



Editors: Olivier Braissant, Hidetoshi Wakamatsu, Isaac Kuo-Kang  
Karel Allegaert, Yongwimon Lenbury, Amy Wachholtz

# RECENT RESEARCHES IN MODERN MEDICINE

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- ⊙ 2<sup>nd</sup> International Conference on Medical Physiology (PHYSIOLOGY '11)
- ⊙ 2<sup>nd</sup> International Conference on Medical Pharmacology (PHARMACOLOGY '11)
- ⊙ 2<sup>nd</sup> International Conference on Biochemistry and Medical Chemistry (BIOMEDCH '11)
- ⊙ 2<sup>nd</sup> International Conference on Medical Histology and Embryology (HISTEM '11)
- ⊙ 2<sup>nd</sup> International Conference on Oncology (ONCOLOGY '11)
- ⊙ 2<sup>nd</sup> International Conference on Psychiatry and Psychotherapy (PSYCHO '11)



Cambridge, UK, February 23-25, 2011

ISSN: 1792-8257  
ISSN: 1792-8273  
ISSN: 1792-829X  
ISSN: 1792-8311  
ISSN: 1792-8338  
ISSN: 1792-8354  
ISBN: 978-960-474-278-3





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Published by WSEAS Press  
[www.wseas.org](http://www.wseas.org)

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All papers of the present volume were peer reviewed by two independent reviewers. Acceptance was granted when both reviewers' recommendations were positive.  
See also: <http://www.worldses.org/review/index.html>



World Scientific and Engineering Academy and Society

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**Preface**

This year the 2nd International Conference on MEDICAL PHYSIOLOGY (PHYSIOLOGY '11), the 2nd International Conference on MEDICAL PHARMACOLOGY (PHARMACOLOGY '11), the 2nd International Conference on BIOCHEMISTRY and MEDICAL CHEMISTRY (BIOMEDCH '11), the 2nd International Conference on MEDICAL HISTOLOGY and EMBRYOLOGY (HISTEM '11), the 2nd International Conference on ONCOLOGY (ONCOLOGY '11) and the 2nd International Conference on PSYCHIATRY and PSYCHOTHERAPY (PSYCHO '11) were held in Cambridge, UK, February 23-25, 2011. The conferences remain faithful to their original idea of providing a platform to discuss medical physiology, pharmacology, biochemistry, histology, oncology, psychiatry, psychotherapy etc. with participants from all over the world, both from academia and from industry.

Their success is reflected in the papers received, with participants coming from several countries, allowing a real multinational multicultural exchange of experiences and ideas.

The accepted papers of these conferences are published in this Book that will be indexed by ISI. Please, check it: [www.worldses.org/indexes](http://www.worldses.org/indexes) as well as in the CD-ROM Proceedings. They will be also available in the E-Library of the WSEAS. The best papers will be also promoted in many Journals for further evaluation.

Conferences such as these can only succeed as a team effort, so the Editors want to thank the International Scientific Committee and the Reviewers for their excellent work in reviewing the papers as well as their invaluable input and advice.

The Editors





## Table of Contents

<b>Plenary Lecture 1: The Meaning of Fluid Responsiveness</b> <i>Karim Bendjelid</i>	15
<b>Plenary Lecture 2: Creatine Deficiency Syndromes, and the Importance of Creatine Synthesis in the Brain</b> <i>Olivier Braissant</i>	16
<b>Plenary Lecture 3: Automatic Control of Physiological State and Function</b> <i>Hidetoshi Wakamatsu</i>	17
<b>Plenary Lecture 4: Nanomechanics and Nanomanipulation of Soft Biological Materials for Tissue Engineering Applications</b> <i>Isaac Kuo-Kang Liu</i>	18
<b>Plenary Lecture 5: Pharmacokinetics, Metabolism and Tolerance of Intravenous Paracetamol in Early Life</b> <i>Karel Allegaert</i>	19
<b>Plenary Lecture 6: Investigating Effects of Drug Therapy for HIV Infection by Double Compartments Cellular Automata Simulations</b> <i>Yongwimon Lenbury</i>	20
<b>Plenary Lecture 7: Proteome analyses of schizophrenia brain tissue: searching for biochemical pathways and potential biomarkers</b> <i>Daniel Martins-de-Souza</i>	21
<b>Plenary Lecture 8: Extended-Spectrum <math>\alpha</math>-Lactamase Producing Escherichia coli Strains Isolated From Male and Female Neonates: Mode of Transmission of CTX-M Gene and a Clinico-Bioinformative Study</b> <i>Asad U. Khan</i>	22
<b>Plenary Lecture 9: Influence of Aluminum on Health and Disease</b> <i>Shunsuke Meshitsuka</i>	23
<b>Plenary Lecture 10: Novel Doped Bioactive Glass for Applications in Orthopedic Surgery: In Vitro and in Vivo Bioactivity</b> <i>Hassane Oudadesse</i>	24
<b>Plenary Lecture 11: Novel Fluorescence Methods as a Base for Biomedical Sensoring: Antioxidants, Reactive Radicals, NO and Superoxide Dynamics, Immunoassay and Biomembranes Fluidity</b> <i>Gertz I. Likhtenshtein</i>	25
<b>Plenary Lecture 12: Recent developments in High Resolution Tandem Mass Spectrometry</b> <i>George A. Zachariadis</i>	26
<b>Plenary Lecture 13: Time to Market and Patient Access to New Oncology Products in Italy: A Multistep Pathway from European Context to Regional Health Care Providers</b> <i>Francesco S. Mennini</i>	27

<b>Plenary Lecture 14: Anxiety and depression in COPD</b>	28
<i>Milena Adina Man</i>	
<b>Plenary Lecture 15: The Role of Spirituality on Pain Perception and Tolerance</b>	29
<i>Amy Wachholtz</i>	
<b>Plenary Lecture 16: Recovery Issues in the Treatment of Schizophrenia: Are We at the End, or Still at the Beginning?</b>	30
<i>Koksal Alptekin</i>	
<b>New Insights in Hypertrophic Cardiomyopathy</b>	31
<i>Georgios K Efthimiadis, Thomas Gossios, Vasileios Kamperidis, Manthos Didangelos, Ioannis H. Styliadis</i>	
<b>Study of DNA Interaction with 1-Phenyl-2-Methyl-Aminopropanol Containing Palladium Compound which Reveal Radiomodifying and Immunostimulatory Activity</b>	37
<i>N. A. Kasyanenko, E. V. Morozova, I. A. Efimenko</i>	
<b>O<sub>2</sub>-Influence on MMSC's Metabolic and Differentiation Status</b>	43
<i>L. B. Buravkova, E. R. Andreeva, J. V. Rylova</i>	
<b>Novel Fluorescence Methods as a Base for Biomedical Sensoring: Antioxidants, Reactive Radicals, NO and Superoxide Dynamics, Immunoassay and Biomembranes Fluidity</b>	49
<i>I. Likhtenshtein Gertz</i>	
<b>Clinical Pharmacology of Propylene Glycol in Neonates</b>	58
<i>Aida Kulo, Jan De Hoon, Maissa Rayyan, Rene Verbesselt, Karel Allegaert</i>	
<b>Pharmacokinetics, Metabolism and Tolerance of Intravenous Paracetamol in Early Life</b>	63
<i>Karel Allegaert</i>	
<b>Targeting Tumor Metabolism: Novel Strategies against Cancer Stem Cells? New Aspects and Changing Paradigms</b>	67
<i>Derek Zieker, Ingmar Koenigsrainer, Russell S. Taichman, Markus Loeffler</i>	
<b>Criteria for the Neuropathological Diagnosis of Dementing Disorders: Routes out of the Swamp?</b>	71
<i>Kurt A. Jellinger</i>	
<b>Theory of Carbon Signaling. Negentropy vs Entropy - Emergence of Self Propagated Biological Systems</b>	98
<i>Radoslav Sabev Bozov</i>	
<b>The Role of Modern Medical Imaging in Evaluation of Tumor Response to Vascular Targeting Therapy</b>	115
<i>Huaijun Wang, Marlein Miranda Cona, Junjie Li, Yuanbo Feng, Feng Chen, Jie Yu, Frederik De Keyzer, Yansheng Jiang, Guy Marchal, Yicheng Ni</i>	
<b>12 Years of Substitution Treatment with Buprenorphine for Opioid Addicts in Austria- Obstacles and Challenges</b>	126
<i>Salvatore Giacomuzzi, Klaus Garber, Yvonne Riemer</i>	

<b>The Repetitive Thinking Questionnaire : Psychometric Properties in Iraninan Students, and Relationship with Depression, Anxiety and Social Anxiety</b>	132
<i>Soheila Khaleghi Y. G., R. Liaghat, M. Shahriary, Y. Ganjdanesh</i>	
<b>Six Almost Unknown Reasons why LMWH is Better than Unfractionated Heparin in Therapy of Patients with Present or Threatening Heart Failure</b>	137
<i>Goran Koracevic</i>	
<b>Perimyocarditis May Coexist with Acute Myocardial Infarction</b>	142
<i>Goran Koracevic</i>	
<b>Increased Bradykinin B1 Receptor Expression in Diabetic Placental Tissue Correlates with both Hyperhistaminaemia and Increased Histidine Decarboxylase (HDC) Activity</b>	145
<i>Dariusz Szukiewicz, Michal Pyzlak, Habib Alkhalayla, Arlena Szukiewicz, Slawomir Maslinski</i>	
<b>Epidemiology of Exercise-Induced Hypoxemia in Athletes and the Role of Expiratory Flow Limitation</b>	151
<i>Gerard Coneys, Peter Lu, Cris Labossiere, Amarjit Arneja, Sat Sharma</i>	
<b>Study of Exercise-Induced Hypoxemia in Athletes: Role of Interstitial Pulmonary Edema</b>	165
<i>Peter Lu, Gerard Coneys, Cris Labossiere, Brett Memauri, Davinder S. Jassal, Sat Sharma</i>	
<b>Investigating Effects of Drug Therapy for HIV Infection by Double Compartments Cellular Automata Simulations</b>	177
<i>Sompop Moonchai, Yongwimon Lenbury</i>	
<b>Drug Resistant and Wild-Type Strains Interaction: Investigating Effects of Conversion Delays for Possible Control Strategies</b>	183
<i>Korsuk Sirinukunwattana, Yongwimon Lenbury, Nardtida Tumrasvin</i>	
<b>Creatine, Central Nervous System and Creatine Deficiency Syndromes</b>	189
<i>Olivier Braissant, Josephine Uldry, Elidie Beard</i>	
<b>Social and Religious Support in Physical and Emotional Functioning in a National Sample of African Americans</b>	197
<i>Cheryl L. Holt, Eddie M. Clark, Katrina Debnam, Beverly Williams, Emily Schulz, Min Qi Wang</i>	
<b>Social Capital and Its Relation to Health</b>	204
<i>Hsieh-Hua Yang, Yi-Horng Lai, Jui-Chen Yu, Shu-Chen Kuo, Hsueh-Chih Lin, Lung- Hsing Kuo , Shang Ming Su, Hung-Jen Yang</i>	
<b>Controlled Release of the Anti-Cancer Drug Paclitaxel from Bioresorbable Poly(Ester-Ether-Ester) Microspheres</b>	210
<i>G. D. Guerra, M. Gagliardi, N. Barbani, C. Cristallini</i>	
<b>Delay Mechanism Involving a Drug Target Candidate G Protein Coupled Receptors in Signal Pathways</b>	218
<i>Warunee Sarika, Yongwimon Lenbury, Wanwarat Anlamlert</i>	
<b>On the Distinction between Lag and Delay in Microorganism Growth</b>	224
<i>Peter Vadasz, Alisa S. Vadasz</i>	
<b>Postnatal Creatinemia in Extremely Low Birth Weight (ELBW) Neonates Reflects Perinatal Renal Maturational Physiology</b>	232
<i>George Isabelle, Maissa Rayyan, Djalila Mekahli, Karel Allegaert</i>	

<b>Anxiety and Depression in COPD</b>	236
<i>Man Milena Adina, Octavia Luiza Necrelescu, Cosmina Bondor, Antigona Trofor, Dana Alexandrescu, Monica Pop</i>	
<b>Depressive Syndrome, Anxiety and Illness Perception in Tuberculosis Patients</b>	243
<i>Man Milena Adina, Octavia Luiza Necrelescu, Cosmina Bondor, Antigona Trofor, Dana Alexandrescu, Elena Dantes</i>	
<b>Evaluation of Alcohol Consumption, Smoking and Aggressivity Among High School Attendees</b>	249
<i>Dana Alexandrescu, Milena Man, Antigona Trofor, Bogdan Ratiu-Duma, Gabriela Sechel</i>	
<b>Study Regarding the Physical and Psychical Recovery of sportsmen and their Recuperation</b>	255
<i>Dana Badau, Adela Badau, Bondoc Ionescu Dragos, Adin Cojocar, Marilena Cojocar, Florin Paraschiv, Milena Adina Man</i>	
<b>Varenieline as First Aid to Treat Nicotine Dependence in Smokers with High Prevalence of Co-Morbidities</b>	261
<i>Antigona Trofor, Milena Adina Man, Dana Alexandrescu, Ramona Miron</i>	
<b>Sensitization of Human Colorectal Cancer Cells to Paclitaxel-Induced Apoptosis by Inhibition of MEK/ERK Pathway is Caspase-4 Dependent</b>	268
<i>Nizar M. Mhaidat, Saied A. Jaradat, Abdulhameed Ghabkari</i>	
<b>Diffusion of a Tracer Sphere in Fibrous Virus (fd) Networks</b>	277
<i>Kyongok Kang</i>	
<b>Neuroprotective Effect of Alcoholic Extract of Terminalia Arjuna Bark in Experimental Stroke Induced Rats</b>	281
<i>Thaakur Santhrani, C. Mangadevi</i>	
<b>Effect of Chrysin Isolated from Oroxyllum Indicum against Cisplatin-Induced Acute Renal Failure</b>	302
<i>Sreedevi Adikay, Usha U., Bharathi Koganti</i>	
<b>Endobronchial Chemotherapy in Malignant Airway Lesions of the Lung Report of 3 Years Experience</b>	308
<i>Hamidreza Jabbardarjani, Shahram Kharabian, Mohammad Reza Masjedi</i>	
<b>Tracheobronchopathia Osteochondroplastica: Presentation of Ten Cases and Review of the Literature</b>	312
<i>H. R. Jabbardarjani, B. Radpey, S. Kharabian, M. R. Masjedi</i>	
<b>Mechanisms and Pharmacological Classification of Ca<sup>2+</sup> Sensitizers</b>	316
<i>Masao Endoh</i>	
<b>Natural Catalytic Antibodies in Norm, Autoimmune and Viral Diseases</b>	321
<i>Georgy A. Nevinsky</i>	
<b>Separation of Macromolecules by Hexagonal Mesoporous Membrane Filters</b>	324
<i>Sherif A. El-Safty, K. Shenashen, A. Shahat</i>	
<b>Towards a Unified Model of Pavlovian Conditioning: Solution to the Extinction Problem</b>	330
<i>V. I. Kryukov</i>	

<b>Effort Capacity Changes under Acute Exposure to Altitude</b> <i>Alina Martoma, Razvan Enoiu, Elena Sabau, Georgeta Niculescu</i>	341
<b>Medical Physiology and Drug Disposition in Special Populations: From Compound Specific Observations to Physiology based Pharmacokinetics</b> <i>Allegaert Karel, Jan De Hoon, Gunnar Naulaers, Jan Depreest</i>	347
<b>Quantitative Measurement of the Serum C Reactive Protein in Different Clinic Categories of Late Spontaneous and Therapeutic Abortion</b> <i>Carmen A. Bulucea, Nikos E. Mastorakis, Mariana F. Paun, Alina D. Neatu</i>	351
<b>Microspheres of Chitosan-Bioactive Glass for Application in Orthopedic Surgery. In Vitro Experiment</b> <i>Xuan-Vuong Bui, Hassane Oudadesse, Yann Le Gal, Amany Mostafa, Guy Cathelineau</i>	359
<b>Studies of Doped Biomimetic Nano-Hydroxyapatite/polymer Matrix Composites for Applications in Biomedical Field</b> <i>Hassane Oudadesse, Amany Mostafa, Xuong-Vuong Bui, Yann Le Gal, Guy Cathelineau</i>	368
<b>Recent Developments in High Resolution Tandem Mass Spectrometry for Biomolecules and Related Compounds</b> <i>George Zachariadis</i>	375
<b>Contributions to Investigation of Oral Biofilms Using Low-Vacuum Scanning Electron Microscopy</b> <i>Stefan-Ioan Stratul, Darian Rusu, Andreea Didilescu, Luminita Nica, Aurel Raduta, Cosmin Locovei, Mircea Nicoara</i>	379
<b>Application of <sup>19</sup>F NMR Spectroscopic Method to the Enantioresolution and Quantitative Determination of Ofloxacin in Pharmaceutical Formulations</b> <i>Mohammad Kazem Rofouei, Nastaran Sohrabi, Mojtaba Shamsipur, Soheila Haghgoo</i>	385
<b>The Orange Domain of Basic Helix-Loop-Helix Transcription Factor SHARP2 Binds to E-Box DNA</b> <i>Mohammed S. Mustak, Riyo Yoshikawa, Kazuya Takahashi, Yuta Nakamura, Ojeiru F Ezomo, Kazuya Yamada, Shunsuke Meshitsuka</i>	395
<b>The Analysis of the Biomechanical Alterations Present During Running at Sportsmen who Suffered from Knee Sprain</b> <i>Corina Pantea, Adrian Ivan, Stelian Pantea, Mihaela Faur</i>	400
<b>Metabolic Supply Chains with Non-Linear Fluxes</b> <i>Dirk Langemann, Achim Peters</i>	406
<b>Biochemical and Molecular Biological Insights into Aluminum Toxicity in Biology and Medicine</b> <i>Shunsuke Meshitsuka</i>	411
<b>A New Perspective Regarding the Rectus Abdominis Muscle-Development and Ontogenesis</b> <i>Lazar L. Onisai, Mihai Greavu, Marinescu Mihnea Cosmin</i>	415
<b>Details Regarding the Arterial Vasculature of the Heart</b> <i>Onisai L. Lazar, Bold Costin Leonard, Marinescu Mihnea Cosmin</i>	421

<b>TELOCYTES – A Novel Type of Interstitial Cells</b>	424
<i>Lawrence M. Popescu</i>	
<b>Burnout in Established General Practitioners The Significance of Supervision</b>	433
<i>Susanne Fuchs, Marcel Fischer, Elke Mesenholl-Strehler, P. C. Ender</i>	
<b>Antitumor Activity of the Polyether Ionophorous Antibiotic Monensin and its Metal(II) Complexes</b>	439
<i>Mariana Mitewa, Ivayla Pantcheva, Radostina Alexandrova</i>	
<b>Gender Differences in Elements of the Brain Regions</b>	445
<i>Yoshiyuki Tohno, Setsuko Tohno, Pasuk Mahakkanukrauh, Takeshi Minami, Nutcharin Ongkana, Lining Ke, Xiao-Zhen Zhao, Patipath Suwannahoy, Apichat Sinthubua, Cho Azuma</i>	
<b>Does Hyponatremia Following Marathon Running Develops During or After the Race?</b>	451
<i>Marcus Blouw, Patrick Harnett, Akash Sharma, Cris Labossiere, Sat Sharma</i>	
<b>Food Components Activating TRPA1</b>	460
<i>Tatsuo Watanabe, Yusaku Iwasaki, Kenji Kobata, Manabu Tanabe, Kanako Koizumi, Yukiko Okumura, Yuko Terada, Masataka Narukawa</i>	
<b>Biochemical Significance of Autoantibody Titers Against Oxidized Low-Density Lipoprotein in Patients with Coronary Heart Disease</b>	463
<i>Mahmoud I. Nasr, Shaden M. Hanafy, M. Osman, Ehab M. Abdel-Fattah, Dalia A., Hassan M.</i>	
<b>Authors Index</b>	472

## Plenary Lecture 1

### The Meaning of Fluid Responsiveness



**Dr. Karim Bendjelid**  
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**Abstract:** Volume expansion is the basis of resuscitation in critically ill patients. It is important to recognize that fluid deficits occur frequently in patients with shock because of decrease in unstressed circulatory volume or alterations in capillary permeability. In this regard, decrease in venous return results in inadequate cardiac output to meet the metabolic requirements of tissues and must be treated urgently to avoid the occurrence of multiorgan failure. Although the importance of fluid management is generally well-known, the prediction of patients' fluid responsiveness in some situations could be difficult to assess. The present lecture reviews the meaning of fluid responsiveness monitoring in critically ill patients.

**Brief Biography of the Speaker:** Karim Bendjelid, MD, PhD is a Cardiologist-Intensivist attending physician at the Geneva University Hospitals (Intensive Care Division) and a Privat Docent at Geneva Medical University. He has also a Master of Science (MSc) in Cardiovascular Pharmacology at University of Pierre-Marie Curie-Paris VI (France) and a PhD in Physiology at University of Claude Bernard-Lyon I (France). Dr Bendjelid succeeds to the Gold Decoration Competition ("Gold Medal awards") of the Lyon University Hospitals. His main research interests concern hemodynamic monitoring (macrocirculation-microcirculation) and reliability of static and dynamic markers to predict fluid responsiveness in critically ill patients. In these fields, he authored or co-authored over 60 scientific papers published in peer reviewed journals or presented at international conferences. He co-authored over 5 Review & Chapters papers books edited by Springer-Verlag, Distribuna Editorial and Elsevier. He was a chairman or keynote lecturer in a number of international conferences organized by different prestigious societies. He is a regular Member of The French Society of Cardiology (echocardiography), the French Cardio-Vasculaire Research Group, the European Society of Cardiology, the American Physiological Society and the European Society of Intensive Care. He is a technical reviewer for the following international journals: IEEE Transactions on Biomedical Engineering, Critical Care Medicine, Intensive Care Medicine, Anesthesia Analgesia, Circulation, Chest, Acta Anaesthesiologica Scandinavica, Anesthesiology, European Journal of Echocardiography, Pulmonary Pharmacology and Therapeutics, the American Journal of Respiratory Critical Care Medicine, Stroke, Critical Care, European Journal of clinical investigation, Journal of Surgical Research, and British medical journal. He is also, member of the editorial board of Current Drug Therapy, Annals of Thoracic Medicine and Open Critical Care Medicine Journal.



## Plenary Lecture 2

### Creatine Deficiency Syndromes, and the Importance of Creatine Synthesis in the Brain



#### Prof. Olivier Braissant

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**Abstract:** Creatine deficiency syndromes, due to deficiencies in AGAT and GAMT, the two enzymes of the creatine synthesis pathway, or in the creatine transporter SLC6A8, are inborn errors of metabolism which lead to a complete absence, or a very strong decrease, of creatine within the brain. Patients suffering from these syndromes show severe neurodevelopmental delay and present neurological symptoms in early infancy such as mental retardation, disturbance of active and comprehensible speech, autism, auto-mutilating behavior and hypotonia. The creatine/phosphocreatine/creatine kinase system plays essential roles to maintain the high energy levels necessary for the brain, through regeneration and buffering of ATP levels. Recent works also suggest new roles for creatine in CNS, where it may act as neurotransmitter and appears as one of the main CNS osmolytes.

While it has long been thought that most, if not all, of brain creatine was of peripheral origin, the recent years have brought evidence that AGAT and GAMT are expressed in the brain, which can synthesize creatine. Moreover, the absence of the creatine transporter SLC6A8 in the astrocytic feet lining microcapillaries made us suggest that blood brain barrier has a limited permeability for creatine. In vivo data confirmed this hypothesis, as the long term treatment of AGAT- and GAMT-deficient patients with high doses of creatine only allows a very slow and in most cases partial replenishment of their CNS creatine. Consequently, the brain most probably depends for an important proportion on its own creatine synthesis rather than on an exclusive supply from the blood. The "brain endogenous creatine synthesis" hypothesis contradicts the in vivo characteristics of SLC6A8 deficiency, which, despite normal expression of AGAT and GAMT in CNS, causes brain creatine deficiency. This apparent contradiction is probably explained by our very recent data showing that in many brain structures, AGAT and GAMT are in most cases not co-expressed but are rather expressed in a dissociated way. This suggests that to allow creatine synthesis, the intermediate guanidinoacetate must be transported from AGAT- to GAMT-expressing cells, most probably through SLC6A8. These observations may explain the absence of creatine in the brain of SLC6A8-deficient patient, despite their normal CNS expression of AGAT and GAMT.

**Brief Biography of the Speaker:** Olivier Braissant, biologist, obtained his PhD thesis at the University of Lausanne, Switzerland, in 1994. After a post-doc on nuclear receptors and their expression in central nervous system, he moved to the University Hospital of Lausanne (CHUV) in 1997, in the Clinical Chemistry Laboratory of the Department of Pathology and Molecular Medicine. There, he started working on inborn errors of metabolism and in particular on their effect on brain development. He is "Privat Docent" and "Maitre d'Enseignement et de Recherche" of the University of Lausanne since 2004, and now head of the research section of the Clinical Chemistry Laboratory of the CHUV. His research interests focus on brain development and metabolism, and how various inborn errors of metabolism, in particular creatine deficiencies, organic acidemias and diseases causing hyperammonemia, can affect them. He is author of about 50 papers published in international journals and conference proceedings, as well as invited book chapters.

## Plenary Lecture 3

### Automatic Control of Physiological State and Function



**Prof. Hidetoshi Wakamatsu**

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**Abstract:** The regulation of physiological phenomena is discussed as an application of system control theory. The concerning concept is not for only the description of biologically regulatory mechanisms, but practically automatic control of specific state and function by approach of medicine using medicine according to control laws and/or by surgery as their structural changes. We discuss first the historical activities in our concerning domain, such as the clinical control of blood sugar, blood pressure and so on. Nevertheless, the conventional methods were sometimes not effective because of their biological characteristics depending on individualities, thus new control methods had been required to overcome such difficulties. From this viewpoint, our control of alveolar CO<sub>2</sub>-concentration by ventilation was realized according to adaptive or fuzzy controls with little influence caused by internal and external characteristics change. Because of general versatility of the methods, they have been applied to various kinds of biological and medical control systems. Practically, temperature regulatory system in hypothermia under constitutional anesthesia has been developed even for a long period of clinical control. We mention, in particular, control of brain temperature by water surface-cooling for the brain hypothermic treatment of patients with cerebrovascular disorders. Thereby, a patient in ICU was regarded as a unity controlled system with water temperature into blanket as an input and brain temperature as an output. During a long period, brain temperature was well controlled according to schedule by physicians and the state of patients without much influence due to various medical treatments including the effect of characteristics of individual patients during the therapeutic course. Furthermore, we describe the automatic control of intracranial pressure, giving optimal amount and timing of administration of medicine for decompression in the brain.

**Brief Biography of the Speaker:** He was born on 15.Nov.1946, received his B.E. and M.E. degrees from Yokohama National University in 1970 and 1972, respectively. He received his Dr. of Eng. degree in 1984 from the University of Tokyo.

Academic Positions: a research Associate at the Institute for Medical and Dental Engineering from 1972-1986, Tokyo Medical and Dental University. From 1973-1974, a Visiting Research Associate, Institute for Biocybernetics, Faculty of Medicine, University of Erlangen-Nuernberg, Germany. From 1986-1988, an Associate Professor at Ashikaga Institute of Technology, Associate professor 1988-1991, Professor 1991-1992 at Fukui University and Professor, Faculty of Medicine in 1992, Professor, Graduate School of Health Care Sciences in 2001, Tokyo Medical and Dental University. In 1994 a visiting professor, Oregon State University and so on. From 2006 a general chair of Asia Pacific Conference on Control and Measurement.

Scientific Activities

1. Automatic control system of physiological state and function for clinical application
2. Biochemical dynamics in the damaged area of brain tissue and during the clinical treatment.
3. Life support system based on simple principle and method using the Internet.
4. Haptic operation of virtual visco-elasto-plastic material by virtual tools and its application to medicine

## Plenary Lecture 4

### Nanomechanics and Nanomanipulation of Soft Biological Materials for Tissue Engineering Applications



#### Professor Isaac Kuo-Kang Liu

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School of Engineering, University of Warwick  
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**Abstract:** Nanomechanics and nanomanipulation of soft biological materials, such as molecular, cell and tissue, are essential for the advancement of the tissue engineering. For example, applying nanoscale force and displacement as mechanical stimuli for tissue regeneration, and for sorting and manipulating cells or molecules to nanofabricate de novo biomimetic systems, are in great need of both the better understanding of nanomechanics and the new techniques of nanomanipulations.

Recent advancements in bio-manipulation instruments, such as micromanipulation and optical tweezers [2], have enabled the nanomechanical characterisation and manipulation of biological cells and soft tissue. Micromanipulation is capable of the micro-force measurement of a single biological cell and tissue membrane at large deformation, while optical tweezers, often incorporated with micro-fluidic systems, allows to the force measurement as low as 100 pN. These measurements can be incorporated with mechanical modelling to facilitate the determination of the mechanical properties, such as the elasticity and rupture strength of cell and tissue membrane. In addition to the mechanical properties, interfacial characterization, e.g. cell-substrate adhesion, can be realized by our recently developed method which is based on Confocal Reflection Interference Contrast Microscopy (C-RICM). In parallel, various theoretical modelling and simulations, such as the cell mechanics theory and capsule-substrate adhesion model, have been developed for interpreting the experimental data and for facilitating the determination of the mechanical properties of biological materials at the cellular/molecular level. Various materials, such as biological/ biomimetic cell and tissue, have been examined by using these new techniques, and their results are presented in this talk.

**Brief Biography of the Speaker:** Dr. Isaac Kuo-Kang Liu is a Reader (Associate Professor) in Nanotechnology at School of Engineering, the University of Warwick, UK. Before joining Warwick in 2009, he was a Reader in Biomedical and Cell Engineering at the Institute of Science and Technology in Medicine, School of Medicine, Keele University, UK and an Associate Professor in the Mechanical and Production School of Nanyang Technological University (NTU), Singapore. He completed his PhD study at the Chemical Engineering Department of Imperial College London, UK in 1995. His research interests include Cellular Bioengineering, Biomechanics, Nanomedicine, Tissue Engineering, and Biomedical Devices. He is a fellow of the Royal Society of Medicine, a fellow of Nanotechnology Institute, and a senior member of American Institute of Chemical Engineers (AIChE). He is an editor of several prestigious journals (e.g. the Open J. Nanomedicine). He has published more than 40 high-impact journal papers in Bioengineering and Biophysical areas and 30 other publications, including 2 US patents.

## Plenary Lecture 5

### Pharmacokinetics, Metabolism and Tolerance of Intravenous Paracetamol in Early Life



#### Assistant Professor Karel Allegaert

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**Abstract:** Neonatal drug dosing needs to be based on the physiological characteristics of the newborn and the pharmacokinetic parameters of the drug. Size-related changes can in part be modelled based on allometry and relates to the observation that metabolic rate relates to weight by a kg 0.75 trend. Until adult metabolic activity has been reached, ontogeny, i.e. iso-enzyme specific maturation and maturation of renal clearance also contributes to drug metabolism, making iso-enzyme specific documentation of maturation necessary.

Changes in body composition and ontogeny are most prominent in neonates. The body fat content (/kg) is markedly lower and the body water content (/kg) is markedly higher in neonates. These findings have an impact on the distribution volume of both lipophilic and hydrophilic drugs. Drugs are cleared either by metabolism (metabolic clearance) or elimination (elimination clearance). While the first is mainly hepatic, the second route is mainly renal. Both hepatic metabolism and renal clearance display maturation in early life although other co-variables (e.g. polymorphisms, co-administration of drugs, first pass metabolism, disease characteristics) further contribute to the interindividual variability in drug disposition.

Documentation of these maturational processes based on in vivo 'case' studies is of value since these drug-specific observations can subsequently be extrapolated to other drugs which are either already being prescribed or even considered for use in neonates by the introduction of these observations in 'generic physiologically based pharmacokinetic' models.

**Brief Biography of the Speaker:** Karel Allegaert graduated from the University Leuven, Belgium in 2000 as paediatrician-neonatologist. After an additional training at Sophia Children's Hospital in Rotterdam, he was appointed as clinical consultant neonatology at the University Hospitals Leuven. After his PhD thesis on neonatal analgesia (2002-2005), he further developed his clinical research in the field of neonatal pain treatment and developmental pharmacology in neonates and was appointed as associated professor at the same university (2005-ongoing). His current clinical research is supported by a grant of the national research council (Fund for Scientific Research, Flanders (Belgium) by a Fundamental Clinical Investigatorship (1800209 N, 2008-2012). This clinical research resulted in about 140 papers published in international peer reviewed journals, conferences proceedings and book chapters and was recently (2009) the Galenus price for research in clinical pharmacology and the Govaerts price for clinical toxicology of the Royal Academy of Medicine of Belgium.

## Plenary Lecture 6

### Investigating Effects of Drug Therapy for HIV Infection by Double Compartments Cellular Automata Simulations



#### Professor Yongwimon Lenbury

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**Abstract:** The progress of human immunodeficiency virus (HIV) infection typically follows a three phase pattern; the primary response phase, the clinical latency phase, and the final phase of acquired immunodeficiency syndrome (AIDS). In order to test the efficiency of different protocols in drug therapy for HIV patients, it is important to have a realistic model which reliably simulates the course of the infection which exhibits two drastically different time scales, days and decades. The classical ordinary or partial differential equations have been found to be inadequate in coping with such extreme spread in time scales. In this paper, we employ a two-compartment Cellular Automata (CA) model to study the dynamics of drug therapy of HIV infection. The levels of healthy and infected CD<sup>+</sup>T cells are tracked in both the lymph node and peripheral blood compartments coupled and updated simultaneously with each time step. The viral loads in the two compartments are also updated through a system of difference equations. Drug therapy is then simulated by incorporating its effects in the update rules of the CA model. By adjusting the rules to update the cells in the CA lattice, it becomes possible to study the efficacies of different treatment strategies or drugs of choice, as well as the repercussion of drug resistance over time.

**Brief Biography of the Speaker:** After Professor Yongwimon Lenbury obtained her Ph.D. in Mathematics from Vanderbilt University, USA, she returned to the Department of Mathematics, Faculty of Science, Mahidol University to teach, and conduct research in dynamical modeling of nonlinear systems in biology and medicine. She was appointed professor of Mathematics in 1996.

Prof. Lenbury has been involved in research work in the field by Mathematical Modelling and Nonlinear Systems in Biology and Medicine. Her work involves dynamical modelling and analysis of nonlinear systems such as food chains coupled by parasitic infections, hormone secretion systems in the human body, and so on. Of particular interest are the pacemaker oscillations and rhythmogenesis in human mechanism which have been proposed as a way to differentiate sickness from health. For example, some of her works involves the construction and analysis of a model for insulin kinetics and the identification of oscillatory behavior subject to various feeding regimens. Her recent interest has been concentrated in the signal transduction system involving GPCR, a major drug target. She received an award from the National Research Council as the Outstanding Researcher in the field of Physical Science in the year 1998. Her continued achievements have resulted in her being granted the prestigious position of Senior Researcher of the Thailand Research Fund in Mathematics, 2000-2002 and a Fellow of the Royal Institute of Thailand. Collaborating with several researchers in various countries such as the United States, Germany, Italy, and New Zealand, Prof. Lenbury has been devoted to the promotion of research and education in the field of Mathematics in Thailand.

## Plenary Lecture 7

### Proteome analyses of schizophrenia brain tissue: searching for biochemical pathways and potential biomarkers



**Dr. Daniel Martins-de-Souza**

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**Abstract:** Schizophrenia is likely to be a consequence of serial alterations of a number of genes and proteins that, together with environmental factors, will lead to the establishment of the illness. Since proteomic analysis of post-mortem schizophrenia brains may lead to the identification of schizophrenia-related proteins that will ensure the comprehension of this pathogenesis as well as indicate potential biomarkers, we have collected post-mortem brain tissue from schizophrenia patients and control individuals of the dorsolateral prefrontal cortex (Brodmann's Area 46), anterior temporal lobe (BA38), Wernicke's Area (BA22p), mediodorsal thalamus and anterior cingulate cortex aiming to analyze their proteomes. We subjected those brain tissues to comparative proteome analysis using a shotgun mass spectrometry approach combining isoelectrofocusing and RP-HPLC prior MALDI-TOF/TOF powered by isotope coded protein labeling (ICPL) for proteome quantitation. Moreover, we used two-dimensional gel electrophoresis/mass spectrometry-based proteome analysis. We have found the most often alterations in energy metabolism, oligodendrocyte-function and myelination, calcium homeostasis and cytoskeleton. Moreover, we have revealed the differential expression of a number of hypothetical or putative proteins, which might be interesting targets to further studies considering their underlie information. Several protein biomarker candidates such as myelin basic protein and myelin oligodendrocyte protein were evaluated and validated by western blot in some of the described brain regions as well as in cerebrospinal fluid from a separate set of samples. A number of glycolysis enzymes have been found differentially expressed in the analyzed brain regions, what have led us to quantify the levels of pyruvate and NADPH in thalamus, which indeed were found altered. The recurrent identification and validation of inter-related protein clusters, determined in different samples by different proteomic approaches not only strongly reinforces the putative involvement of certain pathways in SCZ, but also reveal new potential biomarkers and paves the way to the development of new therapeutic strategies in order to contribute for reducing the social and cognitive consequences of the disease.

**Brief Biography of the Speaker:** Dr. Daniel Martins-de-Souza is an associate researcher in University of Cambridge at Cambridge Centre for Neuropsychiatric Research headed by Prof. Sabine Bahn working on proteomics of psychiatric disorders. Dr. Martins-de-Souza was a postdoc fellow in Max Planck Institute of Psychiatry in Munich, Germany, for 2 years and has obtained his Ph.D. in Biochemistry and Molecular Biology in State University of Campinas (UNICAMP) in Brazil, where he had started the investigations in the proteome analysis of schizophrenia brain tissue, aiming to find differentially expressed proteins which can lead to a better comprehension of this disorder as well as find potential biomarkers to help the clinical diagnosis. Dr. Martins-de-Souza has 32 published scientific articles and 3 book chapters.

## Plenary Lecture 8

### Extended-Spectrum $\alpha$ -Lactamase Producing *Escherichia coli* Strains Isolated From Male and Female Neonates: Mode of Transmission of CTX-M Gene and a Clinico-Bioinformative Study



**Assistant Professor Asad U. Khan**  
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**Abstract:** Due to increase in drug resistance world wide, this study was undertaken to characterize mode of transmission of blaCTX-M among ESBL-producing *E. coli* isolates. ERIC-PCR was used to type the ESBL-producers strains. A search for blaCTX-M genes and integrons in the genomic and plasmid DNA of ESBL positive isolates was performed by PCR amplification. Cloning, sequencing of CTX-M gene was performed and submitted in gene bank (FJ997864, FJ997865, GQ174503, GQ145221 and GQ174504). Modelling and docking was performed by Autodoc. The ERIC typed isolates were screened for blaCTX-M, blaTEM, armA, rmtA and rmtB. PCR amplified blaCTX-M genes were cloned and sequenced. Five blaCTX-M-15, 2 rmtB, 2 blaTEM-1 and 13 Class1 integrons were detected. All the blaCTX-M-15 positive isolates, except one were clonally related. 'Length of stay in NICU' was found as the single independent risk factor. This study concludes that resistant markers were transferred through plasmids in the present setting. Male neonates who are colonized or infected by ESBL-producing *E. coli* might have a longer stay in NICU compared to their female counterparts.

**Brief Biography of the Speaker:** Asad U Khan, male, molecular biologist, graduated from Biochemistry Department, A M University, Aligarh, India in 1998. He joined Interdisciplinary Biotechnology Unit, A.M University as Asst Professor in 1997 and continued till 2000. He later joined Department of Biochemistry, UMDNJ, New Jersey USA in 2000 for three years as post doctoral Research Associate, working on Transcription biology of Yeast and gene expression. He then resumed his services as Asst Professor in the same department till 2006 and became Associate professor in the Interdisciplinary Biotechnology Unit, AMU, India. He was awarded a prestigious fellowship, BOYSCAST Fellowship from Government of India to work as visiting Scientist in University of Napoli, Italy in 2005. He was also awarded Young Scientist Award of Association of Microbiologist of India in 2006 and Alembic award in 2009. His work was well recognized and he has been invited several invited talks as well as reviews articles and chapters. He has been in Editorial board of several number of International journal. He has a total of 85 research articles in his credit. He is a member of several international associations.

## Plenary Lecture 9

### Influence of Aluminum on Health and Disease



**Associate Professor Shunsuke Meshitsuka**

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**Abstract:** Aluminum is not an essential element but is rather toxic and the need to protect themselves from aluminum toxicity is crucial for living organisms. Aluminum is the third abundant element and the most abundant metal in the earth's crust, therefore exposure to aluminum is inevitable in daily life. It was shown that the rate of excretion of aluminum in the urine was assumed to have a limiting value. As a result, an excess intake of aluminum indicated that the aluminum content in the body remained high for several days after the absorption of aluminum from the intestine. It is widely known that accumulation of aluminum in the body has been linked to disease conditions. The toxic effects of aluminum to neuronal cells were examined to show apoptotic cell death via endoplasmic reticulum stress, implicating an influence of aluminum on the gene expression. Also, it was shown that astrocyte-neuron interaction was important in the process of toxic effects in the central nervous system. Renin was the only positively identified up-regulated gene determined by DNA sequencing. The up-regulation of renin was confirmed by RT-PCR and Western blotting experiments in the dose dependent treatments and the time course observation in mice. The up-regulation of the renin expression by aluminum is a strong indication of the influence of aluminum on the renin-angiotensin-aldosterone-system, resulting in the induction of essential hypertension.

**Brief Biography of the Speaker:** Shunsuke Meshitsuka graduated from Waseda University in 1970, and got his Ph.D. from the Faculty of Science of the University of Tokyo in 1977, and got D. Med. from Tottori University Faculty of Medicine in 1987. He got a position of a researcher in Sagami Chemical Research Center in 1972. He moved to Tottori University Medical School as an assistant professor in 1976. After working in the Fox Chase Cancer Center in Philadelphia as a postdoctoral fellow he became an associate professor in 1995. He was an invited researcher of Riken Genome Science Research Center, Yokohama from 2004 to 2006, and also was a visiting researcher of Osaka University Institute for Protein Research from 1981 to 2010. His main research area is inorganic biochemistry and the structure of related biological molecules.



## Plenary Lecture 10

### Novel Doped Bioactive Glass for Applications in Orthopedic Surgery: In Vitro and in Vivo Bioactivity



#### Professor Hassane Oudadesse

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**Abstract:** A bioactive glass is an excellent candidate as a graft for bone tissue regeneration. The insertions of atomic elements such as Zn, Sr and/or Mg, separately or simultaneously, present a high interest in the bone metabolism activity. They were introduced as trace elements at different contents in the glass matrix, according to their concentration in the bone matrix. Their effects consist on the modification of physico-chemical properties of bioactive glass after "in vitro" or "in vivo" experiments. Their role is consequently the improvement of the properties such as crystallographic structure, morphology and density of the apatite layer formation on the surfaces of biomaterials and the bone-bonding ability. In this work, bioactive glass in the ternary system ( $\text{SiO}_2\text{-CaO-Na}_2\text{O-P}_2\text{O}_5$ ) was elaborated by an original method based on the melting process. Additions of these atomic elements have been made with different amounts of each introduced element in the glassy network.

In vitro experiments were achieved to evaluate the crystallographic structure, the morphology and the kinetic of chemical reactivity versus time of soaking in synthetic physiological solution (SBF). Cells adhesion and proliferation on the surfaces of biomaterials were investigated.

In vivo experiments were carried out on the femurs of rabbits to evaluate the biocompatibility, the physico-chemical properties and the kinetic of bioactivity and bioconsolidation in the interface bone-Implant. Several physicochemical and biological methods were employed to highlight the behavior of pure and doped bioactive glass.

Obtained results show different behavior. The presence of magnesium promotes the dissolution of silica network when the presence of strontium or zinc slows down this phenomenon. All doped bioactive glasses show the no toxic character of these biomaterials. However, the introduction of strontium enhances the cells proliferation of about 14.3 % compared to pure bioactive glass.

In vivo experiments demonstrate that 10% BG-Sr seem to be the best implant materials tested leading to beneficial effects in stabilization of the oxidative balance. These beneficial effects were confirmed by histological findings and correlated with the biocompatibility of cells grown. These biomaterials offer to surgeons more opportunities. Because of the variations of the kinetic of bioactivity, they can be adapted for patients according to different parameters such as the age, the gender, the location site and other physiological parameters.

**Brief Biography of the Speaker:** Hassane Oudadesse graduated from the University Blaise Pascal of Clermont-Ferrand France. He obtained his PhD in 1989 and worked as associate Professor and obtained his HDR (Habilitation a Diriger des recherches) in 1998. Since 2001, he works in the University of Rennes 1 as Full Professor in the "Sciences Chimiques de Rennes", UMR CNRS 6226.

His works concern the conception, synthesis and physicochemical studies of new biomaterials for applications in orthopaedic surgery. Biocompatibility, kinetic of bioactivity, kinetic of bio consolidation in the interface bone-Implants, cells enhancement and other properties of biomaterials present the research filed of Professor Hassane Oudadesse.

He is author of more than 80 articles published in international journals and 50 international conferences.

Professor Hassane Oudadesse is a Head of the research unit on Biomaterials since 2001, Vice-President of University of Rennes 1, human resources since 2008, Director of Master 2 Solid State Chemistry and Materials since 2006. He was the President of the Chemical Department from 2002 to 2004 and the President of the specialists commission CNU 33 (Materials Chemistry) from 2003 to 2008.

## Plenary Lecture 11

### **Novel Fluorescence Methods as a Base for Biomedical Sensoring: Antioxidants, Reactive Radicals, NO and Superoxide Dynamics, Immunoassay and Biomembranes Fluidity**



**Professor Gertz I. Likhtenshtein**  
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**Abstract:** We proposed and developed a series of fluorescent methods of analysis and investigation of system potentially important in biotechnology and biomedicine. Three new types of molecular probes have been used: 1) dual fluorophore-nitroxide compounds, 2) fluorescent-photochrome molecules and 3) super molecules containing fluorescent and fluorescent quenching segments. These methods utilize the following photochemical and photophysical phenomena: the fluorescence quenching, photochrome photoisomerization and energy transfer. The fluorescence properties of the new probes was intensively exploited as the basis of several methodologies which include a real time analysis of antioxidants, nitric oxide, superoxide, reactive radicals, trinitrotoluene and metal ions, investigation of molecular dynamics of biomembranes in a wide range characteristic times, detection of protein conformational transition, and characterization of surface system. Owing high sensitivity, simplicity, availability of fluorescence techniques, these methods can be widely employed. The techniques can be adapted to fiberoptic sensing.

**Brief Biography of the Speaker:** Gertz I. Likhtenshtein received his PhD (1963) and Doctor of Science (1972) degrees at the Semenov Institute of Chemical Physics, Russian academy of Science, Moscow. In 1976 this Institute granted him the Professor title. In 1965 he was appointed on the position of Head of Laboratory of Chemical Physics of Enzyme Catalysis. In 1992 Likhtenshtein moved to the Department of Chemistry, the Ben-Gurion University of Negev (Israel) on the full Professor position, was in charge of the Laboratory of Chemical Biophysics and has been emerited in 2003. Among his awards are the Medal of the Exhibition of Economic Achievement, the Diploma of Discovery USSR for works on nitrogen fixation, the USSR State Prize for pioneering research on spin labeling in molecular biology, the V. V. Voevodsky International Prize for Chemical Physics and the Diploma of the Israel Chemical Society. He is a member of the International ESR Society, the American Biophysical Society, the Israel Chemical Society and the Israel ESR Society. At present his main scientific interests focus on mechanism of the light energy conversion and on novel methods of immunoassay, NO and antioxidants analysis. Likhtenshtein authored 10 scientific books and about 380 papers.

## Plenary Lecture 12

### Recent developments in High Resolution Tandem Mass Spectrometry



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**Abstract:** It is widely accepted that the most significant motif for the fast growing field of tandem mass spectrometry was to respond to the requirements of biochemistry, molecular biology, medical and medicinal chemistry. Conversely, the fast development of genomic research during the previous decade, the continuous expansion of proteomics and of metabolomics, as well as the recent interest in metallomics are mainly due to the capabilities offered by modern mass spectrometric instrumentation. The presentation will be focused mainly to the performance of some modern tandem mass spectrometric concepts, as introduced from several manufacturers, although the list is quite large and not all of them can be presented. There are many instruments commercially available for this purpose, capable for direct or hyphenated mass spectrometric analysis in one step (MS). However the demand for structure elucidation of extremely complicated unknown compounds, like proteins and peptides, nucleic acids, carbohydrates and their complexes, and many other types of biomolecules, forced the research to move to the second step, i.e. the development of much more sophisticated spectrometers combining two or three analyzers successively, the so called tandem mass spectrometers. These are capable to provide multi-stage mass spectrometric analysis (MSn), which means selection of precursor ions and further fragmentation of them to produce daughter ions, enabling thus the characterization of the above matrices. In a third step, since there are still many cases with confusion among several possible chemical structures, especially in the field of biochemistry, high-resolution tandem mass instruments (HRMS) were further developed and the current commercial competition shifts the research to even higher standards.

**Brief Biography of the Speaker:** Dr George Zachariadis is an Associate Professor of Analytical Chemistry at the Department of Chemistry of the Aristotle University of Thessaloniki, in Macedonia, Greece. He teaches quantitative analytical chemistry and instrumental analysis to undergraduate and postgraduate students during the past fifteen years. He was the author or co-author of 6 books of Analytical Chemistry and of almost 90 scientific papers and 2 reviews in the field of development, optimization and evaluation of modern instrumental analysis techniques. He has actively participated in almost 25 international conferences with more than 90 announcements. He is reviewer in 15 scientific journals of Analytical, Environmental and Food Chemistry. His main research activities are focused on Atomic and Mass Spectrometric techniques for the determination of heavy metals, trace elements of special interest, because inorganic substances even in very low concentrations play extremely important role in biological systems and also in the environment. He has developed methods also for the analysis of biological materials and determination of organic molecules of biological and medical interest by gas or liquid chromatographic techniques coupled to mass spectrometry. His research is focused on Multi-elemental and Speciation methods. He has also special research activities in Chemometric approaches for Archaeometric and Bioanalytical applications, as well as Food and Drug analysis, with almost a thousand of citations in his published work.

## Plenary Lecture 13

### Time to market and patient access to new oncology products in Italy: a multistep pathway from European context to regional health care providers



#### Prof. Francesco S. Mennini

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**Abstract:** Aim: The main purpose of this study was to identify each sequential phase followed by an oncology product, from European assessment until to patient access in each Italian region (IR). Methods: A panel of oncology products approved by the European Medicines Agency (EMA) in the period 2006–2008 was considered. The explored sequential phases included the times to market for: the EMA; pharmaceutical companies; the Italian Medicines Agency (Agenzia Italiana del Farnaco, AIFA); and IRs as final providers of health care. The IR's time to market was also analyzed by a Cox regression model. Results: The overall mean time required before patients access was 2.3 years. EMA accounted for the greater proportion of time (31.8%), followed by AIFA (28.2%). However, the duration for both pharmaceutical companies and IRs was associated with the highest variability. An oncology product authorized with a risk-sharing agreement showed an early access in the IRs. On the contrary, the introduction in IRs having a compulsory formulary was delayed. Both a high forecast of economic impact and a high oncology product price can also delay the patient access. Conclusion: The process before patient access to an oncology product is time and cost consuming. This study identifies the main predictors that affect the missing overlap between market and patient access in Italy.

**Brief Biography of the Speaker:** Prof. Francesco Saverio Mennini, is presently Professor for Health Economics and Political Economics at University of Rome "Tor Vergata" (both at the Faculty of Economics and Science). He is also Professor for Health Economics at University of Rome "La Sapienza", Faculty of Statistics. Formerly, he has led a career as a researcher in the field of Health Economics and Industrial Economics, at the University of Rome "Tor Vergata" and the National Research Council. His main contributions have dealt with welfare policies, health system analysis, health technology assessment and pharmaco-economics, and pharmaceutical economics. Prof. Mennini has been the scientific coordinator of the Master in Health Economics at University of Rome "Tor Vergata" for several years; he has been a scientific coordinator and member of the Regional Observatory for the HTA, from 2003 to 2006. Prof. Mennini is the chair of the Scientific Committee of the European Conference on Health Economics (ECHE). Prof. Mennini is author of numerous publications, national and international, of Health economics and Economic Evaluation.

## Plenary Lecture 14

### Anxiety and depression in COPD



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**Abstract:** COPD is a disease with multiple co morbidities. Two of the most common and least treated co morbidities are anxiety and depression. The prevalence of depression and anxiety associated with COPD vary considerably because the psychological consequences are rarely screened, because the variety of scales and methods used to measure such symptoms and because the different degrees of illness severity across studies.

The Participants in our study were recruited from patients with COPD, older 40 years old, with Forced Expiratory Volume in one second (FEV1) less than 80%, and FEV1/FVC less 70%, without malignancy, hepatic or renal insufficiency, diabetes mellitus, instable angina pectoris, myocardial infarction within the previous year, cardiac arrhythmias, or other significant diseases, hospitalized in Pneumology Clinic Leon Daniello Cluj, between September 2009-march 2010. The patients were interviewed with Beck Depression Inventory and Beck Anxiety Inventory, and Saint George Questioners for quality of life.

We try to evaluate the risk factors for depression and anxiety like age, gender, lack of social support, severity of disease (COPD), main symptoms, long term use of systemic corticosteroids, value of FEV1, educational level, presence of co morbidity, the total score for depression and anxiety ( for quantification of symptoms). The psychological manifestations of COPD are treated in only a minority of patients.

Untreated depression and anxiety have major implications for compliance with medical treatment (lower adherence), increased frequency of hospital admission, and are associated with poor quality of life (may also be a significant predictor of mortality following hospitalization)

Patients with COPD should be screened for depression and for anxiety by their respiratory doctor and should be treated by physician with skills and knowledge of mental disorders.

**Brief Biography of the Speaker:** Senior Chest Physician, Head of the Pulmonary Department Spitalul Clinic de Pneumftiziologie, "Leon Daniello" Cluj-Napoca, Romania from 2006

Senior Lecturer, University of Medicine and Pharmacy, Cluj-Napoca, Romania from 2004

Participated to WSEAS Conference in Prague, Cambridge, Athena, Bucharest, ERS Congress, National Conference

Published books and articles in the field of competences.

## Plenary Lecture 15

### The Role of Spirituality on Pain Perception and Tolerance



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**Abstract:** Chronic pain is a severe, often intractable, disorder that can severely impede quality of life. Medications for pain management can be useful, but often cause unpleasant side effects. This may leave patients seeking out alternative pain control resources, including those that include their spiritual beliefs and practices. Research has shown the multi-dimensional pain experience can be affected by physical, psychological, and spiritual factors. Many chronic pain patients use religious/spiritual forms of coping, such as prayer and seeking spiritual support, to cope with their pain. The primary objectives of this presentation is to review the current research on 1) potential psychophysiological pathways linking spirituality and health, with a particular focus on chronic pain, 2) adaptive and maladaptive forms of religious/spiritual coping mechanisms, 3) religious/spiritual coping strategies frequently used by pain patients, and 4) empirically supported tools to assess adaptive and maladaptive forms of religious/spiritual coping in the context of chronic pain. The conclusion of this talk encourages providers to assess how religious/spiritual factors may be positively or negatively impacting their patient's experience with chronic pain.

**Brief Biography of the Speaker:** Dr. Amy Wachholtz is an Assistant Professor of Psychiatry at the University of Massachusetts Medical School, and the Health Psychologist on the Psychosomatic Medicine Consult Service at UMass Memorial Medical Center. She is also a clinical supervisor in the UMass Medical School/WSH Psychology Internship program. She is a licensed clinical psychologist in North Carolina and Massachusetts. Dr. Wachholtz graduated Cum Laude with a Master of Divinity degree from Boston University where she specialized in Bioethics. She continued her education to earn a Masters and PhD in Clinical Psychology from Bowling Green State University where she had a dual specialty in Behavioral Medicine and Psychology of Religion. She completed her internship and fellowship at Duke University Medical Center where she focused on psycho-social treatment of medical illness, the promotion of wellness activities prevent illness and injury, and the use of the wellness model in recovery to prevent long term disability after an acute illness and injury. She has become an internationally recognized expert in the areas of pain and spirituality. Her clinical and research interests focus on the bio-psycho-social-spiritual model of health and wellness, chronic pain disorders, the complexities of treating of chronic or recurring pain, and treating disorders that frequently co-occur with pain, such as opioid mis-use and addiction.

## Plenary Lecture 16

### Recovery issues in the treatment of schizophrenia: are we at the end, or still at the beginning?



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**Abstract:** Recovery and normalized psychosocial functioning are the main targets for the treatment of schizophrenia. However pharmacological treatments are not good enough to achieve recovery in schizophrenia. Treatment of schizophrenia and recovery issues are under discussion. Only 10-20 % of all schizophrenia patients achieve full remission of symptoms and good psychosocial functioning during long term treatment of schizophrenia. Positive and negative symptoms are main symptom clusters to treat. Negative symptoms are strongly correlated to cognitive functions whereas both negative symptoms and cognitive dysfunctions predict the patient's ability to work and function independently at the society. But antipsychotics have limited benefit for improving cognitive functions and negative symptoms.

Meta-analytic studies and latest multi center, large scale studies such as CATIE and EUFEST have found that Clozapine, despite its limited use, seemed to be superior compared to all other antipsychotics regarding efficacy in schizophrenia and Olanzapine was associated with significantly longer time to discontinuation although both were significantly associated with metabolic and severe side effects. One of the important results driven from the CATIE trial has shown that the majority of the patients in each antipsychotic treatment group had discontinued their first treatment due to either inefficacy over schizophrenia symptoms or intolerable side effects. Recovery issues in schizophrenia result in polypharmacy as using more than one antipsychotics at the same time. However schizophrenia patients have higher mortality rates. Mortality rate is about two times greater and life expectancy is 20% shorter than general population in schizophrenia mainly due to cardiovascular and metabolic side effects which affect patient's satisfaction with treatment and let nonadherence to treatment.

Advances in our understanding of the etiology, course, and treatment of schizophrenia have led to an increased awareness of the need for defined standards against which to judge clinical improvement, both in clinical trial settings and in daily practice. What we regard as success in treating schizophrenia has evolved substantially, from reducing the risk of harm to self and others, through control of positive (and more recently negative) symptoms, towards preventing relapse and achieving improvements in daily functioning. Remission of schizophrenia symptoms does not always mean to have recovery from the illness. Recovery needs to improve cognitive functions, subjective well-being, quality of life and psychosocial functioning.

Today pharmacotherapy alone is not enough to achieve recovery, therefore psychosocial interventions should be established and be integrated with antipsychotics. However it is not clear which type of psychosocial treatment is best. The most important one is psychoeducational program that has been shown that it may enhance treatment adherence and reduce relapses in schizophrenia. Psychosocial intervention programs that may integrate cognitive, behavioral, educational and psychotherapeutic aspects need to be developed.

**Brief Biography of the Speaker:** Koksal Alptekin has been practicing as professor at the Department of Psychiatry of the University of Dokuz Eylul, Izmir-Turkey since 2002. He had residency training in Psychiatry at the same department. He had been trained in Psychodrama and Psychoanalytically Oriented Group Psychotherapy. Besides many national professional organizations he is a Schizophrenia and Epidemiology Section member of European Psychiatric Association (EPA). He has participated in the task force of WPA for schizophrenia since 2005. He is one of the editors of "Schizophrenia Treatment Guideline" and "Schizophrenia" published by Schizophrenia Section of Turkish Psychiatric Association. Dr. Alptekin's main research focus and publications include psychopharmacological treatment of schizophrenia, cognitive dysfunctions and quality of life in schizophrenia. Nowadays his research interest has been moved towards genetics and epidemiology of schizophrenia.

## Authors Index

Abdel-Fattah, E. M.	463	Endler, P. C.	433	Kuo, L.-H.	204
Adikay, S.	302	Endoh, M.	316	Kuo, S.-C.	204
Adina, M. M.	236, 243	Enoiu, R.	341	Labossiere, C.	151, 165, 451
Alexandrescu, D.	236, 243	Ezomo, O. F.	395	Lai, Y.-H.	204
Alexandrescu, D.	249, 261	Faur, M.	400	Langemann, D.	406
Alexandrova, R.	439	Feng, Y.	115	Lazar, O. L.	421
Alkhalayla, H.	145	Fischer, M.	433	Le Gal, Y.	359, 368
Allegaert, K.	58, 63, 232	Fuchs, S.	433	Lenbury, Y.	177, 183, 218
Andreeva, E. R.	43	Gagliardi, M.	210	Leonard, B. C.	421
Anlamlert, W.	218	Ganjanesh, Y.	132	Li, J.	115
Arneja, A.	151	Garber, K.	126	Liaghat, R.	132
Azuma, C.	445	Gertz, I. L.	49	Lin, H.-C.	204
Badau, A.	255	Ghabkari, A.	268	Locovei, C.	379
Badau, D.	255	Giacomuzzi, S.	126	Loeffler, M.	67
Barbani, N.	210	Gossios, T.	31	Lu, P.	151, 165
Beard, E.	189	Greavu, M.	415	Mahakkanukrauh, P.	445
Blouw, M.	451	Guerra, G. D.	210	Man, M.	249, 255, 261
Bondor, C.	236, 243	Haghighoo, S.	385	Mangadevi, C.	281
Bozov, R. S.	98	Hanafy, S. M.	463	Marchal, G.	115
Braissant, O.	189	Harnett, P.	451	Martoma, A.	341
Bui, Xua.-V.	359	Hassan, M.	463	Masjedi, M. R.	312
Bui, Xuo.-V.	368	Holt, C. L.	197	Masjedi, M. R.	308
Bulucea, C. A.	351	Isabelle, G.	232	Maslinski, S.	145
Buravkova, L. B.	43	Ivan, A.	400	Mastorakis, N. E.	351
Cathelineau, G.	359, 368	Iwasaki, Y.	460	Mekahli, D.	232
Chen, F.	115	Jabbardarjani, H.	308	Memaury, B.	165
Clark, E. M.	197	Jabbardarjani, H. R.	312	Mesenholl-Strehler, E.	433
Cojocar, A.	255	Jaradat, S. A.	268	Meshitsuka, S.	395, 411
Cojocar, M.	255	Jassal, D. S.	165	Mhaidat, N. M.	268
Cona, M. M.	115	Jellinger, K. A.	71	Minami, T.	445
Coneys, G.	151, 165	Jiang, Y.	115	Miron, R.	261
Cosmin, M. M.	415, 421	Kamperidis, V.	31	Mitewa, M.	439
Cristallini, C.	210	Kang, K.	277	Moonchai, S.	177
Dalia, A.	463	Karel, A.	347	Morozova, E. V.	37
Dantes, E.	243	Kasyanenko, N. A.	37	Mostafa, A.	359, 368
De Hoon, J.	58, 347	Ke, L.	445	Mustak, M. S.	395
De Keyzer, F.	115	Kharabian, S.	312	Nakamura, Y.	395
Debnam, K.	197	Kharabian, S.	308	Narukawa, M.	460
Deprest, J.	347	Kobata, K.	460	Nasr, M. I.	463
Didangelos, M.	31	Koenigsrainer, I.	67	Naulaers, G.	347
Didilescu, A.	379	Koganti, B.	302	Neatu, A. D.	351
Dragos, B. I.	255	Koizumi, K.	460	Necrelescu, O. L.	236, 243
Efimenko, I. A.	37	Koracevic, G.	137, 142	Nevinsky, G. A.	321
Efthimiadis, G. K.	31	Kryukov, V. I.	330	Ni, Y.	115
El-Safty, S. A.	324	Kulo, A.	58	Nica, L.	379



Nicoara, M.	379	Sabau, E.	341	Terada, Y.	460
Niculescu, G.	341	Santhrani, T.	281	Tohno, S.	445
Okumura, Y.	460	Sarika, W.	218	Tohno, Y.	445
Ongkana, N.	445	Schulz, E.	197	Trofor, A.	236, 243
Onisai, L. L.	415	Sechel, G.	249	Trofor, A.	249, 261
Osman, M.	463	Shahat, A.	324	Tumrasvin, N.	183
Oudadesse, H.	359, 368	Shahriary, M.	132	Uldry, J.	189
Pantcheva, I.	439	Shamsipur, M.	385	Usha, U.	302
Pantea, C.	400	Sharma, A.	451	Vadasz, A. S.	224
Pantea, S.	400	Sharma, S.	151, 165, 451	Vadasz, P.	224
Paraschiv, F.	255	Shenashen, K.	324	Verbesselt, R.	58
Paun, M. F.	351	Sinthubua, A.	445	Wang, H.	115
Peters, A.	406	Sirinukunwattana, K.	183	Wang, M. Q.	197
Pop, M.	236	Soheila Khaleghi, Y. G.	132	Watanabe, T.	460
Popescu, L. M.	424	Sohrabi, N.	385	Williams, B.	197
Pyzlak, M.	145	Stratul, S.-I.	379	Yamada, K.	395
Radpey, B.	312	Styliadis, I. H.	31	Yang, H.-H.	204
Raduta, A.	379	Su, S. M.	204	Yang, H.-J.	204
Ratiu-Duma, B.	249	Suwannahoy, P.	445	Yoshikawa, R.	395
Rayyan, M.	58, 232	Szukiewicz, A.	145	Yu, J.	115
Riemer, Y.	126	Szukiewicz, D.	145	Yu, J.-C.	204
Rofouei, M. K.	385	Taichman, R. S.	67	Zachariadis, G.	375
Rusu, D.	379	Takahashi, K.	395	Zhao, X.-Z.	445
Rylova, J. V.	43	Tanabe, M.	460	Zieker, D.	67