Pantzaris, Marilia Loizou

### 18:45 – 19:00 POSTER AWARDS - CLOSING CEREMONY

Founder and Congress Chair, Prof. Ioannis Patrikios







### QX200 Droplet Digital PCR





## Bio-medical Scientific Cyprus

## **Speakers CVs**

## Speakers CVs



### Professor Dr Aaron Ciechanover

Distinguished Research Professor in the Faculty of medicine at the Technion - Israel Institute of Technology in Haifa, Israel

Aaron Ciechanover was born in Haifa, Israel in 1947. He is currently a Distinguished Research Professor in the Faculty of medicine at the Technion - Israel Institute of Technology in Haifa, Israel. He received his M.Sc. (1971) and M.D. (1973) from the Hebrew University in Jerusalem. He then completed his national service (1973-1976) as military physician, and continued his studies to obtain a doctorate in biological sciences in the Faculty of Medicine in the Technion (D.Sc.; 1982). There, as a graduate student with Dr. Avram Hershko and in collaboration with Dr. Irwin A. Rose from the Fox Chase Cancer Center in Philadelphia, USA, they discovered that covalent attachment of ubiguitin to a target protein signals it for degradation. They deciphered the mechanism of conjugation, described the general proteolytic functions of the system, and proposed a model according to which this modification serves as a recognition signal for a specific downstream protease. As a post-doctoral fellow with Dr. Harvey Lodish at the M.I.T., he continued his studies on the ubiguitin system and made additional important discoveries. Along the years it has become clear that ubiquitin-mediated proteolysis plays major roles in numerous cellular processes, and aberrations in the system underlie the pathogenetic mechanisms of many diseases, among them certain malignancies and neurodegenerative disorders. Consequently, the system has become an important platform for drug development. Among the numerous prizes Ciechanover received are the 2000 Albert Lasker Award, the 2003 Israel Prize, and the 2004 Nobel Prize (Chemistry; shared with Drs. Hershko and Rose). Among many academies, Ciechanover is member of the Israeli National Academy of Sciences and Humanities, The European Molecular Biology Organization (EMBO), the American Academy of Arts and Sciences (Foreign Fellow), the American Philosophical Society, the National Academies of Sciences (NAS) and Medicine (NAM) of the USA (Foreign Associate), the Pontifical Academy of Sciences at the Vatican, the Chinese Academy of Sciences (CAS; Foreign Member), the Russian Academy of Sciences (Foreign Member), and the German Academy of Sciences (Leopoldina).



### **Prof. Dr Nickolas Papadopoulos**

Oncology Expert, Johns Hopkins, USA

Dr. Nickolas Papadopoulos is internationally known as a co-discoverer of the genetic basis of the predisposition to hereditary nonpolyposis colon cancer (HNPCC), one of the most common hereditary forms of cancer, earlier in his career. He is known for the development of diagnostic tests and he is considered an expert in cancer genetics and diagnostics. He was part of the interdisciplinary team that was first to sequence all of the protein coding genes, determine genetic alterations and construct expression profiles of four common tumor types. Later he was involved in the identification of genetic alterations that drive tumorigenesis in multiple tumor types. Noteworthy discoveries he has made include the identification of novel mutations in chromatin remodeling genes in ovarian clear cell carcinomas and pancreatic neuroendocrine tumors. Currently, he is focused on translating the genetic information derived from cancer genome analyses to clinical applications in early detection, diagnosis and monitoring of cancer. He is a co-developer of sensitive methods for the detection of tumor DNA in liquid biopsy. He is also the co-founder of two companies that develop diagnostics for cancer.

## Speakers CVs



### **Professor Dr Alex C. Spyropoulos**

Professor of Medicine at Hofstra, Northwell School of Medicine and System Director of Anticoagulation and Clinical Thrombosis Services for the multi hospital Northwell Health System in NY, USA

Alex C. Spyropoulos, MD received his medical degree from the University of Pennsylvania School of Medicine in Philadelphia, PA. He completed his internship and residency in internal medicine at the University of New Mexico Health Sciences Center in Albuquerque, NM. He is board certified in Internal Medicine.

Dr. Spyropoulos was Founder and former Medical Director of the Clinical Thrombosis Center in Albuquerque, New Mexico. He is a Professor of Medicine at Hofstra, Northwell School of Medicine and System Director of Anticoagulation and Clinical Thrombosis Services for the multi hospital Northwell Health System in NY. He is also a Professor of the Merinoff Center for Patient-Oriented Research as part of the Feinstein Institute for Medical Research. He is co-chair of the Council on Leadership of Thrombosis at Northwell Health System. He is a Fellow of the American College of Physicians, American College of Chest Physicians, International Academy of Clinical and Applied Thrombosis/Haemostasis, and the Royal College of Physicians, Canada.

Dr. Spyropoulos has helped to develop protocols using LMWH in outpatient-based treatment of venous thromboembolic disease, patient self-testing of warfarin, perioperative "bridging" for patients on chronic anticoagulation, medical inpatient thromboprophylaxis, protocols with regards to the use of anticoagulants for HIT, and clinical use of the direct oral anticoagulants, including their use in special patient populations and periprocedural situations.

He has been involved as Principal Investigator, Scientific Committee member, Steering and Executive Committee member, or member of Data Safety Monitoring Board in multiple international, multicenter randomized trials in thrombosis and anticoagulant therapy. He is the co-Chair of the Executive Committee for MARINER, a global Phase 3 multicenter study of thromboprophylaxis in medical patients with rivaroxaban. He is a founding member of ATLAS, a US-based ARO-CRO in thrombosis-related research. He is a panel member of a US national experts consensus group for clinical excellence in thrombosis management, a member of the Anticoagulation Forum and the Thrombosis/Haemostasis Society of North America, co-Chair of the Scientific Standardization Committees of Predictive Variables and Perioperative Thrombosis and Haemostasis as part of ISTH, and co-author for the 8th, 9th and currently 10th 2017 ACCP Guidelines on Perioperative Antithrombotic Therapy, the 2008 International Consensus Statement Guidelines in Venous thromboembolism, and senior author for the 2013 International Consensus Statement on venous thromboembolic disease. He is also reviewer for the 2014 ESC Guidelines on Pulmonary Embolism. Dr. Spyropoulos' research studies, articles, letters, and editorials have been published in over 170 peer-reviewed journals.



### **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

He 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. 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 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, recently he created the core facility "Center for Clinical Pharmacology and Toxicology" of the Department. This core facility is designed to perform research as well as services for-a-fee to Academic, Industrial as well as Clinical partners. Important part of the activities of the Center aim at facilitating precision medicine decisions by doctors of the Hospitals.

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 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 and the Journal of Biomedical Research. Recently, he has been appointed by the Greek Ministry of Health as vice chairman of the Hellenic National Committee on Pharmacovigilance.

For Prof. Kypreos' most current publication record please refer to PubMed. For updated statistics on his published work please visit google scholar or scopus. Prof. Kypreos' orchid profile may be found at orcid.org/0000-0001-6784-2710.

## Speakers CVs



### Associate Professor Dr Antonis Kirmizis

Department of Biological Sciences at the University of Cyprus

Antonis Kirmizis is an associate professor at the Department of Biological Sciences at the University of Cyprus. He received his PhD in Molecular and Cellular Biology at the University of Wisconsin-Madison, USA. He then completed his post-doctoral work in the field of Epigenetics as an EMBO and Marie Curie fellow at the Gurdon Institute of Cambridge University, UK. In 2010, Antonis has established a research lab in Epigenetics and Gene Regulation (www.kirmizislab.com), which focuses on deciphering functional and regulatory mechanisms of histone modifications in the context of health and disease. His lab was the first to define the cellular role of the previously uncharacterised histone N-terminal acetylation and of its associated enzyme in transcription and cell growth. In general, his studies are driven by the fact that deregulation of epigenetic mechanisms lead to diseases like cancer and the overall goal of his research is to identify new targets and strategies for cancer therapy. Since the launch of his group, Antonis has attracted considerable funding including a prestigious ERC-starting grant. He is also involved in various other collaborative projects and networks such as the EpiGene2Sys network of excellence, the COST action EpiChemBio and LifeTime initiative. Finally, Antonis interacts with many scientists and has important ongoing collaborations with various laboratories nationally and internationally.



### **Assistant Professor Dr. Konstantinos Dimas**

Department of Pharmacology of the Medical School of the University of Thessaly

Dimas is a Biologist with a Doctorate in Pharmacology from the Medical School of the University of Ioannina. Since March 2011 he serves as Assistant Professor at the Department of Pharmacology of the Medical School of the University of Thessaly. Prior to this position, he was a researcher at the Pharmacology Lab of the Academy of Athens's Medical Research Institute since 2003. He was the recipient of a Special Education Award (STA) by the International Organization for Research on Cancer (IARC. Molecular Carcinogenesis Unit), a member of the World Health Organization (WHO) where he remained for the period from October 2001 to December 2002. He has and is collaborating with various universities, research institutes and biotech companies in Greece and abroad. At the Department of Pharmacology of the Medical School of the University of Thessaly (where he serves at various positions since 2007) performs research with his group (the Group of Cancer Biology and Therapy) on the study and development of new anticancer therapeutic approaches, such as putative anticancer small molecules, new inhibitors of kinases p90 ribosomal S6 and novel ligands of sigma receptors. Also he and his group work on the development of new and improved animal models of cancer (such as patient derived tumor xenografts in immunodeficient mice). Recently and in cooperation with the US National Cancer Institute (NCI, NIH, Frederick, MD, USA) his interests expanded to the role of the immune system in the development of new cancer therapies (immunotherapy of cancer).

## Speakers CVs



### Professor Dr Filippos K. Triposkiadis

Director of the Department of Cardiology of the Larissa University Hospital

Dr. Triposkiadis is Professor of Cardiology of the University of Thessaly and Director of the Department of Cardiology of the Larissa University Hospital. He has also served as Chairman of the Internal Medicine Sector of the University of Thessaly and Chief Medical Officer of the Larissa University Hospital. Dr. Triposkiadis is a member of several national and international scientific societies including the European Society of Cardiology, the American College of Cardiology, the Heart Failure Association (HFA) of the European Society of Cardiology (Fellow) and Vice president of the Hellenic Society for the Study and Research of Heart Failure. Dr. Triposkiadis is nationally and internationally known for his research work on the physiology and pathophysiology of the left atrium, the significance of comorbidities in heart failure, the pathophysiology and management of heart failure, the sympathetic nervous system, and the physiological significance as well as the clinical implications of the derangements of the left ventricular ejection fraction. He has served as a member in HFA guideline committees and 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).

Cardiology. He is board member of the British Atherosclerosis Society and one of the founders of the Scientists of Tomorrow of the ESC's council on Basic Cardiovascular Science.


### Professor Dr Aspasia Tsezou

Professor of Medical Genetics at the University of Thessaly and the Director of the Laboratory of Cytogenetics and Molecular Genetics of the University Hospital of Larissa.

Aspasia received her B.Sc. in Biology from Mc Master University, Hamilton, Canada and Ph.D. in Medical Genetics from the National and Capodistrian University of Athens, Medical School (1991). In 2001 she was elected Assistant Professor of Medical Genetics at the University of Thessaly, Faculty of Medicine, Dept. of Biology and from 2010 until today she is Professor of Medical Genetics in the same University. From 2010 until today she is the Director of the Laboratory of Cytogenetics and Molecular Genetics of University Hospital of Larissa. From 2013 until today Prof. Tsezou is the Director of the post-graduate (M.Sc) Program "Human Genetics" at the School of Medicine, University of Thessaly. From 2017-today she has been appointed by the Greek Ministry of Health, as Coordinator of the working group for the establishment of the specialty of Laboratory Genetics in Greece. In May 2018 she was elected as member of the General Assembly of the "Hellenic Institute of Research and Innovation- (ELIDEK) to serve until May 2021.

Prof. Tsezou has given over 50 invited lectures in national and international congresses and/or Universities and has supervised 12 PhD and 43 MSc theses.

She has a sound expertise on genotype-phenotype correlation studies, on gene expression studies and mechanisms controlling gene expression in osteoarthritis (OA), as well as on the epigenetics of osteoarthritis. She was the first to suggest the metabolic aspect of OA based on gene expression studies and the involvement of lipid metabolism in OA. She has many ongoing national and international collaborations in the field of genetics and epigenetics of musculoskeletal diseases and has collaborated as associate member with the FP7 TREAT-OA "Translational Research in Europe Applied Technologies for Osteoarthritis" consortium.

Her research has been supported by several competitive grants as from the European Commission FP7 program "Cooperation" for the project "Osteoarthritis: integrated systematic analysis for targeted biological therapy" (2007-2013), from the STATE SCHOLARSHIP FOUNDATION (IKY) for the projects «microRNAs as novel biomarkers for early diagnosis in musculoskeletal diseases" (2016-2018), and «The role of miR-140 and miR-146 in osteoarthritis (2017-2019) and from the Greek Ministry of Education – ESPA "RESEARCH-CREATIVITY-INNOVATION (2014-2020) for the project "Induced pluripotent Stem cells for cell therapy of degenerative arthritis.

Prof. Tsezou serves as an advisor for scientific organizations, as reviewer for high-impact scientific Journals and has been an evaluator for national projects (from 2009-today) and for the European Commission since 2001 until today.

She has published 126 research articles in peer-reviewed journals and her work has received 3,093 citations (SCOPUS) and 4,618 (Google Scholar) with an h-index of 30 (SCOPUS) and 38 (Google Scholar).



#### **Dr Tassos Georgiou**

Consultant Ophthalmologist at Ophthalmos Educational and Research Institute in Nicosia, Cyprus

Tassos is a Consultant Ophthalmologist at Ophthalmos Educational and Research Institute in Nicosia, Cyprus. He qualified from Leeds University, UK and continued his Ophthalmology training at Leeds Teaching Hospitals.

He has undertaken an anterior segment fellowship followed by a surgical and medical retinal fellowship and he is a member of the Royal College of Ophthalmologist in England. He is the director and founder of the Ophthalmos Research and Educational Institute.

His research and teaching involves around retinal and optic nerve diseases which cause blindness with no therapeutic treatments. He also leads a research team at Ophthalmos Institute which is involved in the development of novel treatments for dry age-related macular degeneration, macular dystrophies, wet macular degeneration ,diabetic macular oedema and other inherited retinal disease, both in the laboratory and also in terms of undertaking clinical trials to determine the safety and effectiveness of these new treatments. The innovative therapy for these blinding diseases is patented in Europe, in USA and other countries.

Dr Tassos Georgiou is the principal investigator of clinical trials in Europe investigating the innovative therapy for dry macular degeneration and Stargardts disease using his patented therapy.



#### **Professor Papacostas**

Head of the Epilepsy and Behavioral Neurology Clinic of the Cyprus Institute of Neurology & Genetics where he established the Clinical Neurophysiology laboratory

completed his medical education at Ohio University, his residency in Neurology and Psychiatry at the University of Rochester, and a fellowship in Clinical Neurophysiology and Epileptology at Columbia University in New York. He is currently Head of the Epilepsy and Behavioral Neurology Clinic of the Cyprus Institute of Neurology & Genetics where he established the Clinical Neurophysiology laboratory, the long term monitoring unit for epileptic seizures and the first Ethics Committee in Cyprus. With the establishment of the Cyprus School of Molecular Medicine, he was appointed Professor of Neuroscience. He has also held a visiting associate professorship at the University of Cyprus in Nicosia and an adjunct associate professorship at the University of Rochester in New York. He has been active in epilepsy research including anti-epileptic drug trials, guality of life in epilepsy issues and has established collaborations with several academic institutions in Cyprus and abroad for the evaluation and surgical cure of epilepsy. He introduced surgical treatments for intractable epilepsy in Cyprus and participated, with intraoperative monitoring, in the first operations performed in Cyprus. Moreover, he performed research on Dementia epidemiology, the psychosocial aspects of the disease, clinical trials for novel medications and conducts studies on animal models of Alzheimer's disease. He has also performed extensive neurophysiological research on new methodologies for the evaluation of the vestibular system. He is on the list of faculty 1000 of International League Against Epilepsy and has been awarded the distinction of Fellow of the American Academy of Neurology. He published extensively and actively participates in local, regional and international scientific meetings. His book "Madness and leadership: From antiquity to the New Common Era' was published in Sept. 2015



#### **Professor Dr Kleopas**

Consultant neurologist, Head of Neurology Clinic E and Neuroscience Laboratory at the Cyprus Institute of Neurology and Genetics (CING) and Professor at the Cyprus School of Molecular Medicine (CSMM)

A. Kleopa, MD, graduated from Medical School University of Wuerzburg, Germany and was trained in Neurology and Neuromuscular Disorders at Drexel University and University of Pennsylvania, USA. He is a consultant neurologist, Head of Neurology Clinic E and Neuroscience Laboratory at the Cyprus Institute of Neurology and Genetics (CING) and Professor at the Cyprus School of Molecular Medicine (CSMM). He is the coordinator of the Neuroscience MSc/PhD Program and course leader of the Molecular and Cellular Neuroscience course at CSMM. He chairs the Academic Committee and coordinates medical student and neurology resident education at CING. He has expertise in the clinical diagnosis and management of neurological and in particular neuromuscular disorders. Furthermore, he has extensive experience in both basic and clinical neuroscience research, with competitive research funding totaling over €3 million for the last 18 years. He has obtained as a principal investigator over 20 research grants and has published over 80 peer reviewed papers in international scientific journals. He received the 2015 Investigator Award from the European Academy of Neurology and the 2017 Distinguished Researcher Award of the Cyprus Research Promotion Foundation.



### Professor Dr Grigoris T Gerotziafas

Université Pierre et Marie Curie and Tenon University Hospital, Paris, France

Prof. Grigoris T Gerotziafas leads 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 Angiogenesis" in INSERM U938 at the Faculté de Médecine, Sorbonne Université.

The fundamental research of Professor Gerotziafas' group is focused on the interactions between cancer cells and blood coagulation and on the pharmacology and the mechanism of action of heparins and the direct oral anticoagulants. His group is active in translational research, principally in the prevention of venous thromboembolism, risk assessment of venous thromboembolism in cancer patients and the management of infertility and vascular complications of pregnancy. Professor Gerotziafas is Principal Investigator of the COMPASS-CAT study which led to a new score for the evaluation of risk for cancer associated thrombosis in ambulatory patients on chemotherapy for solid tumors and leads the ROADMAP-Thrombosis project which investigates clinically relevant biomarkers of hypercoagulability in the prediction of vascular episodes.

Professor Gerotziafas has contributed as an expert to the development of several guidelines, including International Consensus for the Prophylaxis and Treatments of VTE, Thrombophilia and Venous Thromboembolism: International Consensus Statement and International clinical practice guidelines for the treatment and prophylaxis of thrombosis in cancer patients. He chairs the Hellenic consensus statements for the prophylaxis and treatment of venous thromboembolism. He is also member of the French working group on evidence-based recommendations for the laboratory assessment of thrombophilia and member of the Scientific and Standardization Committee for Control of Anticoagulation of the International Society on Thrombosis and Hemostasis. Professor Gerotziafas is President of the Committee for the Therapeutic Protocols for the Prevention and Treatment of Venous Thromboembolic Disease, held under the auspice of the Greek National Organization for Medicines. He is involved in the educational program of the Mediterranean League Against Thromboembolic Disease, he is member of the Scientific Committee of the International Union of Angiology and he co-chairs the scientific committee of the VAS – Vascular Independent Organisation.

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.

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.



### **Dr Periklis Zavridis**

Vice-president of the Board of Directors of the Cyprus Anaesthesiology Society. He was also a member of the Board of Directors of KYSAN (Cyprus Resuscitation Council).

Periklis Zavridis was born and raised in Paphos. He studied medicine at the Semmelweis University of Budapest, Hungary, where he received his Doctors Degree in September 2005.

In September 2012, he acquired the specialty of Anaesthesiology, after being an intern at the Anaesthesiology Department of the General Hospital of Dramas, Greece (one year), and then at the Anaesthesiology Department of the Hippocrates General Hospital in Athens. During his specialty, he was trained for three months at the Anaesthesiology Department of the St. Pierre Hospital of Brussels.

Along with the specialty he received his Master in Science, specialising in Pain Management (MSc Pain Management), at Leicester University of England, and Postgraduate diploma at the Emergency pre-hospital medicine at the National Emergency Department (EKAB), Athens.

He successfully completed the one year refresher education on Algology in 2016, with practical and theoretical practice, which is organised by the Greek Society of Algology under the auspices and approval of the EFIC (European Pain Federation).

He is also a Doctor candidate at the first Propaedeutic Surgical Department of Surgery, at the Kapoditrian University of Athens.

Dr. Periklis Zavrides has also an academic background with several combined publications and presentations at various International and National meetings to his credit. He has attended many conferences as an invited speaker particularly in the field of Pain Medicine.

Additional, he is a representative of the Cyprus Anesthesiology Society to the NASC (National Anaesthesiology Societies Committee) of the European Society of Anaesthesiology (ESA), a member of the European Society of Regional Anaesthesia (ESRA), and a Vice-president of the Board of Directors of the Cyprus Anaesthesiology Society. He was also a member of the Board of Directors of KYSAN (Cyprus Resuscitation Council).

Since November 2012, he has been practicing a private profession of Anaesthetist at the Apollonio Private Hospital and the American Medical Centre in Nicosia. He has developed a private Chronic Pain Clinic at the American Medical Centre, Nicosia, Cyprus.

Since 2013, he is Lecturer at St' George Medical University of Nicosia, while in August of 2016, he has taken the title of Clinical Assistant Professor at the above University.



#### **Associate Professor Dr Marios Pantzaris**

Senior Neurologist in the Neurological Dept and he is the Head of the Neurology Clinic C and the Neurovascular Department

He got his training in Neurology in 1995 in Thessaloniki, Greece. He has been trained in Carotid Duplex Doppler ultrasonography in London, St Mary's Hospital in 1995 and in 1999 he was a visiting doctor in an acute stroke unit in Massachusetts General Hospital, Harvard University Boston, USA.

He is working at the Cyprus Institute of Neurology and Genetics as a Senior Neurologist in the Neurological Dept and he is the Head of the Neurology Clinic C and the Neurovascular Department.

He has a huge experience in carotids – transcranial ultrasound and he has participated in many research projects and publications in this area.

He is also head of the Multiple Sclerosis (MS) clinic with more than 1000 patients where he is running research projects towards the etiology and therapy of MS. He is also interested in movement disorders and pain. With the collaboration of the Cyprus Functional Neurosurgery team they have started operating patients with Parkinson disease (Deep Brain Stimulation) as well as neuropathic pain (Spinal Cord Stimulation.

He has given many lectures about MS, carotids ultrasound stroke and Parkinson's disease in Cyprus and abroad.



#### **Professor Dr Dimitrios Karussis**

Chairman of the Neuroimmunology Unit and MS Center at Hadassah and the neuroimmunology laboratory, Israel

Prof. Dimitrios Karussis, was born in Thessaloniki, Greece on 7-8-1962. He graduated from Aristotelion University of Thessaloniki, Medical school in 1986 with excellency. Since 1988 Prof. Karussis moved and lives in Jerusalem, Israel. He completed at Hadassah his Neurology specialization and his PhD degree. Since 2007 he is the Chairman of the Neuroimmunology Unit and MS Center at Hadassah and the neuroimmunology laboratory. Prof. Karussis has published more than 120 peer reviewed scientific papers, mostly in the field of neuroimmunology and stem cells. He has delivered more than 150 invited plenary lectures and served as chairman in tens of European and world congresses in the field of Neuroimmunology. He serves as ad-hoc reviewer and as member of the editorial board in many major journals. He has been for six years a member of the Executive Committee of the ECTRIMS. Prof. Karussis has pioneered the studies with Linomide and with bone marrow hematopoetic and mesenchymal stem cell transplantation in MS. He is considered one of the world experts in the field of clinical applications of stem cells in neurological diseases. Since 2010, Prof Karussis is the elected President of the Israeli Neuroimmunological society and has organized several International meetings in this field. He has hosted and was President of the International Neuroimmunological meeting in 2016 in Jerusalem.



### **Professor Dr Adina T. MICHAEL-TITUS**

Centre for Neuroscience and Trauma, Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London

Adina Michael-Titus was awarded a Doctorat en Sciences in 1988, after studies in Rouen and Paris on inhibitors of opioid peptide-degrading enzymes. In 1990 she was appointed at Queen Mary University of London, where she was subsequently awarded the title of Professor of Neuroscience in 2010. In addition to her academic activity, she also spent a period of work as head of research in drug discovery, in the pharmaceutical industry. She is the Lead of the Centre for Neuroscience and Trauma and also Programme Director of an MSc in Neuroscience and Translational Medicine focused on the training of the next generation of scientists and physicians involved in clinical translation in neuroscience. A large component of her present translational research is focused on neuroprotective strategies in spinal cord injury and brain injury, and the link between trauma and neurodegeneration. The studies published by her group in the last decade illustrate the significant potential of a particular type of neuroactive lipids, the omega-3 fatty acids, in the treatment of acute neurological injury.



#### **Leonidas Phylactou**

Chief Executive Medical Director of the Cyprus Institute of Neurology and Genetics (CING) and the Provost of the Cyprus School of Molecular Medicin

Leonidas Phylactou was born in Paphos, Cyprus on 2nd January 1970. He studied Medical Biochemistry at the University of Birmingham in the UK and then did a PhD in Molecular Genetics and Gene Therapy in the same University, although most of the time was spent at the University of Connecticut Health Centre in the USA. He then moved back to the UK, to the University of Oxford as a post-doctoral scientist, 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 working on the gene function and gene therapy. In 2005 he was appointed Head of the Department of Molecular Genetics, Function and Therapy in which, apart from the research activities, he is responsible for diagnostic services in Medical Genetics. 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 the Chief Executive Medical Director of the Cyprus Institute of Neurology and Genetics (CING) and the Provost of the Cyprus School of Molecular Medicine, the postgraduate school of the CING.

Leonidas Phylactou sits on the Editorial Boards of the journals Molecules and Pharmaceuticals and has secured international funding from several organisations such as the Association Francaise contres Les Myopathies, the Human Frontiers Sciences Program and the Muscular Dystrophy Campaign of UK. He participates in several European Networks and has published extensively in the areas of his expertise.



### Associate Professor Dr Panos Politis

Department of Chemistry, University of Athens, Greece

received his BSc degree in Biology from the University of Patras, Greece in 1996. Then he moved to Oxford, where he was awarded his Ph.D. in Biochemistry, Molecular Biology and Genetics from the Department of Biochemistry, Oxford University, UK in 2000. During this period, he worked on epigenetic aspects of eukaryotic transcriptional regulation. During his PhD thesis he was supported with studentships from prestigious organizations such as Biotechnology and Biological Sciences Research Council, Florey-EPA studentship from Queen's College of Oxford University and Welcome Trust Fund. He has also been awarded the NASA planetary biology internship that gave him the opportunity to work in the Chemical Evolution Lab in the field of prebiotic Chemistry at the Salk Institute for Biological Studies, CA, USA. He then obtained a post-doctoral position in the lab of Cellular and Molecular Neurobiology of the Hellenic Pasteur Institute, Athens, Greece, His research in Athens focused on the regulation of neuronal differentiation and specification, studying the role of genes that coordinate cell cycle exit and differentiation of neural stem cells during embryonic development. He joined Biomedical Research Foundation of the Academy of Athens in January 2007 as Principal Investigator (Assistant Professor Level) at the Center for Basic Research. He has also been recently elected as Associate Professor of Biochemistry at the Department of Chemistry, University of Athens, Greece. His research interests are focused on how epigenetic mechanisms can regulate cell differentiation and proliferation during development in health and disease. In his research career he has managed to contribute more than 40 peer-reviewed publications in high profile Journals and Books



### **Dr Silviu Brill**

Director of the Institute of Pain Medicine, Tel Aviv Medical Centre Israel

Dr Silviu Brill is Director of the Institute of Pain Medicine, Tel Aviv Medical Centre in Israel that is recognized as an Excellence Center and Host for European Pain Fellowship.

He is Specialist in Anesthesia and in Pain Medicine and he served as the President of the Israeli Pain Association during the period of 2010-2016.

He is Member of the Pain subcommittee of the National List of Health Services, Ministry of Health and Chairperson of Pain Specialization Committee for Accreditation and Control, Scientific Council, Israel Medical Association.

Dr Brill is Co-Founder and Director of BioMed@TAU Research Hub in Pain, Tel Aviv University and he is currently a Reviewer of several journals.

He is Member of the European Pain Federation (EFIC) task force on Cannabinoids and member of Examination Committee, European Pain Federation, Diploma in Pain, Medication. In June 2018 he was the Chairman of the Congress on controversies on cannabis-based medicines, Vienna, Austria.



### Professor Dr Goudevenos John

School of Medicine, University of Ioannina, Greece

John A. Goudevenos is Professor of Cardiology in the School of Medicine, University of Ioannina, Greece. He graduated with distinction from the Medical School, University of Athens. He was a Research Fellow at Regional Cardiothoracic Centre, Freeman Hospital, U.K., and obtained the Certificate of Full Registration as a Medical Practitioner and he was Research Fellow, Senior Registrar and Registrar n Tetiary Regional Cardiothoracic Centre, UK.. He has authored more than 300 papers, 4 of which were followed by Editorial. According to SCOPUS he's got 4500 citations and H-index 34.



#### **Assistant Professor Dr. Pantelis Trompoukis**

School of Medicine, European University Cyprus

Dr Trompoukis graduated from the Charles University 3rd School of Medicine in Prague in 2000. In 2005 he started his specialty in Obstetrics and Gynecology as a Senior House Officer at Queen Elizabeth Hospital, NHS Trust in London and completed it in April 2009 at the 3rd Obstetrics and Gynecology department of the University of Athens at Attikon University Hospital.

In 2008 he received a training permit for endoscopic gynecological surgery and assisted reproductive techniques ART at the Princess Royal University Hospital, Bromley Hospital, NHS Trust under Professor John Erian MBBCh FRCOG.

In October 2009 he was appointed as a consultant of Obstetrics and Gynecology at the 3rd Obstetrics and Gynecology Department of the University of Athens at Attikon University Hospital.

In 2010 he specialized (fellowship) in laparoscopic and robotic surgery at the internationally acclaimed IRCAD / European Institute of Telesurgery and at Hautepierre University Hospital, CMCO hospital and Nouvel Hopital Civil in Strasbourg, France with Professor Arnaud Wattiez, a world-renowned professor. Dr Pantelis Trompoukis is now serves as Instructor of Endoscopic Surgery at the IRCAD Center in training sessions. Since 2014, he is the only Greek medical member and trainer of the international team "Winners Project" that offers proficiency and certification in laparoscopic and hysteroscopic surgery to gynecologists from all countries.

In 2011 he took the title of Lecturer of Obstetrics and Gynecology ( $\Pi\Delta$  407) at the 3rd Obstetrics and Gynecology department of the University of Athens at the Attikon Hospital. In 2012 he begun working as a private physician at the IASO Group.

Since 2013 serves as an Academic Instructor of Obstetrics & Gynecology (former lecturer) in Gynecological Endoscopy of the National Kapodistrian University of Athens at the 3rd Obstetrics and Gynecology Department of "Attikon" Hospital.

In July 2018 Dr Tropoukis was elected as a member of the board of directors of IASO group of Hospitals. At present and since September 2018 he is a member of the Faculty of the School of Medicine, European University of Cyprus as an Assistant Professor of Obstetrics & Gynecology.

He has completed a Master's degree in Pregnancy Pathology and a Doctoral Thesis (PhD) on Fetal Magnetic Resonance Imaging from the 1st Obstetrics and Gynecology Department of the University of Athens, Alexandra Hospital.



#### Associate Professor Dr Konstantinos Evangelou

Medical School of the National and Kapodistrian University of Athens (NKUA)

Konstantinos Evangelou is currently an Associate Professor of Histology and Embryology at the Medical School of the National and Kapodistrian University of Athens (NKUA). He earned his Bachelor of Science in Biology in 1996 and his Medical Degree in 2003 from the NKUA. In 2006 he obtained his PhD in Cancer Biology/Molecular Pathology from the Laboratory of Histology and Embryology of the same institution. In his thesis work he provided novel insights on the role of the WNT (b-catenin) signaling pathway in human Lung carcinogenesis. In 2010 he earned the Medical Specialty of Pathology.

After obtaining his PhD and until today, he participated as a research assistant and recently as an Associate Professor in a significant number of research projects mainly related to Cancer Biology under the supervision of Professor Vassilis Gorgoulis in the Laboratory of Histology and Embryology of the NKUA. Representative research interests include: i) Alterations of pathways and factors implicated in cell cycle control, apoptosis, cellular senescence, DNA damage response, that trigger genomic in cancer, ii) Study of signaling cascades involved in cell adhesion, extracellular matrix regulation, cell plasticity, as well as in invasion and metastasis, iii) Epidemiological analyses in order to determine prognostic molecular markers that predispose to cancer in general populations, iv) Deciphering defects of the immune system and study of the histological response to therapeautic treatments with emphasis to autoimmune diseases such as scleroderma and psoriasis, v) Epidemiological analyses in inflammatory bowel diseases, vi) Study of the interplay between inflammation and cancer. During that time he collaborated with various foreign and domestic researchers/institutions. In the last years he has focused his research in the field of cellular senescence and its role in cancer and other age related diseases. Konstantinos Evangelou has a rich research record. He has published more than 60 Research papers in reputable international scientific journals such as Cell, Nature Cell Biology, Blood, PNAS, Pharmacology & Therapeutics, Cancer Research, Molecular Cell, and Aging and Aging Cell with more than 1700 citations and h-index=25.



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

University of Cyprus

Prof. Deltas graduated in 1982 from the National and Kapodistrian University of Athens with a degree in Pharmaceutics. He then earned a PhD degree in Biochemistry, from Rutgers University, The State University of New Jersey, USA in 1988. Then he worked as Instructor in Medicine and among others as a Research Associate in the Division of Neurology at Duke University Medical Center, at Durham, North Carolina, USA. In 1991 he returned to his home country, Cyprus, at the newly established Cyprus Institute of Neurology and Genetics. He created and directed the Department of Molecular Genetics C' with emphasis on molecular diagnostics and genetics research, mostly engaged in inherited kidney disorders. In 2002 he was elected Professor of Genetics in the newly created Department of Biological Sciences of the University of Cyprus. He is Director of the Molecular Medicine Research Center and teaches undergraduate and graduate courses on human molecular and medical genetics. He served two terms as member of the Cyprus National Bioethics Committee and served as a representative of Cyprus to the Standing Committee of the European Medical Research Council of the European Science Foundation and as a Coordinator of the Committee of the Cyprus Council of the Recognition of Higher Education Qualifications (KY.S.A.T.S.), on the subject of Biology-Biochemistry. He served as an elected member of the Council School of Pure and Applied Sciences and the Senate of the University of Cyprus. Presently he is a member of the newly appointed Cyprus Council for Medically Assisted Reproduction.

His research activities focus on Nephrogenetics while he is developing tools for better understanding of molecular pathomechanisms at cellular and animal level. Recently, with competitive funding of 2m Euro by the European Regional Development Fund and the Republic of Cyprus through the Cyprus Research Promotion Foundation, he founded the Molecular Medicine Research Center at the University of Cyprus (www.ucy.ac.cy/mmrc), of which he is the Director. Also, with competitive funding, he started and established the first Biobank in the country, upon approval by the Cyprus National Bioethics Committee, for archiving samples and patients with genetic diseases. His work has been reported in more than 120 original and review peer-reviewed publications in international journals and in additional local journals.

In 2008, Prof. Deltas was elected as "Eminent Scientist 2008" by the International Research Promotion Foundation, which honoured his innovative research on "Nephrology and Human Genetics" and awarded him with its prestigious Millennium Golden International Award for Europe. Also, he was awarded with the "Cyprus Research Award-Distinguished Researcher 2014". E-mail: Deltas@ ucy.ac.cy



### **Assistant Professor Dr Yiorgos Apidianakis**

University of Cyprus

Yiorgos Apidianakis, PhD, has been trained for 10 years at Harvard Medical School in BiomedicalResearch. He worked for 6 years as a postdoctoral fellow and 4 years as an Instructor in Medicine inthe field of human infectious diseases, practicing his research at the Massachusetts General Hospitaland the Shriners Hospitals for Children in Boston, USA. His is an expert in modeling human infectious diseases and carcinogenesis in model organisms using Drosophila and mice for preclinicaltrials (Apidianakis and Rahme Nat. Protoc. 2009; Apidianakis et al PNAS 2009; Bangi et al EMBO Rep2012). He extends the findings of his team with the use and analysis of human samples from clinical studies. For example, he has found that the Drosophila detoxification gene Glutathione S-transferase S1 (GstS1) and its mouse and human analog (GSTA4) contribute to host defence against infection with the human opportunistic pathogen Pseudomonas aeruginosa (Apidianakis et al PNAS 2005; Apidianakis et al PLoS One 2007; Apidianakis et al FASEB J. 2012). At the University of Cyprus he leads "The Cyprus Intestinal Health Study" (National Bioethics Committee Licence Number: EEBK/EII/2015/38) a translational to clinical study to explore primarily the effect of regenerative inflammation in colon cancer (Panayidou and Apidianakis Pathogens 2013; Panagi et al Oncotarget 2015; Apidianakis and Iliopoulos EMBO Rep 2015).



### Dr George K. Andrikopoulos

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

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 Institute for the Study and Education on Thrombosis and Antithrombotic Therapy (2016), member of the board and 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 124 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 director of the department of Electrophysiology and Pacing.



#### **Professor Dr Charalampos Grassos**

Director of Cardiology Dept 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 bord 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 Co-ordinator or Principal Investigator. He is author of >70 articles in peer-reviewed journals like Hypertension, BMJ,Blood Pressure, Circulation, Atherosclerosis.



#### **Professor Dr Philip Calder**

Professor of Nutritional Immunology within the Faculty of Medicine at the University of Southampton. President of the (UK) Nutrition Society

Professor of Nutritional Immunology within the Faculty of Medicine at the University of Southampton. He is a Registered Nutritionist and a Fellow of both the Royal Society of Biology and the Association for Nutrition. He conducts research at the interface of nutrition, immunity and inflammation. His research addresses both life course and translational considerations. He has received several awards for his work including the Danone International Prize for Nutrition (2016) and the DSM Nutrition Prize in Human Nutrition (2017). He was President of the International Society for the Study of Fatty Acids and Lipids (2009-2012) and Chair of the Scientific Committee of the European Society for Clinical Nutrition and Metabolism (2012-2016). He is currently President of the (UK) Nutrition Society. Professor Calder was Editor-in-Chief of the British Journal of Nutrition (2006 to 2013) and he is currently an Associate Editor of several journals.



### **Professor Dr Ioannis Tentes**

Director of the Laboratory of Biochemistry, Democritus University of Thrace Medical School in Alexandroupolis, Greece.

studied Biochemistry in Salford University (Manchester, UK). Had a four-year fellowship in the Institute of Molecular Biology and Biotechnology (IMBB) in Heraklion, Crete, Greece, and started his academic career in 1993 as a Lecturer in the Democritus University of Thrace Medical School in Alexandroupolis, Greece. In this faculty, he established the Laboratory of Biochemistry wherein he is the Director, as Professor of Biochemistry. For the past thirty years he did his research in the fields of protein chemistry, signal transduction and cancer pharmacogenomics, collaborating with research groups based in Greece and abroad including the Ludwig Institute for Cancer Research (Uppsala, Sweden), the Departments of Oncology, Pathology and Pharmacognosy of the Medical University of Vienna (Austria), the St. George's Hospital in London (UK) and the Laboratory of Molecular Medicine in Boston University (USA).

His current research interests focus on Lipid metabolism/kinetics as part of the pathophysiology of diseases with metabolic background both as a basic as well as translational approach. For this purpose, there has been close translational collaboration between his team and the Clinics of the Medical School, including Cardiology as well as Pathology. He has published more than sixty peer-reviewed papers with more than 1000 citations to this day, and made more than 100 presentations in Congresses throughout the world. From his latter research, novel prognostic biomarkers for Coronary Artery Disease have been postulated. His team received the 2005 Young Investigator Award in Clinical Science by the European Society of Cardiology, and the 2006 Young Investigator Award in Coronary Pathophysiology and Microcirculation by a working group of the European Society of Cardiology.



### Ass Prof. Dr Evangelia Ntzani

Head of the Department of Hygiene and Epidemiology, University of Ioannina, School of Medicine, Greece

Evangelia Ntzani is a pediatrician and an epidemiologist and an Associate Professor and Head of the Department of Hygiene and Epidemiology, University of Ioannina, School of Medicine, Greece. She also holds an adjunct position in the Center for Research Synthesis in Health at the Brown University School of Public Health, Brown University, USA. Dr Ntzani is coordinator and investigator in grants on research methodology, evidence assessment, environmental epidemiology, genetic epidemiology of complex diseases and motivating behavior change across diverse areas. Her research interests yielding publications of more than 7,000 citations include evidence-based medicine, assessment of large-scale clinical and molecular information, clinical and molecular epidemiology, and research methodology and bias.



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

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

completed his medical education in 1983 and obtained his Doctoral Thesis at the Aristotle University of Thessaloniki, Greece in 1989.

He was trained in Cardiology in Thessaloniki and UK where he subspecialized in Invasive Cardiology and Electrophysiology at St Bartholomew's Hospital in London and practiced for several yeas at the Onassis Cardiothoracic Centre in Athens.

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

In 2000 was appointed as a Lecturer at the Aristotle University of Thessaloniki and organized the first invasive electrophysiology and automatic defibrillator implantation program in Northern Greece at the AHEPA University Hospital.

As President of the Hellenic Working Group on Pacing and Electrophysiology, organized the National Registries of Ablations and Devices in Greece under the auspices of the Hellenic Cardiac Society.

He is a committee member of the Working Groups for training in undergraduate and postgraduate Medicine, for the National Guidelines for training in Cardiology and drug prescription on arrhythmias.

Since 2014 is the Director of the 3rd Cardiology University Department at Hippokrateio General Hospital, Thessaloniki where he installed a new, fully equipped Hemodynamic suite and CCU with a "Stavros Niarchos Foundation" grand. In collaboration with the Department of Medical Informatics he developed an ECG signal -analysing platform using wavelet analysis. This method is part of his current research activity, and is used in various groups of patients in order to identify subtle electrophysiological irregularities and their relation with clinical prognosis. He participated in numerous international trials as Primary Investigator.

Professor Vassilikos published extensively and actively participates in local, regional and international scientific meetings.



#### Professor Dr. Wolfgang F. Graier

Professor of Molecular Biology at the Medical University of Graz, Austria; head of the Nikon-Center of Excellence for Super-Resolution Microscopy;

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 focuses on the potential of mitochondria-endoplasmi 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 organelletargeted 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-found 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.



### **Theodoros Xanthos**

School of Medicine, European University Cyprus

Theodoros Xanthos MD, Pg Dip (Ed), MSc, PhD, FHEA, FAcadMEd FERC, FCP has studied Medicine in the University of Athens, and has specialized in Internal Medicine in Cardiology both in Greece and in London (UK). He has obtained his PhD from the University of Athens and he has also a Post Graduate Diploma on Medical Education from the University of Cardiff, an MSc on Clinical Toxicology from the University of Cardiff and an MRes on Higher Education from the University of Liverpool. He is a European Resuscitation Council (ERC) Course Director Organizer for all its courses and he is furthermore an ERC educator. He is a member of the working group of ERC Advanced Life Support and he is one of the authors for the guidelines on Resuscitation for 2015. He is also a reviewer and an author for the International Liaison Committee on Resuscitation and he has worked on the worksheets regarding Hypothermia post arrest. He is also a Fellow of Academy of Medical Educators a Fellow of the Higher Education Academy, a Fellow of the European Resuscitation Council and a Fellow of the American Academy of Clinical Pharmacology. He has worked for the University of Athens and he was appointed as a Professor of Pharmacology for Midwestern University of Chicago and as a Professor of Resuscitation for the School of Specialization for the University of Cagliari. He holds several awards, patents and has received many scholarships from various Organizations. He is also the Current Chair of the ERC Social Media Working Group. He has published extensively on pharmacology, physiology and pathophysiology along with healthcare education. He has an impact factor of more than 890 with publications in prestigious journals, such as the Lancet. His citations are more than 5000 and his h index is 32. He has been a visiting scholar in many Universities and has received several awards for his teaching skills.



#### Dr. Zamba-Papanicolaou

Consultant Neurologist and the Director of Clinic D (Neuromuscular, Neurogenetic diseases and Clinical Electromyography) at the Cyprus Institute of Neurology and Genetics (CING)

Dr. Zamba-Papanicolaou is a Consultant Neurologist and the Director of Clinic D (Neuromuscular, Neurogenetic diseases and Clinical Electromyography) at the Cyprus Institute of Neurology and Genetics (CING). She is also the Coordinator of the Clinical sector at the CING and serves as an Assistant Professor of Neurosciences at the Cyprus School of Molecular Medicine of the CING.

Her research and experience focus on rare monogenic neurological diseases with respect to clinical phenotype, phenotype/genotype correlation, investigation of families and epidemiology. Dr Zamba-Papanicolaou is also involved in clinical trial execution with respect to these diseases. Furthermore, she is involved in clinical electromyography research with a special emphasis on neuromuscular diseases. Lastly, she is active in the field of chronic neuroepidemiology, working on complex diseases such as Parkinson's disease and Dementia.

Dr. Zamba-Papanicolaou teaches at the Cyprus School of Molecular Medicine, and supervises Master's and PhD candidates in neuroepidemiology and clinical neuroscience.



#### **Associate Professor Dr Konstantinos Toutouzas**

Department of Cardiology of University of Athen

Konstantinos 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. Since 2014 he serves as Associate Professor of Cardiology in the First Department of Cardiology of University of Athens. He has also held a visiting associate professorship in University of Bolton. 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, including transcatheter aortic valve implantation, atrial septal defect, patent foramen ovale and left atrial appendage closure, with the use of dedicated devices. Notably, he is a proctor for Evolute R device and for optical coherence tomography imaging.

He has a rich scientific work. His main research interest focuses on invasive assessment of vulnerable or high-risk plaques, including intravascular ultrasound, thermography and optical coherence tomography, non-invasive detection of vulnerable plaque inflammation by novel imaging modalities and the clinical study of patients with severe aortic valve stenosis, undergoing transcatheter aortic valve implantation. He is an author of more than 250 publications in peer reviewed journals.

Finally, Ass. Professor Konstantinos Toutouzas has presented more than 530 abstracts, has given more than 80 invited lectures and chaired in more than 20 lectures in international scientific meetings. He is the editor of two books in Greek language and associate editor of International Journal of Cardiology.



### **Professor Dr Anastasis Stephanou**

Professor of Cell, Molecular Biology and Genetics at the European University, School of Medicine

Professor Stephanou is currently Professor of Cell and Molecular Biology at the European University, School of Medicine (2014 – present). He completed his PhD at the Westminster and Charing Cross Medical School, University of London in 1992. He then did his Post-doctoral training (1992-1995) in the Department of Endocrinology, Cincinnati Children's Hospital, USA, working transcriptional gene regulation. In 1995, he moved as a postdoctoral fellow to the laboratory at the Windeyer Institute of Medical Sciences, UCL where he studied the regulation of heat shock proteins and their cytoprotective properties. During his postdoctoral work, he developed his interest in the Signal Transducers and Activators of Transcription (STATs) factors as key regulators of apoptosis. In 2002, Dr Stephanou became a Lecturer at UCL and in 2005 was promoted to a Reader/Associate Professor. His main research interests is in the field of signal transduction in pathways and mechanisms of cell death (apoptosis), cell cycle regulation and autophagy in disease models such as myocardial infarction injury and also in cancer. Other interests include collaborating with a colleague in the Mechanical Engineering Department at UCL, who has developed a novel technique called bioelectrospraying (BES) for deposition and Other controlled jetting of primary neonatal cardiac myocytes, primary cardiac and endothelial cells, as well as creating a beating cardiac tissue graft and are hoping to use such protocols for transplantation and treatment of severe heart failure models. He has recently edited a book entitled "JAK-STAT Pathway in Diseases" and also in 2012 became Editor-In-Chief of the journal JAK-STAT. He has authored over 150 peer-reviewed articles.



### Assist. Prof. Dr Carsten Werner Lederer

Group leader at the Molecular Genetics Thalassemia Departmentof the Cyprus Institute of Neurology and Genetics (CING) and the head of the MGTD Gene Editing and Therapy unit

Dr Lederer is group leader at the Molecular Genetics Thalassemia Department (MGTD; head: Marina Kleanthous) of the Cyprus Institute of Neurology and Genetics (CING), where he heads the MGTD Gene Editing and Therapy unit. Dr Lederer is Assistant Professor and course coordinator at the Cyprus School for Molecular Medicine, executive board member of the Global Globin 2020 Challenge, co-curator of the ITHANET Portal, board member of the Cyprus Society of Human Genetics and member of the Hellenic Society of Gene Therapy and Regenerative Medicine. Research Interests

Dr Lederer's current research focus is the gene therapy of  $\beta$ -globinopathies and particularly of  $\beta$ -thalassaemia by three different approaches, a) mutation-specific RNAi-supplementation of gene addition, b) genome editing of disease modifiers and c) homology-independent gene repair. Additional scientific activities include involvement in the development of the ITHANET Portal and its classification of pathological variants, as well as the promotion of the Global Globin 2020 Challenge for prevention, disease management and comprehensive epidemiology in low- and middle-income countries.

Publications

Dr Lederer is author of 31 peer-reviewed articles with over 1800 literature citations and an h index of 15.For an updated list of publications, see here.



#### Ass. Prof. Dr Violetta Christophidou Anastasiadou

Founder and first lead of the Clinical Genetics Clinic in Cyprus, which currently offers services at the Archbishop Makarios III Hospital in Nicosia and the Cyprus Institute of Neurology and Genetics

Violetta Christophidou Anastasiadou completed her medical studies at Athens National and Kapodistrian School of Medicine. She obtained her specialty in Pediatrics at P. & Aglaia Kyriakou Hospital and continued specializing in Medical Genetics at Athens and at John's Hopkins University in Baltimore USA. She is the founder and first lead of the Clinical Genetics Clinic in Cyprus, which currently offers services at the Archbishop Makarios III Hospital in Nicosia and the Cyprus Institute of Neurology and Genetics. She has been a lecturer at the European Genetics Foundation in Italy and currently she is an associate professor at the CSMM. She has been active in the field of Rare Diseases for the last 27 years both locally and internationally. She has represented Cyprus in various European Reference Networks. She has been training internists in pediatrics, as well as students of the Cyprus University Medical School and other local universities. Her research interests and publications address the epidemiology of various rare genetic conditions in Cyprus, genetics of mental retardation and bioethics challenges in the application of biomedicine.



#### Professor Dr Loizos G. Loizou

Director of the Pediatric Oncology - Hematology Clinic at the Archbishop Makarios III Hospital in Nicosia, Clinical Professor of Pediatrics, Pediatric Oncology - Hematology at the Medical School of the University of Nicosia and President of the ELPIDA Foundation for Children with Cancer and Leukemia.

Prof. 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 and undertake the establishment and operation of the Pediatric Oncology - Hematology Department at the Archbishop Makarios III Hospital, which he runs until today.

As the founder of Pediatric Oncology-Hematology in Cyprus, he created the clinical and laboratory services, for children and adolescents with cancer and leukemia, which were previously inexistent in our country. He undertook the training of the medical, nursing and other staff as well as the sensitization of the general public and the relevant authorities, in order to create the entire necessary infrastructure to provide the best possible care for the cancerous and leukemic children in our country. 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 Cyprus for storing pluripotent umbilical cord and bone marrow stem cells at the Archbishop Makarios III Hospital in Nicosia.

As a pioneer in the care of children and adolescents with cancer in Cyprus, in 1990 he also created and is the President of the ELPIDA Foundation for Children with Cancer and Leukemia (a nongovernmental charity organization) having as specific aims to strengthen and support the medical and social efforts to create the modern infrastructure for the care of our sick children and offer them the best possible therapies and overall management.

Prof. Loizou, with his unique experience of 35 years of exclusive occupation with childhood cancer and leukemia, continues his clinical and research work in descriptive epidemiology, survivorship issues and cancer predisposition syndromes, 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.



#### 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

Dr 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 (University College London, UK; Hadassah University Hospital, Jerusalem, Israel; Vienna Brain Research Institute, Austria).

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 and the Laboratory of Experimental Neurology and Neuroimmunology.

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 (until 2010), Co-founder and Secretary of the Hellenic Academy of Neuroimmunology. He has recently been elected President of the Hellenic Neurological Society. He is Ad Hoc reviewer in more than 40 international scientific journals, co-ordinator in more than 40 multicenter clinical trials for MS and principal investigator in collaborative research projects for 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; clinical trials. He has published more than 160 papers in peer reviewed journals, and his current citation index is more than 4500 with an H-index: 37.



### Professor Dr Nikolaos Zamboglou

Medical Director of the German Oncology Center in Limassol, Cyprus

Professor Nikolaos Zamboglou was born and raised in Limassol, Cyprus and in 1967 he moved to Germany for his studies. He was awarded a degree in Physics from RWTH Aachen in 1974, and in 1977 he obtained his PhD in Physics at the University of Dusseldorf. He completed his degree in Medicine in 1984 and his PhD in Medicine in 1989, both at the University of Essen.

From 1986 to 1992, Prof. Zamboglou held the post of Consultant of Radiation Oncology at the University of Dusseldorf. He subsequently assumed his appointment as Director and Professor of the Department of Radiation Oncology at Clinikum Offenbach, at the Academic Hospital of Wolfgang-Goethe University, Frankfurt, where he remained until 2016.

Professor Zamboglou is also appointed as Adjunct Research Professor at the Technical University of Athens since 1993. He is elected as corresponding member of the Academy of Athens in 2010. Most notably, he served as President of the German Society of Radiation Oncology between 2005 and 2007, and in 2012 was declared as a Honorary Member of the Austrian Radiation Oncology Society. Finally, in 2015 he was honored with the Alfred-Breit Award of the German Society of RADIATION Oncology (the highest society award).

Since, 2016 Prof. Zamboglou has been acting as Medical Director of the German Oncology Center in Limassol, Cyprus. Since, July 2018 Nikolaos Zamboglou appointed as Professor in Oncology at European University Cyprus.



#### **Professor Dr Theodoros Kyriakides**

Professor at the Cyprus School of Molecular Medicine and Senior Consultant at the Cyprus Institute of Neurology and Genetics

Dr Theodoros Kyriakides is a Professor at the Cyprus School of Molecular Medicine and Senior Consultant at the Cyprus Institute of Neurology and Genetics. He graduated Physiology (BSc Hons) and Medicine (MB ChB) from Bristol University in 1983.

He trained in General Medicine and Neurology in the UK and in Neuropathology in Perth Australia. Since 1992 he works as a Senior Consultant in the Cyprus Institute of Neurology and Genetics where he is also in charge of the Neuropathology Lab. His clinical interests are neuromuscular disorders and Multiple Sclerosis. He sees a variety of myopathies and neuropathies and he is particularly interested in TTRMet30 amyloidotic neuropathy.

He joined the University of Nicosia Medical School in 2011 and he is currently the Module Convenor for Life Control for CS and T Year as well as Lead for NeuroPlus in P Year for the St. George's University of London Medical Programme delivered in Cyprus at the University of Nicosia. In 2013 he was appointed Professor at the University of Nicosia.

His main research interests include the study of Complement C1Q and C5aR inhibition in a mouse model of TTRMet30 amyloidotic neuropathy, the study of modifier genes and epigenetics in disease severity in Multiple Sclerosis.



#### Professor Dr Massimo Filippi

Director of the Residency School in Neurology and Presiden of the Bachelor's Degree in Physiotherapy, Vita-Salute San Raffaele University; Director, Neuroimaging Research Unit, INSPE, Division of Neuroscience; San Raffaele Scientific Institute.

Massimo Filippi is currently Full Professor of Neurology at Vita-Salute San Raffaele University, Milan, Italy; Director Residency School in Neurology, and President of the Bacherlor's Degree in Physiotherapy at the same University; Director of the "BrainMap" Interdepartmental Program and Director of the Neuroimaging Research Unit (NRU), Department of Neurology, Institute of Experimental Neurology, Scientific Institute San Raffaele, Milan. His research activity has always focused on the definition of the mechanisms leading to progressive accumulation of irreversible physical disability and cognitive impairment in various neurological conditions. As Director of the NRU, he coordinated the MRI acquisition and analysis of several large-scale international MRImonitored trials of MS. He is member of various national and international Scientific Societies and Boards where he covered or is covering institutional roles. He is author of over 990 papers; he is Editor-in-Chief of the Journal of Neurology and member of the Editorial Boards of many international scientific journals. He is very often requested as speaker and/or chairman in national and international neurological congresses. In 2001, Prof. Filippi was awarded the Rita Levi Montalcini Prize for his outstanding contributions to the study of MS.



### **Dr Theodoros Christodoulides**

board member of Cyprus Society of Cardiology, currently serving as vice president

Doctor Theodoros Christodoulides completed his medical education at 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 actively involved in heart failure since he is a nucleus member of Cyprus Society of Cardiology heart failure working group serving as a president and vice-president. He served as a national coordinator for the EURObservational Research Program Heart Failure Registry until 2017. He has also been a Task Force Member of the Heart Failure Specialists of Tomorrow committee, which is an initiative aiming to support the development of young professionals in the field of heart failure. He is a board member of Cyprus Society of Cardiology, currently serving as vice president.


### Ass. Professor Dr Apostolos Athanasiadis

Chairman of the 3rd Department Ob Gyn of the Medical School of Aristotle University, Thessaloniki, Greece

Apostolos Athanasiadis was born in Thessaloniki, Greece. He is a Professor in Obstetrics - Gynecology and Maternal Fetal Medicine and the Chairman of the 3rd Department Ob Gyn of the Medical School of Aristotle University, Thessaloniki, Greece, from which he graduated in 1980. He was specialized in the Maternal Fetal Medicine Unit of the Department of Obstetrics and Gynecology at Yale University, USA.

He participates in the educational programs of Greek medical schools and in postgraduate workshops in Europe and especially in South East Europe. He successfully contributed in organizing many congresses and courses in Europe as president, member of the organizing committees and scientific coordinator. His scientific contribution accounts for more than 200 scientific papers, presentations, articles and chapters. His papers have been cited more than 1300 times in the Science Citation Index. He has been invited as lecturer and has given more than 300 lectures in international and Greek congresses and meetings.

He envisioned and realized, with the collaboration of other professors and specialists in the field, the creation of the "South East European Society of Perinatal Medicine", which now consists of 13 countries. He is the Deputy Director of the Editorial Board of the Hellenic scientific journals "Ultrasonography" and "Perinatal and Neonatal Journal" and a member of the Editorial Board of the journal "Gynecology Obstetrics and Reproductive Medicine». He is a peer reviewer in Greek and International scientific journals.

At present, he is the President of the "Hellenic Society on Ultrasound in Obstetrics and Gynecology", Chairman of the Educational Committee of the "European Association of Perinatal Medicine". He was the past President of the "Hellenic Society of Perinatal Medicine" (2002-2004) and Past President of the "South East European Society of Perinatal Medicine" (2013-2015). He participates in 20 Greek and International scientific societies. He is an Associate Member of the "International Academy of Perinatal Medicine", Visiting Professor at Weill Cornell Medical College USA, Visiting Professor at European University Cyprus, an Honorary Member of the "Romanian Society of Perinatal Medicine" and has been awarded with the "Soranos 2011" and Ayash Siban Sifai 2009" scientific awards.

His main scientific interests are fetal medicine, prenatal diagnosis, 3D and 4D ultrasonography and metabolomics in pregnancy.

He is married to Frida Athanasiadis and has two children.

# Speakers CVs



#### **Professor Dr Maddalena Lettino**

Clinical Director for strategic development – Cardiology Clinical Lead, project management group for diagnosis & treatment of chronic cardiovascular diseases at Humanitas Research Hospital, Milan, Italy.

Dr MaddalenaLettino is Clinical Director for strategic development –Cardiology Clinical Lead, project management group for diagnosis & treatment of chronic cardiovascular diseases at Humanitas Research Hospital, Milan, Italy. After graduating in 1982 she developed her practice in research hospitals in Pavia and Milan. Dr Lettino has been a lecturer/adjunct professor at the Universities of Milan and Pavia since 1997. She has been chairperson of the Italian National Working Group of acute Cardiac Care, in charge of co-ordination of all the regional cardiologic initiatives and promotion of education and training in the sector. Nationally, this work concentrated on the management of the cardiologic emergency. Dr Lettino has been a board member and then Committee Chair in the ESC Acute Cardiac Care Association, Europe, and she is now the President of the Association. Additionally, she is an editorial board member of the European Heart Journal: Acute Cardiovascular Care and of the European Heart Journal of Cardiovascular Pharmacotherapy. Dr Lettino's clinical research work is concentrated on antithrombotic therapy of acute coronary syndromes, physiopathological mechanisms of coronary atherothrombosis, management of anti-platelet therapy in revascularized patients who are to undergo non-cardiac surgery and anticoagulation in thromboembolic disorders like atrial fibrillation.



#### **Dr. Marios loannides**

Senior R&D Manager at NIPD Genetics.

Dr. Marios loannides received his BSc and MSc degrees in Microbiology from University of South Florida. He received his PhD in Medical Genetics from the University of Cyprus and the Cyprus Institute of Neurology and Genetics. For 6 years he was a member of the scientific staff at the Department of Cytogenetics and Genomics at the Cyprus Institute of Neurology and Genetics (2005-2010). In 2010, he transferred to the Translational Genetics Team where he was involved in research in the field of non-invasive testing. He also served as acting Head of the Team during which he supervised all the projects of the Team. He has published several peer-reviewed articles, and presented findings at national and international conferences. Since 2015, has been the R&D Senior Manager at NIPD Genetics.

# Speakers CVs



### Professor Dr Achilleas Gravanis,

Professor of Pharmacology, School of Medicine, University of Crete

Professor Dr AchilleasGravanis, Professor of Pharmacology, School of Medicine, University of Crete AchilleasGravanis, Professor of Pharmacology, School of Medicine, University of Crete, Researcher at the Institute Molecular Biology-Biotechnology, Foundation of Research & Technology-Hellas (IMBB-FORTH). Affiliated Research Professor, Center of Drug Discovery Northeastern University, Collaborating Scientist Emulate, WYSS/Harvard. He served as member of the Fellowships Committee of FEBS and participated as Chairman and member in numerous research committees of the European Union, including the Programme Committee of Framework Programmes FP6 and FP7. He was the Chairman of Biosciences Committee of the Hellenic Research & Technology Council, and a Member of the Board of the Hellenic Agency for Evaluation and Accreditation of Higher Education. He is actually a member of the Scientific Council of the Hellenic Foundation of Research & Innovation. He published more 130 papers PubMed journals (h index: 43, citations: 5.100). He is the co-founder of biotechnology spinoff Bionature EA Ltd (www.bionature.net).



#### Professor Dr Kyriacos Kyriacou

The Cyprus School of Molecular Medicine at The Cyprus Institute of Neurology & Genetics

Professor Kyriacos Kyriacou (male) is the Founder and Head of the Department of Electron Microscopy/Molecular Pathology (EM/MP), and Professor, and Dean of the Cyprus School of Molecular Medicine. K. Kyriacou obtained his BSc Honours degree, in Biochemistry/Physiology, from the University of London in 1977, and his PhD from the Faculty of Medicine, Department of Oral Pathology, King's College Schools of Medicine and Dentistry in 1982. In 1983 he was appointed Lecturer in Biochemistry, in the Medical School at King's College Hospital, London. In 1991 he was appointed Senior Scientist, at CING. His main research interests include the genetic epidemiology and molecular pathology of cancer, with emphasis on breast cancer genetics. He was instrumental in obtaining funding for organizing the National research project on characterising the spectrum of mutations in the BRCA genes, in Cypriot families. Through this research unique mutations were also identified in Cypriot families, in BRCA1 and BRCA2 genes and these results led to the establishment of an important cancer genetics service for the whole Cyprus population. Recently he has obtained major funding for establishing the first and only Translational Facility consisting of Genomics and Proteomics platforms at CING. He has co-ordinated more than 50 research projects. has obtained more than 8,000,000 euros in competitive funding and has published more than 130 articles, in peer reviewed journals. He represents Cyprus in several Societies and advisory committees in Europe. He has served as the representative of Cyprus, in the EU-COST programme, in the BMBS (Biomedicine and Biomolecular Sciences) domain. He is an active member of the Electron Microscopy working group which is part of the European Society of Pathology and has served as a Consultant of ESMO, on Genetic Educational Courses. He serves as a reviewer for several scientific journals and research funding bodies. Professor Kyriacou has organized several scientific conferences, at both National and International levels and has been invited to deliver many lectures both locally and at International Conferences. He has graduated 5 PhD and 20 MSc students.



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# Bio-medical Scientific Cyprus

## Abstracts

- Invited Abstracts
- Selected Abstracts
- Poster Abstracts

# Ubiquitin Proteolytic System - From Basic Mechanisms thru Human Diseases and on to Drug Development

#### **Professor Dr Aaron Ciechanover**

The Technion Integrated Cancer Center, Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel

Between the 50s and 80s, most studies in biomedicine focused on the central dogma - the translation of the information coded by DNA to RNA and proteins. Protein degradation was a neglected area, considered to be a non-specific, dead-end process. While it was known that proteins do turn over, the high specificity of the process - where distinct proteins are degraded only at certain time points, or when they are not needed any more, or following denaturation/ misfolding when their normal and active counterparts are spared - was not appreciated. The discovery of the lysosome by Christian de Duve did not significantly change this view, as it was clear that this organelle is involved mostly in the degradation of extracellular proteins, and their proteases cannot be substrate-specific. The discovery of the complex cascade of the ubiguitin solved the enigma. It is clear now that degradation of cellular proteins is a highly complex, temporally controlled, and tightly regulated process that plays major roles in a variety of basic cellular processes such as cell cycle and differentiation, communication of the cell with the extracellular environment and maintenance of the cellular guality control. With the multitude of substrates targeted and the myriad processes involved, it is not surprising that aberrations in the pathway have been implicated in the pathogenesis of many diseases, certain malignancies and neurodegeneration among them, and that the system has become a major platform for drug targeting.

### **Earlier Detection of Cancers Using Non-Plasma Non-Invasive Tests.**

#### **Nickolas Papadopoulos**

Johns Hopkins University School of Medicine

Early detection of cancer provides one of the most effective ways to reduce cancer related morbidity and mortality. Blood based liquid biopsy has provided an opportunity for the development of early detection tests. However, neoplastic conditions are not readily detectable using blood based assays. One of the chief challenges in developing minimally-invasive tests is the identification of the appropriate biofluid and cancer specific biomarkers. Over the past two decades, DNA released from cancer cells has emerged as a specific clinical biomarker of cancer and we have previously developed sensitive methods for detection of this released tumor DNA (rtDNA) and demonstrated its potential applications in variety of clinical

samples. We will discuss a test, called PapSEEK, for the sensitive detection of endometrial and ovarian cancer utilizing liquid from the Papanicolau test. Similarly, we have developed a urine test, called UroSEEK, for the detection of bladder cancer in people with hematuria and monitoring for the presence of minimal residual disease after cystoscopy. We will also discuss similar clinical applications in other bodily fluids. Our vision is to develop non-invasive tests for the detection of cancer.

### Thromboprophylaxis in Medically III

#### **Prof. Dr Spyropoulos Alex**

Clinical geneticist at Archbishop Makarios III; Collaborating with The Cyprus School of Molecular Medicine at The Cyprus Institute of Neurology & Genetics

Venous thromboembolism (VTE) is a major cause of morbidity and mortality in hospitalized medically ill patients. It is estimated that in the US and EU alone, approximately 650,000 VTE-related deaths can be attributed to recent hospitalization in the medically ill population, where rates of VTE linked to hospitalization are estimated to be 35-fold higher than those non-hospital related. Although multifactorial risk factors for VTE have been recognized for some time in this population and linked to both intrinsic (patient-related) and extrinsic (disease-related) causes, it is only recently that evidence-derived, scored, and validated VTE risk models such as the IMPROVE VTE score have been applied to the medically ill population. These models help to assess how individual VTE risk factors can be weighted and combined to determine the overall VTE risk in a particular patient at the bedside.

Anticoagulant-based primary thromboprophylaxis with either unfractionated heparin, low molecular weight heparin (LMWH), or the pentassacharidefondaparinux in the medically ill population has been shown from data that is nearly 20 years old to produce a 50-60% reduction in total VTE risk when given in-hospital. Initial large clinical trials studying extended thromboprophylaxis for 4 weeks of more in medically ill with either LMWH or the direct oral anticoagulants (DOACs) have shown mostly benefit but with an increased risk of major and clinically relevant non-major bleeding, producing an overall unfavorable net clinical benefit in this population. More recently large clinical trials of extended thromboprophylaxis with the DOACs betrixaban and rivaroxaban have finally shown an improved safety profile by careful patient selection, thus making a strategy of extended thromboprophylaxis beneficial. If this extended thromboprophylaxis strategy is applied to the 25-30% of medically ill patients - as modeling estimates suggest - that have a high enough VTE risk to benefit from such a strategy, then there is potential from a populational perspective to reduce the burden of VTE, including VTE-related death, in tens of thousands of patients in the US and EU.

### **New perspectives in Oncology**

#### Professor Dr Nikolaos Zamboglou

Medical Director of the German Oncology Center in Limassol, Cyprus. Since, July 2018 Nikolaos Zamboglou appointed as Professor in Oncology at European University Cyprus

In Modern Oncology there has been much improvement in Surgery, in Radiation Oncology and in Medical Oncology. The most important advances will be presented. Such as:

- a) Staining of tumours during surgery
- b) Interventional Radiation Oncology
- c) Immunotherapy

### **Epidemiology of Rare Diseases in Cyprus**

#### Assist. Prof. Dr Zamba-Papanicolaou

Consultant Neurologist and the Director of Clinic D (Neuromuscular, Neurogenetic diseases and Clinical Electromyography) at the Cyprus Institute of Neurology and Genetics (CING).

**Background:** Huntington disease (HD) and Amyotrophic lateral sclerosis (ALS) are rare progressive neurodegenerative diseases. The epidemiology of ALS and HD in Cyprus, an island in Southern Europe with extensive western European colonization during the past millennium, has never been examined and this was the aim of this study.

**Methods:** All registered Cypriot ALS patients in the Republic of Cyprus from January 1985 until December 2014 and all registered HD patients in the Republic of Cyprus, since 1994, were included. Sociodemographic and clinical information were recorded and maps, showing the geographic distribution of the disorders, were constructed.

**Results:** The study identified 179 ALS patients, seven of whom had a positive family history. The mean age at onset was 58.6 years and a slight male predominance was observed. Average annual crude incidence was 1.26 cases/100,000 person-years and at the beginning of 2015, prevalence of ALS was 7.9 cases/100,000 population. Both incidence and prevalence displayed an increasing trend, even after age-standardization of incidence rates. For HD, the project identified 58 clinically manifested cases of HD belonging to 19 families. Sixteen families were of Cypriot origin and were concentrated in a confined geographical cluster in Southeast Cyprus. In 2015 prevalence of symptomatic HD was 4.64/100,000 population, while incidence was 0.12/100.000 person years.

**Conclusions:** Incidence, prevalence and main sociodemographic characteristics of ALS and HD in Cyprus were similar to those of other European countries. For ALS, an increased

incidence through the years was confirmed. For HD, the geographical clustering of HD families observed supports the possibility for a relatively recent founder effect of HD in Cyprus, which could potentially be of western European origin.

# Interprofessional education – medical and healthcare professionals working in conjunction to treat patients – provides benefits for both the patients and the professionals. Several benefits arise from such education.

### Professor Dr Theodoros Xanthos

School of Medicine, European University Cyprus

### 1. It Empowers Team Members

Until the rise of interprofessional collaboration, and even now in some medical environments, the doctor was viewed as the "quarterback" of patient care. The doctor made most major decisions about how a patient was treated and cared for. With an increased emphasis on interprofessional collaboration, other members of a patient's medical team, such as nurses, radiologists, EMTs, social workers and professionals from any number of other disciplines, are empowered to make recommendations about patient care.

### 2. It Closes Communication Gaps

When all medical and healthcare professionals are working together, a more communicative environment develops. Before interprofessional collaboration practices were adopted, medical professionals would simply look at a patient's chart to review treatments and patient history. Working independently could lead to missed symptoms or miscommunication about patient needs. With increased collaboration, medical professionals are interacting on a personal level, sharing ideas about patient treatment and working together to maintain continuity of care.

### 3. It Enables Comprehensive Patient Care

When team members from different disciplines work jointly, it's easier to form a more comprehensive view of patient care. Think of each medical professional as holding a piece to the puzzle. Bringing all these pieces together enables a better understanding of the patient's needs.

### 4. It Minimizes Readmission Rates

With better care and the closure of communication gaps, patient outcomes are better. Interprofessional collaboration combats ongoing patient care problems such as misdiagnosis. When a patient is misdiagnosed, he or she will probably be back in the hospital soon, at a high cost both to the patient and the medical facility. By increasing collaboration, patients are treated effectively the first time.

#### 5. It Promotes a Team Mentality

Patients aren't the only ones who benefit from interprofessional collaboration. Working independently puts pressure on medical professionals. By working together, medical professionals support each other, breaking down the silos of different disciplines. This team mentality raises morale and encourages camaraderie.

### 6. It Promotes Patient-Centered Care

Ultimately, the goal of all medical and healthcare professionals should be the same: to provide patients with the best care possible. This is easier to achieve with interprofessional collaboration. Instead of having individuals take turns caring for them, patients have a team on their side from the start, working together to provide care that has lasting results. Interprofessional collaboration starts with interprofessional education. When medical and

healthcare students receive training on how to work effectively as a team across disciplines, they're primed to collaborate this way in the workplace. Consider options on how to give your future medical professionals the collaborative training they need to care for patients as a team.

# Mitochondria – endoplasmic reticulum crosstalk as therapeutic target against aging, cancer and diabetes

### Professor Dr Wolfgang F. Graier

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Mitochondria are not only the master of cellular energy metabolism, they are also involved in multiple important processes including signal transduction, biosynthesis and gene expression. Noteworthy, mitochondria are also crucially involved in most pathological processes leading to cell dysfunctions and, ultimately, cell death. The reason of such ubiquitous involvement of mitochondria in cellular physiology and pathology is particularly achieved by intense interaction of the organelle with virtually all other cellular compartments. Very recently the endoplasmic reticulum (ER) – mitochondria axis received enormous attention. This interorganelle interface is organized in, so called, mitochondria-associated membranes (MAMs), the site where the exchange of substrates, products and ions takes place. Particular the latter one, namely Ca2+, appears to be the most important regulator of such inter-organellar communication and recent studies revealed abnormal inter-organellar Ca2+ transfer as hallmark in many diseases like Alzheimer, diabetes mellitus, cancer and aging. Applying state-of-the-art techniques such like super-resolution fluorescence microscopy (Gottschalk et al. Pflügers Arch [in press], 2018),

single Ca2+ channels recordings in the inner mitochondrial membrane (Bondarenko et al. Pflügers Arch. 467: 2509-25018, 2015), NMR or the design of genetically encoded biosensors (Eroglu et al. Nat. Commun. 7: 10623, 2016; Bischof et al. Nat. Commun. 8:1422, 2017; www. ngfi.eu), we discovered a posttranslational arginine metylation of the main regulator of the mitochondrial Ca2+ uptake, MICU1 (Madreiter-Sokolowski et al. Nat. Commun. 7:12897, 2016) that engages UCP2 as crucial facilitator for mitochondrial Ca2+ uptake (Trenker et al. Nat. Cell. Biol. 9: 445-452, 2007) under distinct pathological conditions. Accordingly, we are now able to envisage the specific changes in the ER – mitochondria axis in e.g. aging and cancer (Madreiter-Sokolowski et al Cell. Physiol. Biochem. 39: 1404-1420, 2016; Oncotarget 8: 80278-80285, 2017; Genes [in press], 2018). Based on this work, we are currently successfully testing potential leading compounds that are uniquely designed to counteract (so far) endothelial cell aging- or cancer-specific settings of the ER – mitochondria interface. Latest findings reveal a excellent specificity of these compounds that exclusively hits senescent or cancer cells and highlight the great potential of such strategies and compounds on either aging-associated vascular/endothelial dysfunction or cancer growth.

# The development of invasive therapies for arrhythmias in Greece: past, present and future

### Professor Dr Vassilios P Vassilikos

Director, 3rd Cardiology Department, Aristotle University of Thessaloniki

Arrhythmias are a very important area in Cardiology. Invasive therapies include ablation of tachyarrhythmias and implantation of cardiac rhythm management devices (CRMDs). Technology has made great progress over the last years, allowing successful treatment in the majority of the cases. In order to record and evaluate the extend of use and effectiveness of these techniques in Greece, in 2008 the radiofrequency ablation procedures (RFA) registry was formed. Later in 2015 the CRMD registry was organized. Both registries are under the auspices of the Hellenic Cardiac Society (HCS). This is a dynamic, web-based application, which acts as the interface for storing and retrieving patients' demographic data and procedure data. Access to the site is permitted only to registered users.

There are 30 licensed centers in 26 hospitals performing RFA in Greece. Sixteen are public and 10 private or semi-private hospitals. During the 2008-2017 year-period 15486 procedures in 14702 patients were recorded. In 2017, seven centers were performing more than 100 cases/ year, accounting for 65% of total cases.

The most common procedure until 2012 was slow pathway ablation for atrio-ventricular reentry tachycardia (AVNRT), the second being atrial fibrillation (AF) ablation since 2010. After

2014, AF ablation is in the first place, accounting for 34% of total cases. The third most common type of RFA is tachycardias involving an accessory pathway (the percentage is declining). Electro-anatomic mapping was used in 48.2% of total cases, CARTO being the most often used system. Success rates were high (median 96%, range from 78%-100% according to procedure type), complication rate was 2.3% (serious complications <1%) and total relapse rate was 2.2% at six months follow-up (range 0.2%-21%, according to procedure type).

CRMD registry was started in 2015, but the consistency of data input is not satisfactory. There are 61 centers in 51 hospitals licensed for pacemaker implantation. Sufficient data for analysis were available for 2015 and 2016 from 35 centers. Single chamber, dual chamber and VDD pacemakers account for 25%, 64% and 6% of total implants respectively. The implantation of MRI compatible, CRTP, AAI and wireless pacemakers is low (3.5%, 0.5%, 0.3% and 0.7% respectively).

For ICD implantation there are 31 centers in 27 hospitals. Single chamber, dual chamber and CRTD account for 24%, 50% and 26% of total implants respectively.

The electronic RFA and CRMD registries confirmed that all procedures are performed in Greece with high success and low complication rates, comparable to the European and US standards. The RFA procedures for atrial fibrillation are the majority of the cases since 2014, indicating that electrophysiologists have been through the learning curve for the procedure, and the referral pattern has changed. Although the data completion is high and satisfactory in the RFA registry, this is not true for CRMD registry. The latter requires more effort from the participating centers.

# Functional genomics and epigenetics in osteoarthritis: evidence for metabolic deregulation

#### Professor Dr Aspasia Tsezou

University of Thessaly, Faculty of Medicine, Larissa, Greece

Osteoarthritis (OA) is the most common form of arthritis and a leading cause of chronic pain and physical disability. It is characterized by progressive deterioration and loss of articular cartilage with concomitant structural and functional changes in the entire joint, including the synovium, meniscus (in the knee), periarticular ligaments and subchondral bone. Despite its high prevalence there is no effective method for preventing or retarding the progression of the disease. The main reason for the failures in disease modifying drugs development is the lack of incorporation of the different phenotypes that exist in OA. It is now established that OA is a heterogeneous disease with a variety of pathophysiologic drivers leading to multiple phenotypes. Among the different OA phenotypes are the inflammatory, cartilage-driven, bone-driven, traumatic/injury driven, aging and oxidative stress-related and the most recently identified the metabolic phenotype. The goal of our research was to identify novel biomarkers for prediction of disease progression and drug development and therapeutic targets targeting the metabolic phenotype.

We demonstrated that OA chondrocytes have impaired expression of LXR-a, LXR-B, ABCA1 and ApoA1, genes that are involved in the reverse cholesterol transport (RCT) system and that chondrocytes are capable of internalizing lipids demonstrating that regulation of cellular cholesterol levels is critical for OA pathogenesis. We also showed that Sterol Response Element Binding Protien-2 (SREBP-2), a lipid metabolism gene, is involved in OA pathogenesis and provided novel evidence for its TGF- $\beta$  induced activation through the ITGAV/PI3K/Akt pathway. Furthermore, we demonstrated that miR-33a, which is produced by SREBP-2, is a dual regulator of cholesterol synthesis through the TGF- $\beta$  1/Akt/SREBP-2 pathway and also of cholesterol efflux-related genes (ABCA1 and ApoA1) in OA chondrocytes. In addition, using a high resolution (8 X 60K) miRNA array platform interrogating 2,549 miRNAs we identified three circulating miRNAs in serum, namely hsa-miR-140, hsa-miR-671, hsa-miR-33 which were significantly down-regulated in OA patient's serum compared to healthy controls. Hsa-miR-33 expression was also tested in articular cartilage samples of the same OA patients and controls. In silico analysis predicted that all 3 miRNAs are involved in regulating metabolic processes. Finally, using an animal (rabbit) model of OA, established by Anterior Cruciate Ligament Transection (ACLT), we injected intra-articularly, miRNA-33a-mimic and found significant histological and molecular improvement in the joints with the miRNA-33a-mimic injection compared to the non-injected ones.

In conclusion, we provide evidence, through functional genomics and epigenetics, on the involvement of lipid metabolism in osteoarthritis. We suggest that hsa-miR-33a regulates cholesterol synthesis (SREBP2) and cholesterol efflux-related (ABCA1, ApoA1) genes and that is could serve as a potential biomarker for the evaluation of osteoarthritis risk and progression and also as a potential novel target for the amelioration of the OA phenotype.email: atsezou@ gmail.com

The value of laparoscopic and minimal access surgery in modern medical practice and education.

Assist. Prof. Dr Pantelis Trompoukis School of Medicine, European University Cyprus

Minimal access and laparoscopic surgery in the fields of Surgery and Gynecology in recent years offered to patients better treatment options and quality of life and to doctors new prospective in dealing with surgical practice. However despite the initial enthusiasm the results are not encouraging and minimal access and laparoscopic procedures are not done only in a minority of patients even if the known advantages over open surgery.

This is a matter of education and training. Furthermore laparoscopic surgery is great tool of teaching the medical students anatomy but again not all students have the privilege to learn from modern techniques. We analyze the situation, explain the advantages of laparoscopic and minimal access surgery and the reasons that medical students and residents require special education and training in this fields, in order to learn first and perform themselves later as specialists for the good of education and patient care.

### **Brain Heart Interactions in Heart Failure**

#### Professor Dr Filippos K. Triposkiadis

University of Thessaly and Director of the Department of Cardiology of the Larissa University Hospital

Heart failure (HF) is a complex clinical syndrome including several bidirectional feedback interactions between the heart and other organs, including the brain. The impaired cardiac function affects cerebral structure and functional capacity, whereas neuronal signals impact on the heart and the vessels. These bidirectional heart-brain interactions contribute to the development of the HF phenotype and affect many HF comorbidities of HF. The term cardiocerebral syndrome refers to a state of cognitive impairment of undefined cause in HF patients, beyond that anticipated in age-matched controls, and typically accompanied by anatomic brain changes. Improved cardiac performance and systemic hemodynamics have a positive impact on the brain. Conversely, overactivity of the sympathetic limb of the autonomic nervous system is the main process leading to the development of major cardiac pathologies in neurological disorders. A typical example is the Takotsubo syndrome (TTS), an increasingly recognized type of non-ischemic cardiomyopathy. Although the pathogenesis of TTS remains unclear, a complex interaction between catecholamine-mediated stimulation, myocardial stunning, and subsequent stress-related myocardial dysfunction seems to be the

main pathophysiological mechanism. Moreover, there is a strong association between preexisting psychiatric illness, particularly anxiety and mood spectrum disorders, and TTS. Acute exacerbation of psychiatric illness, rapid up-titration or overdose of certain psychotropic agents, and electroconvulsive therapy may trigger TTS. Treatment options of TTS are largely empiric and supportive; however, when hemodynamics permit, beta blockers seem to be helpful.

### When Cardiology meets Oncology

Ass. Professor Dr Konstantinos Toutouzas National and Kapodistrian University of Athens

During the last decades, there have been significant advances in the field of Oncology leading to improved survival as a result of novel targeted therapies and immunotherapies. Despite the improved outcomes, there is increased recognition of cardiotoxicities associated with these therapies. Moreover, as the population is ageing, many cancer survivor patients and patients undergoing chemotherapy have co-morbid conditions, such as coronary artery disease, hypertension, and diabetes. Recent epidemiological studies, have shown that cardiovascular (CV) disease is the leading cause of non-malignancy related death in this population which at times may be a result of cardiotoxicities associated with their cancer treatments. As such, the field of cardio-oncology has seen significant growth over the last several years.

Cardiotoxicity may be induced by multiple mechanisms and lead to a variety of CV complications (arrhythmias, vascular toxicity, heart failure, thromboembolism, pericarditis). Current preventive strategies for cardiotoxicity include 1) monitoring with imaging tools (echocardiography and/or magnetic resonance imaging-MRI) and biomarkers during therapy with intervention when toxicity signals appear, or 2) chemotherapy limitation (dose/continuous infusion) in high risk groups (primary prevention). Further research is necessary to better understand the mechanisms of action of cancer therapies (tyrosine kinase inhibitors, proteasome inhibitors, histone deacetylase inhibitors, CDK4/6 inhibitors and immunotherapies) and how they affect the CV system. Moreover, it is important to improve our identification of patients at highest risk for development of cardiotoxicities prior to treatment through establishment of guideline-directed screening recommendations. The collaboration between cardiologists and oncologists in the management of treatment-related cardiotoxicities is essential in order for patients to continue receiving optimal cancer care while minimizing both short- and long-term CV risk. Through the establishment of a cardio-oncology service, it is feasible to achieve high rates of cardiac optimisation and cancer treatment continuation.

### **Clinical assessment of hemodynamics in heart failure**

#### **Dr Theodoros Christodoulides**

CardioHealth Center, NicosiaCyprus

Abstract: Heart failure incidence is rising an is expected to rise even more in the next decades. It can cause a variety of signs and symptoms due to reduced cardiac function as well as fluid congestion and has a prognosis comparable to many cancer forms. Knowledge of cardiac hemodynamics is critical in heart failure management since it can guide the selection of treatment and the assessment of its effectiveness. It is also an important tool for risk stratification of heart failure patients. Even though cardiac hemodynamics are measured by introducing catheters in the heart, clinical examination can be a non-invasive and cost-effective way to assess heart hemodynamics which is accurate enough to be used on every day practice.

### CHOLESTEROL AND PHOSPHOLIPID PATTERNS OF THE ERYTHROCYTE MEMBRANE: A POTENTIAL "MIRROR" OR A "TROYAN HORSE" ACTING WITHIN THE CONTEXT OF METABOLIC DISEASE

### **Professor DR Ioannis Tentes**

School of Medicine, University of Alexandroupoli

Perturbation in carbohydrate and lipid metabolism and transport is an integral part of the pathophysiology of a plethora of diseases.

In this presentation, a novel role of the erythrocyte membrane is postulated, as part of the general processes of lipid and cholesterol exchange between plasma and tissues, featuring the paradigm of Coronary Artery Disease (CAD), where the erythrocyte membrane of patients with acute coronary disease (ACS) were observed to bear a higher cholesterol load versus those of patients with chronic stable angina (CSA) [1] and the quantity of cholesterol in those patients was shown to determine plaque progression [2], linking closely with coronary atherosclerotic burden [3] and suggesting a potential interplay between erythrocyte-derived lipid and the expansion of atheromata. This particular cholesterol pool responds to statin administration, displaying different time-course kinetics regarding either ACS or CSA [4].

An animal model aiding proof of principle [5] is also outlined.

Under this perspective, the erythrocyte emerges both as a collateral lipid transporter that can determine the risk of an acute incident, and as a true reporter/biomarker of the state of affairs at tissue level acting as a "Troyan horse" and a "mirror" of CAD.

Finally, a potential involvement of the erythrocyte membrane in other paradigms of diseases manifesting perturbations in lipid metabolism (Hepatitis C, Non- alcoholic steatohepatitis) is outlined, as spin-off projects that are active at present.

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### The role of Omega-3 Fatty Acids in Aging Retina

#### **Dr Tassos Georgiou**

Consultant Ophthalmologist at Ophthalmos Educational and Research Institute in Nicosia, Cyprus

Purpose: To evaluate the therapeutic effects of omega-3 ( $\omega$ 3) fatty acids in aged wild type C57BL/6 mice, in CCL2-/- animal model of retinal degeneration and in patients with dry age-related macular degeneration (AMD); when the blood levels of arachidonic acid (AA)/ eicosapentaenoic acid (EPA) ratio is <2.

Methods: Pre-clinical assessment of  $\omega$ 3 efficacy was performed in two year-old wild type C57BL/6 and in 9 month-old CCL2-/- mice.  $\omega$ 3 treatment lasted 3 months and comprised daily gavage administration of EPA and docosahexaenoic acid (DHA). Blood and retinal fatty acid analysis was performed using gas chromatography. Eyecups were histologically examined using transmission electron microscopy and/or confocal microscopy to evaluate lipofuscin granules and the photoreceptor layer. Mass spectrometry-based proteomics was performed using qRT-PCR and Western blotting.

A clinical observational study was performed in 74 patients with dry AMD (including 119 eyes and with mean initial visual acuity 6/18).  $\omega$ 3 supplementation (3-4 g EPA/day and some DHA) lasted for 6 months, whereas the AA/EPA was examined at different time points.

Results: EPA levels increased and AA levels decreased in the blood and retinas of the treatment group in both animal models. Significantly fewer lipofuscin granules were observed in the aged C57BL/6 treatment group. The thickness of the outer nuclear layer was significantly greater in the treatment group than in the untreated, in both models. Proteomic analysis indicated significant increase in myelin regulatory factor-like protein, myelin basic protein and myelin proteolipid protein in the aged C57BL/6 treatment group. Three different pathways were significantly affected from  $\omega$ 3 treatment, namely fatty acid elongation, biosynthesis of unsaturated fatty acids and metabolic pathways. In the CCL2-/- treated model, there was decreased gene expression of TLR3 and NF- $\kappa$ B and reduced IL-18 protein compared to the untreated control.

Clinical observational studies demonstrated that following a 6-month supplementation with  $\omega$ 3 in patients with dry AMD there was an average of 14 letters gained. Mean AA/EPA ratio was maintained below 2 throughout the study.

Conclusions:  $\omega$ 3 supplementation (when AA/EPA < 2) protects the photoreceptors through different mechanisms, i.e. reduction of lipofuscin granules, decrease in inflammatory markers and increase in myelin-related proteins. The protective effect of  $\omega$ 3 was evident in aged and CCL2-/- mice of retinal degeneration. In addition, there is evidence to support that this effect was also confirmed in patients with dry AMD. Therefore,  $\omega$ 3 supplementation may have the potential as a therapeutic regime for patients who suffer from retinal-related pathologies when the blood AA/EPA is <2.

### Triptolide Promotes Cell Death in Cancer cells by Targeting Na+/K+ ATPase Pump

#### Professor Dr Anastasis Stephanou

Patrikios Ioannis1, Yiallouris Andreas1, Dimas Konstantinos 2, SeretiEvangelia 2, Cristian de Ford3, Natalia Fedosova 4, Graier Wolfgang F. 5, Stephanou Anastasis1.

1School of Medicine, European University Cyprus, Nicosia, Cyprus; 2Department of Pharmacology School of Health Sciences University of Thessaly; 3Department of Pharmaceutical Biology and Biotechnology, Freiburg, Albert Ludwigs University, Germany; 3Department of Biomedicine-Physiology and Biophysics, Aarhus University, Aarhus, Denmark; 4Molecular Biology & Biochemistry, Medical University of Graz, Graz, Austria 5

Chemotherapeutic drugs have improved the prognosis and outcome of a variety of human cancers, however these types of therapies result in limited efficacy as well as cytotoxicity to

the normal tissues and the organs still remain a major problem. There is also the problem that many of the chemotherapeutic drugs also lead to drug resistant and relapsed tumor growth. Therefore, identification of drugs that are able to target the cancer cells without having toxic effects to normal cells would be more beneficial in the long term to the patients. Thus, the challenge is to identify agents that have selective cell death effects in cancer cells that may be derived from natural phyto-extracts. In the healthcare sector, phyto-compounds are known to be beneficial by contributing to alleviating a variety of diseases including exhibiting anticancer abilities. However, the exact molecular mechanism on how these phyto-compounds exert anti-cancer properties is unclear. We have recently been interesting in several phytocompounds and their effects in promoting cell death in cancer cells We have recently reported the phyto-compound annonacin has selective cell death effects in cancer cells that may be mediated via inhibiting Na+/K+-ATPase (NKA) and sarco-endoplasmic reticulum Ca2+ ATPases (SERCA). We now have preliminary data that suggest that another plant extract we are interested in Tripterygium wilfordii Hook F (TWHF) also has selective cell death promoting effects on various cancer cell lines but very little toxic effects on normal cells. In silico analysis suggest that one of the phyto-compounds present in TWHF, triptolide also targets NKA but not SERCA. Moreover, ouabain (1mM) a NKA specific inhibitor was shown to also induce selective cell death in several cancer cells lines. Finally, bio-profiling studies show a strong association between overexpression of both NKA gene expression and reduced survival rates. The present data indicates that TWFH/triptolite is able to promote cell death by targeting and inhibiting Na+/K+ ATPase pump and therefore may be potential therapies for the treatment and prevention of cancer.

# The "Green Revolution": the experience of Patients using Medical Cannabis

### Silviu Bril

Director of the Institute of Pain Medicine, Tel Aviv Medical Centre in Israel

In recent years, there has been a huge increase in the medical use of cannabis in many countries around the world, including USA, Israel and Canada.

Cannabis is still considered a "narcotic drug" as defined by law, but many of the global medical authorities do recognize that cannabis has medical potential that may benefit patients with specific medical indications. The use of cannabis for medical purpose is a very dynamic and emotional field and the regulation of its medical use is an ongoing process in many countries around the world.

It is widely claimed that there is insufficient evidence to support medicinal use of cannabis but

this is not borne out by the facts, let alone 10,000 years of human history.

The State of Israel is one of the leading countries in the world in the sphere of developing cannabis for medical purposes, research and industrial developing.

A real-life analysis clinical practice of the use of cannabinoids for a large variety of chronic pain syndromes will be presented. From this initial snapshot, we determined that the treatment seems to be effective and safe, although more data and subsequent trials are needed to better investigate its ideal clinical indication.

# Gene regulation networks in nervous system development and cancer progression

#### Ass. Prof. Dr Panayiotis Politis

Center of Basic Research, Biomedical Research Foundation, Academy of Athens and University of Athens, Greece

The mammalian brain is the most complex organ of all living organisms. The molecular machinery that regulates the generation of this enormous cellular complexity remains largely unknown. Our goal is to tackle this question by understanding the interplay between extracellular signaling cues and intrinsic gene regulation circuitries that control proliferation vs differentiation decisions in neural stem cells (NSCs) in health and disease. Elucidation of these mechanisms will not only provide insights into the basic principles of brain formation, but will also allow novel therapies for the treatment of brain-related diseases and tumors. To this end, we have recently uncovered the function of such a molecular mechanism in neural stem cells and tumor cells of the nervous system. These observations could provide therapeutic possibilities for treatment of neurological disorders and inhibition of tumor progression in central nervous system.

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### Oligonucleotide-based therapy for Muscular Dystrophy

### Professor Dr Leonidas Phylactou

Chief Executive Medical Director; The Cyprus Institute of Neurology and Genetics (CING)

Muscular Dystrophy is a group of inherited diseases with common characteristics the progressive weakness and loss of muscle. Among the most known muscular dystrophies is Ducchenne Muscular Dystrophy and Myotonic Dystrophy.

Antisense oligonucleotides (AON) are short pieces of nucleic acids which can be designed to target cellular mRNA and inhibit or modulate endogenous gene expression.

In our laboratory we design and use AON in order to correct the genetic defects and consequently the disease phenotype of muscular dystrophies.

During the presentation, data will be shown which support that AON are good candidates for gene therapy of muscular dystrophies.

### Advance techniques for pain management

### Dr Periklis Zavridis

Anaesthesiologist at the Apollonio Private Hospital and the American Medical Centre in Nicosia

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.

Chronic pain may prove to be refractory to conservative treatment or pharmacological treatment because intolerable side effects. When used for the right patient in the right circumstances, interventional pain management techniques may offer pain relief and improvement of quality of life. The last decades these techniques have been studied in controlled and observational studies, developing consensus guidelines.

Simple treatments such as epidural steroids or sympathetic blockade might be used early on, whereas spinal cord stimulation (SCS) or intrathecal drug delivery systems (IDDS) would be used only after more conservative therapies have been tried.

Spinal cord stimulation (SCS) is indicated for the treatment of neuropathic pain. The goal of

SCS is to apply sufficient electrical current over the dorsal columns to result in paresthesias that overlap the painful area while minimisingparesthesias in extraneous areas. The most common indication is failed back surgery syndrome with leg pain, where less common indications are peripheral nerve injury, complex regional pain syndrome (CRPS) and painful peripheral neuropathy.

Intrathecal drug delivery (IDD) is considered an invasive therapy. Therefore, appropriate patient selection and failure of more conservative therapies are essential. Indications for IDD include: nociceptive pain, neuropathic pain that has failed to respond to spinal cord stimulation and multiple pain sites with axial pain.

After viewing this presentation the participants will be able to understand the rationale of evidence based interventional pain medicine.

### The Role of Modern Experimental Biomedical - Translational Research in the Development of New Products with Clinical Applications. Ethical Justification, Implementation, Education and New Frontiers.

**Apostolos E. Papalois (A.Papalois@external.euc.ac.cy and apapalois@elpen.gr)** Director, Experimental – Research Center, ELPEN; Adjunct Professor, School of Medicine, European University of Cyprus.

Drug and new devices development in the medical arena is dependent on a variety of support structures. The introduction of a new molecule or drug or device, ideally begins with innovation responding to clinical need, progresses through engineering and development, is fostered by financing from a variety of sources, and reaches the markets through disparate commercial structures. Along the way, the drug is subject to scientific, clinical, engineering, and regulatory scrutiny and may be lost to the target community by recognition of a lack of validity, safety, or effectiveness, or by mismanagement of its development. It is critical to understand the method by which new products with clinical applications are funded in the period between concept and product launch. Data available reflect the stage of development and therefore reflect the stage of the investment as well as the terms of the development. Nonetheless, diligence must demonstrate at least the following parameters, as organized by stage of development : 1 – Seed stage : a logical mechanical, physiologic and engineering approach to well – defined clinical problem and need for which current solutions remain imperfect.

2 - Early stage : proof of concept as represented by computer modeling, prototype development with in vitro testing or early animal validation.

3 - Pre-clinical stage: demonstrated safety and efficacy in animal models with progression

to phase I testing demonstrating safety in humans.

4 - Pre-launch stage: phase 2 and phase 3 trials demonstrating efficacy and ultimately effectiveness under tightly controlled circumstances.

The foundation stones of most regulations are the internationally established principles of replacement (avoid or replace the use of animals), reduction (minimize the number of animals used per experiment by resorting to other methods or strategy) and refinement (implementation of methods which ensure that animal suffering is minimized and improve welfare). These three principles are very important and are considered to be the common basis for scientists worldwide.

The aforementioned appraisal could guide the development and adoption of a universally lawgiving that meets international standards. In other words, new frontiers in biomedical – translational research and training for healthcare professionals.

# Liquid Biopsy for the early detection of cancer: applications in screening and minimal residual disease.

### **Nickolas Papadopoulos**

Johns Hopkins University School of Medicine

Early detection of cancer in the screening and minimal residual disease settings has the potential to significantly reduce cancer deaths. Our goal is to be able to detect cancer earlier than current modalities. Previously, in-proof-of-principle studies we determined the feasibility of liquid biopsy in detecting cancers in blood and other bodily fluids. We have been able to detect minimal residual disease with exquisite specificity after surgery in patients with stage II colon cancer earlier than recurrence detected by imagining. Recently, we developed Cancer SEEK, a multi-analyte blood test that can detect eight common cancer types through assessment of levels of circulating proteins and mutations in cell-free DNA. In a study involving 1,005 individuals with resectable non-metastatic cancers of the colon, breast, lung, ovary, pancreas, esophagus, liver or stomach, and 812 healthy controls Cancer SEEK tests were positive in a median of 70% of the eight cancer types with specificity greater than 99%. The sensitivities ranged from 69 to 98% for the detection of five cancer types (ovary, pancreas, esophagus, liver and stomach) for which there are no screening tests available for average-risk individuals. Our vision is to develop routine, non-invasive tests for the detection of cancer.

### The effect of seizures on quality of life in Cypriot patients

### **Professor Dr Savvas Papacostas**

Head of the Epilepsy and Behavioral Neurology Clinic of the Cyprus Institute of Neurology and Genetics (CING)

The overall aim of this study was to assess the impact of epilepsy and its treatment on the quality of life of people with epilepsy in Cyprus. Previous studies have demonstrated that reducing side effects of medication and achieving better seizure control are the key to improving the quality of life for people with epilepsy. In addition, continued education, for the lay public and the person with epilepsy is vital in order to increase knowledge, dispel myths about the condition and reduce associated stigma. The results also show that over a third of respondents felt stigmatised by their condition. High percentages of respondents reported that their condition negatively affected their future plans and ambitions and their feelings about themselves. The most commonly experienced side effects were sleepiness/drowsiness, memory problems, behavioural problems, nervousness and headache.

# Imaging brain networks in demyelinating and neurodegenerative diseases

#### Prof. Dr Massimo Filippi

Director of the Residency School in Neurology and President of the Bachelor's Degree in Physiotherapy, Vita-Salute San Raffaele University; Director, Neuroimaging Research Unit, INSPE, Division of Neuroscience

San Raffaele Scientific Institute, Milan, Italy MRI is playing an increasingly important role in the study of demyelinating and neurodegenerative diseases such as multiple sclerosis (MS), Alzheimer's disease, frontotemporal dementia, amyotrophic lateral sclerosis, and Parkinson's disease, delineating the structural and functional alterations associated with these conditions. New evidence from the application of MRI in patients with clinically isolated syndromes has guided the 2017 revision of the McDonald criteria for MS diagnosis, which has simplified their clinical use while preserving accuracy. Other MRI measures (e.g., cortical lesions and central vein signs) may improve diagnostic specificity, but their assessment still needs to be standardized, and their reliability confirmed. Novel MRI techniques are providing fundamental insights into the pathological substrates of the disease and are helping to give a better understanding of its clinical manifestations. It has been recently hypothesized that clinical progression in neurodegenerative diseases involves the systematic spreading of misfolded protein aggregates along neuronal pathways. Such aggregates would trigger misfolding of

adjacent homologue proteins in newly-affected regions, and this would propagate across anatomical connections throughout the central nervous system, eventually leading to structural and functional rearrangements that are responsible for clinical symptoms. In this context, advanced MRI techniques are of special interest for their potential to characterize the signature of each neurodegenerative condition and aid both the diagnostic process and the monitoring of disease progression.

All these techniques allow us to investigate the different features of inflammation and neurodegeneration. This aspect will become crucial when disease-modifying (personalized) therapies will be established.

# From the ESC guidelines to the everyday practice: how to fill the gap in 2018

#### Prof. Dr Maddalena Lettino

Humanitas Research Hospital, Milan, Italy; President of the European Society of Cardiology (ESC) Acute Cardiac Care Association, Europe.

Cardiovascular (CV) diseases are still the leading cause of death in the European countries, despite the efforts of the scientific community to run clinical trials and to produce new evidences that should contribute to reduce mortality and morbidity of CV patients. The mission of the European Society of Cardiology (ESC) is "to reduce the burden of cardiovascular disease" and, in order to achieve such endpoint, the ESC issues international guidelines on diagnosis and management of cardiovascular diseases, with the ultimate goal of helping health professionals to improve the quality and quantity of life of their patients. I will focus my attention on the process of generating guidelines and also of bringing evidence-based recommendations from the scientific ground to the everyday clinical practice, evaluating points of strength and limitations of the whole journey and the different roles of researchers, guidelines task force members, international and national societies and, finally, decision makers and healthcare administrators.

International guidelines should reflect national country needs and try to propose solutions that could be applicable in different socio-economic contexts; guideline task forces should incorporate all the stakeholders and not only physicians, thus including patient representatives, nurses and professionals different from doctors. Epidemiologists and experts in health economics are also expected to be more and more engaged in the future. Last but not least, quality indicators to properly monitor process of care and outcomes should be defined for each CV disease and quality improvement strategies should be included in the guidelines, particularly when recommended interventions fail to achieve their goal despite a strong scientific evidence of their efficacy.

### What is new in updated STEMI guidelines 2017

#### Prof. Dr Maddalena Lettino

Humanitas Research Hospital, Milan, Italy; President of the European Society of Cardiology (ESC) Acute Cardiac Care Association, Europe.

New ESC STEMI guidelines were issued in 2017, 5 years after the prior edition, to include the last evidence concerning diagnosis, risk stratification and treatment of patients with acute MI. Some relevant key points should be highlighted: 1) Patients should undergo primary PCI as first choice reperfusion therapy, provided that the procedure can be done in a timely fashion by an experienced team, and this is recommended even in patients with resuscitated out-of-hospital cardiac arrest. DES and the radial approach should be privileged on other revascularization strategies as many times as possible; 2) time limits for primary PCI are clearly given as well as timing for coronary angiography after successful thrombolysis, with a more clear definition of first medical contact; 3) there are precise indication about the extension of revascularization of a multivessel coronary disease in the acute phase and the use of ancillary antithrombotic therapies. Among the new parts there is a chapter completely dedicated to myocardial infarction with non-obstructive coronary artery disease (MINOCA), making the point on both diagnosis and potentially effective treatment. There is also a chapter addressing the gap between optimal guideline-based therapy and actual care of STEMI patients. In this regard the Authors stress the role of measuring established quality indicators to audit practice and improve outcome in real life and recommend the use of such quality indicators to monitor and improve STEMI care.

# How to improve the survival rates and quality of life of children and adolescents with cancer or leukemia: The role of the pediatrician and the family doctor

#### Professor Dr Loizos G. Loizou

Director of the Pediatric Oncology-Hematology Clinic; Archbishop Makarios III Hospital, Nicosia, Cyprus

Cancer and leukaemia in children and adolescents (CLCA) are recorded with an increasing incidence over time. They constitute a major cause of mortality and morbidity in this age group. They are the leading cause of disease related mortality in the pediatric population in many developed, high income countries. Nevertheless, in these well-resourced countries the outcome and survival rates for the majority of pediatric cancer patients have been significantly improving over the last few decades with cure rates in the order of 80%. On the contrary, in the

less-developed countries where most cases of CLCA are diagnosed, the majority of these patients do not survive because of insufficient resources for a successful management and outcome. This situation is unsatisfactory and has to change. Our actions nationally and globally should be centered on improving a) diagnosis and therapy, b) facilitating fundamental research so that the advances achieved would be applied (translational medicine) with innovative therapies in the frame of collaborative, international protocols, c) support the search of etiology by the means of descriptive, and in particular, of analytical epidemiology studies, and d) promote national plans where health professionals and others would cooperate for improving not only the cure rates but also the quality of life of children and adolescents with cancer or leukemia during the therapeutic phases, but also for the survivors in their adult life. Our model of approach is based on 12 pillars of actions for which the role of the community pediatrician and the family physician (CP&FP) is of capital importance in our guest for improving the cure rates and the guality of life of patients and survivors. The 1st sector of actions (SA) is the continuous education of the CP&FP for the timely diagnosis. As the first line health counselors, they should be ready to promptly recognize conditions necessitating immediate exploration. The 2nd SA is increasing awareness and skills of the CP&FP for the clinical detection of signs of the de novo or acquired cancer predisposition syndromes (CPS). The contribution of the CPS in CLCA appears to be much higher than what it was thought before. Recognizing them promptly can increase survival rates and decrease morbidity by establishing adapted personalized therapy and/or surveillance protocols. The 3rd SA should improve the ability of the CP&FP not only to refer the patient whenever there is a high degree of suspicion for a malignant disease but also to know when to refer to the Pediatric Geneticist for further exploration. The 4th SA focuses in helping the CP&FP in the management of the short term complications of cancer therapies, monitor the common problems, acquire pain control knowledge and provide assistance in nutrition issues. The 5th SA is monitoring the medium and long term toxicities or adverse effects. As patients and also survivors may experience serious late effects, it is of capital importance for the CP&FP to recognize the problems and provide adequate advice and management. The vaccinations issues before, during and after cancer therapies for CLCA is a continuously evolving and sometimes controversial issue and therefore they constitute the 6th SA. In the era of internet and the overwhelming, often inaccurate information, providing correct guidance and information to the patients is of primordial importance. Therefore our 7th SA is helping the CP&FP in acquiring the skills for providing this much needed adequate medical information and thus protecting the patients from unproven therapies and charlatans. The provision of psychological support and social assistance is a field in which the CP&FP can have one of the most important roles and therefore this domain constitutes our 8th SA. As the role of the CP&FP is decisive in preventing adulthood cancer through education of the verv young and their parents, the 9th and 10th SA focus is precisely in these issues. Monitoring the

quality of life of CLCA during therapy and when cured, can decrease morbidity and increase survival and therefore this is the 11th SA. Finally the survivorship issues with the much needed medical, social, professional and psychological support is of increasing importance as the number of childhood cancer survivors is constantly increasing. Although these SA can be dealt and grouped differently, we believe that by individualizing and approaching each one of them as a separate entity, we may yield better results in awareness and effective actions with substantial improvements of the survival rates and quality of life of children and adolescents with cancer or leukemia in our country.

### Gene therapy of $\beta$ -hemoglobinopathies: trials and trends

### Ass. Prof Dr Carsten Werner Lederer

Laboratory Scientific Officer and Assistant Professor, Molecular Genetics Thalassaemia Department The Cyprus Institute of Neurology and Genetics & The Cyprus School of Molecular Medicine

As severe monogenic diseases of the haematopoietic system, sickle cell disease and  $\beta$ -thalassaemia are ideal target for gene therapy. In preclinical research, substantial success has been achieved in the correction of critical disease parameters by three principal therapeutic approaches of (i) gene addition of  $\beta$ -globin-like transgenes, (ii) repair of the primary mutation by genome editing and (iii) functional correction of  $\beta$ -globin deficiency by re-activation of the primarily fetal  $\gamma$ -globin chain. Gene addition is the longest-established of these approaches and is the only one as yet applied in the clinic and informing future development of improved therapies. Second, repair of the primary mutation is still hampered by low efficiencies in primary cells but is based on nascent genome and base editing technology with substantial scope for improvement. Finally, an array of strategies dedicated to the activation of fetal hemoglobin has led to the registration of clinical trials based on genome editing and shRNA-mediated knockout, respectively.

Accumulating data for clinical trials based on gene addition indicate significant therapeutic benefits but also a high level of variability in treatment outcomes for  $\beta$ -haemoglobinopathies. This talk will extrapolate how the approach might be improved based on the current state of knowledge and technology development, and where gene correction and activation of fetal hemoglobin might offer superior performance in future clinical trials and, eventually, in routine curative treatment of patients.

# The Contemporary Contribution of genetics in the diagnosis and treatment of Cancer

#### Professor Dr Kyriacou Kyriakos

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Cancer is the second leading cause of mortality and morbidity and in 2015 nearly 9 million people died from cancer (1). Although cancer encompasses more than 200 different types, they all share the common characteristic, in that cancer develops as a result of genetic mutations. These mutations may be inherited in the germline, or they may arise as a result of somatic mutations, which develop due to the interactions between the genome and the environment (2,3). It is no surprise then that in the era of molecular medicine, cancer represents the model disease, where advances in DNA technologies and the ability to analyse the whole human genome, is transforming the field of cancer diagnosis, prognosis and disease management. In particular, there are two main areas where genetics is impacting the management of cancer. The area that has been historically developed first is the use of genetics, in identifying individuals who are at a high risk of developing cancer. This has been made possible since the early 1990s when key genes such as the APC and BRCA genes were discovered. Molecular analysis which detects mutations in the genes, enables the identification of individuals who have a strong family history and carry mutations in these highly penetrant genes (2,4). Currently more than 40 familial cancer syndromes are known in which more than 100 genes are involved, fuelling the use of application of NGS panels, for performing such molecular genetic testing across many cancer types (5,6).

The second area that currently represents one of the most exponentially advancing fields in medical practice, is precision medicine and personalized treatment. The major interest in this field is to analysetumour DNA, in order to detect mutations in driver genes which are actionable and can be inhibited, by the use of small molecule inhibitors, such as Tyrosine kinase inhibitors (7). Indeed over the past decade the Cancer Genome Atlas (TCGA) has generated a vast amount of molecular profiling data across 33 cancer types, leading to the identification of key driver genes (https://cancergenome.nih.gov/publiations) (8).

In future it is anticipated that cancer will no longer be classified based on its primary anatomic location, such as colorectal cancer, breast cancer, lung cancer or its histological features, but rather based on its specific molecular profiles. Indeed at the Institute we established a department of Molecular Pathology since the early 1990s and have built an extensive experience in the development of molecular genetic tests related to both cancer genetics and personalized medicine. The aim of this presentation is to provide a contemporary overview

of the significant contribution of genetics in the diagnosis, prognosis and management of cancer patients.

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### The role of complement in the amyloidoses-a new therapeutic avenue?

### Professor Dr Theodoros Kyriakides

Senior Consultant at the Cyprus Institute of Neurology and Gene

Complement is known to co-precipitate and be activated by amyloid deposits in both peripheral and central nervous system amyloidoses and most probably contributes to the pathological cascades in amyloid diseases. Complement has been called a double edged flower in Alzheimer Disease because of at least two opposing actions. C1q, the initiator of the classical pathway activation, can opsonize foreign material, including amyloid fibrils, and enhance their destruction by phagocytes thus protecting the recipient tissue bed. On

the other hand complement activation, when completed, creates the membrane attack complex (C5b9) which is cytotoxic and detrimental to the resident tissue bed. Component C5a, produced by complement activation, drives inflammation in nerve tissue, exacerbates amyloidogenesis and also drive neuro-inflammation, all of which are detrimental. We present additional evidence that complement plays a crucial role in both central and peripheral amyloidosis based on experiments with two transgenic mouse models of amyloidosis (Transthyretin peripheral neuropathy and Alzheimer Disease) and also demonstrate that by manipulating complement amyloid deposits may be ameliorated thus opening up another therapeutic avenue for treating these diseases.

### **Novel Aspects of HDL Biochemistry and Pharmacology**

#### Professor Dr Kyriakos E. Kypreos

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High density lipoprotein (HDL) has been for years an intriguing lipoprotein which attracted the attention of biomedical community, mainly because of its important role in atheroprotection. Even though HDL-cholesterol is usually referred to as the "good cholesterol", certainly it is far more than just a "cholesterol". HDL is a macromolecular assembly of proteins and lipids formed in the circulation as a result of a concerted action of apolipoproteins, lipid transporters and plasma enzymes. Studies in cell cultures as well as in experimental mice showed that biogenesis of classical Apoa1-containing HDL particles (Apoa1-HDL) involves lipid transporters ATP-binding cassette A1 (Abca1) and G1 (Abcg1) and plasma enzyme Lecithin:Cholesterol Acyl Transferase (Lcat).

Previously, we showed in mice that other apolipoproteins such as apolipoprotein E (APOE) and apolipoprotein CIII (APOC3) are also capable of promoting the de novo biogenesis of HDL in the absence of a functional APOA1. In addition to the studies in mice, we recently observed the existence of APOE-HDL and APOC3-HDL particles in the circulation of morbidly obese human subjects; analysis of HDL particle composition showed that rapid weight loss was associated with a significant switch from primarily APOE-HDL and APOC3-HDL to primarily APOA1-HDL displaying increased antioxidant capacity. In another clinical paradigm we observed that young asymptomatic subjects (≤35 years of age) who suffered an acute non-fatal myocardial infarction possessed elevated levels of plasma APOE-HDL and APOC3-HDL that correlated with reduced antioxidant potential. These clinical observations supported the hypothesis that variations in HDL apolipoprotein composition may set basis for its functional heterogeneity.

Indeed, our more recent data support the contention that APOA1-HDLs are functionally distinct from APOE-HDL particles and that HDL proteome determines its lipidome. The apparent differences in the HDL apolipoprotein content, lipidome and functionality between APOE3-HDL and APOA1-HDL that we identified through our preclinical and clinical studies reinforce the idea that not all HDL particles are equally active and that apolipoprotein composition is a key factor for defining HDL lipid content and particle functionality. Therefore, creation of effective pharmaceuticals that aim at improving HDL functionality requires deep understanding of the impact of apolipoprotein composition of HDL on its properties associated with protection from atherosclerosis and possibly from other metabolic disorders. Acknowledgement Dr. Eleni A. Karavia and Ms. Eva Xepapadaki are supported by a Postdoc-Research Scholarship (2017-2019), and a graduate studentship (2017-2019), respectively, both funded by the Hellenic Scholarships Foundation (I.K.Y).

### Escaping from oncogene induced senescence: Role in cancer

### Ass. Prof. Dr Konstantinos Evangelou1

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Oncogene induced senescence (OIS) is activated by the coordinated action of the DNA damage response (DDR) pathway and ARF, alternatively to apoptosis, in early stages of cancer, preventing transformation of incipient cancer cells. Progression to cancer requires antitumor barrier bypass and occurs when critical DDR and ARF pathway components like p53 are impaired, fueling genomic instability. This explains the frequent p53 mutations in cancer and how apoptosis results in "clearance" of incipient cancer cells while escape from OIS, which is a viable state, remains an uncharted territory.

Detection of senescence is of paramount importance, especially in vivo, as it plays a bimodal role in cancer and seems to be related to prognosis. Moreover, estimations on the outcome of senotherapeutics that target senescent cells require a reliable senescence biomarker. Until recently, available methods failed to accurately recognize senescent cells in vivo. This conundrum was lately addressed by the development of an innovative biotinylated Sudan Black-B (SBB) analogue (SenTraGorTM) and hybrid histochemical/immunohistochemical method, that allows detection of senescent cells in any biological material (including archival one).

As shown for the first time in vivo, using the SenTraGorTM methodology, senescence occurs

in primary human malignancies and is related to adverse clinical outcome. This might be attributed either to the pro-tumorigenic effect of SASP or to the fact that neoplastic cells "trapped" in senescence exhibit tolerance against classical antitumor strategies and can subsequently escape from senescence. In this context, tumor relapses and a worse clinical outcome may occur rendering their elimination in primary lesions, as a complementary strategy, an attractive perspective.

To examine these issues and to recapitulate the in vivo findings in vitro, we developed prototypical cellular OIS models. Various manipulations that resulted in aberrant chronic stabilization of the replication licensing factors Cdc6 and/or Cdt1 led to an evolutionary recapitulation of cancer development. Initially, a senescence-like state was observed, characterized by replication stress, DNA-damage and an error-prone DNA repair process that eventually altered the genome. Following, a subpopulation of cells emerged that re-entered the cell cycle. Interestingly, these "escaped" cells exhibited aggressive features and increased chemo-resistance, while epithelial derived ones underwent epithelial to mesenchymal transition.

These findings have uncovered an unprecedented mode of how oncogenes drive cancer development, through escape from senescence, providing also new opportunities for cancer treatment.

# Developing cell-targeted gene therapy for neuromuscular and neurological disorders

#### Professor Dr Kleopas Kleopa

Head of Neurology Clinic E and Neuroscience Laboratory at the Cyprus Institute of Neurology and Genetics (CING)

The discovery of genetic causes underlying many neurological and in particular neuromuscular disorders in the last few decades has stimulated efforts to develop genetic therapies. Our group focuses on cell-targeted gene therapy approaches to treat genetic disorders of myelinating cells in the peripheral and central nervous system. These include X-linked and autosomal recessive Charcot-Marie-Tooth inherited neuropathies as well as hypomyelinatingLeukodystrophies. Using lentiviral and Adeno-associated (AAV) viral vectors we have demonstrated successful and cell-specific gene delivery to Schwann cells and oligodendrocytes of disease related genes driven by cell-specific promoters. Delivery of these vectors into well-characterized experimental models of these disorders resulted in improvement of function and myelin pathology. Further steps towards clinical translation of these gene therapy approaches are currently underway.

### Epigenetic deregulation in cancer: the case of histone acetyltransferase Naa40

**Ass. Prof. Antonis Kirmizis** University of Cyprus

Epigenetic modifications such as those occurring on histone proteins are important regulators of chromatin structure and gene expression. Deregulation of these histone marks has been implicated in the development of cancer. Due to the fact that epigenetic modifications are reversible, understanding their cellular function and role in cancer offers new opportunities for therapeutic interventions. N-alpha-acetyltransferase 40 (NAA40) is an epigenetic enzyme, which catalyzes histone H4 N-terminal acetylation (N-acH4) and its role in oncogenesis is poorly understood. In this study, we show that NAA40 protein and mRNA levels are commonly increased in colorectal cancer (CRC) primary tissues compared to non-malignant specimens. Importantly, depletion of NAA40 inhibits cell proliferation and survival of CRC cell lines and delays the growth of human CRC xenograft tumors. Intriguingly, we found that NAA40 knockdown and loss of N-acH4 reduce the levels of an adjacent histone modification, namely symmetric dimethylation of histone H4 (H4R3me2s), through transcriptional downregulation of protein arginine methyltransferase 5 (PRMT5), NAA40 depletion and subsequent repression of PRMT5 results in altered expression of key oncogenes and tumor suppressor genes leading to inhibition of CRC cell growth. Consistent with this, NAA40 mRNA levels correlate with those of PRMT5 in CRC patient tissues. Taken together, our results demonstrate a deregulated epigenetic mechanism in colon cancer cells and establish the oncogenic function of the epigenetic enzyme NAA40.

### A Single NIPT for Aneuploidies, Microdeletions and Point Mutations

Dr Marios Ioannides Michalis Nicolaou, Achilleas Achilleos, Charalambos Loizides, Kyriakos Tsangaras, Petros Mina, Elena Kypri, George Koumbaris, Philippos C Patsalis R&D Senior Manager at NIPD Genetics

**INTRODUCTION:** We hereby present the development of a NIPT of major aneuploidies, microdeletions and 50 monogenic diseases by leveraging parental carrier status information. All monogenic diseases under investigation are associated with moderate or severe phenotype, including Hematological, Kidney, Opthalmological, Neurological, Inherited Metabolic Diseases, such as Thalassaemia, Cystic Fibrosis, Phenylketonuria and Tay-Sachs.
**MATERIALS AND METHODS:** The carrier status of maternal cfDNA referred for NIPT and paternal DNAwas investigated for 496 causative mutations in 49 disease associated genes. An enriched sequencing library was prepared using custom TArget Capture Sequences (TACS) as previously described. TACS were designed based on genomic locations of known causative mutations for the 50 monogenetic diseases, in addition to select regions on chromosomes 13, 18, 21, X, Y and critical regions of 22.q11, 1p36, Wolf-Hirschhorn and Smith-Magenis microdeletion syndromes. Enriched products were sequenced using NGS and the data was processed using a custom bioinformatics pipeline.

**RESULTS:** Atotal of 325 mutations were identified in 266 samples, 78 of which were unique pathogenic mutations. All unique point mutations were confirmed by Sanger sequencing. All aneuploidies and microdeletions were correctly classified with 100% specificity and sensitivity. **CONCLUSIONS:** The fetal risk for the 50 monogenic diseases can be determined by identifying the carrier status of the parents using our targeted capture enrichment assay. This is the first time that NIPT is made available for a high number of single gene diseases together with aneuploidies and microdeletions, opening a new chapter in prenatal screening. This novel NIPT is expandable to hundreds of single gene diseases and can be taken potentially by all pregnant women as early as the 10th week of gestation.

# Stem cell therapies in neuroinflammatory and neuro-degenerative diseases: The hurdles, the existing evidence and the promise

#### Professor Dr Dimitrios Karussis

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Due to the limited capacity of CNS for regeneration, more effective treatment of chronic degenerative and inflammatory neurological conditions, may involve the use of stem cells which seem to carry the potential for regeneration and neuroprotection. Embryonic cells have strong pluripotent and self-renewal properties and represent the prototype of stem cells, but there are additional somatic stem cells that may be harvested from various tissues during adult life, such as the mesenchymal stem cells (MSC), which offer several practical advantages for clinical application. MSC can be obtained from every adult, are easily expanded to large numbers and carry less risks for malignancies.

Our pilot trial (Phase I/II, 2006-2009) with intrathecal (IT) and intravenous(IV) injection of autologous MSC included 19 patients with ALS and 15 with MS. No major side effects were reported. The mean disability score of ALS (ALSFRS) was stabilized during the 6 first months following the treatment in the ALS patients, indicating a halt of the progression of this severe

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paralytic disease. In MS patients, the mean disability score (EDSS) showed a clear trend of improvement.

A more recent phase I/II and IIa study in our Center, with IT or IM injections of modified MSCs (Brainstorm technology) in 26 ALS patients, revealed that 87 % of the patients treated IT showed an improvement in the rate of progression of either general disability or respiratory function.

Since the beginning of 2015 we have initiated a large double-blind crossover trial that enrolled 48 progressive MS-patients. The study started in February-2015 and completed in June 2018. During the 2-month run-in period, functional evaluations (EDSS, walking speed test, 9-hole peg test, neurocognitive evaluation, quantitative and functional MRI, OCT, VEP, and visual functions' assessment in the static and dynamic domains) were performed monthly before the transplantation and at 3 months intervals after the treatment, for a total of 12 months. Patients were randomized and treated with either autologous, bone marrow-derived MSC (1x106/Kg) or placebo, IT or IV. At 6-months the patients were re-treated with a second injection of MSC or placebo and followed for safety and all the efficacy measures for additional 6 months. The study was approved by the local Ethics committee and MOH, registered to NIH (NCT02166021) and monitored by an external CRO and an external safety committee.

No serious treatment-related adverse events were observed during the whole period of the trial. Only one patient withdrew his consent and stopped the trial, at one month after the first transplantation. Most of the (mild) side effects were related to the lumbar puncture (headaches and back pain).

Twenty-two, out of the 48 patients deteriorated in EDSS during the 2-3 months before the treatment (indicating that our group included patients with very active disease). A scheduled interim analysis of the 32 first patients was performed and showed a significant beneficial effect of the treatment in terms of EDSS progression and a positive trend in terms of the relapses frequency. The first analysis of the currently available data from all 48 patients is now running and will be presented upon completion.

Both our animal studies and our data from this study indicate that the clinical beneficial effects were more significant in patients receiving intrathecally the cells (a method advocated first by our group, so that the cells will reach easier the damaged CNS areas) than intravenously.

In my talk, I will summarize the clinical experience with stem cells in neurological diseases, the promise, the hardles and the risks of such experimental therapeutic approaches.

#### **CNS-Immune System Dynamic Dialogue in Neurology**

#### Professor Dr Nikolaos Grigoriadis

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

The brain and spinal cord parenchyma are populated by resident microglia, which enter the central nervous system (CNS) as precursors early in embryonic development. Interestingly enough, microglia and CNS infiltrating monocyte-derived macrophages are now identified to be functionally distinct and of separate origin. In addition, there is increasing evidence indicating that the generalized perception of the CNS as 'immune-privileged sites' may no longer be realistic. Indeed, it is now clear that circulating leukocytes play a crucial role in maintenance and repair of the CNS. Innate and adaptive immune cells may exhibit protective and/or healing properties in the CNS, provided their activity is well-regulated, and their recruitment and migration well-controlled. Moreover, the CNS-immune system relationship is important even early during development, particularly for the differentiation of neural precursor cells (NPCs). On the other hand, it has been found that NPCs are also able to control the immune reactions within CNS. Later in development, all immune related components aim to contribute to CNS homeostasis and plasticity for a life span in health, aging, and chronic neurodevelopmental and neurodegenerative diseases. Importantly enough, the CNS barriers are not uniform both in their construction and interactions with the circulating immune cells. In particular, Blood Brain Barrier (BBB) is a true barrier thatensures brain function without any disturbance. However, blood-CSF barrier serves as a functional interface and as a selective gate for immunosurveillance and immune cell entry upon need. Overall, there is growing indication that CNS and immune system not only interact but also have a mutual dependency.

#### Neurogenic compounds as inducers of brain self-repair

#### Professor Dr Achilleas Gravanis

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Chemical approaches using small molecules have yielded exciting results in induction and differentiation of pluripotent stem cells, lineage conversion of somatic cells, and ex vivo as well as in vivo modulation of adult stem cells. The application of small molecules, either as probes to dissect the underlying mechanism of stem cell biology or as key tools to manipulate stem cell fate, will continue to facilitate the progress of future stem cell research and cell-based clinical

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interventions, combining conventional synthetic pharmacology and stem cell technology. Applications of regenerative therapeutic technologies in the age-related neurodegenerative diseases represent one of the largest future burdens. The definition of mechanisms controlling adult neural stem self-renewal, migration and differentiation will provide new insights and therapeutic targets to pharmacologically induce brain self-repair processes. Deficiencies in neurotrophins are implicated in the pathogenesis of many age-related neurodegenerative disorders, due also to their central role in controlling adult neurogenesis. Central nervous system networks are effectively maintained through aging by neuroprotective, neuroplasticity and neurogenesis signaling mechanisms which are predominantly controlled by neurotrophin receptor signaling. Neurotrophin receptors are single pass receptor tyrosine kinases that form dimeric structures upon ligand binding to initial cellular signaling events that control many protective and plasticity-neurogenesis related pathways. While the therapeutic applications of cognate polypeptide ligands for neurotrophin receptors are limited, the development of nonpeptidergic, small-molecule ligands can overcome these limitations, and productively regulate this important receptor system with beneficial effects. Our group develops blood brain barrier-permeable small molecules, agonists of neurotrophin receptors (microneurotrophins) which induce fetal and adult neural stem cell self-renewal and differentiation, in vitro and in vivo. We are testing our neurogenic microneurotrophins in animal models of Alzheimer's disease, showing decreased hippocampal neurogenesis and deficient memory.

#### Air pollution and cardiovascular diseases

**Charalampos Grassos** 

Director of Cardiology Dept. in General Hospital of Attica "KAT"

Ambient air pollution (AAP) and particulate matters (PM) have been closely associated with adverse health effects such as respiratory disease and cardiovascular diseases. Previous studies have examined the adverse health effects associated with short- and long-term exposure to AAP and outdoor PM on respiratory disease. However, the effect of PM size (PM2.5 and PM10) on cardiovascular disease has not been well studied. Thus, it remains unclear how the size of the inhalable particles (coarse, fine, or ultrafine) affects mortality and morbidity. Airborne PM concentrations are commonly used for ambient air quality management worldwide, owing to the known effects on cardiorespiratory health. In this article, we assess the relationship between cardiovascular diseases and PM, with a particular focus on PM size. We discuss the association of PM2.5 and PM10, nitrogen dioxide (NO2), and elemental carbon with mortality and morbidity due to cardiovascular diseases, stroke, and altered blood pressure, based on epidemiological studies. In addition, we provide evidence that the adverse health effects of

AAP and PM are more pronounced among the elderly, children, and people with preexisting cardiovascular and respiratory conditions

#### Perioperative management of anticoagulant and antiplatelet therapy

#### Professor Dr Goudevenos John

President of Hellenic Society of Cardiology

A significant number of patients with stents or atrial fibrillation (AF) under antiplatelet or anticoagulant(warfarin or DOACs) therapy respectively undergo noncardiac surgery and may require therapy interruption. This poses a significant clinical dilemma because antithrombotic therapy interruption exposes patients to the potential risk of stent thrombosis, or stroke. Conversely, continuing therapy may be associated with excess bleeding complications. In patients with AF who are receiving a DOAC, simple interruption and resumption protocols are available but require validation in prospective studies. Finally, while continuation of aspirin appears safe for cardiac surgery, high-quality data are lacking to discern which the best perioperative strategy is for patients on other antiplatelet agents or DOACs.

# Personalized management of cancer associated thrombosis: Actual status and perspectives

#### Grigoris T Gerotziafas1,2

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More than 150 years after its first description by Armand Trousseau, the association between cancer and thrombosis remains a major clinical problem. Venous thromboembolism (VTE) occurs in up to 15% of cancer patients during the disease course and remains the second leading cause of death after malignancy itself. Overall, cancer accounts for an estimated 18% of the total number of VTE cases. The incidence of VTE is near 6-fold higher in patients with cancer than in patients without cancer. In addition, cancer patients developing VTE present lower survival rates, worse prognosis and higher healthcare costs compared with VTE patients without cancer. Thus, being an independent prognostic factor of both cancer progression and death, VTE occurrence has been proposed as a secondary endpoint in many oncological trials.

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A routine assessment to identify patients at high risk for CAT is recommended by international and national guidelines. Nevertheless, according to the European Society of Medical Oncology (ESMO), "most oncologists underestimate the prevalence of CAT and its negative impact on their patients". A routine assessment to identify patients at high risk for VTE is recommended. Moreover, the collaboration between oncologists and specialists of angiology/vascular medicine is still weak. During the last decade, important progress has been made in the comprehension of CAT pathogenesis and in the efficacy and safety of antithrombotic agents in prophylaxis and treatment of CAT.

The LMWHs dalteparin, enoxaparin and tinzaparin, emerge up to now as a cornerstone therapeutic strategy for primary prevention and treatment of cancer associated thrombosis (CAT). The CLOT trial, which demonstrated the superiority of the LMWH dalteparin over warfarin for recurrent VTE, established LMWH as the standard of care for cancer-associated VTE. This was further supported by the results from the CATCH trial which compared tinzaparin versus warfarin in the treatment of CAT. While more patients with CAT require long-term anticoagulant treatment, daily subcutaneous injections are associated with discomfort, reduced patient compliance and injection fatique. The direct specific factor Xa inhibitors rivaroxaban, apixaban and edoxaban and the direct specific thrombin inhibitor dabigatran became the first line therapeutic option for the acute phase treatment and the secondary prevention of VTE. Direct oral anticoagulants (DOACs) have a stable and predicted anticoagulant effect, do not show any food interactions and have few drug-to-drug interferences. Thus, DOACs appear as attractive alternative for CAT treatment. Meta-analysis of subgroup data from the large phase III clinical trials of DOAC in the treatment of VTE and data from small non-randomized studies indicate that the efficacy and safety profile of DOAC is similar in patients with cancer as compared to the non-cancer ones. Though, the decision to switch the antithrombotic treatment from LMWH to DOAC should not be based on the argument of the predictive pharmacokinetics and pharmacodynamics of DOAC since these properties have been studied in healthy population. The management of CAT has not yet been paralleled with the above scientific achievements. Health authorities and expert panels in EU and USA recognize an increasing knowledge translation gap between the actual status of knowledge in pathogenesis and treatment of CAT and the clinical practice. The distance between fundamental and translational/clinical research and the lack of an overall structure for the management of the risk for vascular complications in cancer patients figure among the major causes of this gap. An additional major barrier for the prevention and treatment of CAT is given by the absence of reliable risk assessment tools with high positive predictive value (i.e. accurate to identify patients at high risk for CAT who should receive thromboprophylaxis). According to the most modern concept, such tools should incorporate predictors related with the cancer and its treatment, as well as patients' intrinsic risk factors and biomarkers of hypercoagulability and specific biomarkers of coagulation and vascular activation.

Personalize prevention and treatment of CAT is based on the evaluation of clinical profile of the patients (cardiovascular risk factors and comorbidities), on cancer related characteristics, on the presence of hypercoagulability of plasma or cellular origin and on the genetic profile of the patient. This strategy requires a new multidisciplinary concept in the management of oncological patients and is expected to improve the efficacy/safety profile of the antithrombotic strategies.

#### **Oedipus Tyrannous: A lesson in genetics**

**Professor Dr Constantinos Deltas** University of Cyprus

Oedipus the King or Oedipus Tyrannous is a famous play of Sophocles, one of three ancient Greek tragedians whose plays have survived. According to the narrative of this play by Sophocles (c. 497/6 – winter 406/5 BC), Oedipus was the son of lokasti and Laios, the King of Thebes, in ancient Greece. When Oedipus was born, Laios received an oracle of Apollo at Delphi according to which Oedipus was going to kill his father Laios and then marry his mother lokasti. To avoid this oracle coming to truth, the royal couple gave Oedipus away immediately after birth, with the purpose to having him die out in the wild. Instead, the infant was collected by a shepherd and eventually was adopted and raised by king Polybus and gueen Merope of Corinth, thinking they were his biological parents. When he grew up, after an accident, Oedipus killed his father Laios during a fight without knowing and after responding to the aenigma of the Sphinx outside Thebes, he married lokasti, his mother, also without knowing the truth. Oedipus and lokasti had four healthy children, always according to the play by Sophocles, Polynices, Eteocles, Antigoni and Ismini. The important question is: what is the probability of two persons who are genetically related by first degree (consanguineous marriage), to have four children and all be healthy? To answer this question we need to have information about the human genome and its polymorphic nature, and of the frequency of deleterious DNA variants. During this lecture we will calculate together the likelihood for this to happen and prove that Sophocles did not know of genetics when he wrote this play.

#### Omega-3 fatty acids have a role in prevention of coronary heart disease" Professor Dr Philip C. Calder

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The long chain omega-3 fatty acids EPA and DHA are found in seafood, especially fatty fish. Supplemental forms of EPA and DHA from fish oil, algal oil, krill oil and concentrates are also available. In the absence of consumption of fatty fish or supplements, intakes of EPA and DHA are low and well below what is recommended. Most recommendations are based upon the reported beneficial effects of omega-3 fatty acids with regard to cardiovascular diseases particularly coronary heart disease (CHD). The benefits of EPA and DHA were first identified in Inuit populations who had a very high intake but low mortality from CHD. Studies in the Japanese showed similar findings. Data from several large prospective cohort studies (e.g., Nurses Health Study; Physicians Health Study) showed inverse associations between dietary intake of EPA and DHA or blood levels of EPA and DHA and risk of CHD, CHD morbidity and CHD mortality. A meta-analysis published in 2014 (Choudhury et al.) identified a significantly lower risk of coronary outcomes in those with high compared to low dietary intake of EPA+DHA and in those with high compared to low blood levels of EPA, DHA or EPA+DHA. More recently, delGobbo et al. reported lower risk of fatal CHD in those with higher blood or tissue status of EPA or DHA. These findings provide robust evidence that dietary intake of long chain omega-3 fatty acids, which results in higher blood and tissue levels, is linked to lower risk of CHD. The explanation for this protective effect is the beneficial impact of EPA and DHA on a range of risk factors for CHD, demonstrated in numerous individual trials and in a number of metaanalyses. Older studies (e.g. GISSI, GISSI-HF, JELIS) also reported that long chain omega-3 fatty acids could be used in secondary prevention to reduce mortality in individuals who already had advanced CHD. More recent studies have failed to replicate the earlier findings. Metaanalyses of mortality in such at-risk patients report a range of findings depending upon which studies are included. The 2017 AHA advisory supports the use of long chain omega-3 fatty acids in secondary prevention. Thus, while evidence for the role of EPA and DHA in (primary) prevention of CHD is robust, their role in secondary prevention is less certain and remains hotly debated.

# Diet-depended competition between Pseudomonas aeruginosa and Escherichea coli in the host intestine

#### Ass. Prof. Dr Yiorgos Apidianakis

**Theodoulakis Christofi, Irini Dieronitou, Christina Michael, Yiorgos Apidianakis** Department of Biological Sciences, University of Cyprus

Gut microbiota acts as a barrier against intestinal pathogens, but the functions of specific bacterial species in the presence of other microbes and the host intestine remain poorly understood. We assessed thirty-five strains of human intestinal bacteria species in inducing

intestinal regeneration and lethality in Drosophila melanogaster. Virulence profiles of single bacterial strains in flies significantly match the anticipated pathogenicity of the corresponding species in humans. Furthermore, among all possible one-to-one bacterial combinations we identified Pseudomonas aeruginosa and Escherichia coli antagonizing each other in eliciting midgut regeneration and fly lethality. Oral antibiotic-induced dysbiosis and associated elimination of commensal E. coli in mice, favours intestinal P. aeruginosa colonization and concomitant mouse mortality. This effect can be explained by the glycolytic fermentation of sugars in E. coli and the production of lactic acid, which inhibits P. aeruginosa growth. Nevertheless, in the absence of high levels of sugars P. aeruginosa is capable of producing the quorum sensing regulated virulence factor pycyanin, which can inhibit E. coli growth. Assessing three extreme and a conventional diet in mice we find that, in addition to sugar fermentation to lactic acid, a fat-based diet can also induce E. coli to inhibit P. aeruginosa colonization in the mouse gut. These results aim to explain why although P. aeruginosa infection is a formidable clinical problem in sever wounds and predisposed human lungs, it doesn't commonly affect the human gut. We propose that dysbiosis induced by antibiotics and unbalanced diet eliminate lactic acid producing bacteria imposing an environment conducive to P. aeruginosa infection.

# NEW DRUGS, NEW TOOLS FOR INVASIVE TREATMENT AND NEW DATA FROM CLINICAL TRIALS ON ATRIAL FIBRILLATION

#### Is there any hope for the treatment of the "incurable" arrhythmia? Dr Giorgos Andrikopoulos

Henry Dunant Hospital, Cardiology and Department Director

Atrial Fibrillation is the most common arrhythmia in the industrialized world. The prevalence of this disease may exceed 10% of the population among the elderly. Atrial fibrillation is a significant cause of morbidity and mortality mainly because it increases 5-fold the incidence of stroke and heart failure. In addition, it deteriorates quality of life and increases health care costs, being the most frequent cause of admission in the hospital due to an arrhythmic event. Although antithrombotic therapy has successfully reduced the incidence of stroke and the development of novel anticoagulants (NOACS) expanded the use of proper antithrombotic therapy, our efficacy to prevent relapses of atrial fibrillation has been always very low due to the modest efficacy of antiarrhythmic medical therapy and its unfavorable influence on long-term prognosis of our patients. The introduction of invasive therapy of atrial fibrillation in the form of catheter and surgical ablation has substantially improved our antiarrhythmic strategies. The remarkable advances of catheter ablation techniques during the last 20 years

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and the development of holistic approaches that include catheter ablation, prevention and modification of hypertension and obesity and in specific cases combination of invasive and medical treatment, have enriched our therapeutic armamentarium against an arrhythmia that had been rightfully characterized as the "same of cardiology".

Recent technological developments and accumulating experience from the widespread use of atrial fibrillation ablation and appropriate use of antiarrhythmics have resulted in remarkable improvements in the management of atrial fibrillation, which have been recently verified by several large-scale clinical trials. Can we expect the definite cure of atrial fibrillation soon? Optimism should be tempered by reality, because atrial fibrillation is a disease of complex and still largely unknown pathophysiology, but surely this not "the same of cardiology". Not anymore.

# Hereditary Cancer syndromes, genetic counseling and testing: the experience in Cyprus

#### Ass. Prof. Dr Violetta Anastasiadou

Clinical geneticistat Archbishop Makarios III; Collaborating with The Cyprus School of Molecular Medicine at The Cyprus Institute of Neurology & Genetics

Hereditary Cancer syndromes include various rare conditions of associated cancers caused by germline mutations. The most well-known being Hereditary Breast and Ovarian Cancer syndrome, several other cancer associations meet the criteria for making a diagnosis such as Lynch syndrome, Cowden disease, Li-Fraumeni syndrome and others. Furthermore genetic disorders such as Neurofibromatosis type I (von Recklinghausen disease), Noonan syndrome and other Rasopathies, raise the risk for early onset cancers in various organs and tissues. Symptoms and signs beyond cancer, such as macrocephaly, dysmorphic features and autism, can also be indicative of a diagnosis in the group of hereditary cancer syndromes.

Genetic testing is vital for better management of patients and relatives at risk of hereditary cancer syndromes. Genetic counseling is a communication process aiming to discuss with patients all relevant information and implications of testing for them and for other family members. It is absolutely mandatory in order to assist patients to take their own personal informed decisions before testing.

In this presentation we will present data on hereditary cancer syndromes in Cyprus. We will also illustrate our experience in genetic counseling and testing patients at risk of hereditary cancer syndromes, who have been referred to the Genetics Clinic by their oncologists and other treating physicians.

# The Periprocedural Management of Patients with Atrial Fibrillation on Direct Oral Anticoagulants

#### Professor Dr Spyropoulos Alex

The Donald and Barbara Zucker School of Medicine at Hofstra/ Northwell in NY, USA

It is estimated worldwide that 1 in 6 patients on chronic oral anticoagulation with atrial fibrillation, or approximately 6 million patients per year, will require temporary interruption of their anticoagulant therapy for an elective procedure or surgery. Direct oral anticoagulants or DOACs have recently surpassed warfarin as the oral anticoagulant of choice in patients with atrial fibrillation. However, the management of such patients in periprocedural situations remains uncertain, including the timing of their interruption, the necessity of using heparin bridging therapy as temporary anticoagulation, and the routine need of preoperative coagulation testing.

Recent data to inform management principles of the DOACs suggest that any periprocedural management strategy should consist of an estimation of the procedural bleeding risk, patient renal function, and pharmacokinetic characteristic of each DOAC. Using these simple principles, the clinician can expect a very low 30-day periprocedural adverse outcome event rate of thrombotic and bleeding complications that is similar to, and in some instances safer, than that with warfarin. Consistent clinical data also points to the fact that the use of heparin bridging therapy with DOACs lead to a multifold increased risk of major bleeding without an accompanying reduction in the risk of stroke or systemic embolism. The recently completed large multicenter, multinational PAUSE trial assessed clinical outcomes with DOACs in atrial fibrillation patients undergoing elective procedures using a simple, standardized DOAC protocol based on DOAC pharmacokinetic properties and bleeding risks associated with the procedure/surgery. This trial will provide for the first time high quality data as to the optimal periprocedural management of this population with the DOACs.

#### Neuroprotection and neurorepair in brain and spinal cord injury A link between neurotrauma and neurodegeneration

#### Professor Dr Adina T. MICHAEL-TITUS

Centre for Neuroscience and Trauma, Blizard Institute; Barts and The London School of Medicine and Dentistry' Queen Mary University of London

Traumatic injury in the central nervous system triggers a cascade of pathophysiological processes and is for many individuals a life-changing event. Spinal cord injury and brain injury

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can lead to significant disability, and no neuroprotective or neuroregenerative treatment is currently available, in spite of more than two decades of effort. There is ample evidence across a range of experimental models of traumatic injury of the brain and spinal cord, that there are several compounds that could limit the secondary injury, but translation to the clinic has failed. We will explore potential causes of this failure and will discuss the specific case of omega-3 fatty acids, which have been shown in several models of central nervous system injury to have therapeutic and prophylactic potential. The talk will review the accumulating evidence that supports the therapeutic potential of long-chain omega-3 fatty acids in central nervous system trauma and will highlight some of the remaining questions that need to be answered in order to improve the chances of success in translation. The link between neurotrauma and neurodegeneration will also be discussed, and placed in the perspective of new concepts in the diagnosis and management of neurodegenerative conditions.

# Inflammatory prothrombotic pathways in Multiple Sclerosis. The role of the antiphospholipid antibodies

#### Ass. Prof. Dr Marios Pantzaris

Senior Neurologist and Head of the Neurology Clinic C and the Neurovascular Department at the Cyprus Institute of Neurology and Genetics

There are several scientific evidences to support that the coagulation cascade is activated prior other metabolic or immunological pathways in Experimental Allergic Encephalomyelitis. Following that activation fibrinogen and/or fibrin is extravasated and attract locally the microglia (CNS macrophages) which is the promoter of local inflammation and chemo-attraction of immune cells to finally lead to demyelination andaxonal degeneration. New data will be presented from the literature and from our research projects at the Cyprus Institute of Neurology and Genetics.

#### DHA, EPA and antioxidants for multiple sclerosis: where we stand

#### Evangelia Ntzani

University of Ioannina School of Medicine

Multiple sclerosis (MS) is a potentially disabling autoimmune disease of the brain and spinal cord (central nervous system). It attacks the myelin sheaths insulating the axons of the central nervous system, thereby impeding neural signaling. This damage was initially thought to be solely caused by the adaptive immune system's T cells; recent scientific

data shed light to the major role B cells play in this destructive process. Multiple sclerosis usually begins in its relapsing-remitting form in early to mid-adult life with periodic attacks of neurological dysfunction followed by stabilization and often, early in the disease, partial or complete recovery. Over time, the relapsing form may transition to secondary progressive MS, exhibiting worsening symptoms, with about 2% to 3% of people with relapsing MS converting to secondary progressive MS annually without treatment. Under treatment, there is incomplete but increasingly convincing data that the long-term course of MS has been favorably modified and that the transition from relapsing to progressive MS has been decreased perhaps to about 1% a year. Treatment typically focuses on speeding recovery from attacks (abortive therapies), slowing the progression of the disease (preventive therapies) and managing MS symptoms (symptomatic therapies). Due to the partial effectiveness of the currently available conventional treatments and their side effects, most patients with MS use complementary or alternative therapies. The most common dietary interventions used by MS patients are supplementation with polyunsaturated fatty acids (PUFA), allergen-free (gluten and milk) diets, and vitamins. Preclinical data show that polyunsaturated fatty acids, including omega-3 and omega-6 fatty acids, ameliorated experimental autoimmune encephalomyelitis in association with decreased IFN-y, IL-17, inflammatory leukocyte activity, and matrix metalloproteinase activity, and with induction of regulatory T cells.A number of observational studies and randomized clinical trials have been conducted attempting to define and establish the potential role of polyunsaturated fatty acids as a treatment modality in the management of multiple sclerosis. The accumulated different design strategies, studied populations, assessed exposures/interventions and outcomes and varying follow-up periods pose challenges in the assessment of this evolving evidence base and hinder its translational potential.



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### SA01 Heavy recreational cannabis use negatively impacts on bone health – A cross-sectional study

### Antonia Sophocleous1,2, Roy Robertson3,4, Nuno B. Ferreira5, James McKenzie2,3, Stuart H. Ralston2

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Preclinical studies have shown that the endocannabinoid system plays a key role in bone metabolism via the type 1 (Cnr1) or type 2 (Cnr2) cannabinoid receptors. These observations together with the recent developments in the medical use of cannabis worldwide and the full legalisation of marijuana for recreational purposes in some countries, prompt us to investigate the impact of recreational cannabis use on bone health. The study was conducted with 284 individuals recruited from a local community in Edinburgh. Bone mineral density (BMD), fat mass and other relevant clinical variables were recorded. Of the 284 individuals recruited 170 (59.9%) were regular cannabis smokers, and were divided into two groups based on lifetime cannabis smoking episodes; moderate users (<5000 episodes; n=56,) and heavy users (>5000 episodes; n=114). Controls were tobacco smokers who did not smoke cannabis (n=114). Heavy cannabis users were younger than controls (p<0.005), had a higher dietary calcium intake (p<0.005), a lower body mass index (BMI) (p<0.01) and were more likely to use other illicit drugs (p<0.005). Heavy cannabis users had lower BMD in the hip (p<0.005), lumbar spine (p<0.005) and femoral neck (p<0.05) than controls. Fractures were more common in heavy cannabis users (rate ratio=2.17; p< 0.001). Serum biochemical analyses showed that heavy cannabis users were significantly likely to lose (p<0.045) and form new bone matter (p<0.01) when compared to controls, suggesting a higher bone turnover. Multiple regression analysis showed that heavy cannabis use was an independent predictor of low BMD at lumbar spine, femoral neck, and total hip, accounting for 5.4% (p=0.035), 3.9% (p=0.01) and 5.8% (p=0.001) of the variance, respectively. Mediation analysis showed that the effects of heavy cannabis use on total hip and femoral neck BMD were direct, but on spine BMD were indirect and mediated through low BMI. We conclude that recreational heavy cannabis use has a negative impact on bone health, and that more studies are needed to ascertain the potential impact of regulated cannabis consumption for medicinal purposes.

### SA02 Proteomic analysis in mouse kidneys reveals novel lupus nephritis biomarkers

#### Orthodoxia Nicolaou1,2 Kleitos Sokratous1,2, Anastasis Oulas1,2, George M. Spyrou1, 2, Kyriaki Michailidou1,2, Christiana Demetriou1,2, Andreas Hadjisavvas1,2, Bernard R. Lauwerys3, Kyriacos Kyriacou1,2

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Background: Approximately 50% of Systemic Lupus Erythematosus (SLE) patients develop nephritis, which is among the most severe complications of the disease and a leading cause of morbidity and mortality. Although therapy has improved in the past two decades, up to 26% of lupus nephritis (LN) patients still develop end-stage renal disease. Due to the complex and unpredictable course of the disease, diagnosing LN remains a challenge. Despite intensive research, there are still no reliable LN markers in clinical use that can assess renal damage and activity with high sensitivity and specificity. The aim of this study was to identify new clinically relevant tissue specific protein biomarkers and possible underlying molecular mechanisms associated with renal involvement in SLE, using mass spectrometry (MS)-based proteomics.

Methods: Kidneys were harvested from female triple congenic B6.NZMsle1/sle2/sle3 lupus mice model and the respective sex and age-matched C57BL/6 control mice at several stages of disease development: pre-nephritic (3 months), full-blown-disease (6 months) and end-stage renal disease (9 months). Serum samples from 36 LN patients (18 active, 18 inactive) and 20 age- and sex-matched healthy controls were used for validation experiments. Proteins were extracted from kidneys, purified, reduced, alkylated and digested by trypsin. Purified peptides were separated by liquid chromatography and analyzed by high resolution MS. Data were processed by the ProgenesisQIp software and functional annotation analysis was performed using multiple bioinformatics resources. Immunofluorescence (IF) and multiple reaction monitoring MS (MRM-MS) methods were used to confirm prospective biomarkers.

Results: Comparative proteomic analyses lead to the identification and quantification of around 3000 proteins within all samples. Pathway analyses revealed a number of proteins to be implicated in important pathways previously shown to be associated with LN and autoimmunity including, phagosome pathway. Significantly dysregulated proteins were further compared with human kidney transcriptomics data, revealing 4 potential protein targets. Three of these proteins were confirmed with targeted methods. In addition, one of these protein targets was found to be secreted in human serum and its concentration levels were able to discriminate LN patients from healthy controls.

Conclusion: Proteomic analyses enabled the mapping of molecular pathways involved in renal responses to the systemic insult characteristic of SLE. Interestingly, our results were found to be in agreement with results obtained from human kidney biopsies. This enabled us the selection of 4 potential protein biomarkers for further validation. It is of interest that one of these proteins was

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found to be secreted in human serum, enabling the discrimination of LN patients from healthy controls. This provides the prospect for further investigation of this protein as potential SLE biomarker.

### SA03 Therapeutic trial of an oral c5a agonist in a mouse model of Alzheimer's disease

Elena Panayiotou1, Rana Abu Manneh2, Eleni Fella2, Savanna Andreou2, Revekka Papacharalambous1, Petroula Gerasimou3, Paul Costeas3, Stella Angeli2, Ioanna Kousiappa4, Savvas Papacostas4,2, Theodoros Kyriakides1,2.

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According to the amyloid hypothesis of Alzheimer Disease the deposition of prefibrillar and fibrillar a peptide sets off pathogenic cascades of neuroinflammation and neurodegeration that lead to synaptic and neuronal loss and cognitive decline. Various approaches to reduce amyloid load by reducing prefibrillar production of a peptide (secretase inhibition) or enhance amyloid clearance (anti-a peptide antibody mediated clearance) has proven unsuccessful in clinical trials.

Complement is activated from the very early stages of Alzheimer disease. Complement C1q has been found to modulate disease and in particular neuronal loss in the Alzheimer mouse model but its mechanism of action is controversial and has been called a double edged flower.

C1q has been shown to opsonize prefibrillar  $\alpha\beta$  peptide aggregates and facilitate phagocytosis yet complement activation leads to neuroinflammation and more amyloid deposition due to the production of cytokines creating an "inflammatory environment". Macrophages and neutrophils carry C5a receptors but also neurons, microglia and astrocytes in the brain.

Experiments in the Alzheimer mouse model show that complement component C5a receptor inhibition by PMX205 reduces amyloid load, attenuates pathology and improves cognitive testing. More recent evidence suggests that C5a is toxic to mouse neurons in vitro both directly and by enhancing the toxic effects of fibrillary  $\alpha\beta$ . Furthermore C5a enhances migroglia phagocytosis of synapses initiated by pre-fibrillar  $\alpha\beta$  early on in the disease in mouse models of the disease.

In the ATTR neuropathy mouse, an animal model of transthyretin amyloidosis, C5a receptor inhibition exacerbates amyloid deposition while full C5a agonist administration significantly reduces amyloid deposition. This model of amyloidosis differs from the Alzheimer models in that the amyloidogenic peptides are imported into the tissue beds from the circulation (since the TTR peptides are made in the liver). Any activation of complement in the tissue bed and the release of pro-inflammatory mediators are not expected to have any major impact on local pre-fibrillar TTR production unlike the  $A\beta$  situation with AD mouse models.

We have treated 3 month-year-old 5XFAD mice with 1 dose of the C5a full agonist for one week and then evaluated their cognitive capacity, amyloid deposition and expression of various secondary effector markers. We have also compared our results to our data set obtained when 5XFAD mice were treated with the modified EP67 agonist (devoid of neutrophil activating potential). Both

agonists appear to ameliorate cognitive decline and amyloid deposition, however, the modified agonist seems to be more beneficial in respect to overall symptom improvement.

#### SA04 TRANSPORTERS CONTROL INTESTINAL HOMEOSTASIS, INFECTION-INDUCED REGENERATION AND CANCER IN DROSOPHILA

#### K. Neofytou and C. Pitsouli

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The intestine is a fast-renewing tissue exposed to a massive number of pathogens and it is therefore susceptible to acute and chronic infection that can elicit intestinal inflammation. Inflammation and carcinogenesis are intimately connected and recent studies have shown that infection can lead to cancer in individuals predisposed for oncogenic mutations. However, infection of flies harboring different oncogenic backgrounds, leads to the development of morphologically distinct tumors. Specifically, pathogenic bacterial infection in combination with the Ras oncogene leads to dysplastic, large tumors with cellular heterogeneity and loss of apicobasal polarity, whereas infection combined with a dominant negative form of the Notch tumor suppressor leads to dysplastic, large tumors composed almost exclusively of stem cells that do not lose apicobasal polarity. Here, using genomics, genetics and advanced microscopy we characterized tissue- and cell-specific regulators of inflamed Ras tumors. Transcriptomic experiments identified six genes encoding transporters (sterol, vitamin, sugar, ion) that were upregulated in Ras dysplastic intestines compared to healthy and Notch dysplastic intestines. Tissue-specific RNAi experiments showed an intestinal stem cell requirement for these transporters during homeostasis and regeneration upon infection. Strikingly, knockdown of these six genes in the intestinal progenitor population almost completely inhibited homeostasis and regeneration upon infection and made the flies susceptible to the pathogen. Importantly, among the identified genes, those coding for transporters of essential sterols and vitamins were also shown to regulate maintenance of intestinal stem cells and their differentiation into the hormone-secreting enteroendocrine cells. Additionally, the same genes were also found to control autonomously infection-promoted tumorigenesis. The number of mitotic cells, as well as the size and the number of Ras tumors in intestines lacking the expression of these transporters were significantly reduced. In conclusion, our work revealed novel regulators of homeostasis and regeneration upon inflammation leading to tumorigenesis in Drosophila, which might allow us to elucidate the effect of dietary components on the function of intestinal stem cells during infection-induced inflammation and carcinogenesis.

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#### SA05 Moderating effect of Psychosocial factors in the relation between Symptom Severity and Quality of Life in Irritable Bowel Syndrome (IBS)

#### Hester Bowers1, Nuno Ferreira1,2, David Gillanders1

1 Department of Clinical and Health Psychology, University of Edinburgh; 2 Department of Social Sciences, University of Nicosia

ObjectiveNo study to date has attempted to reconcile multiple psychosocial factors in a single account of IBS experience and outcomes. The present study will present and test a theoretically driven model of how gastrointestinal anxiety, behavioural response, symptom severity, quality of life and psychological flexibility interact to determine how people cope and respond in IBS.

Methods A model of moderated serial mediation was tested using Ordinary Least Squared Regression-based Path Analysis. Secondary, cross-sectional data was utilised from 166 gastrointestinal outpatients attending a tertiary care Gastrointestinal Motility disorders clinic. Measures of IBS Symptom Severity (IBSSS), Visceral Anxiety (VSI), Behavioural Response (IBS-BRQ), Psychological Flexibility (IBS-AAQ) and Quality of Life (IBS 36) were used.

Visceral anxiety and behavioural response were found to serially mediate the relationship between symptom severity and quality of life. Each specific path of the indirect effect was significant at the p<.001 level. A significant interaction was also found for psychological flexibility as a moderator at the level of the indirect effect (-.0091, 95%Cl = .-.0163 to .0019). The strength of the mediatory effect appears to be linearly related psychological flexibility.

Conclusions The results suggest multiple psychosocial variables interact to shape IBS experience and outcomes. This study provides a clearer picture on the variability of Quality of Life across patients that present with similar Symptom Severity. The theoretical and clinical implications of these findings are discussed in the light of a biopsychosocial approach.

#### SA06 GENE REPLACEMENT THERAPY FOR CMT1X NEUROPATHY

### Kagiava A1, Richter J2, Tryfonos C2, Karaiskos C1, Sargiannidou I1, Christodoulou C2, Kleopa KA1,3.

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GJB1 gene mutations affecting the gap junction protein connexin32 (Cx32) cause the X-linked Charcot-Marie-Tooth disease (CMT1X), one of the commonest forms of inherited demyelinating peripheral neuropathy. Clinical studies and experimental models indicate that loss of Cx32 function leads to the manifestations of the disease suggesting that gene replacement therapy could offer a therapeutic benefit. In previous studies we showed targeted expression of virally delivered Cx32 in Schwann cells following a single intrathecal injection of lentiviral vectors in the Cx32 knockout (KO) mouse model. This approach resulted in improved outcome of the progressive neuropathy that develops after 3 months of age.

To further examine the potential for translating this approach, we used repeated intrathecal

injections to increase the expression rates, as well as late injections in 6-mo old Cx32 KO mice with already established nerve pathology. Compared to mice injected only once, repeated injections resulted in a non-significant increase in the expression levels of either EGFP in wild type (WT) mice using the mock vector (LV.Mpz-EGFP) or of Cx32 in Cx32 KO mice using the full (LV.Mpz-GJB1) vector. Intrathecal delivery of the full vector in 6-mo old Cx32 KO mice resulted in expression of WT Cx32 in lumbar roots and sciatic nerves correctly localized at the paranodal areas similar to the expression in 2-mo old mice.

We have proceeded to treatment trial where 6-mo old Cx32 KO mice were randomized to receive either the mock or the full vector in order to examine the outcome at 8 and 10 months of age by behavioral, electrophysiological and morphological analysis. These studies are expected to provide further evidence for the potential to treat CMT1X by gene replacement therapy after the onset of the disease.

Funding: Muscular Dystrophy Association and Charcot-Marie-Tooth Association (Grant MDA 480030 to KAK) and Cyprus Research Promotion Foundation (KOYATOYPA/BP-NE/0416/06 to AK).

# SA07 Analysis of polymorphism in the TLR3 gene of NK cells from Multiple Sclerosis patients

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Background: Multiple Sclerosis (MS) is a chronic demyelinating disease of the central nervous system (CNS) where both environmental and genetic risk factors play a role. Among the environmental risk factors, EBV and HSV infections have been suggested as strong candidates contributing to MS pathology/progression. Viral recognition and control is largely tasked to the NK cells via TLR recognition and various cytotoxic and immunoregulatory functions. Objective: The present work aimed to characterize NK cells isolated from MS patients for genetic polymorphisms in the gene encoding for TLR3. Method: Highly purified NK cells isolated from peripheral blood of MS patients (n=30) and healthy controls (n=30) were used to sequence all five exons of the TLR3 gene using sanger sequencing. Alignment of the obtained sequences with the wild-type TLR3 sequence was used to identify genetic polymorphisms within the TLR3 gene. Results: The alignment identified multiple substitution mutations across the 5 exons of the TLR3 gene (rs116729895, rs3775296, rs377529, rs3775290, rs3775291, rs376735334 and rs73873710). A significant difference was observed in the allele distribution of rs3775291 (Leu412Phe) between MS patients and HC, whereby the minor allele was detected in 36.7% of MS patients versus 20% of HC (p=0.04). Interpretation: There appears to be a possible association between the TLR3 missense mutation rs3775291 and Multiple Sclerosis, which might be attributed to changes in the TLR3 functional properties. Future work can look further into TLR3 expression and/or functional differences in the NK cells of MS patients.

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### SA08 EPTRI - European Paediatric Translational Research Infrastructure: a bridge towards the future of paediatric medicine

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EPTRI Project Communications Team, Consorzio per ValutazioniBiologiche e Farmacologiche (CVBF) INTRODUCTION: Minors cannot be compared to adults as they are continuously developing and their metabolism is changing over time. While they comprise 20% of the European population, only 30% of medicines have a paediatric authorization. On the whole, only 1 out of 2 authorized paediatric medicines have been properly tested, uncovering a serious lack of suitable medicines for children.

**OBJECTIVE:** The European Paediatric Translational Research Infrastructure (EPTRI) is a project that arises from the need to find answers to that severe gap. It aims to propose developmental models for a future basic Research Infrastructure (RI) fostering high level basic and applied research from drug discovery to paediatric formulation. The future RI will be complementary to the existing RIs, by putting together and networking all the available competences and technologies useful to enhance paediatric research in paediatric medicines.

**METHODS:** For this purpose, EPTRI will prepare a Concept Design Report (CDR) describing the scientific and technical requirements as well as the key components of the future RI. This CDR will act as a basis for political decisions for future implementations and will represent a relevant strategy for the design and future set-up of the new RI. Plus, the project will cover the main areas of need in paediatric medicines technology, creating 5 thematic platforms: 1) Paediatric medicines discovery and early drug development; 2) Biomarkers use in paediatric medicines development; 3) Paediatric pharmacology; 4) Formulation science; 5) Underpinning paediatric clinical studies. EPTRI is coordinated by Consorzio per ValutazioneBiologiche e Farmacologiche (CVBF) and involves 26 partners from 19 EU/Associated countries including existing RIs and the major paediatric expertise to cover the scientific topics in the proposal. Moreover, EPTRI has received relevant supports from several national/regional authorities, patients associations, academy and health institutions, thus demonstrating a favorable framework for the future technology-driven RI focused on paediatrics. The project includes 11 Work Packages and will last 2 years.

**CONCLUSION:** Creating a framework for a future paediatric RI will help to accelerate peadiatric drug development processes, resulting in a substantial improvement of children's quality of life. Key Words: Paediatric medicines; research infrastructure; children; biomarkers; pharmacology;

formulation

This project has received funding from the European Union's Horizon 2020 research and innovation programme under Grant Agreement No 777554

### SA09 CRISPR/Cas9- and TALEN-mediated disruption of aberrant regulatory elements restores normal splicing and gene function

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**Background:** The rapidly evolving field of genome-editing has raised hopes for the permanent therapy of a plethora of human diseases, including  $\beta$ -thalassemia. However, most of the correction approaches are based on homologous recombination and suffer from low efficiencies, impeding their progress to clinical trials. The severe and common HBBIVSI-110(G>A)  $\beta$ -thalassemia mutation creates an aberrant splice acceptor sites and leads to by the production of a non-functional aberrant mRNA and insufficient amounts of normal HBB mRNA.

**Aim:** Limitation of current mutations-specific editing approaches prompted us to develop a novel mutation-specific and nuclease-based approach for the correction of missplicing, based on the disruption of aberrant regulatory elements (DARE) and exploitation of the common and efficient non-homologous end-joining repair mechanism (NHEJ). In this context, the intronic, exon-proximal HBBIVSI-110(G>A) mutation was used as a missplicing mutation model for the evaluation of the DARE strategy

**Material and Methods:** DARE was applied to a humanised HBBIVSI-110(G>A) murine erythroleukaemia clonal cell line (MEL HBBIVS) via plasmid-based delivery of designer nucleases, and to patient-derived haematopoietic and stem and progenitor (CD34+) cells via nucleofection of in vitro synthesized mRNA for TAL effector nucleases (TALEN) or of ribonucleoprotein for CRISPR/ Cas9 RNA-guided nucleases (RGN). On- and off-targeting of designer nucleases was assessed by T7 endonuclease I (T7E1) assay and targeted deep sequencing. Restoration of normal splicing was assessed at the level of mRNA (by reverse-transcription quantitative PCR) and protein (by immunoblots and high-performance liquid chromatography). Correction of late-stage erythropoiesis was assessed with differential counts of cytocentrifuged slides after histological staining.

**Results and Conclusion:** In MEL HBBIVS cells, DARE by a RGN or TALEN restored correct splicing, and clonal analyses showed that disruption of the upstream region of HBBIVSI-110(G>A) was sufficient

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to correct splicing. In patient-derived CD34+ cells, DARE allowed for up to 95% on-target disruption, with comparable performance by both platforms. Based on conditions and designs that minimized off-target modification of the HBB paralog HBD, DARE achieved significant correction of two key parameters defining  $\beta$ -thalassemia pathology, globin-chain synthesis and erythroid differentiation, in gene-edited CD34+ bulk populations. DARE would be applicable to any of a great number of human diseases caused by aberrant regulatory elements outside open reading frames. The present study validates DARE as a novel virus-free and DNA-free mutation-specific therapy at efficiencies in primary patient-derived cells suitable for direct clinical translation without enrichment of modified cells.

# SA10 ActivinA signaling regulates IL13Rα2 expression to promote breast cancer metastasis

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**Introduction:** Metastatic dissemination of cancer cells to distal organs is the major cause of death for patients suffering from the aggressive basal-like breast cancer (BLBC) subtype. Recently, we have shown that interleukin 13 receptor alpha 2 (IL13Ra2) is a critical gene that is overexpressed in a subset of BLBC primary tumors associated with poor distant metastasis-free survival (DMFS) and can promote extravasation and metastasis of breast cancer cells to the lungs. However, the upstream signaling mechanisms that promote aberrant IL13Ra2 expression during tumor progression remain unknown.

**Results and Discussion:** By leveraging our previously published gene expression profiling data from a well-characterized cell line model for basal-like breast cancer progression we show that both INHBA and IL13Ro2 genes exhibit similarly higher expression levels in metastatic compared to non-metastatic cells and that overexpression of both genes predicts worse metastasis-free survival of patients with high grade tumors. Activin A, a member of the TGF $\beta$  superfamily comprised of two INHBA subunits has been shown to context-depended roles in cancer progression. Here, we demonstrate that INHBA depletion downregulates IL13Ro2 expression in metastatic breast cancer cells, whereas treatment with Activin A in non-metastatic cells increases its expression levels. We also found that Activin A predominantly induces Smad2 phosphorylation and to a lesser extend activates Smad3 and Akt. Interestingly, Activin A-mediated upregulation of IL13Ro2 was Smad2-dependent since knocking down Smad2 or using the ALK4/ALK5 inhibitors EW-7197 and SB-505124 abolished this effect. Most importantly, our data indicate that knocking-down INHBA levels delays primary tumor growth, suppresses migration suppresses formation of lung metastases of breast cancer cells in vivo.

**Conclusion:** Conclusively, our findings suggest that the development of therapeutic interventions employing small molecule inhibitors against Activin receptors or neutralizing antibodies targeting Activin A ligand, could serve as alternative approaches against breast tumors overexpressing INHBA and/or IL13Ra2.

Acknowledgments: This work was supported by the Cyprus Research Promotion Foundation (KOULTOURA/BP-NE/0415/03).

# SA11 Normalization of tumor microenvironment in combination with cytotoxic nanomedicine reprograms macrophages, suppresses metastasis and improves overall survival.

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The dense extracellular matrix (ECM), compressed blood vessels and hypo-perfusion are major physiological barriers to the delivery of nanomedicines to solid tumors. Despite progress in strategies to normalize the tumor microenvironment (TME) to improve nanomedicine efficacy, their effect on metastasis remains unexplored. In this study, we re-purposed tranilast (Rizaben®), an approved anti-fibrotic drug, to normalize the TME, increase perfusion and improve nanomedicine delivery to metastases. Employing two metastatic syngeneic mammary tumor models, 4T1 and E0771, we demonstrate that combination of tranilast with Doxil-nanomedicine, but not with doxorubicin, delayed primary tumor growth, reduced the number of spontaneous lung metastases and increased overall survival of mice. Immunohistochemical analysis of both primary and metastatic lesions indicated a pronounced reduction in the ECM components for the tranilast-Doxil group. Furthermore, we found an increase in pericytes coverage of intratumoral blood vessels and an increase in mean vessel diameter causing a significant increase in perfusion in primary and metastatic tumors. Improved perfusion in metastatic nodules resulted in increased nanomedicine delivery, demonstrated by Doxil-induced DNA damage. We further found that only the combination of tranilast-Doxil reprogrammed macrophages by directing macrophage polarization towards M1 phenotype. We also provide evidence that tranilast normalizes immune TME by decreasing the distances between cancer-associated fibroblasts and CD4+/CD8+T cells. Our findings suggest that normalization of not only the primary but also the metastatic TME is more effective when combined with nanomedicine. Therefore, normalization of the TME using nanomedicine could be a potential treatment strategy to enhance drug penetration and suppress metastasis.

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### SA12 Systemic sclerosis susceptibility in the Greek-Cypriot population: a replication study of HLA and non-HLA genetic variants

### Paraskevi Chairta1, Savvas Psarelis2, Kyriaki Michailidou3, Christiana Demetriou4, Paschalis Nicolaou1,Kyproula Christodoulou1

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**Background:** Systemic sclerosis (SSc) is a multisystemic rheumatic disease, characterised by vasculopathy, immune system abnormalities and excessive deposition of collagen leading to fibrosis. Although the aetiology of the disease is still unclear, genetic studies showed that Human Leukocyte Antigens (HLA) and non-HLA genetic variants are associated with SSc development in some populations.

**Aim:** The aim of this study is to assess whether specific HLA as well as non-HLA genetic variants that are associated with SSc in other populations, confer SSc protection or risk within the Greek-Cypriot population.

**Methods:** This study included 33 SSc patients and 132 healthy age/sex-matched controls for the Greek-Cypriot population. Eighteen single nucleotide polymorphisms (SNPs) associated with SSc in other populations have been selected through a literature search and investigated in this study using either the SNaPshot technique, Sanger sequencing or RFLP analysis. Statistical significance was assessed using different genetic models. A p-value of < 0.05 was considered as nominal significant.

**Results:**Genotyping and log-additive model analyses showed that none of the selected SNPs is significantly associated with SSc and its subgroups in our population. However, recessive model analysis of SNP rs131654 located upstream of UBE2L3 showed that it is nominally significantly associated with SSc anti-topoisomerase I (ATA) + and diffused cutaneous SSc (dcSSc) subgroups, in our population.

**Conclusions:** Reported association of SSc with genetic variants, in other populations, was not confirmed in the Greek-Cypriot population for the vast majority of tested loci. Further investigation with a larger sample size may increase the statistical power of the study and decrease the probability of false-positive or false negative results.

# SA13 Tissue-intrinsic Eiger/TNF as a dual switch of intestinal stem cell divisions

#### Vasilia Tamamouna, Myrofora Panagi, Andria Theophanous, Maria Demosthenous, Savvas Teloni, Maria Michael, Markella Papadopoulou, Chrysoula Pitsouli, Yiorgos Apidianakis

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Although the rate of mitosis has been proposed to explain differences in the prevalence of cancer in different tissues and organs, the inherent factors controlling adult tissue mitosis remain obscure. Our quantitative population genetics analysis reveals that the cytokine Eiger/TNF - independently of its systemic role - acts as a dual tissue-intrinsic switch of the Drosophila intestinal mitosis. While abundant and inducible in the fat body, Eiger/TNF has a basal expression in midgut stem cells and differentiating enterocytes that is unaltered by intestinal infection and concomitant signaling. In the midgut progenitor cells, Eiger/TNF accelerates regeneration, stem cell intrinsically, via the wgn-JNK-Upd module. In mature enterocytes Eiger/TNF signals the visceral muscle via the grnd/ wgn-JNK module to inhibit the expression of wg, a growth factor that sustains stem cell mitosis. We identify zones of high and low Eiger/TNF expression in the midgut with distinguished progenitor and enterocyte expression. We demonstrate that the intensity of Eiger/TNF signal in progenitors vs. enterocytes explains differences in regeneration and tumorigenesis potential among individuals of different genetic backgrounds, and along the midgut of each individual.

# SA14 Depletion of Ras Suppressor-1 (RSU-1) promotes cell invasion of breast cancer cells through a compensatory upregulation of a truncated isoform

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Extracellular matrix (ECM)-adhesion proteins and actin cytoskeleton are pivotal in cancer cell invasion. Ras Suppressor-1 (RSU-1), a cell-ECM adhesion protein that directly interacts with PINCH-1, thus being connected to Integrin Linked Kinase(ILK), alpha-parvin(PARVA), and actin cytoskeleton, is up-regulated in metastatic breast cancer (BC) samples. Apart from the originally-identified gene

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(RSU-1L herein), an alternatively-spliced isoform (RSU-1-X1) has been reported. We used noninvasive MCF-7 cells, expressing only RSU-1L, and highly invasive MDA-MB-231-LM2 expressing both isoforms and generated stable shRNA-transduced cells lacking RSU-1L while siRNA-mediated silencing was also employed to deplete the truncated RSU-1-X1 isoform. RSU-1L depletion in MCF-7 cells resulted in complete abrogation of tumor spheroid invasion in three-dimensional collagen gels, whereas it promoted invasion in MDA-MB-231-LM2, through a compensatory upregulation of RSU-1-X1. When RSU-1-X1 was also eliminated by siRNA, the RSU-1L-depletion-induced migration and invasion was drastically reduced being accompanied by reduced urokinase plasminogen activator expression. Protein expression analysis in 23 human BC samples corroborated our findings showing RSU-1L to be upregulated and RSU-1-X1 downregulated in metastatic samples. We demonstrate for the first time, that both RSU-1 isoforms promote metastasis while elimination of RSU-1L induces RSU-1-X1 upregulation to compensate for the loss. Hence, both isoforms should be blocked to effectively eliminate metastasis.

### SA15 Mutational signatures and kataegis across distinct cytolyticsubgroups of colorectal cancer.

#### Apostolos Zaravinos1,2, Konstantinos Roufas3, Christos Dimopoulos2,3

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**Background:** The catalogue of somatic mutations in cancer (COSMIC) bears the signatures of the mutational processes that have been operative. Kataegis is a mutational process that results in hypermutation in localized genomic regions. Cytolytic activity (CYT) is a useful tool to assess anticancer immunity. Here, we hypothesized that distinct mutational signatures are associated with different cytolytic subgroups in colorectal cancer and that they exhibit different patterns of kataegis.

**Methods:** We extracted MAF files for 633 cases of colorectal cancer from the TCGA-COAD and TCGA-READ datasets and processed them computationally, after classifying them into cytolytic-high (CYT-high) and CYT-low subgroups. Tumor heterogeneity in the both datasets was inferred by clustering variant allele frequencies (VAF). The extent of intra-tumor heterogeneity of each tumor was measured calculating the width of the VAF distribution and assigning a mutant-allele tumor heterogeneity (MATH) score. The total number of genetic variations within each cytolytic subgroup was calculated and tumors were sorted based on the mutation rate.

**Results:** We discriminated five different subsets of CYT-high and three different subsets of CYTlow colon cancer samples in the TCGA-COAD cohort. More than half of CYT-high and -low COAD samples, was mainly characterized by signature 1. The other two groups presented a higher level of signatures predominantly associated with MMR deficiency (signatures 6, 15 and 20) and defects in polymerase  $\varepsilon$  (signature 10). The contribution of signatures 6, 15, 20, 28 and 7 differed significantly between the two cytolytic subgroups. The majority of COAD tumors exhibiting kataegic sites were CYT-high (70%), and none of them CYT-low. Importantly, a significant number of the mutations in both datasets (51% in TCGA-COAD, 31% in TCGA-READ) were C>T transitions, consistent with the notion that kataegis results from DNA replication over cytidine deamination of resected DNA. **Conclusion:** The reconstruction of mutational signatures highlights the impact of the different underlying causes of mutations that are present in diverse cytolytic cancer samples. CYT-high colon cancers are closely associated with MMR deficiency and are thus, enriched in signatures 6, 15 and 20. Our data on kataegis suggest that the activated cytidine deaminase APOBEC is more actively involved in this cytolytic subgroup.





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#### PA01 NOVEL BARBITURIC ACID-BASED TOTAL INHIBITOR OF LEUKOCYTE TRANSMIGRATION

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Leukocyte transmigration is one of the most important events in the physiological tissue immune response. However, over-activation of the immune system leads to damage of healthy tissues. Thus, effective leukocyte transmigration inhibitors are considered as a very promising potential therapeutic agents against autoimmune diseases. In addition, inhibition of the homing of B-lymphocytes to lymphoid organs may be envisioned as a new therapeutic strategy to reduce B-cell lymphoma proliferation and their capacity to reach supportive lymphoid microenvironments. PECAM-1 protein is belonging to the immunoglobulin superfamily, localizes in endothelial surfaces and regulates leucocyte transmigration via endothelial cell intercellular junctions. Based on a pharmacophore model derived based on activated dimer of PECAM-1, fifteen new molecules with modified barbituric acid scaffold were designed in-silico, synthetized and tested in vitro. Human endothelial cells and human monocytes were used for the evaluation of the effect of synthetized compounds on the leucocyte transmigration. Three out of 15 compounds were active in a pharmacological concentration range. Importantly, one of the compounds (GT-73) completely blocked leukocyte transmigration, without damaging monocytes or endothelial cells (IC50=2.4  $\mu$ M). So far, even pan-antibody blockers of the beta-1 and 2 integrins were not able to block completely monocyte transmigration. GT-73 (10 mg/kg) was also extremely active in-vivo; in Crohn's disease, non-alcoholic fat liver, arthritis and multiple sclerosis mice models. Finally, a possible effect on the rolling of lymphocytes was tested using a B-cell lymphoma homing assay. GT-73 was injected together with human B-lymphoma cells IV to NOD mice. GT-73 significantly reduced the amount of cancer cells in the spleen and liver. Detailed acute toxicity profile of the compound was also studied and demonstrated not to have any toxic effects in the administrated doses. Such type of molecules might therefore provide a unique starting point for designing a novel class of leukocyte transmigration blocking agents with broad therapeutic applications.



GT-73 effect on lipid accumulation in the mice liver. Mice were kept on high fat diet.

# PA02 The role of hypoxia in ovarian carcinogenesis in BRCA mutation carriers

#### Theodora Kyriakou, Mira Mousa, Chindera Kantaraja

University College of London, Cancer Research Institute

Introduction High-grade serous ovarian carcinoma (HGSOC) is the most common and offensive histotype of epithelial ovarian cancer. Mutant BRCA as well as TP53 mutations have been considered as early events in HGSOC in patients with germ-line mutations. Recent studies are focused on the presence of a lesion in called serous tubal intraepithelial carcinoma (STIC), which has cytological appearance of HGSOC and it's mostly detected at the fimbriae of the fallopian tube suggesting the fimbrial end of fallopian tube as the primary site of origin for the ovarian tumor in the presence of STIC and HGSOC. Majority

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of the somatic mutations (including P53) are mediated by overexpression of physiological mutator enzymes collectively called as AID/APOBECs that are highly expressed in the fimbrial end of fallopian tube and could mediate pathways leading to STIC formation. This aim of this project was to investigate whether BRCA mutation stabilize hypoxia-induced factor (HIF-1 $\alpha$ ) under hypoxia, leading to activation of cyclooxygenase pathway which in turn activates AID/APOBEC expression and subsequently mutagenesis in the fimbrial end of the fallopian tube.

**Methods** Ovarian cancer cells and primary fimbrial cells were plated into 6 well plates and exposed to normoxia and hypoxia (1% 02, 2% 02 and 3% 02) for 18, 24, 48, 72 and 96 hours. At the end of the incubation cells were processed for DNA/RNA/protein isolation and the effect of hypoxia on inflammation and AID/APOBEC expression was assessed.

**Results** The results showed that hypoxia mediates inflammatory environment by up-regulating COX2 in a range of ovarian cancer cells. Also, COX2 pathway increases expression of mutagenic enzymes (AID/APOBECs) which induce somatic mutations and are significant in ovarian carcinogenesis in patients with BRCA mutations.

**Conclusion** We have successfully shown that tissue oxygenation status has a key role in ovarian cancer initiation and progression in BRCA mutation carriers. Hypoxia upregulates COX-2, TNF- $\alpha$  and IL-1B inflammatory cytokines that are crucial in the induction of key mutator enzymes such as AID and APOBECs that cause somatic mutations in tumor-related genes.

#### PA03 Siramesine induces cell death through autophagy and apoptosis in primary patient derived pancreatic cancer cell populations

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**Introduction**: Pancreatic cancer is a highly malignant tumor, poorly responsive to conventional systemic therapies that result in a progressive resistance to treatment. Sigma receptors (sigma-1 and sigma-2) have been shown to be overexpressed in cancer and their selective ligands (agonists and antagonists) specifically label tumor sites, induce cancer cells to undergo apoptosis and inhibit tumor growth. However, the mechanisms

of action underlying the anticancer activity of sigma ligands and their signaling pathways are reported to be highly dependent both on the type of the ligand and the type of the tumor they target. Siramesine, a selective sigma-2 receptor agonist, has been shown to exhibit a potent anticancer activity however, its mechanism of action is still elusive. The aim of this study is to investigate the expression levels of sigma receptors, their relation to pancreatic cancer development and the potential use of siramesine as drug against this cancer using patient derived animal cancer models.

**Materials and Methods:** The expression of sigma receptors was examined in clinical samples of patients with pancreatic cancer (pairs of cancer and adjacent normal tissue), in primary patient derived ex vivo pancreatic cancer cell populations and in established pancreatic cancer cell lines using Western Blot. The antiproliferative effect of multiple sigma ligands was studied in vitro with Sulforhodamine B assay. Additionally, the mechanism of action whereby siramesine induces cell death as well as the impact of siramesine on the cell cycle of established and patient derived ex vivo pancreatic cancer cell populations has been investigated using Flow Cytometry and Western Blot. The toxicity evaluation of siramesine was studied both in zebrafish examining the impact on lethality, toxic effects and hatching rate on embryos, as well as in immunodeficient mice SCID for the determination of maximum tolerated dose (MTD) and no-observed-adverse-effect level (NOAEL). Further, the in vivo potency of siramesine, either as single agent or in combination with established drugs, has been studied in patient derived xenograft models of cancer.

**Results and Discussion:** Expression of sigma receptors was observed in all examined pancreatic cancer cell lines and tumor tissues. Sigma-2 receptor is highly expressed in cancer compared to adjacent normal tissues and seems to be overexpressed compared to sigma-1 receptor. Amongst the sigma ligands that have been tested, siramesine exhibits good and in fact the best anticancer activity in established cell lines and primary patient derived ex vivo pancreatic cancer cell populations. Furthermore, siramesine induces cell death through autophagy in a dose and time dependent manner followed by apoptosis in higher concentrations and latter time points. Flow cytometry results suggest, that siramesine arrests cells at the G0/G1 phase. In vivo, siramesine exhibits good anticancer activity and enhances significantly the action of the known chemotherapeutic drug gemcitabine resulting in tumor growth inhibition.

**Conclusion**: Sigma receptors seems to be a key component for targeting pancreatic cancer and developing novel therapeutic approaches. Sigma-2 receptor agonist, siramesine, shows promising anticancer activity against ex vivo pancreatic human cellular populations and in vivo human-to-mouse cancer models.

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# PA04 Dermatofibroma- Dermatofibrosarcoma Protuberans: rare types of skin tumors

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DFSP is a very rare type of skin cancer that begins in connective tissue cells in the middle layer of the skin and may at first appear as a bruise or a scar. As it grows, lumps of tissue (protuberans) may form near the surface of the skin. This type of skin cancer often forms on the arms, legs and trunk. It grows slowly and rarely spreads beyond the skin. Dermatofibroma is pleomorphic soft tissue sarcomas presumably derived from histiocytes that are capable of fibroblastic transformation, and nowadays are called pleomorphic soft tissue sarcomas. Dermatofibromas and DFSPs appear to be associated with multiple systemic diseases (such as Systemic Lupus Erythematosus, myasthenia gravis, altered immune status) and some genetic basis.

Our project is concentrated on Dermatofibrosarcoma Protuberans (DFSP) and in generally Dermatofibromas. It is an epidemiologic study of patients who suffer from either DFSP or dermatofibroma. Our sample size is 6725 cases, 5 of which presented with DFSP and 120 with dermatofibromas, all found and analyzed from the patients' records of Dr. Mantas, plastic surgeon in Apollonion private hospital, in Nicosia, Cyprus. This study focuses on the common characteristics of the patients such as age, gender and genetic predisposition (chromosomal translocation association). Aim of this study is to confirm the worldwide epidemiology as well as to raise awareness to doctors.

For the conduction of the study we used Microsoft Forms and "Aktis" software which is used as database for the patients' records in Dr. Mantas private practice, as well as histological reports of each of our cases.

The results confirmed the worldwide literature. Dermatofibroma is a common cutaneous benign tumor with a high prevalence even in a small country like Cyprus. DFSP remain a rare type of cutaneous malignant skin tumor with a very good prognosis.

This study is not sponsored by any pharmaceutical or other kind of company/ association and has no intention for promotion and profit.

# PA05 Gene editing for genetic disorders: therapy development in the fast lane

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Gene editing and in particular the advent of CRISPR/Cas9 technology may turn the tide on therapy development for many genetic disorders. As pharmaceutical companies have begun to embrace gene therapy for the treatment of human disease, the principle of gene editing fundamentally changes the scope and speed of development for molecular medicines. Gene therapy by gene addition took decades to reach the clinic by incremental disease-specific refinements of vectors and methods, whereas gene therapy by genome editing in its basic form merely requires certainty about the causative mutation and access to target cells of interest. CRISPR/Cas9 technology in particular went from concept to first clinical trial in three years instead of thirty: therapy development in the fast lane. This presentation will summarise key achievements to date in therapy development based on different gene editing tools and will give a perspective on their employment for the treatment of genetic disorders. With emphasis on CRISPR/Cas9 technology, this talk will then highlight ongoing improvements to specificity, delivery and efficiency of existing tools, discovery of new enzymes, and ingenious reengineering and reemployment of gene editing tools as genome disruptors, transcriptional regulators, epigenetic modifiers and base editors. Thousands of orphan diseases are up for adoption, and recent developments in the gene therapy field finally conspire to find many of them a good home.

# PA06 Effect of folic acid supplementation on homocysteine levels in obese patients: results of meta-analysis

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**Background.** Due toinapropriate diet many disorders can develop in the human body, among others overweight/obesity, metabolic syndrome or atherosclerosis. One of the biochemical factors which was found to be especially high in obese patients is homocysteine (HCys). HCys is a sulphuric amino acid synthesized during the transformation of methionine and cysteine. It is produced in all types of cells in the human body. HCys shows cytotoxic effect towards endothelial cells, causes strong oxidative stress as well as can chronic inflammation. Folic acid plays an important role in the transformation of HCys since it is necessary for the synthesis of tetrahydrafolate, a substrate for 5,10-methylenetetrahydrofolate reductase (MTHFR), which is a main enzyme

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involved in the remethylation of homocysteine into methionine. Thus, supplementation of the folic acid may be helpful to decrease the level of homocysteine. The aim of the present meta-analysis was to determine the efficacy of folic acid supplementation on homocysteine level in overweight/obeses patients.

**Methods.** We have searched PubMed with appropriate key words (last search February 2018). Finally, 5 studies, including 133 patients and 134 placebo cases, corresponded to the inclusion criteria for meta-analysis [1-5]. Time of the end-point was from 8 to 12 weeks for all of the included studies. Folate dose was 5mg/day for all of the patients. Fixed or random effects models were used depending on the heterogeneity between the studies. Data were analyzed using MedCalc software version 13.7.

**Results.** Asignificant decrease of HCys level in patients with obesity supplemented with folic acid compared to obese cases from placebo group (standardized mean differences SMD -1.973 µmol/L; 95%Cl: -2,926 to -1,021; p<0.001) was observed. There were also significant differences in HCys levels in the study group before and after supplementation with folic acid (SMD 1.433 µmol/L; 95%Cl: 0,812 to 2,054; p<0.001) as well as in the case of the comparison of HCys levels between obese patients and placebo group before the trial (SMD -0,795 µmol/L; 95%Cl: -1,421 to -0,169; p=0,013). In the case of HCys level in the placebo group before and after the trial no difference was demonstrated (SMD -0,197 µmol/L; 95%Cl: -0,576 to 0,182; p=0,308). The significant heterogeneity between the analyzed studies was found.

**Conclusions.** Folate supplementation significantly decreases serum level of homocysteine in patients with overweight/obesity. Routine monitoring of serum HCys levels may be beneficial for overweight/obese patients since its decreasing with folic acid can lowered the risk of cerebro- and cardiovascular diseases. problems.

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### PA07 Effects of the Lazaroid Antioxidant U-74389G in a Surgically Induced Liver Ischemia Reperfusion Injury

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**Introduction:** Ischemia-reperfusion injury (IRI) is tissue damage triggered when blood flow returns to tissue after a period of ischemia.

Aim: The aim of this study was to determine whether pigs undergoing hepatectomy for IRI treatment using the Pringle procedure would have reduced inflammatory activity effect, quantified by specific blood inflammatory markers, when prior injection of the antioxidant lazaroid U-74389G molecule has been administered directly into the Liver.

**Methods:** Fourteen landrace pigs  $(30 \pm 2 \text{ Kgr})$  were obtained for use in the study. The animals were randomly assigned to experimental (Pringle procedure + receiving antioxidant lazaroid U-74389G) and control groups (Pringle procedure alone). The Pringle procedure being portal triad clamping. Blood was taken from all pigs at the phases: 1) Before 2) After 3) Two hours after and 4) 24 hours after Hepatectomy. Quantitative analyses of Blood Inflammation biomarker were performed on all samples. In order to perform histopathologic evaluation, tissue samples were taken from the liver at phases 3 and 4. The hepatic tissue should have included at least one big vessel.

**Results:** Histological analysis revealed the presence of inflammation and apoptosis, of the same density, both in the untreated (control) and the experimental group. Biochemical analysis revealed a statistically significant decrease (P<0.001) in TNF $\alpha$  biomarker at 2 hours and at 24 hours post reperfusion of the clamped vessels.

**Conclusion:** There was a statistical significant effect in the lowering of a pro-apoptotic chemokine (TNFa) following the administration of antioxidant U-74389G in swine when compared to the control group. But, the effect of antioxidant U-74389G did not appear to be sufficient in decreasing hepatocyte apoptosis at 24 hours. Further clinical research on the aforementioned molecule Vs TNFa and other pro-apoptotic mechanisms might give important and useful knowledge on lazaroid antioxidants and especially the molecule U-74389G.

#### PA08 ANTICONVULSANT DRUGS DURING PREGNANCY: THE CASE OF PHENYTOIN

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**INTRODUCTION:** Maternal use of anti-seizure medications such as phenytoin results in multiple effects on the developing embryo, including Fetal Hydantoin Syndrome (FHS). This syndrome is mostly caused by a combination of specific genetic and environmental factors, and women under anti-epileptic treatment with mutations in the methylenetetrahydrofolate reductase gene are at an increased risk of having an affected infant, as the protein product of this gene plays a role in the proper metabolism of phenytoin. FHS affects equally males and females, with the incidence rate being approximately 5%-10%. This report addresses the causes of FHS, provides epidemiological data and familiarizes readers with diagnostic techniques and treatment methods applied to avoid the syndrome's incidence.

**METHODS:** A literature search was performed on PubMed. This review focuses on articles published from May 1990 - September 2017, with priority given to articles reporting original research, case reports and randomized controlled trials.

**RESULTS:** FHS is associated with different signs and symptoms, but not all of them occur in each case. Exposure during 3rd week of gestation may lead to mild mental disability, delays in reaching developmental milestones and heart defects. Exposure during 4th week of gestation can result to defects as malformed or undeveloped digits, as well as strabismus, epicanthal fold, ptosis, hypertelorism, or down slanted eyes. Other common symptoms are cleft lip/palate, low weight and umbilical hernias. The diagnosis of FHS is clinically based upon identification of characteristic symptoms in affected infants along with a history of phenytoin exposure during pregnancy. A specific diagnostic test does not exist, but techniques as, ultrasounds for the detection of malformations in the eyes, radiographies for skeletal defects and echocardiography for associated congenital heart defect can be used.

**CONCLUSIONS:** Pregnant women should be treated with a single anticonvulsant drug prior conception, since exposure to many anticonvulsants poses a greater risk for birth defects. Females under phenytoin therapy should take folic acid supplements prior conception and during pregnancy, to reduce the risk of neurological malformations. Treatment for FHS depends on the symptoms and their severity. For heart defects, possible treatments include medicines and cardiac rehabilitation. For undeveloped or

missing limbs, prosthetic/plastic surgery and reconstruction are needed. Cleft lip/palate is also treated with plastic surgery. Enlarging or painful hernias require surgery to relieve discomfort and prevent serious complications. Strabismus treatment includes eyeglasses, vision therapy, or eye muscle surgery, while hypertelorism is treated either with box osteotomy or facial bipartition.

## PA09 Identification of pathogenic antibodies that may trigger inflammatory-thrombotic mechanisms in multiple sclerosis

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**Background:** Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system. Although the cause of MS is still unclear, many findings point toward the crosstalk between coagulation and inflammation due to the presence of specific antibodies, which act as procoagulant factors leading to thrombosis, in a condition characterized clinically as the Antiphospholipid Syndrome (APS). Taking into account the overlap of symptoms in MS and APS, particularly venous thromboembolism, the identification of antibodies against procoagulant and/or anticoagulant serine proteases namely Factor VIIa (FVIIa), Factor Xa (FXa) and plasmin should be considered. Furthermore, the presence of antibodies against the subunits of the excitatory NMDA receptor (NMDAR) has been recently suggested as a candidate biomarker in MS with only a handful of studies examining this association. In the present study, we aim to evaluate the prevalence of antibodies against procoagulant serine proteases which have not yet been investigated in MS, in addition to antibodies against the NR2B subunit of NMDAR.

**Methods:** Serum samples from 100 MS patients [83 Relapse-Remitting patients (RRMS), 13 Secondary Progressive (SPMS) and 4 Primary Progressive patients (PPMS)] and 60 age and gender matched HCs were analyzed for IgG antibodies against FVIIa, FXa and plasmin, as well as against the NR2B subunit of NMDAR using ELISA.

**Results:** Increased levels of IgG anti-FVIIa were detected in MS patients compared to HC (3.2% and 0% respectively, p<0.05). Additionally, anti-Xa were associated with 4% of MS individuals in comparison to none of the HC (p<0.05). Likewise, IgG anti-plasmin were detected in MS patients (3.2%) compared to none of HCs indicating a significant association of antibodies with MS (p<0.001). Interestingly, anti-NR2B were identified in

6% of MS patients in comparison to 1% of HCs (p<0.05). Of equal importance is the finding that patients with RRMS had the higher levels of antibodies compared to other types of MS. Conclusion: This study demonstrated increased prevalence of antibodies against various coagulation factors and against the NMDAR subunit in the serum of MS patients. These findings may prove valuable in future studies, to evaluate possible mechanisms involving these antibodies and in clarifying their role as potential risk factors in MS.

#### PA10 Coagulation parameters in children with arterial ischemic stroke in dependence to the presence of focal cerebral arteriopathy Ilona Kopyta1, Beata Sarecka-Hujar2\*, Magdalena Machnikowska-Sokołowska3, Katarzyna Gruszczyńska3, Dorota Raczkiewicz4

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**Background:** One of the state which predispose to the development of arterial ischemic stroke (AIS) in children is arteriopathy. Focal cerebral arteriopathy (FCA) is often found in children with AIS and applies to cases with focal cerebral arterial stenosis with no apparent cause. It is also a risk factor for stroke recurrence. However, it is not the only cause of paediatric stroke. In the present study we assessed whether levels of some coagulation parameters i.e. fibrinogen, activated partial thromboplastin time (APTT), protein C (PC) and antithrombin (AT) differ between stroke children with FCA and stroke children without FCA.

**Methods:** Total group consisted of 67 cases with AIS (age at the time of AIS up to 18 years). Children were hospitalized in the Department of Paediatric Neurology at the Medical University of Silesia in Katowice. The presence of FCA was confirmed by a radiologist. Data were analysed using STATISTICA 12.0 software.

**Results:** We observed that stroke subtypes is related to FCA however age and sex were not. Only stroke children with FCA were characterized by seizures and aphasia which occurred after stroke. No differences in the levels of fibrinogen, APTT, PC and AT between stroke children with and without FCA. Decreased level of PC was observed in 3 children without FCA (12.5%). 82.5% of children with AIS and FCA had normal level of fibrinogen

while fibrinogen level above normal was present only in stroke children without FCA (8%). **Conclusions:** FCA is associated with stroke subtypes and the presence of post-stroke consequences but the levels of the analyzed coagulation parameters did not differentiate children with AIS and FCA from children with AIS but without FCA.

## PA11 RISK OF MERCURY EXPOSURE IN THE MEDITERRANEAN AREA: PILOT STUDY IN CYPRUS

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**Introduction:** Mercury is a bioaccumulating global pollutant. Depending on dosage and timing, acute and chronic prenatal exposure to mercury has adverse effects including neuro- nephro- and immunotoxicity. Methylmercury (MeHg), a highly fat-soluble agent, penetrates the placental barrier to affect developing fetuses in the uterus. Thus, even in low concentrations MeHg causes developmental abnormalities including microcephaly, mental retardation, vision and hearing loss. This review aims to explain the increased baseline levels of mercury in Cyprus biomonitoring samples by investigating alternative methods of mercury exposure apart from fish consumption.

**Methods:** A systematic review was performed on databases as PubMed. This review was restricted to articles published from January 1988 to January 2018. Priority was given to original research reports and randomized controlled trials.

**Results:** Recent epidemiological studies show that mercury concentration in Cyprus is higher than the average concentration-although within the normal range. Follow-up studies performed during non-fasting periods confirm that this increase is not due to dietary fish consumption. Our review supports this statement not only because the regional diet is not rich in fish, but also because seawaters surrounding Cyprus lack nutrients and plankton vital for the growth of large marine fish populations. Alternatively, 3 fossil fuel power plants and 2 landfills were found in Cyprus. Cyprus also holds a high car ownership rate (742 cars per 1000 people), thus emissions from vehicles contribute to the mercury levels. Collectively, emissions from those sources pose risks including, but not limited to, mercury inhalation. Air transfer of mercury could also explain the elevated levels in the areas suggested by the latest biomonitoring study; as southwestern Cypriot winds aid in transporting the mercury which may then land by precipitation and vapor and thus contaminate the air, soil and water hence the food chain in locations corresponding with the aforementioned areas.

**Conclusion:** Mercury exposure in pregnancy is associated with both pregnancy complications and developmental problems in children. In the case of Cyprus, exposure is not due to fish consumption; alternatively emissions from power-plants, landfills, vehicles and precipitation to residential and agricultural areas, results in a significant increase of mercury levels in such areas.

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# PA12 Increasing apolipoprotein A1 levels improves the pharmacological effect of metformin on plasma glucose homeostasis and HDL levels

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Apoliprotein A1 (APOA1) is the major protein component of High Density Lipoprotein (HDL) in plasma which has been identified as a key lipoprotein in the protection against atherosclerosis and coronary heart disease. Recent data of our laboratory indicate that APOA1 modulates the pharmacological action of metformin, the first-line medication for the treatment of type 2 diabetes, particularly in overweight patients with metabolic syndrome. Specifically, we reported that mice deficient in APOA1 remained unresponsive to the pharmacological actions of the drug. Based on our experimental data and the current state of the art in the field, in the present study we aim at exploring how select APOA1 raising compound may augment the antidiabetic action of metformin. One of the most effective APOA1 inducers is niacin which has long been used in the treatment of dyslipidemia and cardiovascular disease (CVD). We found that co-administration of niacin and metformin in mice results in a substantial increase of functional HDL accompanied by an improvement in glucose homeostasis, when compared to each drug alone. The potential benefit of a fixed dose combination of niacin and metformin should be further explored in human subjects.

## PA13 Opposing effects of RSU-1 silencing in glioma cell invasion depending on their aggressiveness

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Most gliomas are invasive tumors formed from glial cells and associated with high mortality rates. In this study, we characterized four glioma cell lines of varying degree of aggressiveness (H4, SW1088, A172 and U87-MG) in terms of morphology, cytoskeleton organization and stiffness, and evaluated their invasive potential by performing invasion, colony forming and spheroid invasion assays. Cells were divided into two distinct groups: aggressive cell lines (A172 and U87-MG) with more elongated, softer and highly invasive cells and less aggressive cells (H4 and SW088). Interestingly, we found that Ras Suppressor-1 (RSU-1), a cell-matrix adhesion protein involved in cancer cell invasion, was significantly upregulated in more aggressive glioma cells compared to less aggressive. Importantly, RSU-1 silencing had opposing effects on glioma cell invasion depending on their aggressive cells. Finally, we found that RSU-1 silencing in aggressive cells led to decreased Signal Transducer and Activator of Transcription6 (STAT6) phosphorylation and Matrix Metalloproteinase13 (MMP13) expression in contrast to less invasive

## PA14 Genetic Susceptibility to Triple-Negative Breast Cancer in Cyprus

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**Introduction:** Triple negative breast cancer (TNBC) is a very aggressive form of breast cancer (BC), characterized by lack of expression, of the estrogen and progesterone

receptors (ER/PR), as well as by the human epidermal growth factor receptor 2 (HER2). Recently, it has been reported that 14.4% of TNBC patients have deleterious mutations in established BC genes, as well as other cancer susceptibility genes. Of these 8.4% had mutations in the BRCA1 and BRCA2 genes, and 6% in non-BRCA1/2 genes including BARD1, PALB2 and RAD51D, which are TNBC high risk genes (odds ratio > 5.0) and BRIP1, RAD51C and TP53, which are TNBC moderate risk genes (odds ratio >2.0). The aim of this study was to assess the distribution of germline mutations in non-BRCA1 and BRCA2 cancer susceptibility genes in Cypriot TNBC patients.

**Materials and Methods:** Genomic DNA from 124 TNBC patients was extracted from peripheral blood lymphocytes and sequenced using the TruSight Cancer panel (Illumina) on a NextSeq 500 instrument (Illumina). Analysis was performed using the Genome Analysis Toolkit (GATK) guidelines. Rare variants of uncertain significance (VUS) were evaluated using nine in-silico pathogenicity prediction algorithms, and those predicted as pathogenic from at least seven tools, were selected for further investigation. All variants were verified by Sanger sequencing.

**Results:** Five deleterious mutations in BC susceptibility genes (4 in PALB2 & 1 in TP53) were identified in 5 unrelated TNBC patients. Furthermore, five deleterious mutations in genes not proven to be associated with TNBC were found in ERCC2, ERCC5, FANCL and PRF1 genes in 5 unrelated TNBC patients. In addition, 20 VUS in established and other promising BC susceptibility genes were identified and predicted as deleterious by in-silico prediction tools. Six out of the 20 predicted deleterious VUS in the PALB2, RAD51C, BRIP1, CHEK2, ATM, PMS2 genes respectively, were identified in more than one sample (PALB2 (3), RAD51C (2), BRIP1 (3), CHEK2 (2), ATM (2), PMS2 (3)).

**Conclusion:** In summary, 5 deleterious mutations were identified in five Cypriot TNBC patients in established BC susceptibility genes other than the BRCA1 and BRCA2 genes (frequency 4.03%). Shimelis et al. reported that pathogenic mutations in TNBC susceptibility genes (BARD1, PALB2, RAD51D, BRIP1, RAD51C and TP53), were detected in 3.7% of all study participants, similar to our population's frequency. A combination of functional studies, case-control association studies and/or co-segregation analyses are needed in order to be able to classify the VUS identified.

## PA15 A Gene Silencing Approach To Treat Charcot-Marie-Tooth Disease Type 1A

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Charcot-Marie-Tooth disease type 1A (CMT1A) is the commonest inherited demyelinating peripheral neuropathy mainly resulting from the duplication of the peripheral myelin protein 22 gene (PMP22). This duplication causes destabilization of the architecture and function of the myelin sheath formed by Schwann cells leading to demyelination and ultimately to axonal loss. Despite the early characterisation of the disease, none of the various therapeutic approaches that have been studied so far has provided any significant benefit in improving the disease phenotype. The aim of this project was to develop and test two gene silencing approaches for CMT1A through lentiviral delivery of microRNA29a and a PMP22-specific shRNA which are predicted to post-transcriptionally downregulate PMP22 protein expression. In order to prove this we first developed a stable cell line overexpressing human PMP22 which was then transfected with microRNA29a 3p-precursor or anti-PMP22 shRNA-A loop under a ubiquitous promoter. Four days after transfection cells were harvested and their PMP22 levels were evaluated in repeated experiments using immunocytochemistry and western blot analysis. Normalized PMP22 immunoreactivity was reduced by over 30% in microRNA29a and shRNA-A transfected cells, while western blot results showed that microRNA29a and shRNA-A reduced human PMP22 protein levels by 29% and 53% when compared to scramble or non-targeting agents, respectively. These results provide an initial proof of principle that the above two agents can reverse PMP22 overexpression and potentially ameliorate CMT1A peripheral neuropathy. Currently, we are working on testing our hypothesis in vivo in the C61 mouse model of CMT1A, overexpressing the human PMP22 gene, using intraneural and intrathecal injections of viral vectors to deliver microRNA29a and PMP22 specific shRNA-A.

#### PA16 CRISPR/CAS9-BASED DISRUPTION OF BETA-THALASSEMIA DISEASE MODIFIERS

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Background: Beta-hemoglobinopathies such as beta-thalassemia and sickle cell anemia

are the most common genetic disorders and major sources of morbidity and mortality worldwide. Importantly, disease severity of  $\beta$ -hemoglobinopathy can be alleviated by increased expression of fetal  $\gamma$ -globin, as observed in patients with coinheritance of hereditary persistence of fetal hemoglobin. Reactivation of  $\gamma$ -globin has thus long been pursued as a major therapy approach for  $\beta$ -hemoglobinopathies. The complex puzzle of mechanisms underlying the normal postnatal fetal-to-adult hemoglobin switch and silencing of  $\gamma$ -globin is still incomplete, despite intense research efforts. Numerous studies have put forward genes with involvement in hemoglobin regulation, but only few of them have been evaluated as therapeutic targets of genome disruption.

Aim: The present study aimed to analyze potential or tentatively described  $\gamma$ -globin repressors as therapeutic targets for beta-hemoglobinopathies by genome disruption based on CRISPR/Cas9-based RNA-guided nucleases (RGNs). To this end, specific RGNs were expressed from integrating lentiviral vectors in erythroid cells before erythroid differentiation, followed by analysis of differentiated cells for  $\gamma$ -globin expression.

Methods and Results: Single guide RNAs (sgRNAs) were designed using the MIT CRISPR design tool to target ten candidate genes, cloned into dual-promoter Cas9-encoding LVs and efficiently delivered in erythroid HUDEP-2 cells. Targeted disruption efficiencies of the designed sgRNAs were evaluated using the T7EI endonuclease assay, whereas changes in γ-globin expression were assessed by reversed-phase high-performance liquid chromatography (RP-HPLC) and immunoblot.

Analyses revealed targeted disruption efficiencies of the RGNs in the range of 21-49% and $\gamma$ -globin reactivation after genome disruption of two of the candidate genes, CHD4 and MIR96. However, levels of induction compared to those for the positive control target, BCL11A, were low, indicating a minor role of the investigated candidate genes in HUDEP-2 cells, or elevated cell death and reduced proliferation because of target gene disruption.

**Conclusion:** The current study demonstrates the ease and efficiency of employing genome-editing technology for functional dissection of complex processes, such as haemoglobin switching. Moreover, disruption of as yet undercharacterized  $\gamma$ -globin repressors in erythroid cells has the clear potential to define promising therapeutic targets for beta-hemoglobinopathies. In this vein, our data shortlisted CHD4 and MIR96 as candidates for individual and combinatorial deactivation in primary patient-derived cells.

### PA17 A GENE THERAPY APPROACH FOR TREATING CHARCOT-MARIE-TOOTH DISEASE TYPE 4C

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Charcot-Marie-Tooth Disease Type 4C (CMT4C) is the most common recessively inherited demyelinating neuropathy and results from loss of function mutations in the SH3TC2 gene. Sh3tc2-/- mice represent a well characterized disease model developing early onset progressive peripheral neuropathy with hypo- and demyelination, slowing of nerve conduction velocities and disturbed nodal architecture. The aim of this project was to develop a gene replacement therapy for treating CMT4C in order to rescue the phenotype of the Sh3tc2-/- mouse model.

We generated a lentiviral vector LV-Mpz-SH3TC2.myc to drive expression of the human SH3TC2 cDNA under the control of the myelin protein zero (Mpz/P0) promoter specifically in myelinating Schwann cells. The vector was delivered by lumbar intrathecal injection at 3 weeks of age in Sh3tc2-/- mice and gene expression was assessed 8 weeks after injection. Immunofluorescence analysis showed immunoreactivity of hSH3TC2 and antimyc in sciatic nerves and lumbar roots in the perinuclear Schwann cell cytoplasm in a dotted pattern intracellularly colocalizing with physiologically interacting protein Rab11. Real time PCR analysis confirmed SH3TC2 mRNA expression in different PNS tissues.

A treatment trial was performed in Sh3tc2-/- littermate mice randomized to receive intrathecally at 3 weeks of age either the full or mock (LV-Mpz-Egfp) vector. Behavioral analysis 8 weeks after injection showed improved motor performance in rotarod and foot grip tests in treated Sh3tc2-/- mice. Moreover, motor nerve conduction velocities were significantly increased in fully treated Sh3tc2-/- compared to mock injected mice. Morphological analysis confirmed significant improvement in g-ratios, myelin thickness, and numbers of demyelinated fibers in lumbar roots and sciatic nerves of fully treated compared to mock-treated Sh3tc2-/- mice. Finally, treated mice showed improved nodal molecular architecture assessed by immunostaining of nodal and paranodal markers. This study provides a proof of principle for viral gene replacement therapy targeted to Schwann cells to treat CMT4C.

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## PA18 Functional investigation of a nonsense Ano10 mutation associated with Autosomal Recessive Cerebellar Ataxia

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Autosomal Recessive Cerebellar Ataxias (ARCAs) comprise a genetically and clinically heterogeneous group of rare neurological disorders characterized by degeneration of the cerebellum and/or the spinal cord. ARCAs include Friedreich Ataxia, ataxia-telangiectasia and many other rare forms such as the ARCA3; a form of ARCA caused by Ano10 (Anoctamin10) mutations. ARCA3 affects both children and adults with a vastly variable age of onset, presenting either with pure ataxia or with more complex phenotypes. Disease progression is slow and most patients remain ambulant for up to 25 years after onset.

We have previously identified a novel nonsense homozygous mutation in the Ano10 gene in a Cypriot ARCA family with three affected individuals. This mutation is located at the beginning of the open reading frame of the gene, permitting the translation of only one fifth of the main Ano10 isoforms, while allowing the full translation of only two of the five known isoforms.

Mutations in Ano10 have been associated with the ARCA3 form within the last decade and few functional studies have been performed thus far in order to determine their pathomechanisms. Ano10 is a member of the Anoctamin family of proteins that is comprised by ion channels and phospholipid scramblases. Ano10 has not been thoroughly characterized so far. The present literature data point Ano10 to be involved in calcium signalling, ions transport, cellular volume regulation and apoptosis. It is also considered a key protein for the innate immune defence. Its ortholog in Drosophila, Axs, is necessary for mitotic spindle generation and is implicated in an ER (Endoplasmic Reticulum) system controlling Ca2+ cytosolic concentration.

In order to perform functional analysis, lymphoblastoid cell lines were established from the proband and healthy individuals' blood and used for RNA and protein extraction. Three antibodies for Ano10 from different manufacturers were employed. Also, plasmid constructs expressing shRNA oligostargeting Ano10 were generated.

RT-PCR confirmed that the main expressing isoforms in all the tested subjects, cell lines and tissues are those carrying the nonsense mutation. Furthermore two novel Ano10 isoforms were identified and cloned. Immunoblot analysis showed similar protein expression of Ano10 in the patient and controls, thus indicating that the used antibodies are not suitable for immunoblotting.

Preliminary data showed a reduced growth rate when the Ano10 isoforms carrying the nonsense mutation were silenced. An even more reduced rate is exhibited when all the Ano10 isoforms were targeted.

Immunofluorescence experiments with the use of two of the Ano10 antibodies showed the presence of Ano10 in various subcellular organelles such as microtubules, centrosomes, cilia and nucleolus, portraying a possible multitasking role for Ano10.

Further experiments are currently performed to unravel the effect of silencing Ano10 in ER stress response, autophagy, mitosis and ciliogenesis.

Source of funding: Cyprus School of Molecular Medicine, The Cyprus Institute of Neurology and Genetics

## PA19 Co-inheritance of βo or β+ mutation with β-silent +33 C $\rightarrow$ G mutation: Genotype/Phenotype correlation

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Beta-thalassaemia, is an autosomal recessive inherited disorder of beta haemoglobin chain production, is a global health burden. It is mainly caused by point mutations in the  $\beta$ -globin gene with currently more than 400 point mutations being identified. The disease is characterised by reduced beta globin chain production, ineffective erythropoiesis and anaemia.

Aims: In this study we aim to investigate and describe the phenotypic characteristics of 8 patients after co-inheritance of the  $\beta$ -silentmutation CAP +33 (C>G) (HBB: c.-18C>G) with a  $\beta$ 0 or  $\beta$ + mutation.

Methods:Eight patients that co-inherited the  $\beta$ -silent mutation +33 C>G with a  $\beta$ 0 or  $\beta$ + mutations, previously identified through routine genetic diagnosis were selected for this study. Sanger Sequencing was performed to confirm the genotype. The samples were also analysed for a possible  $\alpha$ -thalassaemia mutation using GAP PCR, RED PCR and MLPA. Haematological tests, Full blood count and haemoglobin electrophoresis measuring HbA2 and HbF were performed.Clinical data was collected for the 8 patients

including transfusion dependency, age of first transfusion, frequency of transfusion, bone deformities, splenomegaly, splenectomy and presence of osteoporosis.

Results/Conclusion:The study demonstrated that 3 patients are transfusion dependant, 2 of which having a genotype C-39 (HBB: c.118C>T) /+33 began transfusion at the ages 31(bone deformities on face and splenomegaly) and 35 years of age while the other patient having a genotype IVSI-110 (HBB: c.93-21G>A) /+33 began transfusion at 3 years. One 51-year old patient with the genotype C-39/+33 was transfused only 2 times, once post birth and the other post-surgery.Three patients with genotypes IVSI-110/+33 and one with C-39/+33 were never transfused. One patient with the genotype IVSI-110/+33 was also a carrier of the  $\alpha$ -thalassaemia mutation - $\alpha$ 3.7 (NG\_000006.1:g.34164\_37967 del3804). The presence of the  $\alpha$ -thalassaemia mutation - $\alpha$ 3.7 may ameliorate the clinical picture of the patient.

The study displayed phenotypic variation amongst the 8 patients. It appears that the phenotype is more severe (increased need for transfusion) with the combination  $\beta$ 0(C-39)/+33 compared to the  $\beta$ + (IVSI-110)/+33 combination. While theco-existence of the $\beta$ + (IVSI-110)/+ 33 combinations with the  $\alpha$ -thalassaemia mutation- $\alpha$ 3.7 seems to ameliorate the clinical picture of the patient.

## PA20 Pre-graduate Suturing Skill Training with a Multimodal Hands-on Workshop

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The paper reviews how important is for medical students to learn how to handle the suturing instruments, tie knots and do sutures, but also shows that practicing these skills during their university studies is really beneficial. A multimodal hands-on suturing workshop was created by EUC faculty members and student peer-teachers in order to train medical students for their surgical rotation of clinical years. By using an electronic booklet, video demonstration and a Power-Point presentation, students were taught how to tie knots and do simple interrupted sutures. After the training the students were asked to perform simple interrupted sutures and an academic surgeon assessed their performance. There were 25 students participating in the workshop (40% 1st year students, 60% 2nd year students). The training was evaluated positively by the students in a similar training course. In conclusion, objective structural workshops motivate and doesgood to students for their career.

## PA21 Laparoscopic Skills Training for Pre-graduate Students with a Structured Hands-on Program

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Background: Minimally invasive surgery (MIS) is an integral part of all surgical subspecializations. It requires hand-eye coordination and psychomotor skills translating a 2D video image to a 3D working field. Introduction of MIS skill training in the pre-graduate years has several advantages: familiarization with medical technology, motivation for continuous skill training, and early exposure to surgery.

Materials & Methods: A multimodal task training workshop was created by EUC faculty members and student peer-teachers with the aim of teaching basic laparoscopic surgery skills to pre-clinical medical students.

The workshop included a series of tasks progressing from simple to complex ambidextrous tasks. The tasks description with images as well as a video demonstration was available to the participants before the workshop.

The hands-on session involved four skill stations on lap trainer boxes: placement of rubber band on pegs, rubber band maze, rope maze and paper cutting. There was a 15 minute time allocation per station per student for a total hands-on training time of 1 hour per student.

An electronic self-evaluation form was filled-in six months after the workshop by the participants with questions assessing the workshop and self-assessment items on a five point Likert scale.

Results: Ten 4th year medical students participated in the workshop. All participants answered the on-line evaluation form. For 90% of the participants this was their first laparoscopic training workshop and 70% are considering a surgical specialization. The course evaluation was generally positive but revealed that the 1 hour training time was considered inadequate. When asked about the course impact, all students would like to participate in similar courses.

Conclusion: Basic laparoscopic surgery skills can be taught to pre-graduate medical students with objective structured work-shops. Medical students of clinical years are eager to learn laparoscopic skills but seem to downsize the importance of hands-on workshops and continuous training because they have limited chances to apply this knowledge in a clinical setting.

### PA22 Alterations in atrial excitation patterns revealed by wavelet analysis a year after successful ablation for paroxysmal atrial fibrillation

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**Introduction:**Atrial fibrillation (AF) is the most frequently encountered cardiac arrhythmia, affecting about 2% to 3% of the population. Pulmonary vein (PV) electrical isolation is a therapeutic option for patients with drug refractory paroxysmal AF (PAF).

**Purpose:**P-wave morphology analysis can reveal information regarding abnormal propagation of the electrical activity on the atrial substrate. The aim of this study is to investigate mid-term changes in atrial excitation patterns following PV ablation.

**Methods:**We studied 31 patients (17 male, mean age 56.3 ± 8.1 years) who underwent PV ablation (20 with radiofrequency ablation, 11 with cryoablation) due to drug refractory PAF. Electrocardiographic (ECG) recordings were obtainedduring sinus rhythm before and several months (10.2 ± 1.97) after PV ablation with a 3-channel digital recorder for 10 minutes at a sampling rate of 1000 Hz. The Morlet wavelets analysis was applied over the P wave ECG recordings using a custom made software.Wavelet parameters expressing the mean and maximum energy ( $\mu$ V<sup>2</sup>) of P wave were calculated in the three orthogonal leads (X, Y, Z) and in the vector magnitude (VM), in three frequency bands (high: 161-200, mid: 91-160 and low: 50-90 Hz). Wilcoxon signed-rank test was used for comparing continuous variables, while p<0.05 wasconsidered significant.

**Results:**Ten months post PV ablation, both mean and max energies at high frequency band were significantly lower in allaxes, while wavelet energies where also lower at mid range band in X and Y axes. No significant changes werenoted at low band. Furthermore, P wave duration was shorter in all axes (X: 120.7±7.3 vs 113,5±7.2, p: 0.024, Y:130.4±7.0 vs 109.5±5.3, p: 0.014, Z: 125.8±7.2 vs 109.2±6.1, p: 0.009, VM: 125.3±5.9 vs 115.6±7.5, p: 0.030).

**Conclusion:**P-wave wavelet analysis identifies spectrotemporal alterations in atrial excitation patterns, remaining severalmonths after successful PV ablation.

High freq. band	Before PV Ablation	Follow-up	р	Mid freq. band	Before PV Ablation	Follow-up	р
mean (X)	11.0±7.9	3.5±1.9	0.001	mean (X)	17.5±11.5	9.7±4.2	0.030
mean (Y)	7.9±3.9	3.3±1.2	<0.001	mean (Y)	14.8±7.2	8.4±3.8	0.017
mean (Z)	6.2±3.5	3.7±0.9	0.016	mean (Z)	13.1±6.4	10.5±4.0	0.129
mean (VM)	4.4±1.1	2.4±0.4	<0.001	mean (VM)	7.7±2.0	6.6±1.8	0.098
max (X)	14.9±3.1	10.2±2.1	0.002	max (X)	19.4±3.9	16.3±2.8	0.019
max (Y)	13.7±2.9	11.0±1.8	0.003	max (Y)	19.3±4.0	16.2±3.0	0.021
max (Z)	15.2±5.0	12.3±1.7	0.007	max (Z)	18.8±3.7	18.6±3.3	0.525
max (VM)	11.3±1.3	9.2±0.8	0.003	max (VM)	15.4±1.9	14.3±1.7	0.262

Wavelet parameters before and ten months post PV ablation

## PA23 Acute Promyelocytic Leukemia AML M3: Clinical presentation and Treatment

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#### **PA24 Evans Syndrome Case Report**

Philip Papadimitriou, Eleana Strouthou, Themis Gkraikou School of Medicine, European University Cyprus

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