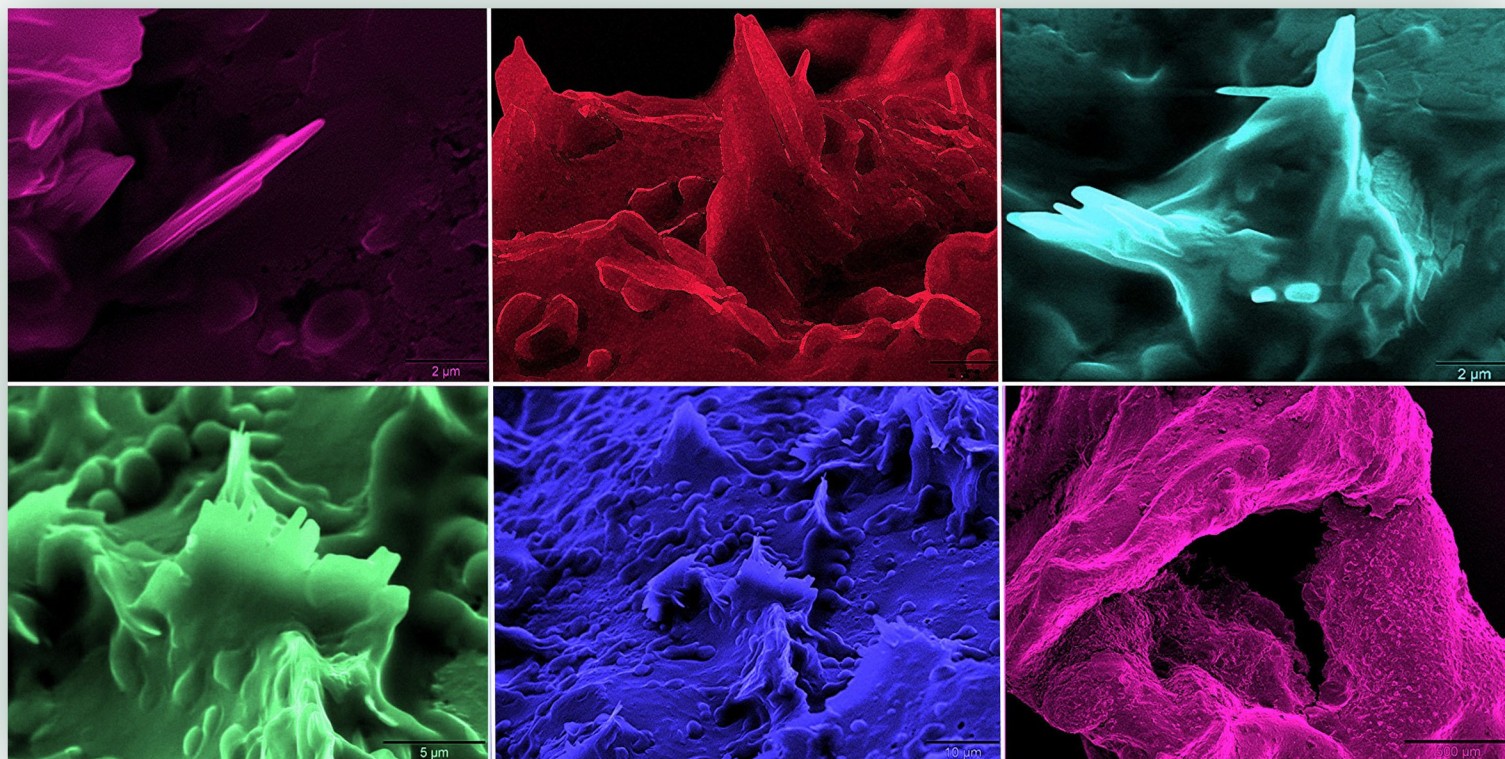




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**Editors: Vadim V. Sumbayev, Alessandra Pica, Shi-Ping Luh,
Hyun Kyoong Lim, Kazuhiko Natori,
Shunsuke Meshitsuka**

Proceedings of the WORLD MEDICAL CONFERENCE



Malta, September 15-17, 2010

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Plenary Lecture 1

Toll-like Receptor Signalling in Host Defence, Tissue Regeneration and Autoimmune Disorders



Professor Vadim V. Sumbayev
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University of Kent
United Kingdom
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Abstract: Toll-like receptors (TLRs) specifically recognise pathogen-associated molecular patterns and thus induce inflammatory/innate immune reactions to pathogens. Both cell membrane-associated and endosomal TLRs lie at the core of resistance to infectious disease allowing the host to specifically detect pathogen and promote further stages of the immune defence. Recent evidence clearly demonstrated the role of TLRs in development of autoimmune disorders and tissue regeneration. This appears possible because of the ability of some TLRs to recognise host-derived endogenous ligands. Here we analyse the intracellular signalling pathways recruited by TLRs and used for cellular adaptation to inflammatory stress and promotion of innate immune reactions in the cases of host immune defence, tissue regeneration and autoimmune reactions. Possible cross-links between pro-inflammatory/stress-adaptation pathways and formation of inflammasome are considered. Molecular mechanisms employed for suppression of the inflammatory responses and programmed death of the effector cells are discussed as well.

Brief Biography of the Speaker:

I achieved my PhD degree in 1999 from the Palladin Institute of Biochemistry, National Academy of Science of the Ukraine. After graduating, I worked as Assistant, then Associate, Professor at the Department of Biochemistry, Mechnikov Odessa National University in the Ukraine. Then I moved to Germany where I received an Alexander von Humboldt research fellowship and worked as a Humboldt fellow in the Institute for Cell Biology, University of Kaiserslautern. Upon complete of my fellowship, I spent three years in Denmark at the University of Aarhus, working as Assistant Professor at the Department of Molecular Biology at the Interdisciplinary Nanoscience Centre. In December 2006, I joined the Medway School of Pharmacy, University of Kent as a Lecturer in Biochemistry where I have established my research group.

Plenary Lecture 2

A Novel Form of Manganese Superoxide Dismutase: Its Role as anti-Cancer, anti-Necrotic and Tumor Marker for Imaging Analysis



Professor Alessandra Pica

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Abstract: The manganese superoxide dismutase from liposarcoma (LSA-MnSOD) is a tumor protein isolated and sequenced, for the first time, in human liposarcoma cells (LSA) in the Laboratory of Experimental Oncology, Cancer Institute of Naples, G. Pascale, by Dr. Aldo Mancini. This protein showed a rapid and effective anti-cancer activity consisting of a selective cytotoxicity on certain human breast cancer cells (MCF-7), and no cytotoxic effect on normal cells, such as normal human mammary epithelium (MCF-10) and fibroblasts (MRC-5). This protein was sequenced and produced as recombinant form (rMnSOD). The rMnSOD demonstrated the ability to enter both normal and cancer cells and to perform antioxidant activity by neutralizing free radicals, turning them into hydrogen peroxide that only normal cells are able to transform into molecular oxygen and water, due to their normal levels of catalase. In cancer cells – by their well known catalase underproduction, up to 10-100 times, as compared to normal cells – the peroxide can not be converted in oxygen, so that only cancer cells will reach the threshold of toxicity that will cause apoptotic death. The surprising effect of this molecule is, however, due to its ability, following injection in vivo, to penetrate all cells giving off its antioxidant potential, through its enzymatic activity. Both LSA-MnSOD and the rMnSOD were sequenced and compared to the common mitochondrial form. The difference lies in the presence of a leader peptide detected only in LSA-MnSOD, thus explaining the unusual characteristic of the protein of entering cells, while the native protein remains confined to the mitochondrial compartment. So the leader peptide has been synthesized (rMnSOD-LP) and injected in vitro and in vivo, thus demonstrating its ability to enter cells. These experiments highlighted its role as a molecular carrier. Further studies about its carrier function were performed by conjugation of this peptide to radioactive ^{68}Ga and its subsequent injection into animals affected by mammary tumors. PET analysis, performed two hours after injection in animals (dogs and cats), demonstrated internalization of the synthetic construct in the tumor and in its metastasis, thus allowing a more accurate identification in the body. Experiments in progress are demonstrating the ability of the leader peptide to deliver a conjugated cisplatin directly inside the tumor cells (as quantitatively demonstrated by atomic absorption spectrophotometry) and delivering cisplatin toxic load. This internalization rapidly leads to cell death in vitro and in vivo. As a further demonstration of the ability of rMnSOD to repair the damage caused by radical excess, its topical formulation has been used to treat animals affected by extended necrotic lesions, which quickly returned to the structural and functional integrity of all tissues affected by necrosis. More recently, a significant reduction of tissue injury from X ray damage was demonstrated by using MnSOD-plasmid/liposome treatments in the protection of murine lung. The latter studies demonstrated that rMnSOD not only exerts radioprotective effect on normal cells, but it is also radiosensitizing for tumor cells.

Brief Biography of the Speaker:

Alessandra Pica B.Sc., Associate Professor of Hematology, Faculty of Mathematical Physical and Natural Sciences of University of Naples, Federico II, Italy

Teaching:

Human Anatomy ;Embryology and Experimental Morphology;Histochemistry and Cytochemistry; Human Development, Growth and Anatomy - Course of General and Applied Biology - Curricula Nutritional Biology, University of Naples, Federico II, Italy.;- Hematology – Course of first Degree in Biological Sciences University of Naples, Federico II, Italy.;General and Comparative Hematology - Course of Biological Sciences -Curricula in Physiology-Pathology, University of Naples, Federico II, Italy.; - Biology in Doctorate School in Bioethics of University of Naples, Federico II, Italy.;- Hematology of Sea Turtles in Training Course On Sea Turtle Rescue and Rehabilitation

RAC/SPA (Regional Activity Centre for Specially Protected Areas - United Nations Environment Programme Mediterranean Action Plan (UNEP)) of Zoological Station, A. Dohrn, (Naples, Italy) devoted to foreign researcher of Mediterranean Areas; Hemopathology of Sea water Vertebrates in 1st Level Master in Biotechnology applied to reproduction and repopulation of marine species. 2007 School: Mathematics, Physics and Natural Sciences of University of Naples, Federico II, Italy

Current Scientific Activities

Consulting Hematologist of Sea Turtle Rescue and Rehabilitation Program of Zoological Station of Naples A. Dohrn, Italy

Member of Research Unit of project granted by Fidia Pharmaceutical: "Study of a Superoxide Dismutase modified (mMn-SOD-2), secreted by human liposarcoma displaying antitumoral and antioxidant properties" (Coordinator: Dr. Aldo Mancini, Cancer Institute of Naples, A. Pascale): immunocytochemical study of anti-tumoral action of LSA-Mn-SOD treatment on MCF-7 cultured breast cancer cells.

Member of Research Unit of the project granted by Space Agency (Coordinator: Dr. Aldo Mancini, Cancer Institute of Naples, A. Pascale) "From Molecules to Man: Biotechnological Applications of Space Research. Pharmacological countermeasures "on: Prevention and care from the radiation damages through a modified form of Manganese Super Oxide Dismutase (mMnSOD-2) of human origin.

Main fields of interest: Comparative hematology; hematological characterization of the Mediterranean loggerhead *Caretta caretta*; Histology of human endometrial cancer cells and leukemia cells of children, following a treatment with a new anticancer agent; Detection of biomarkers of blood cell damage due to sea water pollution.

Academic activities: Member of Doctorate School in Bioethics; teacher in 1st Level Master in Biotechnology applied to reproduction and repopulation of marine species. School: Mathematics, Physics and Natural Sciences of University of Naples, Federico II; Member of Animal Experimentation Ethics Committee (CESA) of A.O.R.N. "A. Cardarelli" Napoli, Italy; member of Regional Center of Competence for New Technology for Productive Activities: biological and medical imaging; Revisor, Hematology expert, for Comitato di indirizzo per la valutazione della Ricerca (CIVR) MIUR, Italy.

PROFESSIONAL MEMBERSHIPS: Italian Society of Anatomy; Italian Society of Histochemistry; Italian Zoological Society; Italian Group of Neuromorphology; Member of Scientific Committee of C.I.R.U.B. (Centro interdipartimentale per l'ultrastruttura biologica) of University of Naples, Federico II.

AUTHORED BOOK: Erythrocytes of the Poikilotherms: a Phylogenetic Odyssey

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Plenary Lecture 3

Video-Assisted Thoracoscopic Surgery (VATS) – Our 3,000 Cases Experiences, and Future Perspectives



Professor Shi-Ping Luh

Professor of Surgery

Vice Superintendent, St Martin De Porres Medical Center and

National Chiao-Tung University

Taiwan, R.O.C.

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Abstract: Video-assisted thoracoscopic surgery (VATS) has replaced conventional thoracotomy as a standard procedure for some simpler thoracic operations as well as an option or a complementary procedures for some other complex operations. From 1992 to now, about 3,000 cases (not including sympathectomy for hyperhidrosis) have undergone this procedure by my service for the diagnosis and treatment of intrathoracic diseases. My experiences in VATS will be presented. Some specific issues in the application of VATS, which will be very important in the future will be discussed:

1. The role of VATS in the diagnosis and treatment for undetermined pulmonary nodules.
2. The VATS approach of pulmonary sub-centimeter ground glass opacity.
3. Timing of VATS approach for complicated pleural effusions or empyemas.
4. The role of VATS in indeterminate pleural effusions (suspect malignancy).
5. Timing of VATS for primary spontaneous pneumothorax. Choice of VATS for secondary spontaneous pneumothorax and giant bullous emphysema.
6. The VATS approach for spontaneous hemopneumothorax and bilateral lesions.
7. The VATS approach for simple or thymomatous myasthenia gravis (MG), and invasive or metastatic thymomas.
8. Newer instruments and techniques that facilitate the VATS procedures.

Plenary Lecture 4

The Evolution and Future of Magnetocardiography in Identification of Heart Disease-Induced Electrophysiological Changes



Professor Hyun Kyoon Lim

Co-authors: Y. H. Lee, N. S. Chung

Division of Convergence Technology

Center for Emerging Measurement Standards

Korea Research Institute of Standards and Science (KRISS)

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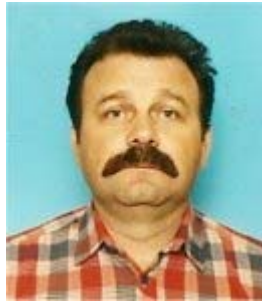
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Abstract: It has been more than 100 years since electrocardiography (ECG) began to be studied, and 60 years since it became a standard of care for patients with cardiac pain. Cardiac electrophysiological information using ECG has provided crucial data for heart disease diagnosis. However, the fundamental principles of ECG have not much changed since that time, and its low sensitivity has been unfavorably contrasted with those of new technologies that provide anatomical or biochemical information. Nevertheless, ECG is still the primary screening tool in the emergency department because no alternative medical device has been demonstrated to provide comparable physiological information directly. Multichannel magnetocardiography (MCG) has recently shown higher accuracy in detecting abnormal cardiac electrophysiology than that of ECG. MCGs are especially known for their superior ability to detect ischemic heart disease and fetal arrhythmias. In this paper, we focus on recent studies, including our own, demonstrating the ability of MCG to detect ischemic heart disease.

Realization of the benefits of MCG, such as its non-invasive and non-contact nature, has been anticipated for more than for 40 years. In addition, its signal is free from sensor artifacts and human organ artifacts including muscles and/or tissues. Regardless of the benefits, few MCG studies were published until the late 20th century for several reasons, particularly its high cost, bulky instrumentation, and difficulty in reading. Recently, MCG studies in the emergency department began to reveal additional crucial information. In particular, MCG showed a higher sensitivity than that of ECG, echocardiography and troponin-I for detecting patients with coronary artery disease, and MCG even predicted high-risk patients with chest pain without ST-segment elevation. We also found a similar diagnostic ability: sensitivity of 86 % and specificity of 75% using a single MCG parameter to detect non ST-segment elevation myocardial infarction (NSTEMI) compared with healthy controls (age-matched). The diagnostic performance to detect NSTEMI versus healthy controls was increased when multiple MCG parameters were used together. The use of magnetic field map pattern analysis and spatio-temporal electrical action graph (STAG) increased our understanding of how electrical conduction patterns were abnormal comparing to those of healthy controls. We were also able to observe consistent results including MCG parameter value change, magnetic field map change, and STAG from an animal model using a pig that had acute occlusion from 0 to over 90% at the middle portion of the left anterior descending (LAD) artery. In addition, an adenosine stress test in angina patients showed similar and significant MCG changes pre and post adenosine injection in several parameters ($p < 0.05$). These favorable study results were facilitated by newly developed computing techniques. In conclusion, MCG may have valuable implications in detecting abnormal cardiac electrophysiology, especially for non ST-segment elevation myocardial infarction patients.

Plenary Lecture 5

Harm-Reduction as Risk Decreasing Strategy in Heroin Dependence



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Abstract: Harm reduction is a relatively new concept in the armamentarium of methods used for decreasing abuse and complications of the drug dependence, in patients who don't actually intend to give up completely their substance use. The main strategies of this intervention are drug substitution with a less dangerous pharmacological agent, information dissemination in consumer communities about long-term negative effects of drug use and possible complications (sexually transmitted diseases, traumatism, death by intoxication) and other strategies like needle-exchange or promoting less aggressive criminalization policies. This strategy tries to reduce the high-risk situations encountered by drug dependent patients and was implemented in several countries from Europe (Great Britain, Holland, Switzerland, Germany) and America (United States, Brazil). Several strategies of harm-reduction are applied also in Romania, in adolescent population, with high risk for overdose and other drug dependence complications. Although at a conceptual level harm reduction seems an interesting and useful approach, there are needed more controlled data in order to verify its efficacy versus other methods.

Brief Biography of the Speaker:

Dr. Daniel Vasile is Associate Professor of Clinical Psychopharmacology at University of Medicine and Pharmacy "Carol Davila", Bucharest and chief of the Clinic of Psychiatry at the University Emergency Central Military Hospital "Dr. Carol Davila", Bucharest, Romania. He is a psychiatrist and psychopharmacologist. He received his M.D. and Ph.D. in medical sciences from the University of Medicine and Pharmacy "Carol Davila", Bucharest and his M.A. from University of Bucharest, Faculty of Sociology and Social Assistance.

Postgraduate work in research and clinic in France, Belgium, Spain, Netherlands, Romania. He published 10 books as first author, regarding drug dependences, psychopharmacology and general psychopathology. 160 papers published in international and national journals of psychiatry and psychopharmacology. Seven of these studies were published in ISI indexed journals (2 in "The World Journal of Biological Psychiatry" and 5 in "The International Journal of Neuropsychopharmacology"). He was distinguished with four awards at international scientific meetings.

He worked in 16 multicentric clinical trials (phase IIa, IIb, III) as Principal Investigator.

Plenary Lecture 6

Malignant Lymphoma Complicated by Gastrointestinal Perforation: Experience of 7 Cases in our Department



Associate Professor Kazuhiko Natori

Co-authors: Haruka Izumi, Susumu Ishihara, Yukitoshi Toyoda, Akiko Shibuya, Yoshinori Fujimoto, Daisuke Nagase, Motohiro Kato, Masanori Umeda, Yasunobu Kuraishi and Kazutoshi Shibuya

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Abstract: Malignant lymphomas frequently invade the gastrointestinal tract, and concomitant perforation often occurs due to the response of the invasive regions to chemotherapy. We encountered 7 patients with malignant lymphoma complicated by gastrointestinal perforation. Herein, we report these cases.

The patients were 5 men and 2 women with a median age of 64 years. The histopathological type was non-Hodgkin's lymphoma in all cases, and the clinical stage was IEA in 1, IIIA in 1, IVA in 1, and IVB in 4. The perforated site was located in the stomach in 2, duodenum in 1, jejunum in 2, and ileum in 2, and emergency laparotomy was performed in 6 cases. The median survival time after perforation was 14 days, showing that the prognosis was very poor.

When gastrointestinal perforation occurs during chemotherapy, the life-saving rate is generally low due to pancytopenia-associated infection and hemorrhage. For surgery in malignant lymphoma patients complicated by gastrointestinal perforation, curative resection is not essential, and initiation of chemotherapy early after surgery is important. Complete resection of the lesion is not always necessary, and a safe surgical procedure prioritizing saving the life should be selected according to the systemic condition.

Plenary Lecture 7

N - Nitrosodiethylamine (NDEA) Genotoxicity in Primary Hepatocytes: Influence of Metabolic Activation by Cytochrome P450



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Abstract: Nitrosamines are converted enzymatically into a methylating agent sparked an interested in the mechanism of carcinogenesis through alkylation of proteins and nucleic acids. The comprehension of formation of N-nitroso compounds from precursors (that are amine and nitrites) common in our environment, including formation in the stomach became clear that many nitrosamines, including a number of suspected carcinogens, could be formed in acid solution. Because of the gastric secretion of hydrochloric acid, the stomach of humans provides a milieu in which nitrosamines could form from ingested nitrite and amines. The more direct source of exposure to N-nitroso compounds is the nitrosamine present in tobacco. Tobacco contains by itself many volatile amines, which are formed by thermal degradation. In addition, tobacco is cured with the aid of nitrates, which become reduced to nitrites and react with nitrosable amines, such as nicotine, to form nitrosamines. Local exposure to nitrosamines present in tobacco is almost causally related to the oral and lung cancer common for tobacco chewers and snuff dippers. During the last few years, there has been a great interest in developing rapid and simple tests to identify the effects of exposure to environmental agents that can induce DNA damage. Drug enzyme induction is usually investigated in animal models by repeated administration of the tested compound, followed by the assessment of the metabolism of a reference compound, or changes in the pharmacological action of a metabolisable drug. Using the methodology described by Eckl and Raffelsberger (1997), in primary hepatocytes cultures, we study cell viability, induction of necrosis and apoptosis, mutagenicity and DNA repair in CYP (cytochrome P-450) pre-induction cultures in the presence of N-nitrosodiethylamine (NDEA), and correlate enzyme expression in rats with that in man, and their potential cancer risk. NDEA is activated by cytochrome P450 enzymes, resulting in ethylation of N and O atoms of most bases from DNA. The N7, and O6 positions of guanine are preferable ethylated, and a lower level of ethylation is also observed at the O4 position of thymine. O6-ethylguanine and O4-ethylthymine, if not repaired, will lead to mutation and tumour formation.

Brief Biography of the Speaker:

Claudia AF Aiub, PhD (doctor in Biology, Area Nuclear Biosciences by Rio de Janeiro State University) is a researcher at Rio de Janeiro State University and professor in Environmental Toxicology, Brazil. Her area of expertise is metabolism of natural products, including endogenous formation of nitrosamines, mutagenesis and carcinogenesis. She is an author of 15 papers and member of Environmental Mutagenesis, Carcinogenesis and Teratogenesis Brazilian Society (SBMCTA), Genetic Brazilian Society (SBG) and Biology Regional Council (CRB). She has an active participation as adhoc reviewer for Toxicology Letters, Marine Drugs, Anais da Academia Brasileira de Ciencias, Genetics and Molecular Biology and, Environmental Toxicology and Pharmacology. She was awarded in 2009- Distinction on Chagas Disease during the 100th anniversary, FIOCRUZ; 2004-Young Investigator Grant, Cancer Research Institute, Cancer Research Foundation, Gregor Mendel/s Genetic Society; 2001-Special Fellow to 8? Internacional Mutagens Congress, in Japan, by Associacao Latino Americana de Mutagenese e Carcinogenese e Teratogenese Ambiental, ALAMCTA and 1998- Young Scientist – Eminence, UFRGS.

Plenary Lecture 8

Efficacy of Anti-VEGF Agents in the Treatment of Age-Related Macular Degeneration



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Abstract: Choroidal neovascularisation (CNV) is a leading cause of loss of central vision in developed countries. The potentially poor natural history of many subfoveal CNV lesions and the limitations of thermal laser photocoagulation for these lesions have prompted the search for alternative treatment modalities, including photodynamic therapy. More recently agents that block the effects of vascular endothelial growth factor (VEGF) have been used to treat CNV secondary to age macular degeneration. Bevacizumab binds all biologically active forms of VEGF, as ranibizumab does.

In this presentation the authors summarize their experience on the treatment of CNV due to age-related macular degeneration (AMD). Also they assess the efficacy of the treatment by means of multifocal-Electroretinogram (mf-ERG) and optical coherence tomography (OCT) before and after the intravitreal injection of bevacizumab and ranibizumab.

Brief Biography of the Speaker:

Marilita M. Moschos graduated the Pharmacy School of the University of Patras and the Medical School of the University of Athens. She is actually working as a senior lecturer of Department of Ophthalmology of Athens University where she has the clinical and scientific co-responsibility of the Laboratory of Electrophysiology of Vision and the department of Glaucoma. She authored or co-authored over 45 scientific papers in pubmed reviewed journals and presented over 60 at international conferences, in some of them as invited speaker. She also wrote the chapter on 'Multifocal-Electroretinogram in retinal vascular diseases' in the annual edition of SFO (Societe Francaise d'Ophthalmologie). Finally she is a member of many international ophthalmological societies and reviewer in several ophthalmological journals, like, Clinical and Experimental Ophthalmology, Expert Review of Ophthalmology, Journal of Neuroscience Methods, Graefe's Archive for Clinical and Experimental Ophthalmology, BMC Ophthalmology, Clinical Ophthalmology, Indian Journal of Ophthalmology and others.

Plenary Lecture 9

The Influence of Aluminum on the Expression of Genes



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Abstract: 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. High aluminum excretion continued for several days after taking aluminum laden analgesics on account of a limiting threshold of renal aluminum excretion. It is widely known that accumulation of aluminum in the body has been linked to disease conditions such as dialysis encephalopathy, renal osteodystrophy, and hypochromic microcytic anemia. Therefore, the influence of a dose of aluminum on gene expression was interested in. It was shown by differential display analysis that aluminum caused up-regulation of eight and down-regulation of five renal genes. Renin was the only positively identified up-regulated gene by DNA sequencing of 13 genes. The up-regulation of renin was confirmed by RT-PCR and Western blotting experiments in the dose dependent treatments and the time course observation after aluminum citrate injection 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.