“Glial Interactions and Brain Experiments”
4th CaribeGLIA Symposium
Organized by Drs. Skatchkov, Eaton, Inyushion and Cubano

Molecular mechanisms of neuron-glial interactions in vivo and in vitro

January 29-31, 2015
San Juan/Bayamón, Puerto Rico
UNIVERSIDAD CENTRAL DEL CARIBE
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Serguei Skatchkov

Seminar Title:

Polyamines and Brain Signaling

Biography:

Serguei N. Skatchkov, the organizer of the CaribeGLIA symposium, is the Director of the Integrative Center for Glial Research in Puerto Rico and Professor of Biochemistry and Physiology, School of Medicine, Universidad Central del Caribe (UCC), Bayamon, PR, USA. He obtained his rank of Distinguished Research Professor in 2011 after remarkable achievements in glial biology and teaching at the UCC.

He studied chemistry, biology, biophysics and physiology at the Leningrad (Saint Petersburg) State University (LGU), received his PhD degree in Biophysics there in 1990. He has started his research on phototransduction in rod and cone photoreceptor cells and on the role of Müller glial cells in retinal potassium homeostasis in 1979 together with Drs. A.V. Dmitriev, K. A. Bykov and V.I. Govardovsky (his name was spelled Sergey N. Skachkov in his earlier articles). After visiting (1992-1993) the Institute of Brain Research at Leipzig University, Germany (C/O Dr. Andreas Reichenbach) and collaborating at the Institute of Neurobiology in Puerto Rico (C/O Dr. Richard Orkand during 1993-1996), he decided to permanently reside in the Caribbean and started his research group focused on “Polyamines and Glial Signalling” at the UCC, School of Medicine, in Bayamón, PR, USA. In 2007 he with his colleagues was awarded the Cozzarelli Prize from the National Academy of Sciences (PNAS Office) for the discovery of a new function of glial cells as light cables.

In 2009, he was appointed as full professor at the Universidad Central del Caribe. From 2009-2013 he has collaborated as the Expert Visiting Scientist for the International program “EduGLIA” being associated with Drs. Alexej Verkhratsky, Andreas Reichenbach, Eva Sykova, Arthur Butt, Menachem Hanani, Frank Kirchhoff and many others. He has given more than 60 oral presentations internationally and has obtained several grants. He has been an invited reviewer for such journals as PloS ONE, PloS Biology, Cell. & Mol. Neurobiol., J. Neurosci. Lett., NeuroReport, J. Neurosci. Res., Cell Death & Disease (Nature Publishing Group) and others.

He is a co-author of several reviews and book chapters on glial cell function and pathology and his research addresses the ionic, molecular and cellular mechanisms of glial cell behavior and signaling using different models and techniques. The main questions his work addresses are: (i) What are the mechanisms of light propagation in glial cells? (ii) How do glia but not neurons accumulate polyamines? (iii) How do polyamines function as new glial mediators? (iv) Why do interneurons and pyramidal cells respond differently to polyamine signals released from glia? (v) How do glial polyamines modulate neuronal networks and (vi) how does polyamine homeostasis participate in trauma, diseases and aging in CNS?

His work is supported by grants from NIH (NINDS, NIGMS, NIMHD).

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Alexej Verkhratsky (coming Jan 24-31)

Seminar Title:
Astroglial reparation as a way to brain longevity

Biography:
Professor Alexei Verkhratsky, MD, PhD, D.Sc., Member of Academia Europaea, Member of the German National Academy of Sciences Leopoldina, Member of Real Academia Nacional de Farmacia of Spain, graduated from Kiev Medical Institute in 1983, and received PhD (1986) and D.Sc. (1993) in Physiology from Bogomoletz Institute of Physiology, Kiev, The Ukraine. From 1990 to 1995 A. Verkhratsky was Head of Laboratory of Cellular Signalling in Bogomoletz Institute of Physiology. In 1992 - 1995 he also was a Deputy Director of the International Centre of Molecular Physiology, Kiev, The Ukraine. Between 1989 and 1995 he was visitor scientist in Heidelberg and Gottingen, and between 1995 and 1999 he was a Research Scientist at Max Delbrück Centre of Molecular Medicine in Berlin. He joined the Division of Neuroscience, School of Biological Sciences in Manchester in September 1999, became a Professor of Neurophysiology in 2002 and served as Head of the said Division from 2002 to 2004. From 2007 to 2010 he was appointed as a visitor professor/Head of Department of Cellular and Molecular Neurophysiology at the Institute of Experimental Medicine, Academy of Sciences of Check Republic. In 2010 A. Verkhratsky was appointed as a Research Professor of the Ikerbasque (Basque Research Council), in 2011 as a Honorary Visitor Professor at Kyushu University, Fukuoka, Japan and from 2012 he acts as Adjunct Scientific Director of the Achucarro Basque Center for Neuroscience (Bilbao, Spain).


Prof. Alexei Verkhratsky is an internationally recognised scholar in the field of cellular neurophysiology. His research is concentrated on the mechanisms of inter- and intracellular signalling in the CNS, being especially focused on two main types of neural cells, on neurones and neuroglia. He made important contributions to understanding the chemical and electrical transmission in reciprocal neuronal-glial communications and on the role of intracellular Ca2+ signals in the integrative processes in the nervous system. Many of A. Verkhratsky’s studies are dedicated to investigations of cellular mechanisms of neurodegeneration. A. Verkhratsky was the first to perform intracellular Ca2+ recordings in old neurones in isolation and in situ, which provided direct experimental support for “Ca2+ hypothesis of neuronal ageing”. In recent years he studies the glial pathology in Alzheimer disease. He authored a pioneering hypothesis of astroglial atrophy as a mechanism of neurodegeneration.

Scientometry: Prof Verkhratsky authored and edited 11 books and published more than 300 papers and chapters. His papers were cited ~11000 times, H-index 61 (ISI, 2014).

Webs:
http://www.ikerbasque.net/alexei.verkhratsky;
http://www.ls.manchester.ac.uk/people/profile/?alias=verkhratskya;
http://www.manchester.ac.uk/research/alexej.verkhratsky/publications

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Seminar Title:

Age-related changes in neuroglial communication in neocortex: implication to synaptic plasticity.

Biography:

Dr Ulyana Lalo, Senior Research Fellow at the School of Life Sciences, Warwick University, graduated from Moscow Institute of Physics and Technology in 1992. She studied calcium signalling and mastered ‘patch clamp’ methods in the famous laboratories of Prof. Kostyuk and Prof. Kryshtal in Bogomoletz Institute of Physiology, Kiev, Ukraine, where she obtained her PhD (1999) in Biophysics.

She moved to England in 2003 to join the lab of Professor R.A. North in the University of Sheffield and, later, in Manchester. Ulyana’s work was focused on molecular physiology of ATP and glutamate receptors and role for ATP in glial signalling and glia-neuron interactions. Among her main achievements are: finding functional P2X and P2Y receptors in the neocortical neurons; discovery of the lack of Mg$^{2+}$ block of astrocytic NMDA receptors; the first evidence of functional P2X receptors in cortical astrocytes which have a different subunit composition and higher affinity to ATP than those in neurons. These results give a new insight on role of P2X and NMDA receptors in the fast astroglial signalling and neuron-glial communication in the brain.

Ulyana studied molecular physiology of purinoreceptors in the Prof. R. Evans lab, University of Leicester 2007-2011 where she mastered molecular biology techniques, confocal imaging, FRAP. Using GFP tagged P2X receptors she found that their mobility and turn over are sensitive to disruption of lipid rafts and inhibition of polymerization of actin cytoskeleton. She also has shown that inhibitors of molecular chaperone heat shock protein 90 reduced mobility of selective P2X receptors and reduced their cell surface expression.

In 2013, she was appointed at the University of Warwick as a Co-Investigator on project funded by BBSRC UK. In recent years, Ulyana was engaged in the study of role for astrocytes in brain ageing with particular focus on age-related changes in Ca2+-dependent gliotransmission and its impact on synaptic plasticity.

Ulyana is an invited reviewer for Cell Calcium, Cell Death and Disease, British Journal of Pharmacology, Brain Research.

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Robert Zorec* (coming Jan 27-31)

Seminar Title:

Physiopathology of vesicle dynamics in astrocytes

Biography:

Robert Zorec is Professor of Pathophysiology at the University of Ljubljana, Medical Faculty, a Full Member of Academia Europaea (London) and Slovenian Academy of Sciences and Arts (cont. of Academia Opereorum Labacensis from 1693), as well as a Member of the Committee for Advanced Medical Products at the European Medicine’s Agency (London). Dr. Zorec received his Ph.D. from the University of Ljubljana in 1986 for his work conducted at the Newcastle Medical School and at the MRC Neuroendocrinology Unit in Newcastle upon Tyne, U.K, and introduced the “patch-clamp” method in Ljubljana in 1985. Dr. Zorec's postdoctoral experience was at Cambridge in Dr. W. T. Mason's laboratory. Further, independently of the laboratory of the Nobel Laureate Erwin Neher, he developed his own membrane capacitance measurements (MCM) to monitor processes such as endo-and exocytosis in real time. In Prof. M. Berridge's laboratory at the Cambridge University, he studied cytosolic calcium homeostasis by the imaging related to MCM approach. He also worked in Dr. R.N. McBurney's laboratory studying single channel chloride currents activated by GABA and glycine in spinal cord neurons. In 1991 he was conducting experiments on plant secretory cells at the University of Adelaide, Australia and his MCM technique rounded up by the papers in Nature Protocols in 2013 (8:1169) and in Nature Communications in 2014 (5:3780), focusing into the mechanisms of regulated exocytosis in endocrine pituitary cells, plant cells, hepatocytes, adipocytes, skeletal muscle, taste cells, neurons and glia. Since 1991 he has been the Head of Laboratory of Neuroendocrinology-Molecular Cell Physiology and in 1997 he received the Republic of Slovenia Prize for Science. In 2000 he established the Cell Engineering Laboratory at the Celica Biomedical center, Ljubljana Tech Park (http://celicabiomedical.com/) where he has been a CEO since 2006 and the head of the Carl Zeiss Reference Center for Confocal Microscopy. During the last 15 years he developed research on astrocytes, the most abundant glial cells in the brain, to learn how vesicle traffic and regulated exocytosis is altered in these cells under pathological conditions, specifically related to the mechanisms of cytotoxic edema and astroglial scarring in the acute and chronic trauma.

In addition to MCM, Dr. Zorec developed Super-Resolution Fluorescence Microscopy to study subcellular vesicle traffic and collaborates with wide circle of scientists such as Drs. B. Betz, M. Kreft, B. J. Teng, N. Vardjan, V. Parpura, M. Potokar, A. Araque, G. Carlingnot, A. Verkhratsky, P. Haydon and has published over 155 peer reviewed papers. He has lectured at over 100 distinguished Universities, International Meetings and Research Institutions worldwide. He has been a reviewer for leading scientific journals including Nature, Science, PNAS, J. Neurosc., J. Physiol., Biophys J., Brain Res. and others.

Recently, together with Dr. Teng from Harvard he found a robust new endogenous mechanism of cytotoxic edema reduction in astrocytes, which leads to new paradigms of treatment of CNS trauma. Importantly, not only in trauma, astrocytes also play a pivotal role in neuron-glia signaling in other pathological conditions and represent a target for new therapeutics including those for regeneration to be developed in the future for neurological diseases. In addition to basic research focusing into physiological and pathological problems, the lab is also developing advanced cell-based medicines such as hybridoma cells to treat cancer.

His work was and is supported by different grants from EU and other countries (the British Council and The Wellcome Trust Fellowships, Fulbright Scholarship, Research Council of Slovenia, Nuffield Foundation, EduGLIA, NIH).

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Liliya Vitanova* (coming Jan 25-Feb 1)

Seminar Title:
Membrane Receptors in the Retinal Glia of Lower Vertebrates (Immunofluorescent Study)

Biography:

Liliya Vitanova is a Professor at the Department of Physiology, Medical University, Sofia, Bulgaria-EU. She graduated medicine in 1973 and received her MD from Medical University Sofia. Immediately after this she started her scientific and teaching career as Assistant Professor at the Department of Physiology, Medical University Sofia. In 1982 she obtained her PhD at Pavlov's Institute of Physiology, St. Petersburg, Russian Academy of Sciences and in 1993 became Associate Professor at the Department of Physiology, Medical University, Sofia.

Liliya Vitanova obtained extensive training at the Visual Lab, Pavlov’s Institute of Physiology, Russian Academy of Sciences, St. Petersburg during 1978–1982 and at the Biophysics of Receptors Lab, State University of St. Petersburg in 1988. In Great Britain she was trained at the Neurobiology Lab, Imperial College, London in 1993. In the period 2000 - 2003 she worked for several months at the Neuroanatomy Lab, Max-Planck-Institute of Brain Research in Frankfurt/Mein, Germany.

In 2006, Dr. Vitanova defended Doctor of Science dissertation (DSc) at the Medical University and in 2008 she achieved full Professor level at Dept. Physiology, Medical University Sofia.

Vitanova’s teaching activities covers the whole course of Physiology, including Neurosciences, for medical, dental medical and pharmacy students. Her major scientific projects are related to processing the information in visual cortex, and the synaptic transmission in the retina. Her studies on the participation of different neurotransmitter systems (glutamate, gamma-aminobutyric acid - GABA, glycine etc.) in the intensity and colour coding and the contrast sensitivity of the lower vertebrate retina are ones of the first in this region. She performs and teaches in electrical activity of the distal and proximal retina, as well as in immunocytochemistry of the retinal neurotransmitters and membrane receptors. In the immunocytochemical Lab in Sofia, established by the support of Max-Planck Foundation, Vitanova’s group studies the neurotransmitters and their receptors in lower vertebra tes retina. The results concerning the glial localization of glutamate (AMPA, NMDA), and purines P2X receptors as well, are the first in this region.

Dr. Vitanova is a member of the Bulgarian Society for Physiological Sciences, the Bulgarian Neuroscience Society and the Society of EEG and Clinical Neurophysiology. Since 2011, she is President of the Bulgarian Society for Physiological Sciences.

Her work is supported by different grants from Bulgaria and EU.

For more information about Dr. Vitanova at: http://www.vision-research.eu/index.php?id=152
and
http://medfac.mu-sofia.com/kf/?q=node/134

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Phone: + 3592 9172544 and + 3592 9172543; Fax:+35929520345
Victor Arvanian (coming Jan.26-Feb.1)

Seminar title:

Search and neutralize the glial scar-related inhibitory factors in damaged spinal cord to improve transmission and function.

Biography:

Victor Arvanian (former Arvanov) is a Research Professor and Project Director at Northport VAMC and Stony Brook University, New York. Current Research Focus of his laboratory: (1) Cellular, molecular and genetic aspects of neural plasticity in damaged CNS. (2) Understanding mechanisms (including role of various glial cells), underlying diminished transmission through the spared fibers in damaged spinal cord. (3) Based on this knowledge, design and develop novel gene therapy and activity-based treatments with potential to promote plasticity, strengthen synaptic connections and improve function after spinal cord injury (SCI) and traumatic brain injury (TBI) in adult mammals. To approach these goals, Dr. Arvanian established an international team of collaborators. He still conducts experiments himself, in addition to supervising research work of his laboratory.

He obtained degrees in biophysics: MS (1975, from the Tbilisi State University, Georgia), PhD (1981, from Academy of Sciences of Armenia), and D.Sc. (1990, from Bogomoletz Institute of Physiology, Kiev, Ukraine). 1990-1992: Guest Research Fellows Award from the Royal Society London, collaboration with Dr. Robert Walker (Southampton) and Dr. Peter Usherwood (Nottingham, UK). 1992 – 1993: Visiting Professor at National Taiwan University. In 1993 he with family moved to New Zealand and then to USA to “look for new beginnings”. 1993-1994: Research Scientist, UTMB Galveston Texas. 1994-current: Stony Brook University, NY: Research Assistant Professor > Research Associate Professor > Research Professor. 2000-2008: Group head within laboratory of Dr. Lorne Mendell and Associate member at the Christopher Reeve and Dana Foundation. 2008 – current: Head of laboratory, Project Director and SRS Chair at Northport VAMC.

Recent Awards and Honors. One paper [Schnell et al., & Arvanian (senior and corresponding author), 2011] describing novel combination treatment that induced formation of novel detour functional connections around the lesions in damaged spinal cord following SCI has been awarded by the Forum of European Neuroscience as the “Best research paper of 2010-2013”. His scientific achievements have been highlighted and awarded by the Army and Congressionally Directed Medical Research Programs (10/5/2012 and 8/9/2013). Dr. Arvanian has been invited as Keynote speaker at several domestic and international scientific meetings, including 4th CaribeGLIA Symposium.

He is internationally recognized and one of the leading scientists in the field of spinal cord neurophysiology. Current goals are to translate into clinical applications a set of treatments that have been developed through animal studies in Arvanian laboratory. Since year 2000 to current his research has been continuously funded, including awards from the Department of Veterans Affairs, Department of Defense, Craig Nielsen Foundation, etc.

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Fax: (631) 544-5317
Email: victor.arvanian@va.gov or victor.arvanian@stonybrook.edu
Alexander Mongin (coming Jan.29-Feb.2)

Seminar Title:

**GLIAL VOLUME-REGULATED ANION CHANNELS IN HEALTH AND DISEASE: New molecular insights on swelling-activated and agonist-induced release of gliotransmitters in astrocytes and microglia**

Biography:

Alexander A. Mongin is an Associate Professor in the Center for Neuropharmacology and Neuroscience at Albany Medical College (AMC, Albany, NY). He graduated from the Belarusian State University (Minsk, Belarus) with M.S. degree in Biochemistry in 1989, and received Ph.D. degree in Biophysics from the National Academy of Sciences of Belarus (NASB, Minsk, Belarus) and Moscow State University (Russia) in 1995. Dr. Mongin's Ph.D. work was focused on regulation of cell volume and K⁺ transport in astroglial cells. In 1997 Dr. Mongin was awarded John E. Fogarty International Research Fellowship to continue and expand his studies in the laboratory of Prof. Harold Kimelberg at AMC. After completion of Fogarty Fellowship, Dr. Mongin accepted a faculty position in the AMC’s Center for Neuropharmacology and Neuroscience, where he continues to work at the present time.

The interests of Dr. Mongin and his colleagues revolve around complex roles of the non-excitable cells in the brain – glia – in normal brain functioning and neurological disorders. By employing molecular biology, cell physiology, and in vivo techniques, Dr. Mongin's laboratory explores how astrocytes and microglia modulate neuronal communication and contribute to progression of neurological conditions, such as stroke, traumatic brain injury, hyponatremia, and others.

The major recent findings of this group include: (i) identification of the molecular nature of glial glutamate-permeable, volume-regulated anion channel (VRAC), (ii) elucidation of intracellular mechanisms governing activity of VRAC in glial cells, (iii) discovery of effects of oxidative stress on VRAC and glutamate release in vitro and in vivo, (iv) association of oxidative stress and glutamate release in stroke, (v) characterization of the impact of cellular swelling on brain glutamate-glutamine cycle, and (vi) exploration of critical role of Ca²⁺-sensitive K⁺ and anion channels in malignant astroglia, which give a rise to the most dangerous brain tumor, glioblastoma multiforme or GBM.

Current research in Dr. Mongin’s laboratory is funded by the National Institute for Neurological Disorders and Stroke (NIH), and the American Heart Association.

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Web: http://www.amc.edu/Research/CNN/cnnresearcher.cfm?ID=141
Min Zhou (coming Jan.29-Feb. 2)

Seminar Title:  
**mGluR3 activation regulates TWIK-1 membrane expression in hippocampal astrocytes**

Biography:  
Dr. Min Zhou is an **Assistant Professor of the Department of Neuroscience**, The Ohio State University, School of Medicine, Columbus, OH, USA. Dr. Zhou received his MD from Tongji Medical College, Wuhan, China and PhD in Neurophysiology, Friedrich-Shiller-University Jena, Germany. He accomplished his post doctoral training at Albany Medical College with Dr. Harold K. Kimelberg, where he was also appointed as an Assistant Professor. He later moved to the Ordway Research Institute, Albany, USA where he served first as a Staff Scientist then Senior Staff Scientist. In 2011, he transitioned to The Ohio State University at the current position.

Dr. Zhou's current research project studies the expression and function of two-pore domain K+ channels (K_2P) in astrocytes. K_2Ps are newly appreciated potassium channels that can interact with and be substantially modulated by a variety of physiochemical stimuli. Following our recent observation of rat hippocampal astrocytes expressing K_2P isoforms of TWIK-1 and TREK-1, the continuing research examines the unique features of K_2Ps enabling astrocytes to maintain brain homeostatic function and subserve neuronal function with high efficiency. The ongoing projects address 1) the biophysical features of K_2Ps of astrocytes in brain slices as well as expression system; 2) crosstalk of astrocyte K_2Ps with neurotransmitters and its impact on astrocyte homeostatic function, and 3) interaction of K_2Ps and gap junction channels that in turn regulates the communication of astrocytes in their network.

Dr. Zhou is also interested in the role of astrocyte K_2Ps in stroke pathology. His laboratory studies the K_2Ps mediated mechanisms that protect astrocytes surviving through the early cerebral ischemic attack, the role of K_2Ps in the process of induction of reactive astrocytes in stroke brain, and the potential role of altered K_2Ps in reactive astrocyte in the post-stroke recovery of neuronal function.

Astrocyte is the most populous cell type in the brain. The goal of our research aims at unveiling the mysterious function of astrocytes and identifying glia-oriented therapeutic strategy for stroke treatment.

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E-mail: zhou.787@osu.edu  
Web: http://medicine.osu.edu/neuroscience/people/faculty/min-zhou-m-d-ph-d/pages/index.aspx
Timothy Hendricks

Seminar Title

Is astrocyte diversity determined by a developmental genetic program?

Biography

Timothy Hendricks is a Research Professor at Inter American University of Puerto Rico, Bayamón campus, a position he has held since 2011. He studied Biomedical Engineering at Johns Hopkins University where he started his research career as an undergraduate in the area of biosensor design. Dr. Hendricks earned his Ph.D. in Neuroscience at Case Western Reserve University in 2003. His thesis work led to the identification Pet-1 as a central genetic determinant for all mammalian serotonergic neurons in the CNS. Behavioral analysis of Pet-1 deficient mice demonstrated marked elevation of both anxiety and aggression.

Dr. Hendricks then joined the laboratory of Dr. Martyn Goulding at the Salk Institute where as a postdoc he studied the genetic origins of interneurons diversity in the murine spinal cord. His work led to the identification of previously unknown molecular subtypes of interneurons and helped to reveal the precise temporal control of gene expression during neurogenesis.

Since starting his laboratory at Inter American University he has demonstrated a key role for the transcriptional regulator Wt1 in the development of a genetic subclass of inhibitory commissural interneurons in the mammalian central pattern generator (CPG). For the future he is interested in studying the gene expression dynamics during gliogenesis to understand the origins of phenotype diversity in astrocytes.

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Colin Nichols* (coming Jan.29-Feb.2)

Seminar Title

“Neuro-glio-vascular KATP: Some new insights and ideas”

Biography

Dr. Colin Graham Nichols, is the Carl Cori Endowed Professor, and Director of the Center for Investigation of Membrane Excitability Diseases at Washington University in St. Louis, Missouri, elected a Fellow of the Royal Society (FRS) in 2014.

Dr. Nichols was awarded a B.Sc. degree in Biochemistry and Physiology (1982), followed by a PhD (1985) for research on cardiac muscle in mammals supervised by Brian R. Jewell and has completed his postdoctoral research at the University of Maryland, College Park in the laboratory of W. Jonathan Lederer. He was appointed Assistant Professor at Washington University School of Medicine (1991), Full Professor (2000) and the Carl Cori Endowed Professor in 2006.

Colin Nichols is distinguished for his contributions to our understanding of cellular excitability and its role in disease. He was instrumental in cloning the first inward rectifier channel and the regulatory subunit of the KATP channel. He elucidated the mechanism of inward rectification, generated new insights into lipid regulation of ion channel function, determined the physiological role of cardiac KATP channels and identified one type of congenital hyperinsulinism. Animal models that he generated predicted the mechanism of human neonatal diabetes, and ultimately helped enable patients to switch from insulin injections to oral drug therapy.

Prof. C.G. Nichols research investigates the biology of ion channels, particularly potassium channels, and their role in diabetes mellitus, cardiac dysrhythmias and epilepsy. Nichols uses models to investigate the structure, function and regulation of ion channels, which control what cells do by controlling their electrical polarity.


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Maria Remedi * (coming Jan.29-Feb.2)

Seminar Title

“KATP channels: Linking metabolism to excitability in diabetes and epilepsy”

Biography

Dr. Maria S. Remedi, is an Assistant Professor in the Department of Cell Biology and Physiology and a member of the Center for Investigation of Membrane Excitability Diseases at Washington University School of Medicine in St. Louis, Missouri, USA.

Dr. Maria S. Remedi accomplished her education with M.S. in Biochemistry (1987) and M.S. in Pharmacy (1989), National University of Cordoba, Argentina and obtained her Ph.D.in Chemical Sciences, School of Chemical Sciences, National University of Cordoba, Argentina. Dr. Remedi performed Postdoctoral training in the Department of Biological Chemistry, School of Medicine, National University of Cordoba, Argentina, and in the Department of Cell Biology and Physiology, Washington University School of Medicine in St. Louis.

Dr Remedi’s primary interest and funding are for K_ATP channels, which constitutes a critical link between glucose metabolism and insulin secretion in pancreatic β-cells. In humans, K_ATP gain-of-function (activating) mutations in both K_ATP subunits (Kir6.2 and SUR1) underlie Neonatal Diabetes Mellitus (NDM). NDM is a disease characterized by persistent hyperglycemia presenting in the first six months of life. In contrast, K_ATP loss-of-function mutations cause congenital Hyperinsulinism of Infancy (HI), a rare disease characterized by high insulin levels in parallel with low blood glucose. The manipulation by gene transfer of ion channels in pancreatic β-cells or the use of transgenic animals models that Dr. Remedi and colleagues generated (mice which overexpress, underexpress or have mutations in the K_ATP) give the exciting possibility to explore in more detail the consequences of K_ATP channel alterations in the development of NDM, HI and type-2 diabetes.

On the other hand, a hypo- or hyper- glucose level(s) are very critical for brain function. Hyperinsulinemia can precede the development of diabetes and, interestingly, many HI patients can cross-over to a diabetic phenotype in later life. Type-2 diabetes requires interaction of genetic and environmental factors (i.e. obesity) for its development, therefore, Dr. Remedi is studying the consequences of high-fat feeding on diabetic or hyperinsulinemic transgenic mice. She directly examined the temporal progression of β-cell function and the contribution of genetic and environmental factors in the development of these diseases. In a mouse model of K_ATP-induced NDM, Dr Remedi study not only factor/s involved in the development of the disease, but also the mechanism/s underlying long-term secondary consequences of diabetes. Her recent findings demonstrate β-cell dedifferentiation to progenitor cells in severe diabetes, and re-differentiation to mature β-cells following normalization of blood glucose by insulin therapy. These findings may explain secondary loss of β-cell mass in diabetes and point the way to novel strategies to manipulate this process in humans.

Recently, Dr. Remedi developed an interest to study role and consequences of K_ATP channels in the brain. In the most severe cases of human NDM induced by K_ATP mutations, the patients demonstrate developmental delay and epilepsy in addition to neonatal diabetes (DEND syndrome). By expression of K_ATP mutations in neurons and glia, Dr Remedi is studying the consequences of altered K_ATP channels in the development of the brain features in DEND. Better understanding of key signaling cascades involved in diabetes and brain disorders will be of interest not only for the development of these diseases, but may also contribute to the understanding of other diseases induced by altered K_ATP channels in these tissues.

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