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2nd International Multithematic Bio-Medical Congress



Bio-Medical Scientific CYPRUS

Saturday, 15 November 2014

CULTURAL CENTER, EUROPEAN UNIVERSITY CYPRUS, NICOSIA

SCHOOL OF MEDICINE,
EUROPEAN UNIVERSITY
CYPRUS



Under the auspices of Ministry of Health and the
Cyprus Medical Association (CYMA).

Credits of Continues Education will be awarded

General Congress Supervision:
Professor Dr. Ioannis Patrikios





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NOTES



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Maria Christodoulou, Events Officer
European University Cyprus

M.Christodoulou@euc.ac.cy Tel.: 22 713047

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WELCOME ADDRESS BY 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 2nd Multidisciplinary Scientific Bio-Medical Congress, entitled “Biomedical Scientific Cyprus”.

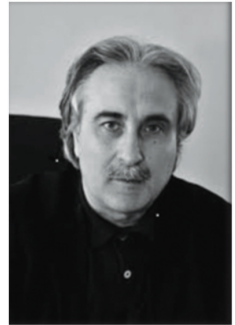
The European University Cyprus is becoming an Institution with high quality targets aiming to new frontiers of science, innovation, research and excellence. We are investing with particular emphasis on Bio-Sciences like the opening of the Medical School at our University in September 2013. High caliber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

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 PROF DR IOANNIS PATRIKIOS

Dear Congress participants and guests

It is my great pleasure to welcome you to the 2nd 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 15th of November 2014.

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 so to make this an unforgettable date of our calendar through the years.

It was my strong desire to establish this congress: “Biomedical Scientific Cyprus, (BSC)” so to become a yearly event with global recognition. I am more than sure that this is an achievable target and here we are for a second consecutive year.

Finally, I would like to thank the sole 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.

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

Professor Dr. Ioannis Patrikios
Faculty of Medicine, School of Medicine
European University Cyprus
Founder and General Congress Supervisor
2nd International Multithematic Medical Congress



CHAIRMEN & SPEAKERS

Chairmen

Dr Agathangelou Petros
Dr Christodoulou Christina
Dr Christou Christos
Dr Economides Panayiotis
Dr Hadjipanayis Adamos
Dr Ioannides Adonis
Dr Kadis Savvas
Dr Kadi Stelia
Dr Karagiannis Petros
Dr Miltiadous George
Dr Pantzaris Marios
Dr Patrikios Ioannis
Dr Philaktou Leonidas
Dr Savva Savvas
Dr Stephanou Anastasis

Keynote Speaker:

Professor Dr Robert Huber

Plenary Speakers:

Professor Dr George P. Chrousos
Professor Dr Richard Atkinson
Dr Chiara Guglielmi
Professor Dr Panos Vardas
Professor Dr Philippe Froguel

Session for:

Cyprus National Health

Insurance Plan: Zero Hour

Speakers:

Dr Christodoulos Kaisis
Theodoulos Charalambides
Emily Mavrokordatou

Coordinator:

Nikos Nouris



PROGRAMME



PROGRAMME

Program Date 15/11/2014

2nd International Bio-Medical Scientific Cyprus Congress

Under the auspices of the Cyprus Ministry of Health and the Cyprus Medical Association
(in Collaboration with the Cyprus Medical Association)

8:00 - 9:00

Registration

9:00 - 9:10

EUC/Medical School Virtual Tour

Opening Introduction/welcome-address By:

Prof. Dr Ioannis Patrikios

School of Medicine/ European University Cyprus

9:10 - 9:40

Opening Ceremony

Salutation by:

Ms Roula Mavronikola, member of the Parliament, on behalf of the President of the House of Representatives, **Mr Yiannakis Omirou**

Dr Stavros Stavrou on behalf of the President of the Cyprus Medical Association, **Dr Andreas Demetriou**

Prof. Kostas Gouliamos, Rector of European University Cyprus

Conferment: Honorary Professorship for Professor R. Huber;

Prof. Andreas Efstathiou, Vice Rector of European University Cyprus

9:40 - 10:35

Prof. Dr Robert Huber (Nobel Laureate)

Max-Planck-Institut fuer Biochemie, Emeritusgruppe Strukturforschung D-82152 Martinsried - Germany; Technische Universität München, TUM Emeritus of Excellence D-85747 Garching, Germany; Universität Duisburg-Essen, Zentrum für Medizinische Biotechnologie D-45117 Essen, Germany; Cardiff University, School of Biosciences Cardiff, UK

Chairs: Dr Adonis Ioannides, Dr Petros Karagiannis, Dr Ioannis Patrikios

Protease control in Health and Disease and my Experience with its Translation into Practice and Business

10:35 - 10:55

COFFEE BREAK

I. Sessions on Research of Excellence *Endocrinology - Obesity - Diabetes*

10:55 - 11:45

Prof. Dr George P. Chrousos
University of Athens Medical School

Chairs: Dr Stelia Kadi, Dr George Miltiadous

Systems Biology and the Stress Response: From Pythagoras and the Epicureans to Modern Medicine.

11:45 - 12:35

Prof. Dr Richard Atkinson

Emeritus Professor of Medicine and Nutritional Sciences, University of Wisconsin, Madison; Director of the Obetech Obesity Research Center, Richmond, VA, USA

Chairs: Dr Leonidas Philaktou, Dr Christina Christodoulou

Re-evaluation of the Etiologies of Obesity

12:35 - 1:30

LUNCH BUFFET

1:30 - 2:20

Prof. Philippe Froguel

Lille Pasteur Institute, France; Imperial College London

Chairs: Dr Savvas Kadis, Dr Anastasis Stephanou

From Diabetes and Obesity Genomics to Metabolic Personalized Medicine

2:20 - 3:10

Dr. Chiara Guglielmi

University Campus Bio-Medico, Rome, Italy

Chairs: Dr Panayiotis Economides, Dr Adamos Hadjipanayis

The new prognosis of type I diabetes

3:10 - 3:25

COFFEE BREAK

2. Obesity and Cardiovascular Diseases

3:25 - 4:15

Prof. Dr Panos Vardas

**President of the European Society of Cardiology; University Hospital of Heraklion
Crete, Greece**

Chairs: Dr Petros Agathangelou, Dr Christos Christou, Dr Marios Pantzaris

Obesity as a potential key factor in cardiovascular diseases

4:15 - 4:30

COFFEE BREAK

3. Cyprus National Health Insurance Plan

The following Session Will be in Greek Language

Το υπόλοιπο μέρος του προγράμματος θα διεξαχθεί στην Ελληνική Γλώσσα

Cyprus National Health Insurance Plan: Zero Hour

Σχέδιο Υγείας: Ώρα Μηδέν

Open Discussion

4:30 - 7:00

Ομιλητές:

Speakers:

Representative of the Cyprus Ministry of Health:

Εκπρόσωπος του Υπουργείου Υγείας Κύπρου

Δρ Χριστόδουλος Καϊσής

Manager of the Cyprus office of Health Insurance:

Διευθυντής Οργανισμού Ασφάλισης Υγείας

Κος Θεόδουλος Χαραλαμπίδης

Representative of the Pharmaceutical Bureau:

Εκπρόσωπος Φαρμακευτικών Υπηρεσιών

Κα Έμιλυ Μαυροκορδάτου

Συμμετέχοντες

Συμμετέχουν για ανοικτή συζήτηση αντιπρόσωποι από: Φαρμακευτικό Σύλλογο, Ιατρικό Σύλλογο, ΠΑΣΥΚΙ, Σύλλογο Ιδιωτικών Γιατρών, Σύλλογο Κλινικών & Ιδιωτικών Νοσοκομείων, ΣΦΕΚ, ΚΕΦΕΑ, Σύλλογο Κλινικών Εργαστηρίων

Συντονιστής: Κος Νίκος Νουρής, Φαρμακοποιός και Βουλευτής Λευκωσίας

7:00 - 7:05

CLOSING

General Congress organizer and general Supervision
Professor Dr Ioannis Patrikios
School of Medicine
European University Cyprus

We would like to thank the Congress Main Sponsor
Byer - Novagem Limited for their valuable contribution

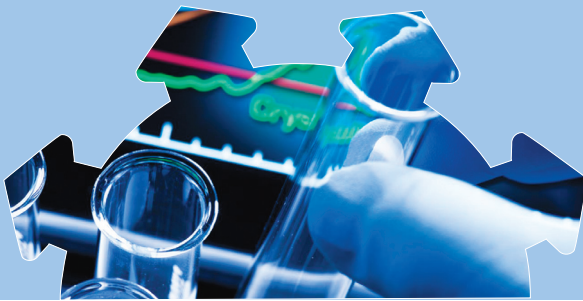


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SPEAKERS CVs



Professor Robert Huber, PhD, Nobel Laureate

Huber was born in 1937 in Munich. He studied chemistry at the Technische Universität München (TUM), where he also completed his Ph.D. and habilitation. Since 1972, he has been a member of the Max-Planck-Gesellschaft and Director at the Max-Planck-Institut für Biochemie until his retirement in 2005. Since 1976, he also serves at the TUM as a Professor. He holds appointments as Guest Professor at the Universität Duisburg-Essen (Germany), the Cardiff University (Great Britain), the Universidad Autonoma de Barcelona (Spain), and the Seoul National University (Korea). He serves as a member of the Board and/or Scientific Advisory Board of a number of pharmaceutical and crop science companies, and he is co-founder of two companies, Proteros and Suppremol, located in Martinsried and offering services for drug discovery and development and for the development of novel therapies for autoimmune diseases, respectively. Huber has made major contributions to the understanding of the structure and function of biological macromolecules. He has studied proteases and their natural and synthetic inhibitors, metalloenzymes (iron, nickel, molybdenum, copper), proteins of the immune system (antibodies and antibody receptors), protein hormones and their receptors, protein kinases, enzymes of amino acid biosynthesis, enzymes of cofactor and vitamin biosynthesis and proteins of energy and electron transfer. In addition, he has contributed to the development of instruments for data collection and to methods in protein crystallography, particularly Patterson methods, graphic methods, and refinement, to the use of electron rich metal clusters, and most recently to the methods and instruments for crystal improvement. He has been honoured by numerous honorary doctorates, professorships, memberships in learned societies and awards, including the Otto-Warburg Medal, the Emil von Behring Medal, the Sir Hans Krebs Medal, the The Linus Pauling Medal, Max Tishler Prize and, in 1988, the Nobel Prize for Chemistry together with H. Michel and J. Deisenhofer.



Professor Richard Atkinson, M.D.

Richard L. Atkinson, M.D. is Emeritus Professor of Medicine and Nutritional Sciences, University of Wisconsin, Madison; Adjunct Professor of Molecular Medicine and Drug Research, University of Karachi, Pakistan; Visiting Professor of Molecular Medicine, Karolinska Institute, Stockholm, Sweden; Director of the Obetech Obesity Research Center, Richmond, VA; and President of Obetech, LLC. He is Editor of the International Journal of Obesity and of Nutrition and Diabetes; Regional Vice-President of The Obesity Society; Member of the Board of Directors of the World Obesity Federation; Past President of the American Obesity Association, the North American Association for the Study of Obesity, and the American Society for Clinical Nutrition. NAASO-The Obesity Society established the annual Richard Atkinson-Judith Stern Public Service Award in 2006 to honor his service to the field of obesity and awarded him the Mickey Stunkard Lifetime Achievement Award for 2014. He has been consultant to the NIH, FDA, USDA, National Academy of Sciences, Department of Defense, Department of Veterans Affairs, Federal Trade Commission, and numerous companies and foundations. His interests are research, obesity policy and young investigator programs nationally and internationally. Recently, his research has focused on virus-induced obesity and he and colleagues demonstrated that human adenovirus 36 (Adv36) produces obesity in animals and is associated with obesity in humans. Dr. Atkinson has 200 publications and over 200 abstracts in the medical literature.



Professor George P. Chrousos, MD, PhD

George P. Chrousos is Professor and Chairman of the First Department of Pediatrics at the University of Athens School of Medicine, Athens, Greece, and former Chief of the Pediatric and Reproductive Endocrinology Branch of the National Institute of Child Health and Human Development (NICHD), National Institutes of Health (NIH), Bethesda, Maryland. He also holds the UNESCO Chair on Adolescent Health Care at the University of Athens and held the 2011 John Kluge Distinguished Chair in Technology and Society at the Library of Congress, Washington DC. Prof. Chrousos is internationally recognized for his research on the glucocorticoid signaling system of the cell, on the diseases of the hypothalamic-pituitary-adrenal axis, and on the physiological and molecular mechanisms of stress. His work has opened new horizons in our understanding of a spectrum of human complex disorders, including depression, the eating disorders, the metabolic syndrome and the inflammatory autoimmune and allergic diseases. His contributions span a range of medical disciplines, including Medicine, Pediatrics, Endocrinology, Psychiatry, Rheumatology, Allergy, Surgery, Oncology and Reproductive Medicine.



Dr. Chrousos has written over 700 original scientific papers and over 500 book chapters and journal reviews and his work has been cited in more than 69,000 other scientific articles, an irrefutable testimony to the importance and influence of his research. He is one of the 250 most cited scientists internationally (ISI highly cited) included not only in the list of Clinical Medicine, but also in that of Biology and Biochemistry, and the highest cited endocrinologist and pediatrician in the world. With an H index of 132, Dr. Chrousos is a top cited Clinician and Clinical Researcher. Dr. Chrousos has received numerous national and international awards and has given many lectures in the USA, Europe, Latin America and Japan. His awards include the 1987 Richard E. Weitzman Memorial Award, US Endocrine Society, the 1992 Superior Service Award, U.S. Public Health Service, the 1997 Clinical Investigator Award, US Endocrine Society, the 1997 Hans Selye Award, Hans Selye Foundation,

Montreal, Canada, the 1999 Pharmacia-Upjohn International First Prize for Excellence in Published Clinical Research, US Endocrine Society, the 1999 Novera Herbert Spector Award, International Society for Neuroimmunomodulation, Lugano, Switzerland, the 2000 Henning Andersen Prize, European Society for Pediatric Endocrinology, Brussels, Belgium, the 2002 Sir Edward Sharpey-Schafer Medal, British Endocrine Societies, the 2004 Lifetime Achievement Award, International Society for Psycho-Neuro-Endocrinology, Glasgow, UK, the 2007 Henning Andersen Prize, European Society for Pediatric Endocrinology, Helsinki, Finland, and the 2008 Geoffrey Harris Prize in Neuroendocrinology, European Society of Endocrinology, Berlin, Germany. Among others, he is a Doctor Honoris Causa of the University of Liege, Liege, Belgium (2003), Universita Politecnica delle Marche, Ancona, Italy (2006) and University of Patras, Patras, Greece (2011). He is an honorary professor of the University of Warwick, Coventry, UK. He was honored with the 2011 Aristeion Bodossaki Award, the highest distinction for accomplishment in the Sciences in Greece. In 2012, he received the Albert Struyvenberg Medal of the European Society of Clinical Investigation (ESCI). He is a distinguished visiting scientist of NICHD, NIH, Bethesda MD, USA. He served as President of ESCI from 2008 to 2011. In 2014 he received the highest honor of the Endocrine Society, the Fred Conrad Koch Award. Dr Chrousos was inducted as a Master of both the American College of Endocrinology and the American College of Physicians and a Fellow of the Royal College of Physicians, London, UK. He is an elected member of the American Society for Clinical Research, the Association of American Physicians, the Institute of Medicine of the National Academy of Sciences, Washington DC, USA, and the Academia Europaea, London, UK. Prof. Chrousos runs one of the best endocrine training programs in the world and fostered the careers of over 60 distinguished, award-winning, world-class physician-scientists. After a 25 year distinguished career in the Intramural Program of the NIH, where he made seminal original contributions and trained a generation of international leaders in Endocrinology, Dr. Chrousos returned to his country and has assumed leadership roles at the University of Athens and in Greek and European Medicine and Academia.

<http://scholar.google.com/citations?user=rMgCyBUAAAAJ&hl=en&oi=ao>

Dr. Chiara Guglielmi, MD, PhD

Her Degree in Medicine and specialized in Endocrinology & Metabolic Diseases from University “Campus Bio Medico” of Rome, Italy. After the MD degree she moved to Augusta (GA, USA) at the Medical College of Georgia where she was admitted as Post Doc Fellow in the Center for Biotechnology and Genomic Medicine directed by Dr. Jin-Xiong She. During this period, Dr Guglielmi focused her research on genetics of type 1 diabetes and participated at the



PANDA (Prediction and Prevention of Type 1 Diabetes) study. This project was established in 1997 and seeks to screen newborns and young relatives of type 1 diabetes patients using genetic markers.

In 2004 she began under the supervision of Professor Paolo Pozzilli her International PhD in Endocrinology and Metabolic Medicine: the first joint PhD program in diabetes including two Universities (Barts and The London, UK and University Campus Bio-Medico, Rome, Italy). In 2013 Dr Guglielmi completed her specialization in Endocrinology & Metabolic Diseases and in these years she acted as Investigator and Study coordinator in several international studies focused on immunotherapy of type 1 diabetes: DEFEND, GAD65, DIAPE277. Dr Guglielmi has received national and international fellowships to carry out her projects in particular a Fellowship from the Italian Society of Diabetology (Lazio Region), a Fellowship Italian Consortium for Organ Transplantation and the Albert Renold Fellowship from the EASD. She has worked mainly in the field of diabetes with particular interest into type 1 diabetes (T1D) pathogenesis and prevention in collaboration with investigators around the world. She is an active member of the IMDIAB group (immunotherapy of T1D) founded by Prof. Paolo Pozzilli in the late 1980s. She has published numerous peer reviewed articles (Pubmed).

Professor Philippe Froguel, MD, PhD

Professor Philippe Froguel passed his Medical Degree in 1986 in Paris and he obtained a PhD in 1991 from Paris University. He is currently Professor of Genomic Medicine and head of the department genomics of common disease at the Hammersmith hospital, Imperial College London, UK. He is also Professor of Endocrinology-Diabetology at Lille University hospital and director of the CNRS research group "genomics of metabolic diseases" at Pasteur Institute, Lille, France.



Professor's scientific carrier is focused on the genetics of diabetes and obesity. He is author of 579 Pubmed indexed publications and his H-index is 117. Professor Froguel identified in 1992 the first type 2 diabetes gene (glucokinase) and has published in February 2007 the first Genome Wide Association Study in T2D, in 2008 the first GWAS analysis related to quantitative traits related to glucose control, and in 2010 the first identification of a common Genome Structure Variant causing obesity. Professor's major breakthroughs include several MODY genes neonatal diabetes gene such as ABCC8/SUR1; obesity genes leptin receptor, MC4R, FTO, GPR120, Amylase.

Professor Panos E. Vardas, MD, PhD

Professor Vardas is Head of the Cardiology Department at Heraklion University Hospital, Crete, Greece; the immediate Past President of the ESC and Chairman of the Managerial Council of the ESC European Heart Agency in Brussels.

His career started at the University of Athens, where he obtained his Medical Degree and his MD Thesis. During the same period, he specialized in Internal Medicine and Cardiology in the clinics of the same University. In 1985 he started working at the Westminster Hospital in London, Cardiology Department (director: Prof. Richard Sutton), where he stayed until 1989, focusing on Clinical Electrophysiology and Cardiac Rhythm Management Devices. In 1993 he obtained his PhD in Clinical Electrophysiology from the Charing Cross & Westminster Medical School.

In Greece, Prof. Vardas held major academic positions, such as Dean of the Medical Faculty of the University of Crete (2003-2007) and President of the Hellenic Cardiological Society (1999-2001). Furthermore, he has been Editor of the Hellenic Journal of Cardiology since 2002 and President of the Hellenic Cardiovascular Society since 2007.

In Europe, Prof. Vardas was elected to significant scientific positions. He was President of the European Society of Cardiology (2012-2014) and President of the European Heart Rhythm Association (2009-2011). He also served as Chairman of the Review Committee for the 2010 and 2012 Guidelines on AF, and Chairman of the European Working Group of Pacing and Electrophysiology (2002-2003).

Prof. Vardas was awarded the Gold Medal of the ESC in 2014 and he has been further honored as Invited Professor in several Universities and Honourary Member of a significant number of National Cardiac Societies. Prof. Vardas has participated as an author in 463 publications included in the MedLine as well as in a considerable number of chapters of well-known medical books, the Text Book of the ESC being one of them. He has been a fervent contributor to the activities of the European Society of Cardiology for twenty years.

Apart from the wide range of Cardiovascular Medicine, Prof. Vardas' main interests today lie in Health Economics, Health Technology Assessment, and Business Administration.





ABSTRACTS



Protease control in Health and Disease and my Experience with its Translation into Practice and Business

Robert Huber

Max-Planck-Institut fuer Biochemie

Emeritusgruppe Strukturforschung

D-82152 Martinsried – Germany;

Technische Universität München, TUM Emeritus of Excellence

D-85747 Garching, Germany;

Universität Duisburg-Essen, Zentrum für Medizinische Biotechnologie

D-45117 Essen, Germany;

Cardiff University, School of Biosciences

Cardiff CF10 3US, UK

As a student in the early nineteen sixties, I had the privilege to attend winter seminars organized by my mentor, W. Hoppe, and by M. Perutz, which took place in a small guesthouse in the Bavarian-Austrian Alps. The entire community of a handful of protein crystallographers assembled in a room which served as living and dining room and as auditorium for the lectures.

Today structural biologists organize large congresses with thousands of attendants and there exist many hundreds of laboratories specialized in this field. It appears to dominate biology and biochemistry very visibly if we count covers in scientific journals displaying macromolecular structures. Structural biology was successful, because it was recognized that understanding biological phenomena at the molecular and atomic level requires to see those molecules.

Structural biology revealed the structure of genes and their basic mechanism of regulation, the mechanism of enzymes' function, the structural basis of immune diversity, the mechanisms of energy production in cells by photosynthesis and its conversion into energy- rich chemical compounds and organic material, the mechanism that makes muscle work, the architecture of viruses and multi-enzyme complexes, and many more.

New methods had an essential impact on the development of structural biology. Methods seemed to become available in cadence with the growing complexity of the problems and newly discovered methods brought biological problems within reach for researchers, a co-evolutionary process of the development of methods and answerable problems.

An important additional incentive for structural biology came from its potential application for drug design and development by the use of knowledge of drug receptors at the atomic level. The commercial interest in application spurred this direction of research enormously.

My lecture will start out with a very brief review of the history of protein crystallography and continue with our studies since 1970 on proteolytic enzymes and their control. Proteolytic enzymes catalyse a very simple chemical reaction, the hydrolytic cleavage of a peptide bond. Nevertheless they constitute a most diverse and numerous lineage of proteins. The reason lies in their role as components of many regulatory physiological cascades in all organisms. To serve this purpose and to avoid unwanted destructive action, proteolytic activity must be strictly controlled. Control is based on different mechanisms which I will discuss and illustrate with examples of systems and structures determined in my laboratory:

- a) by specific inhibition with natural and synthetic inhibitors
- b) by enzymatic specificity
- c) by activation from inactive precursors accompanied or not by allosteric changes
- d) by co-localization of enzyme and substrate
- e) by cofactor binding accompanied or not by allosteric changes
- f) by controlled access to the proteolytic site.

The regulatory principles offer new opportunities of intervention for therapeutic purposes and use in crop science.

I then will let you share my experience with the foundation and development of two biotech companies with different business models, but both based on basic academic research in structural biology:

Proteros (www.Proteros.com) offers enabling technology services for Pharma- and Crop science companies imbedding all steps of the workflow molecular and structural biology can provide and commands and uses its platform for the generation of leads from identified targets to in vivo Proof of Concept (PoC).

Supremol (www.Supremol.com) specializes in the development of novel immunoregulatory therapeutics for the treatment of autoimmune diseases on the basis a recombinant, soluble, non-glycosylated version of the human Fcγ receptor IIB.

Re-evaluation of the Etiologies of Obesity

Richard L. Atkinson, Obesity Research Center, Richmond, VA, USA

Obesity is a chronic, life-long disease of multiple etiologies. About 1980, the prevalence of obesity began to rise in most countries of the world, both developed and undeveloped. In the USA, the prevalence of obesity in adults rose from 15% of the population in 1980 to over 30% in 2000. The prevalence of obesity tripled in children and similar rises were seen in children across the world. The increasing obesity in poor countries occurred despite great differences in access to fast foods, sugary beverages, television, and computers compared to the USA. Likely of greater importance than these factors are genetics and novel concepts including epigenetic factors in women of childbearing age, certain drugs, insufficient sleep, and environmental factors such as infections and chemical pollutants. This talk will focus on two important etiologies of obesity that recently have been identified: factors affecting women of childbearing age and infection with adenovirus 36. There is a cluster of factors that affect women before and during pregnancy that produce weight gain and obesity in offspring, both in childhood and as adults. These include the mother being either large or small for gestational age at her birth, being obese at the onset of pregnancy, excess weight gain during pregnancy, smoking during pregnancy, lack of exercise during pregnancy, later age at first pregnancy, and development of gestational diabetes. The magnitude of risk for offspring obesity may be 20 fold or more if all of these factors are present vs none being present. This dwarfs the contributions of fast foods, sugary beverages, TV, and computers to the development of obesity in children and adolescents.

Adenovirus 36 (Adv36) may be a major contributor to the worldwide epidemic of obesity. Experimental infection of chickens, mice, rats, and monkeys causes obesity in 60%-70% of lower animals and 100% in monkeys, producing a rise of 50% to 150% of total body fat or visceral fat. Adv36 infection does not increase food intake or decrease activity in animals. Prior Adv36 infection can be detected in humans by presence of antibodies to Adv36 or Adv36 DNA in adipose tissue biopsies of humans. Initial studies in the USA found that 30% of obese humans and 11% of non-obese humans had been infected. Infected individuals were heavier than uninfected. Multiple studies across the world confirm the higher prevalence rate of Adv36 infection in obese humans, especially in children. Prevalences of Adv36 infection range from 6% to 65% in obese adults and 22% to 30% in obese children. Prevalence in lean individuals ranges from 4% to 35%. Obesity due to a virus may be preventable by effective vaccines. In conclusion, obesity is a complex disease that is greatly misunderstood and underappreciated. Much research is needed to identify all the causes of obesity and to identify appropriate, individualized treatments for affected people.

Systems Biology and the Stress Response: From Pythagoras and the Epicureans to Modern Medicine.

George P. Chrousos, Medical School of the University of Athens, Athens, Greece

“Stress” is defined as the disturbance in the “dynamic balance” or “homeostasis” of a complex system, such as the human organism or society, “stressors” as the forces that produce this disturbance, and “adaptive response” as the forces from within the complex system that strive to return homeostasis to normal. In the case of the human organism, the adaptive response is subserved by a specialized system in our brain and body, the “Stress System”, which is activated to help us deal with stress when a stressor of any kind exceeds a certain threshold. In itself, stress that is dealt with efficiently by the adaptive response of a complex system is neutral or even potentially beneficial to that system, be that an organism or a society. In contrast, the chronic dynamic state in which the adaptive response fails to fully reestablish homeostasis during stress, which I call “dyshomeostasis” or, more correctly, “cacostasis”, may have detrimental effects on the system. In human beings, the crucial beneficial hormones that are activated to reestablish homeostasis, the “homeostatic or stress mediators”, including adrenaline, noradrenaline, cortisol and the inflammatory mediator interleukin-6, are also, paradoxically, responsible to a great extent for the damage the organism sustains when in cacostasis. These mediators may impair the physiology of our cells, disturb their metabolic activity, increase their inflammatory response and stimulate their oxidative functions, all potentially damaging changes, ultimately accelerating aging, causing obesity, metabolic problems and osteoporosis, promoting atherosclerosis and cardiovascular disease and increasing the chance of the organism to be infected or get cancer.

The pre-Socratic philosophers Pythagoras and Alcmaeon, respectively, used the terms “harmony” and “isonomia” to express the dynamic balance or homeostasis of life, while the Hippocratics equated this harmony with health and disharmony with disease. Both the Stoics and the Epicurians, philosophic schools that concentrated on the study of stress and its management, considered the attainment of “ataraxia”, or imperturbability of the mind to stressors, as the ultimate goal of life, while Epicurus himself spoke of “eustatheia” -or “eustasis”, if we extrapolate from homeostasis-, the serene emotional state of a harmonious balance in a human being. The not uncommon Greek first name “Eustathios ” is a remnant of that era. Based on these ancient seminal ideas, we suggested that appropriate responsiveness of the human stress system to stressors is a crucial prerequisite for a sense of wellbeing, adequate performance of tasks, and positive social interactions, and hence for the survival of the self and the species. By contrast, inappropriate, over- or under- responsiveness of the stress system through its hormonal and inflammatory mediators may impair growth and development, and may account for the many chronic behavioral, endocrine, metabolic, and allergic/autoimmune disorders that plague contemporary humanity. The development and severity of these conditions primarily depend on the

Our first model disorders of stress system over- and under-responsiveness were, respectively, melancholic depression, which we showed to be a disease characterized by chronic hyperactivation of the stress system, explaining its behavioral and somatic manifestations, and its mirror image, atypical depression, characterized by chronically decreased activation of this system, also explaining its clinical manifestations through a similar but alternative pathway. This realization allowed us to extrapolate our thoughts to the larger nosology of the human population, identifying many other such states. Starting from animal models, and with some surprise, we realized that hyporesponsivity of the stress system to inflammatory signals and resistance of immune tissues to cortisol characterize several inflammatory disorders, such as rheumatoid arthritis and septic shock, phenomena that we elucidated at the molecular level. Similarly, we identified other human states characterized by hypoactivity of the stress response, including seasonal depression, the chronic fatigue and fibromyalgia syndromes, postpartum blues/depression and the late luteal phase dysphoric syndrome disorder.

We suggested that the genetic vulnerabilities of our species leading to the contemporary “chronic non-communicable diseases”, which include obesity, the chronic pain and fatigue syndromes, depression, hypertension, the metabolic syndrome and cardiovascular diseases, resulted from selective pressures of evolutionary stressors upon our genome during our evolution to modern human beings. To these genetic vulnerability changes, stress in prenatal and early life adds the so-called epigenetic ones. Prenatal life, infancy, childhood and adolescence are critical periods characterized by great plasticity and, hence, increased vulnerability to stressors. During these critical periods of life, stress mediators exert major organizational effects on the neural circuits of the brain and epigenetic effects throughout the brain and body. Such neural and epigenetic changes are environmentally acquired, and as such, are fully preventable.

Well beyond depression, currently affecting approximately 20% of the adult population and predicted by the World Health Organization to soon be the number 2 morbidity factor in the world, we suggested that chronic common, every day stress and the resultant cacostasis are also a major factor for all cause morbidity and mortality in today's societies, encompassing all the chronic non-communicable diseases and, to a lesser extent, certain infections and cancer. At this time, and despite the stupendous advances in hygiene and medicine that have prolonged our lives, we believe that over 50 percent of the human disease burden is due to chronic socioeconomic distress, a result -to a great extent- of the ever increasing complexity and alienation in the modern world. We should note that the effects of prolonged distress go well beyond the causation of the chronic non-communicable diseases. Prolonged human cacostasis disturbs normal growth and development in children, causes emotional deprivation, upsets sleep, destroys family and social life, increases criminal behavior, multiplies violent accidents, and stimulates the abuse of and dependence on substances. Chronic distress also accelerates aging, reflected in decreasing chromosomal telomere length, and increases frailty, curtailing healthy life expectancy.

Finally, the health care related costs of prolonged distress are enormous, probably accounting for a significant proportion of the total expenditures.

The dysphoria that most frequently accompanies cacostasis and the “happiness” of equanimity and sense of wellbeing are mutually inhibitory of each other. We now understand the neurochemical mechanisms of this crucial relation and can employ this knowledge in our quest for happiness and good health. We actually can, with the power of our will, lead ourselves to a dynamic state of homeostasis that is at a level higher than what would have been expected from our genetic and epigenetic constitution and our environment, a condition that I call “hyperstasis”. The latter state allows the full experience and appreciation of the gift of life, extends its duration and influences propitiously those around us. This state gives materialism its true proportions and promotes virtue, spirituality and a better Society.

Through our work, we established the common biological pathways connecting a large array of ostensibly disparate psychological and somatic disorders, including depression, anxiety, obesity, hypertension, metabolic syndrome, diabetes, allergic and autoimmune inflammatory disorders, sleep disturbances, such as insomnia and sleep apnea, hypofertility, and osteoporosis. We contributed to the understanding of how stress through its mediators, including components of the inflammatory reaction, causes premature aging, and promotes cardiovascular and neurovascular diseases. A common pathophysiology suggests that prevention and curative means have common bases.

Today, the presence of stress and cacostasis in an individual can be evaluated and graded. There are rational and proven methods to prevent and ameliorate distress that start from changes in lifestyle (healthy diet, exercise, stable daily timing, adequate sleep), to cognitive and behavioral therapies, to the use of appropriate medications. Indeed, the currently available medications that control risk factors and prolong life function primarily by blocking the stress system and inflammatory mediators. The key issue is that nature is not destiny and wellbeing and hyperstasis are attainable.

Granted that chronic distress in early life augments the risk of developing chronic behavioral and non-communicative disorders, preventing distress in pregnancy and the first 5 years of life or interrupting the vicious cycle of distress during this period is imperative and, in the long run, the most cost-effective approach. Interventions beyond the age of 5 may be quite useful, but one should note that major stress-related brain organizational and epigenetic damage has already occurred. At this point I should mention what L. Tolstoy had intuitively said: “From the child of five to myself is but a step. But from the newborn baby to the child of five is an appalling distance”. Now, this is based on robust evidence and makes early interventions, starting with the education of prospective mothers, a must.

In summary, to interrupt the vicious effects of stress in a society and its members, one should, first, eliminate or at least moderate the stressors and, second, one should improve the coping of

Political actions can influence both strategies: Granted that stress in today's industrialized world is mostly anthropogenic, a well run country itself in homeostasis, in which people feel enfranchised, dignified and dealt with fairness and justice, is bound to have happier and healthier citizens. On the other hand, preventing early life stressors and their effects on the very young will eliminate development of risks for the later behavioral and chronic non-communicable disorders that plague our societies today. Finally, like many human endeavors, coping with stress is an eminently learnable process and the basis of the most effective psychological therapy employed today, cognitive behavioral therapy. It is the duty of a Society to ensure the wellbeing and happiness of its people with political strategies that prevent stress and enhance the ability of its citizens to cope.

The new prognosis of type 1 diabetes

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Immune intervention at diagnosis of type 1 diabetes (T1D) aims to prevent or reverse the disease by blocking autoimmunity, thereby preserving/restoring beta cell mass and function. In the last year several clinical trials of non-specific and of antigen-specific immune therapies tried to demonstrate the feasibility of modulation of islet-specific autoimmunity but unfortunately only few studies were able to give positive results. In part, this failure results from the considerable disease heterogeneity associated with diverse genetic and non-genetic disease determinants and the spectrum of clinical phenotype at diagnosis.

Thus, a younger age at onset is associated with stronger genetic susceptibility, more intense immune response to beta cell antigens, shorter duration of symptoms, more severe metabolic derangement at diagnosis and a more rapid rate of beta cell destruction. Therefore, designing therapies that would be effective in all clinical settings is definitely challenging.

Over the last years new treatment options for T1D has been considered and great interest is now coming from incretins (DPP-IV inhibitors and GLP-1 analogs). Incretin-based therapies, since their approval, have demonstrated their clinical utilities in type 2 diabetes (T2D). GLP-1, in addition to its insulinotropic action in alleviating hyperglycemia, possesses beneficial effects in protecting progressive impairment of pancreatic beta cell function, preservation of beta cell mass and suppression of glucagon secretion, gastric emptying and appetite.

A combination therapy should be the way to tackle T1D and clinical trials in this respect are needed.

Diabetes and Obesity Genomics to Metabolic Personalized Medicine

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Type 2 Diabetes (T2D) and obesity are both multifactorial diseases due to the interaction of genes with the environment. A non negligible fraction of these metabolic disorders are due to mutation in a single gene or to chromosome abnormalities. The elucidation of these forms of disease has important implication for physiopathology and for clinical care. Recent progress in Next Generation Sequencing has made possible the molecular diagnostic of these patients.

Genome Wide Association Studies have discovered more than 200 genes that contribute to common T2D and/or obesity.

However, altogether these genetic markers don't explain more than 10% of disease heritability: rare variants and epigenetics can contribute to the development of metabolic disorders and to their complications and may help to make progress towards more personalized metabolic medicine.

The lecture will present state of the art in genomic medicine of T2D and obesity.

Obesity and cardiovascular disease

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Obesity is a new epidemic not only in industrialised countries but also in countries of average or low Gross Domestic Product.

Through a large number of epidemiologic studies, it has been widely recognised that obese individuals have higher cardiovascular disease related morbidity and mortality rate, and weight reduction is associated with improved risk factor profile.

Focusing partly on coronary heart disease and its connection to obesity, it seems that the pathophysiology of the disease is indirectly related to obesity through common covariants for both diseases. The most important covariants are arterial hypertension, dyslipidemia, particularly reduction in HDL cholesterol, and impaired glucose tolerance or non-insulin dependent diabetes mellitus. Insulin resistance and accompanying hyperinsulinemia are typically associated with these comorbidities. Although most of the two situations mentioned above relating obesity to Coronary Artery Disease (CAD) increase as Body Mass Index (BMI) increases, they are also connected with body fat distribution. Left ventricular hypertrophy is quite common in obese patients and, to some degree, associated with systemic hypertension. Abnormalities in left ventricular mass and function also occur in the absence of hypertension and may relate to the severity of obesity. Hypertension is three times more common to obese individuals than to normal-weight ones.

While quite a few studies have linked obesity to the occurrence of CAD, other important studies in the last years have shown that among patients having been reperfused or suffered acute coronary syndromes, morbidity and mortality rates are lower for those with moderate obesity. In other words, it seems that the relation between BMI and mortality is U shaped.

In conclusion, obesity as a new epidemic from childhood to adulthood is directly and mainly indirectly connected to a series of cardiovascular diseases leading to high morbidity and mortality rates.

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