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## 3rd International Multithematic Scientific Bio-Medical Congress



# Bio-medical Scientific Cyprus

- Saturday, November 14, 2015
- Cultural Center,  
European University Cyprus

5 Credits of Continued Education will be awarded

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



Organized & Supervised by: Professor Dr Ioannis Patrikios



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# Welcome Address

By the Rector Prof 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 3rd Multidisciplinary Scientific Bio-Medical Congress, entitled "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 international university organization, Laureate International Universities-- a worldwide network of Higher Education institutions founded in 1998 in the United States; it is currently made of more than 80 institutions in 28 countries, with more than 200 campuses and over 1,000,000 students worldwide.

Furthermore, Laureate International Universities is an international community of universities that encourages learning without boundaries, with a unique multicultural perspective.

European University Cyprus has secured a momentous distinction following the assessment by QS TOP UNIVERSITIES (QS Stars™), 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.

Dear Colleagues,

The European University Cyprus is becoming an Institution with high quality targets aiming to new frontiers of science, innovation, research and excellence. We are investing with particular emphasis on Bio-Sciences like the opening of the Medical School at our University in September 2013.

High caliber events and symposia like this one, with distinguished scientists as speakers and participants from all over the world, are the vehicles driving to the accomplishment of our goals and they have our full support.

It is really an honor for us to have world known scientists and of your caliber participating and lecturing in our Institution.

Saying this, I salute and welcome every and each one of the congress participants and congratulate Professor Dr. Ioannis Patrikios, 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.

I would also like to acknowledge Bayer / Novagem Ltd, the sole sponsor of the congress for their genuine, valuable contribution.

I wish you all a successful and productive congress.

Professor Kostas Gouliamos  
*Rector, 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 3rd 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 14th of November 2015.

The School of Medicine of the EUC and I personally welcome all distinguished invited speakers and the scientific community of Cyprus that is attending this high quality Multidisciplinary Scientific Symposium.

As the founder and general organizer of the congress, I would like to thank the Ministry of Health and the Cyprus Medical Association for their support and recognition.

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 to me and my abilities to organize this event at the highest possible level. I thank all of my colleagues participating as chairmen of the session committees; 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. I am more than sure that this is an achievable target and here we are for a third consecutive year.

Finally, I would like to thank the sponsor of the congress, 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. We hope to have them for many more.

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 wish you all the best and a productive Congress

Dr Ioannis Patrikios

*Professor, Faculty of Medicine, School of Medicine, European University Cyprus  
General Congress Supervisor*

# Chairmen / Speakers

## Chairmen

- Dr Agathangelou Petros
- Dr Christodoulou Christina
- Dr Christou Christos
- Dr Ioannides Adonis
- Dr Ioannou Kyriakos
- Dr Johnson Elisabeth
- Dr Kaisis Christodoulos
- Dr Kiamides Yiannakis
- Dr Kyriakides Theodoros
- PhD Cand. Loukaides George
- Dr Miltiadous George
- Dr Nikolousi Elpida
- Dr Pantzaris Marios
- Dr Philaktou Leonidas
- Dr Stephanou Anastasis
- Dr Ioannis Patrikios

## Keynote Speaker

- Professor Dr Yonath Ada

## Plenary Speakers

- Professor Dr Achilleas Gravanis
- Professor Dr Deltas Konstantinos
- Professor Dr Kleopa Kleopas
- Professor Dr Manolis Athanasios
- Associate Professor Dr Pantzaris Marios
- Associate Professor Dr Poulas Konstantinos
- Professor Dr Riccio Paolo
- Professor Dr T. Michael-Titus Adina

Special Thanks to the Medical Students that have contributed to the organization of the conference.

- |                       |                        |
|-----------------------|------------------------|
| - Christofides George | - Panjiyar Sony        |
| - Demetriou Karolos   | - Papamichael Michael  |
| - Hadjivasilis Alex   | - Poupoutsi Ioanna     |
| - Ioakim Kalliopi     | - Stefanidi Diamanto   |
| - Ioannidou Ioanna    | - Theodorelou Charitou |
| - Kapnisi Stella      | - Sofia-Andriana       |
| - Kleinaki Zoe        | - Tsouvali Chara       |
| - Kouklidou Anastasia | - Tzanis Alex          |
| - Manolopoulos Philip | - Vasilakou Andriana   |
| - Masoura Vasiliki    |                        |
| - Neokleous Anastasia |                        |

# Program

Saturday, November 14, 2015

- 8:00-9:00 Registration
- 9:00-9:20 Opening Ceremony  
Introduction to the EUC School of Medicine  
Welcome Addresses  
Prof. Dr Ioannis Patrikios, *School of Medicine, European University Cyprus*  
Representatives of Cypriot Government and Cyprus Medical Association  
Prof. Kostas Gouliamos, *Rector, European University Cyprus*
- 9:20-9:35 Conferment Ceremony  
Doctor Honoris Causa  
Prof. Dr Ada Yonath (Nobel Laureate), *Weizmann Institute of Science, Israel*  
Recognition of Invited Speakers  
Prof. Andreas Efstathiou, *Vice Rector, European University Cyprus*

## Sessions on Research of Excellence

- 9:35-10:15 Combating species-specific antibiotics resistance  
Prof. Dr Ada Yonath (Nobel Laureate), *Weizmann Institute of Science, Israel*  
Chairs: Dr Christodoulos Kaisis, Dr. Yiannakis Kiamides, Dr Ioannis Patrikios

- 10:15-10:35 Coffee Break

## Neurodegenerative Diseases-Multiple Sclerosis-Trauma and Neuroprotection Neuroregeneration Vs Structured molecules (PUFA) and Antioxidant Vitamins (New Treatment Approaches)

- 10:35-11:10 Neuroprotective microneurotrophins: selective agonists of Nerve Growth Factor (NGF) receptors  
Prof. Dr Achilleas Gravanis, *University of Crete School of Medicine, Dept. Pharmacology, Greece*  
Chairs: Dr Yiannakis Kiamides, Dr Elizabeth Johnson, Dr Christodoulos Kaisis
- 11:10-11:45 Nutrition Facts in Multiple Sclerosis. From Bench to Bedside and Back Again: Translational Research in an Auto-inflammatory Disease  
Prof. Dr Paolo Riccio, *University of Basilicata, Potenza, Italy*  
Chairs: Dr Leonidas Philaktou, Mr George Loukaides, Dr Marios Pantzaris
- 10:15-10:35 Coffee Break

- 12:05-12:40 Omega-3 Fatty Acids for Brain and Spinal Cord Injury: Neuroprotection and Beyond...  
Prof. Dr Adina T. Michael-Titus, *Barts and the London School of Medicine and Dentistry, Queen Mary College, University of London, UK*  
Chairs: Dr George Miltiadous, Dr Anastasis Stephanou

- 12:40-1:15 Biochemical Pathways Affected by PLP10 Intervention  
Assoc. Prof. Dr Marios Pantzaris, *Cyprus Institute of Neurology and Genetics-Cyprus School of Molecular Medicine, Cyprus*  
Chairs: Dr Theodoros Kyriakides, Dr Elizabeth Johnson

- 1:15-2:00 Lunch Buffet

## Gene Therapy as a New Therapeutic Approach for Neurodegenerative Diseases

- 2:00-2:35 Towards a Gene Therapy Approach to Treat Inherited Demyelinating Neuropathies  
Prof. Dr Kleopas Kleopa, *Cyprus Institute of Neurology and Genetics-Cyprus School of Molecular Medicine, Cyprus*  
Chairs: Dr Ioannides Adonis, Dr Christina Christodoulou

## Other

- 2:35-3:10 Hypertension and Atrial Fibrillation  
Prof. Dr Athanasios Manolis  
*Asklepeion Hospital, Athens Greece; Adj. Professor of Medicine, Emory University, Atlanta; Adj. Ass. Professor of Hypertension, Boston University, USA*  
Chairs: Dr Petros Agathagelou, Dr Christou Christos
- 3:10-3:25 Coffee Break
- 3:25-4:00 Familial Microscopic Hematuria as a Paradigm for a "Multifactorial" Mendelian disease: A Unique Cyprus Experience  
Prof. Dr Konstantinos Deltas, *University of Cyprus, Cyprus*  
Chairs: Dr Kyriakos Ioannou, Dr Anastasis Stephanou
- 4:00-4:35 Electroceuticals: Paving the Path to Non-invasive Therapies  
Assoc. Prof. Dr. Konstantinos Poulas  
*University of Patras, Dept. Pharmacology, Greece*  
Chairs: Dr Elizabeth Johnson, Dr Elpida Nikolousi
- 4:35-4:40 Closing Ceremony  
Prof. Ioannis Patrikios, *School of Medicine, European University Cyprus*

## Speakers CVs



**Professor Dr Ada Yonath**  
*Weizmann Institute of Science, Israel*

Ada Yonath, who is focusing on protein biosynthesis, graduated the Hebrew University, earned Ph.D. and from Weizmann Institute and completed postdoctoral studies at Mellon-Institute and MIT, USA. In the seventies she established the first structural-biology laboratory in Israel. She is the Kimmel Professor and Director of Kimmelman Center for Biomolecular Structure. During 1986-2004 she also headed Max-Planck-Research-Unit for Ribosome Structure in Hamburg. She is a member of US-National-Academy-of-Sciences; Israel Academy of Sciences and Humanities; German Science Academy (Leopoldina); EMBO; International Academy of Astronautics, UK Royal Society for Chemistry, the Pontificia Accademia delle Scienze (Vatican) and more. She holds honorary doctorates from Oslo, NYU, Mount Sinai, Oxford, Cambridge, Hamburg, Berlin-Technical, Patras, De La Salle University and most Israeli Universities. Her awards include the Israel Prize; Paul-Karrer Medal; Louisa-Gross-Horwitz Prize; Ehrlich-Ludwig Medal; Linus Pauling Gold Medal; Wolf Prize; UNESCO/L'Oreal Award; Albert-Einstein World Award for Excellence; Erice Peace Prize; Nobel Prize for Chemistry.



**Professor Dr Achilleas Gravanis**  
*Medical School University of Crete*

Professor of Pharmacology Medical School University of Crete, Researcher Institute of Molecular Biology & Biotechnology Foundation of Research & Technology-Hellas (IMBB-FORTH), Collaborating Scientist Dept. of Neuroscience, Harvard Medical School. His lab is interested in developing synthetic agonists of neurotrophin receptors, with neuroprotective and neurogenic properties and potential applications in therapeutics of neurodegenerative diseases. It also focuses in the development of 3D micro-scaffolds hosting neural stem cells to develop Neuroimplants (brain-on-Chip) for spinal cord injury and Neurobiosensors for screening for new neurogenic compounds.

He obtained his Diploma in Pharmacy from the University of Athens (1980) and his Master's in Endocrine Pharmacology (1981) and PhD in Pharmacology (1983) from the University Pierre Marie Curie, Paris 6. Then, he moved to Mount Sinai School of Medicine in New York as a post-doctoral fellow (1983-1986). He was elected Assistant Professor (1987), Associate Professor (1991) and Professor of Pharmacology (2001) at the School of Medicine, University of Crete, and Director of the Laboratory of Pharmacology, University Hospital of Crete (2002-2008).

He served as vice-president of the Hellenic Pharmacological Society (1996-8), and the Hellenic Society of Biochemistry and Molecular Biology (2003-4), member of the steering committee of the European Pharmacology Network. He participated as a member and Chairman of many research committees of the European Union: the Project Review Board of BIOMED 2 (1995-7), the 5-year Assessment Committee of BIOMED 1 (1997) the 1996 Monitoring Committee of BIOMED 2, the BIOMED 2 Assessment Committee (1998), Co-Chairman of the BIOMED 2 Assessment Committee (2001), Greek National Delegate in the Program Committee of Life Sciences-Genomics Research Framework Program 6 (2000-3), Member of the Genomics Assessment Committee of FP5 programme (2004), Member of the Steering Committee, Population Genomics-Pharmacogenomics Program, Wellcome Trust (2005), Member of the Biotechnology and Biological Sciences Research Council (BBSRC) of UK (2005), Elected Member of the Fellowships Committee της Federation European Biochemical Societies (FEBS) (2007-11), Reviewer Panel LS5, European Research Council (ERC) (2007), Member of the Council, Hellenic Quality Assurance Agency for Higher Education (HQAA). (2008-10), Member of Bioethics Committee of the General Secretariat of Research and Technology (2008), Chairman of Biosciences Committee, Hellenic National Research Council (ESET) 2011-2014, Collaborating Scientist, Dept of Neuroscience, Harvard Medical School 2014, 120 Medline papers, h index: 39



### **Professor Dr Konstantinos Deltas**

*University of Cyprus, 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. Between the years 1988-1990 he worked as Instructor in Medicine, Jefferson Institute of Molecular Medicine, Thomas Jefferson University in Philadelphia, PA, USA. He worked 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 served twice as elected Chairman and had a key role in establishing the Department, implementing undergraduate and graduate programs of study and hiring new faculty. 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](http://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" upon nomination by the Cyprus Research Promotion Foundation, based on long standing research experience in Cyprus and demonstration of outstanding achievements with local and international impact honoring Cyprus, significant publication record in high impact journals, development of innovative molecular diagnostic methods, success on attracting competitive research funding, the creation of significant research infrastructures and the training/guidance of young researcher.



### **Professor Dr Kleopas A. Kleopa**

*Neurology Clinic E and Neuroscience Lab at CING, Cyprus*

Dr. Kleopas A. Kleopa is currently Head of Neurology Clinic E and Neuroscience Lab at CING, and Professor at the Cyprus School of Molecular Medicine, coordinating the graduate MSc/PhD program in Neuroscience. He has completed his medical studies at the University of Wuerzburg, Germany in 1987-1993, and obtained his doctoral degree from the same University in 1994 with magna cum laude. He completed his residency in Neurology at Drexel University in Philadelphia, USA in 1999. He then completed a fellowship in neuromuscular disorders and electromyography at the University of Pennsylvania in 2001, and was appointed as clinical instructor in Neurology at the Faculty of the Hospital of the University of Pennsylvania.

He has engaged in translational and basic neuroscience research since 2000 focusing on the molecular mechanisms of peripheral and central nervous system involvement in inherited neuropathies, and continued his research after his recruitment at the Cyprus Institute of Neurology and Genetics in 2002, where he was appointed Senior Consultant Neurologist. His team has generated and studied cellular and animal models of inherited and acquired neuropathies, multiple sclerosis, and leukodystrophies. Additional research projects in the lab include the molecular mechanisms of autoimmune encephalopathies, mechanisms of multiple sclerosis in post-mortem human brain tissue focusing on gap junction pathology, and chemotherapy-induced neuropathy. More recently, his research team has developed new therapeutic approaches for gene replacement in inherited neuropathies and leukodystrophies using lentiviral and adenoviral vectors to deliver genes to peripheral nerves and to the central nervous system.

Prof. Kleopa has authored more than 70 papers in international peer reviewed scientific journals, in most of which as leading author (<http://www.ncbi.nlm.nih.gov/pubmed/?term=kleopa>). He has been the principal investigator in more than 16 research projects with total external funding from national and international sources exceeding 2 million Euros in the last 15 years. He has established collaborations with leading scientists in top rank academic institutions in Europe and the USA. He is member of numerous American and European professional societies and associations. He has recently won the European Academy of Neurology 2015 Research Award for peripheral neuropathies.



**Professor Dr Athanasios J. Manolis**

*Asklepeion Hospital, Athens Greece; Adj. Professor of Medicine, Emory University, Atlanta; Adj. Ass. Professor of Hypertension, Boston University, USA*

Professor Athanasios J. Manolis graduated from the Athens University, Medical School in 1979.

At present he is the Director of the Cardiology Department of the Asklepeion Hospital, Athens, Greece. Moreover, he has a position as Adj. Professor of Medicine, Emory University, Atlanta, USA and Adj. Ass. Professor of Hypertension, Boston University, Boston, USA. Athanasios J. Manolis is Past-President and General Secretary of the Mediterranean Association of Cardiology and Cardiac Surgery, ex-member of the Council of the European Society of Hypertension, past Chairperson of the Working Group "Hypertension and Heart" of the European Society of Cardiology, and President of the Working Group "Hypertension Arrhythmias and Thrombosis" of the ESH. He is Past President of the Hellenic Society of Hypertension, and was President of the Joint Meetings of ESH/ISH 2014 in Athens. Dr Athanasios J. Manolis is member of the editorial Board and reviewer of several journals in the field of Hypertension and Cardiology. He has been involved as member of the steering committee or principal investigator in more than 100 multicenter trials in the field of hypertension, coronary heart disease, heart failure atrial fibrillation and genetics. He published more than 200 papers in peer-reviewed international journals about several aspects of hypertension, heart failure, coronary heart disease, preventive cardiology and genetics, and more than 50 chapters in books.

Professor Athanasios J. Manolis is member of the American College of Cardiology, the American Heart Association, the Hypertension Council of the American Heart Association, the European Society of Hypertension, the International Society of Hypertension, the Mediterranean Association of Cardiology and Cardiac Surgery. His special areas of interest and expertise are in all aspects of hypertension, coronary heart disease, neurohormonal activation and treatment of heart failure, and atrial fibrillation.



**Associate Professor Dr Marios Pantzaris**

*Cyprus Institute of Neurology and Genetics-Cyprus School of Molecular Medicine, Cyprus*

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.





**Associate Professor Dr Konstantinos Poulas**  
*University of Patras, Dept. Pharmacology, Greece*

Konstantinos Poulas was born in 1970 in Athens. He studied biology at the Athens University where he has also completed his Ph.D. Since 2003, he has been a faculty member of the Department of Pharmacy at the University of Patras. He serves as Scientific Advisor of two biotechnological companies in Greece and he is the co-founder of one. He is currently offering services within the University of Patras for the diagnosis of autoimmune diseases' and biochemical/chemical analysis.

He has been working for 20 years on the elucidation of the structure and function of Acetylcholine Receptor(s) and on its interaction with autoantibodies or monoclonal antibodies. Moreover, his scientific work included the studying of the molecular structure of monoclonal antibodies and fragments of the acetylcholine receptor. In addition, he developed two new methodologies for the crystallization of proteins, for one of which he owns an international patent. For the last three years he is working on a new scientific field, the ELECTROCEUTICALS. He is studying the effect of Wireless Microcurrent Stimulation (WMCS) technology and Pulsed Electromagnetic Fields (PEMF) technology on wound healing, burns and pain. Since last year he is studying and analyzing the e-liquids (before and after vaping) and also the effects of vaping at molecular, cellular and histological level.

He has about 60 publications in peer reviewed journals and he is currently participating in HORIZON2020 but also on national projects.



**Professor Dr Paolo Riccio**  
*University of Patras, Dept. Pharmacology, Greece*

Professor Paolo Riccio was born in 1942 in Bari, Italy. In 1969, he completed his studies in Chemistry at the University of Bari, and in 1970 he started his research activity working on mitochondria with Prof. Martin Klingenberg at the Faculty of Medicine, University of Munich, Germany. The most outstanding achievements were the original purification of the ADP/ATP carrier, the first mitochondrial carrier to be isolated, and the chromatographic purification of the mitochondrial respiratory chain complexes. In 1975 Paolo Riccio moved to the Institute of Biological Chemistry, Faculty of Science, in Bari, and in 1983 started with the study of the myelin membrane. The most important result in this field was the isolation of myelin basic protein (MBP) in the native, lipid-bound form. This was the first example of a membrane protein purified through a procedure able to discriminate non-raft from raft regions. The study of purified MBP promoted the setting up of new studies regarding diseases such as NeuroAIDS and Multiple Sclerosis, and their relationship with myelin structure, including neuroimmunological aspects and proteolytic activities. In 1994 Paolo Riccio joined the Faculty of Agriculture of the University of Basilicata, in Potenza, Italy, and began his studies in the field of Food Sciences. The studies regarded wine and dairy production, fishery, and zymoproteomic analysis of fruits, vegetables and unifloral honey. Most innovative was the production of cheese from crustacean enzymes. The studies in food science allowed him to explore the aspects regarding the impact of nutrition on Multiple Sclerosis and hence on human health.

Paolo Riccio is an ex-Alumnus of EMBL, the European Molecular Biology Laboratory in Heidelberg, where he has been visiting professor three times between 1979-1983. He has been a member of the Italian Association for Multiple Sclerosis (AISM) and of the Italian Foundation for Multiple Sclerosis (FISM) (1993-2012), as well as an elected member of the National Council of the Italian Association of Neuroimmunology (AINI) (1998-2001). In 1996 he has been awarded the Quagliariello Foundation Prize for his scientific activity and moral qualities.

From 1978 to 2010, Paolo Riccio has been Lecturer of Neurochemistry at the Postgraduate School of Neurology, Faculty of Medicine, University of Bari. He also served as member of the PhD School on "Alimenti e Salute" ("Food & Health") at the 2nd University of Naples (SUN), Italy. He has participated in two BIO-MED Projects (1996-1999) on "High resolution structures of myelin proteins" and on "T cell autoimmunity in MS", and has been the chair of the European Network 'MARIE' (Myelin Autoimmunity Research In Europe) of the European Science Foundation (ESF) on Myelin Structure and Its Role in Autoimmunity, 2004-2006.

After his retirement in 2010 and until 2014, Paolo Riccio has been Adjunct Professor at the Department of Sciences in Potenza. One of his more recent findings has been the discovery that metalloproteinase isoforms exist in the form of charge variants (2014). Now he is continuing his studies on the molecular and cellular mechanisms by which dietary factors can influence the course of Multiple Sclerosis and other chronic inflammatory diseases (FISM grant 2014/S/2).



**Professor Dr Adina Michael-Titus**  
*Barts and the London School of Medicine and Dentistry,  
Queen Mary College, University of London, UK*

Adina Michael-Titus is Professor of Neuroscience at Barts and the London School of Medicine and Dentistry, at Queen Mary, University of London. She is Lead of the Neurotrauma and Neurodegeneration Group in the Centre for Neuroscience and Trauma, at the Blizard Institute. Professor Michael-Titus is also Director of Graduate Studies and Program Director of an MSc in Neuroscience and Translational Medicine whose aim is to train the next generation of scientists and physicians involved in clinical translation in neuroscience. Her research in neuroscience has covered a variety of topics and is at present focused on neurotrauma. The work in her group in recent years has explored the development of neuroprotective strategies for spinal cord injury and brain injury, areas in which she is leading an active translational program. 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.



# Bio-medical Scientific Cyprus

## Abstracts

## Combating species-specific antibiotics resistance

Ada Yonath

*Department of Structural Biology, Weizmann Institute, Rehovot 76100, Israel*

The current global escalation in resistance to antibiotics is a serious threat, as it seems that the world is headed for a post-antibiotic era, in which common infections and minor injuries that have been treatable for decades could become fatal again. Ribosomes, the universal cellular machines that translate the genetic code into proteins, are paralyzed by many clinically useful antibiotics. The structures of ribosomes from non-pathogenic bacteria, used as models for genuine pathogens, illuminated the antibiotics binding modes, inhibitory actions, synergism pathways, the differentiation between patients vs. pathogens and mechanisms leading to bacterial resistance. However, as species specific diversity was detected in susceptibility to infectious diseases and in developing specific resistance mechanisms, our structural studies have been extended to ribosomes from genuine pathogens. The high resolution structures of ribosomal particles from multi-resistant pathogens and from eukaryotic parasites with several antibiotics, highlighted subtle, albeit highly significant structural elements that can account partially or fully for species specificity and may be exploited for improving known antibiotics and for the design of novel compounds.

## Neuroprotective microneurotrophins: selective agonists of Nerve Growth Factor (NGF) receptors.

Achilleas Gravanis

*Dept. of Pharmacology, School of Medicine, University of Crete & IMBB-FORTH, Heraklion Greece.*

Neurotrophins, like NGF, are important factors for the development and maintenance of nervous tissue. Their decline has been associated to neurodegenerative disorders. Despite the demonstrated beneficial effects, the therapeutic usefulness of neurotrophins is compromised by their polypeptide nature and their restricted penetrance to the blood-brain barrier (BBB). We have recently developed synthetic C17-derivatives of neuroprotective neurosteroid Dehydroepiandrosterone (DHEA) (Charalampopoulos et al, PNAS 101:8209-8214, 2004), shown to interact with TrkA and p75NTR NGF receptors (Lazaridis et al, PLoS Biol 9(4):e1001051, 2011). Derivative BNN27 does not bind to TrkB and TrkC receptors, has nor affinity for steroid receptors and is deprived of any estrogenic or androgenic effects, described for endogenous DHEA (Calogeropoulou et al, J Med Chem 52:6569-6587, 2009). Derivative BNN27 effectively displaced binding of [3H]DHEA to membranes isolated from HEK293 cells transfected with the cDNAs of TrkA and p75NTR receptors (IC50: 1.86 and 3.9 nM respectively). BNN27 dose-dependently induces TrkA tyrosine phosphorylation in the functionally relevant tyrosine residues, affecting downstream prosurvival kinases Akt and MAPKs in primary sympathetic neurons. BNN27 induces internalization and fast return of TrkA into neuronal cell membrane in a different manner than NGF, securing higher levels of surface TrkA and potentiating the efficacy of NGF. BNN27 promotes also the interaction of p75NTR receptor with its effector proteins RhoGDI, RIP2 and TRAF6 (Charalampopoulos et al, Cell Reports 2:1563-1570, 2013). BNN27 effectively rescues from apoptosis NGF receptor positive sensory neurons of Dorsal Root Ganglia (DRG) in *ngf*<sup>-/-</sup> mouse embryos. Our findings suggest that synthetic, lipophilic compounds, like BNN27, may represent lead molecules to develop BBB-permeable, neurotrophin agonists with potential therapeutic applications in neurodegenerative diseases and brain trauma (Gravanis et al, Science Signaling 16:5(246):pt8, 2012). The *in vivo* neuroprotective efficacy of microneurotrophins is now tested in experimental animals models of human neurodegenerative diseases.

## Familial microscopic hematuria as a paradigm for a “multifactorial” Mendelian disease: A unique Cyprus experience

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Familial microscopic hematuria (blood in urine) is a genetically heterogeneous group of autosomal dominant conditions that present with microscopic hematuria (MH) since childhood and may or may not be progressive on follow-up. Several genes are involved that include mainly collagen IV genes of the glomerular basement membranes (GBM), CFHR5, MYH9, and FN1. In Cyprus we have a unique experience with a large cohort of patients who inherit heterozygous mutations in the COL4A3/COL4A4 genes and develop a condition which is known as Thin Basement Membrane Nephropathy (TBMN) (basement membrane of the glomerulus is thinner than normal). In particular, among several other mutations, there is a wide founder effect for mutation COL4A3-p.G1334E, where there is a substitution of glutamate for glycine at aminoacid residue 1334 of the collagenous domain of the alpha 3 chain, of the trimer  $\alpha 3(\alpha 4)5$  in the GBM. Remarkably, this and the other mutations, result in a broad phenotypic spectrum. Specifically, on one end of the spectrum are patients who present with MH in childhood and will reach advanced age with either isolated MH or MH with added low grade proteinuria, without clinical significance. Importantly however, a significant percentage of the patients will progress to high grade proteinuria and chronic renal failure later in life, in the presence of focal and segmental glomerulosclerosis. According to our cohort with more than 250 patients, about 30% of all patients will reach end-stage renal failure by the age of 70 years, thereby coming into contrast with older literature, which considered this condition as benign, with excellent prognosis on long follow-up. Our group at the Molecular Medicine Research Center, in collaboration with many clinicians Cyprus wide, were the first to document these findings and alert the international community of this potential outcome of TBMN patients. Molecular genetic studies in our lab are focused on these patients and offer timely accurate diagnosis to patients with microscopic hematuria. In conclusion, the finding of familial MH with or without proteinuria of glomerular origin should be investigated further and the option for a genetic analysis be offered before a renal biopsy is considered. Also, the full spectrum of this monogenic condition behaves as a multifactorial trait, as additional genetic modifiers are implicated to play a crucial role in disease development.

## Towards a gene therapy approach to treat inherited demyelinating neuropathies

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Inherited demyelinating neuropathies are genetically heterogeneous but all result from mutations affecting myelin-related genes expressed in Schwann cells. X-linked Charcot-Marie-Tooth disease (CMT1X) is one of the commonest types and is associated with mostly loss-of-function mutations in the GJB1 gene encoding the gap junction protein Cx32. In order to develop a gene replacement therapy for this disease, we cloned a novel lentiviral vector in which the GJB1 gene is placed under the control of the Schwann cell-specific rat Mpz/P0 promoter. This LV.Mpz-GJB1 vector was delivered by a single intraneural injection into adult mouse sciatic nerves distal to the sciatic notch or, to achieve a more widespread expression, by a single lumbar intrathecal injection. EGFP reporter gene expression was detected throughout the length of the injected nerve in up to 50% of Schwann cells starting two weeks after intraneural injection and remaining stable for up to 16 weeks. By comparison, lumbar intrathecal vector delivery led to widespread expression in various components of the peripheral nervous system, including the spinal roots, dorsal root ganglia and along the sciatic and femoral nerves, remaining stable for up to 16 weeks, with similar expression rates ranging from 35%-55% of Schwann cells. Using the Cx32 knockout mouse, an authentic mouse model of CMT1X, we demonstrated that intraneural gene delivery restores Cx32 expression and improves the pathology of the injected nerve. Furthermore, intrathecal gene delivery in the same model resulted in widespread pathology rescue as well as in significant improvement of behavioral motor and electrophysiological parameters of peripheral nerve function. Our studies provide a proof of principle that gene therapy may be feasible for CMT1X and other inherited neuropathies that share similar cellular mechanisms.

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## Hypertension and Atrial Fibrillation

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Hypertension is the most common cardiovascular disorder and atrial fibrillation is the most common clinically significant arrhythmia. Both these conditions frequently coexist and their prevalence increases rapidly with aging. There are different risk factors and clinical conditions predisposing to the development of atrial fibrillation, but due to its high prevalence, hypertension is still the main risk factor for the development of atrial fibrillation. Several pathophysiologic mechanisms (such as structural changes, neurohormonal activation, fibrosis, atherosclerosis, etc.) have been advocated to explain the onset of atrial fibrillation. The presence of atrial fibrillation per se increases the risk of stroke but its coexistence with high blood pressure leads to an abrupt increase of cardiovascular complications. Different risk models are available for the risk stratification and the prevention of thromboembolism in patients with atrial fibrillation. In all of them hypertension is present and is an important risk factor. Antihypertensive treatment may contribute to reduce this risk, and it seems some classes are superior to others in the prevention of new-onset atrial fibrillation and prevention of stroke. Old fashioned warfarin became standard of care outperforming antiplatelets in every trial but novel classes of anticoagulants that overcome many of warfarin drawbacks have been introduced and are already guideline recommended regimens. The new oral anticoagulants are direct thrombin (dabigatran) and factor Xa inhibitors (rivaroxaban, apixaban, edoxaban) and many trials examining their use in AF have published or are in final phase (RE-LY, ROCKET-AF, AVERROES, ARISTOTLE, and ENGAGE-AF). In all the above trials new antithrombotics were more effective in reducing stroke with less hemorrhagic events. All the new guidelines suggest the use of new anticoagulants as preferred treatment for the prevention of stroke in patients with atrial fibrillation and CHA<sub>2</sub>DS<sub>2</sub>-VASc >1.

## Biochemical Pathways Affected by PLP10

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The polyunsaturated fatty acid (PUFA) composition of membrane phospholipids plays an important role in immune-related and non-immune-related inflammation. PUFA and antioxidant deficiencies, along with decreased cellular antioxidant defense mechanisms, have been reported in MS patients. The cause of PUFA deficiencies is not entirely clear and may involve metabolic and nutritional alterations. Increased or uncontrolled inflammation contributes to several different acute and chronic diseases, and it is characterized by the production of inflammatory cytokines, arachidonic acid (AA)-derived eicosanoids (prostaglandins (PGs), thromboxanes (TXs), leukotrienes (LTs) and other oxidised derivatives), and other inflammatory agents such as reactive oxygen species (ROS), nitric oxide (NO) and adhesion molecules. During inflammation, glutamate homeostasis is altered by the release of increased quantities of glutamate by activated immune cells, which can result in the over activation of glutamate receptors and, in turn, excitotoxic oligodendroglial death. Among others, membrane-related pathology, immune-mediated inflammation, oxidative stress and excitotoxicity provide potentially useful combined targets for intervention in MS. In vitro and in vivo studies have demonstrated that dietary eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), linoleic acid (LA) and  $\gamma$ -linolenic acid (GLA) can be implicated and modulate almost all known complex networks of events and pathways in MS pathophysiology. The brain membrane fatty acid composition can be modified with dietary supplementation, but the process has been shown to be age dependent (taking much longer in adults vs developing brains) and possibly dependent on the quantity of the dietary/supplemented PUFAs.

The anti-inflammatory properties of  $\Omega$ -3 PUFAs include the production of PGs and TXs of the 3-series and of LTs of the 5-series. Resolvins and protectins are biosynthesised from  $\Omega$ -3 fatty acids via cyclooxygenase-2/lipoxygenase (COX-2/LOX) pathways, and they promote the control of inflammation in neural tissues. T-cell proliferation in acute and chronic inflammation can also be reduced by supplementation with either  $\Omega$ -6 or  $\Omega$ -3 PUFAs. Furthermore, vitamin E is an important antioxidant that can interrupt the propagation of free radical chain reactions. Specifically, vitamin E ( $\alpha$ -tocopherol, an isoform of vitamin E) efficiently detoxifies hydroxyl, perhydroxyl and superoxide free radicals, whereas  $\gamma$ -tocopherol (another isoform of vitamin E) appears to be more efficiently implicated in trapping NO radicals. In addition,

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$\alpha$ -tocopherol exerts non-antioxidant properties, including the modulation of cell signalling and immune functions, regulation of transcription and induction of apoptosis. Moreover,  $\Omega$ -3 fatty acid electrophilic derivatives formed by COX-2 in activated macrophages can stimulate the nuclear respiratory factor (Nrf), which induces the transcription of neuroprotective and antioxidant-related genes and can activate the peroxisome proliferator-activated receptor  $\gamma$  (PPAR $\gamma$ ) for an anti-inflammatory response. In animal studies, EPA and DHA have proved to be endogenous ligands of the retinoid X receptor (RXR), with positive effects on neurogenesis. Additionally, in 2008, Salvati et al reported evidence of accelerated myelination in DHA-treated and EPA-treated animals. Moreover, DHA and EPA have been reported to significantly decrease the levels of metalloproteinases (MMP)-2, MMP-3, MMP-9 and MMP-13, which have a significant role in the migration of lymphocytes into the central nervous system by inducing the disruption of the blood brain barrier, an important step in the formation of MS lesions. Based on the aforementioned observations, specific PUFAs and antioxidant vitamins fulfil the criterion of biological plausibility and have the potential to diminish the severity and activity of MS symptoms, potentially even promoting recovery (remyelination).

## Electroceuticals: paving the path to non-invasive therapies

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Electroceuticals are a “pharmaceutical” form of Bioelectronics, in other words the science of developing medical devices that use electric or electromagnetic impulses to modulate the body’s circuits, neural or other, as an alternative to drug-based interventions and therapies. There are many examples of electroceuticals in use today, including mainly implantable devices (pacemakers, defibrillators, cochlear implants etc.). In our lab we are working with two non-implantable devices (external use) based on innovative technologies: Wireless Microcurrent Stimulation (WMCS) and Pulsed Electromagnetic Fields (PEMF), which are proved to be very effective for the treatment of hard-to-heal wounds and burns, while minimizing the pain following these pathologies.

We will present clinical results of patients with pressure ulcers, venous stasis ulcers, diabetic foot wounds and burns that were treated with the W200 device (WMCS - Wetling®, Denmark) and the consumable, wearable PEMF device (Actipatch®, USA) as well. The W200 device is adjusted to a distance of about 10–15 cm straight onto the wound, with an intensity of 1,5 $\mu$ A. Each therapy lasted 1 hour daily. The patients that used in parallel or separately the PEMF technology applied the device so that the therapeutic area was within the loop, for at least 8 hours daily or usually for almost 24 hours. All the patients demonstrated substantial improvement up to complete healing, regardless the underlying cause or the extension of the wound (ulcer, burn etc.). Although the duration of the therapy varies, in the majority of the cases the therapeutic outcome was optimal. Histochemical and microbiological studies will be presented, proving the reformation of the wounded tissue. Additional experiments are performed and we strongly believe that the application of such technologies could replace conventional pharmaceuticals in the near future.

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## Nutrition facts in Multiple Sclerosis From bench to bedside and back again: translational research in an auto-inflammatory disease

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Multiple sclerosis (MS) is a chronic and autoimmune disease of the central nervous system, leading to focal breakdown of the myelin sheath and axonal damage. There are two main forms of MS: relapsing-remitting (RRMS) and primary-progressive (PPMS). Both forms are inflammatory in nature, but disease-modifying therapies are currently available only for RRMS, not for PPMS.

Some years ago,<sup>1,2</sup> we have introduced the idea that the lifestyle and dietary habits can influence the course of the disease. In fact, MS is a complex and multifactorial disease and it is acknowledged that environmental factors may contribute in some way to the disease and exacerbate or ameliorate its symptoms. In particular, the target of a nutritional intervention may be the control of the inflammatory status. This can happen in two ways: 1) modulating the inflammatory and metabolic activity of the human cell, and/or 2) by controlling the composition of gut microbiota and its inflammatory activity in the intestine.<sup>3</sup>

What increases inflammation are energy-dense Western-style diets, characterized by high salt, animal fat, red meat, sugar-sweetened drinks, fried food, alcohol, low fiber, and lack of physical exercise. The persistence of this type of diet, on one hand up-regulates the metabolism of human cells toward biosynthetic pathways, including the synthesis of pro-inflammatory molecules and, on the other hand, leads to a dysbiotic gut microbiota, alteration of intestinal immunity and low-grade systemic inflammation.

Conversely, exercise and calorie restricted diets based on the assumption of vegetables, fruit, legumes, and fish act on nuclear receptors and enzymes that up-regulate oxidative metabolism, while down-regulating the synthesis of pro-inflammatory molecules, and restoring or maintaining a healthy symbiotic gut microbiota. Anti-inflammatory dietary supplements, prebiotics and probiotics may be added to the diet to achieve a more robust effect of the nutritional intervention.

In a seven-month pilot study we investigated the effects of a calorie-restricted, semi-vegetarian diet and administration of vitamin D and other dietary supplements in 33 patients

with RRMS, under therapy with IFN-beta and 10 patients with PPMS, with no therapy. At 0/3/6 months, patients had neurological examination, filled questionnaires and underwent anthropometric measurements and biochemical analyses. Serum fatty acids and vitamin D levels were measured as markers of dietary compliance and nutritional efficacy of treatment, whereas serum gelatinase levels were analyzed as markers of inflammatory status.

All patients had insufficient levels of vitamin D at baseline, but their values did not ameliorate following the administration of vitamin D equivalent to 914 I.U./day. Conversely, omega-3 polyunsaturated fatty acids increased already after three months, even under dietary restriction only.

After 6 months nutritional treatment, no significant changes in neurological signs were observed in any group, but physical and inflammatory conditions of the patients were improved. Only 4 patients withdrew from the study, indicating that the nutritional treatment was well accepted. Further nutritional clinical trials are needed, but in the meantime it may be possible to provide nutritional guidance and physical activity opportunities to MS patients helping them to stay healthy. This may be especially relevant for PPMS, for which all efforts are still oriented only towards druggability and no attention is reserved to dietary habits and life style.

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**Adina T. MICHAEL-TITUS**

Traumatic injury in the central nervous system triggers a host of tissue destructive processes and is for many individuals a life-changing event. Spinal cord injury and brain injury can have dramatic and irreversible consequences, and no neuroprotective or neuroregenerative treatment is currently available. It is appropriate to review the pathophysiology concepts and the proposed sequence of events which leads to tissue demise following neurotrauma, and consider the principles governing the present clinical translation. There is emerging evidence across a range of experimental models of traumatic injury of the brain and spinal cord, that omega-3 fatty acids have therapeutic and prophylactic potential. The endpoints used to characterize the efficacy of these compounds range from behavioural functional outcomes to histological evidence of tissue protection. The data suggest an intrinsic protection of neuronal and non-neuronal cells and a reduction of the damaging neuroinflammation that is triggered by injury. Results supporting this concept continue to be generated through use of transgenic mice with altered production of long chain omega-3 fatty acids, or through the use of various treatment regimes, from acute administration of fatty acids to dietary supplementation with fatty acids or with complex preparations enriched in fatty acids. 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 in peripheral nervous system injury and will highlight some of the questions that need to be answered concerning the molecular and cellular mechanisms that underlie the observed beneficial effects. Concerning neurodegeneration, one of the most important trends in the neurotherapeutics of the future is the temporal shift in the critical period of intervention aimed at aborting neurodegenerative processes. Neurodegenerative diseases such as Alzheimer's disease or Parkinson's disease, which have been historically considered distinct entities, although heterogeneous, are now viewed from a novel angle, influenced by network modelling and with a new understanding of common features such as the non-random propagation of abnormal protein aggregates. Interestingly, such pathological aggregation can be initiated by traumatic injury – thus, the challenge of neuroprotection bridges the acute and the chronic dimensions and requires entirely new approaches.

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