

## The Third International Symposium on

## Sigma-2 Receptors: Role in Health and Disease

November 3, 2018 San Diego, CA

### The Third International Symposium on Sigma-2 Receptors: Role in Health and Disease

Sigma-2 receptors have been implicated in central nervous system disorders ranging from anxiety and depression to Alzheimer's disease. This satellite symposium will review the role of the sigma-2 receptor in the neurobiology of health and disease and will examine controversies still present in this emerging field.

At Cognition Therapeutics, we are leveraging our understanding of the role the sigma-2 receptor plays in the pathology of Alzheimer's disease to develop CT1812 (Elayta<sup>™</sup>), a sigma-2 antagonist. By sponsoring this satellite symposium, we encourage researchers to share their findings with the larger neuroscience community and spur further growth in this area.

Sincerely,

Susa Catelan

Chief Science Officer Cognition Therapeutics, Inc.

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Principal Scientist Cognition Therapeutics, Inc.

### The Third International Symposium on Sigma-2 Receptors: Role in Health and Disease

When: 9:00am - 12:00pm on Saturday, November 3, 2018 Where: The Big Island Room of Roy's Restaurant, San Diego, California

#### AGENDA:

Each presentation will be allotted 10 minutes followed by 5 minutes of Q&A

Introduction	Susan Catalano, Ph.D. Cognition Therapeutics
Differential Sigma-2 Receptor/TMEM97-Mediated Cytotoxic and Metabolic Stimulative Properties of Monovalent and Bivalent SN79 Analogs	Wayne D. Bowen, Ph.D. Brown University
Targeting Sigma-2 Receptor (σ2R)/TMEM97 to Address Unmet Medical Needs in Neuroscience	Stephen F. Martin, Ph.D. University of Texas at Austin
Sigma 2 Receptor-Interacting Protein PGRMC1 is Descended from the Hopanoid Synthetic Pathway of the Endosymbiotic Proto-Mitochondrion	Michael A. Cahill, Ph.D. Charles Sturt University
Let7i as a Key Regulator of PGRMC1 and Progesterone-Induced Neuroprotection	Meharvan Singh, Ph.D. UNT Health Science Center
Clinical Evidence of Synaptic Protection in Alzheimer's Patients following Treatment of CT1812	Susan Catalano, Ph.D. Cognition Therapeutics
Sigma-2 Antagonist CT1812 Protects Synapses from Abeta Oligomer-Induced Loss, In Vitro	Nicholas J. Izzo, Ph.D. Cognition Therapeutics
<b>KEYNOTE ADDRESS</b> : APOE4 Associated Changes in the Synaptic Proteome in Human Alzheimer's Disease Brain	Tara Spires-Jones, DPhil University of Edinburgh, UK
The Essential Role of Sigma-2 Receptor/TMEM97 and Progesterone Receptor Membrane Component 1 in the Internalization of Low-Density Lipoprotein via and Interaction with the Low-Density Lipoprotein Receptor	Aladdin A. Riad, Ph.D. University of Pennsylvania
A Novel Mechanism Underlying Synaptic Plasticity: Roles for PGRMC1 and TMEM97?	Timothy E. Kennedy, Ph.D. McGill University, Montreal
Biological Roles of TMEM97 and PGRMC1 in Cell Growth and Sigma-2 Ligand- Induced Cell Death	Chenbo Zeng, Ph.D. University of Pennsylvania
Identification of a Second [ <sup>3</sup> H]DTG Binding Site on TMEM97-KO Cell Membranes	Robert H. Mach, Ph.D.

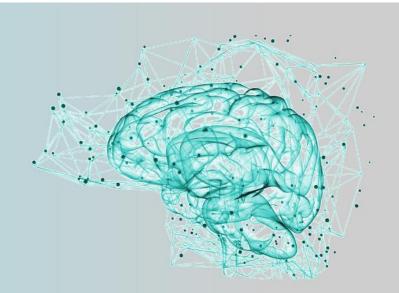
Following the satellite symposium, please join your colleagues in the 1:00-5:00pm poster session (Session 045.08) at Neuroscience 2018

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# **SPEAKER BIOS**



Wayne D. Bowen, Ph.D. Upjohn Professor of Pharmacology Professor of Biology Chair of the Department of Molecular Pharmacology, Physiology & Biotechnology Brown University

A nationally recognized leader in research on sigma receptors, Wayne Bowen, Ph.D. is generally credited with the discovery and initial characterization of the sigma-2 receptor. He has shown that activation of sigma-2 receptors induces apoptotic cell death and therefore they may serve as regulators of cell proliferation and survival. He has most recently provided evidence that sigma-2 receptors may play a role in metabolic regulation in cancer cells. Trained initially as a chemist, Dr. Bowen maintains a strong interest and involvement in medicinal chemistry and drug design, particularly in relation to the development of selective sigma receptor agonists and antagonists. He is exploring these compounds as potential anti-neoplastic, tumor diagnostic and neuroprotective agents.

Dr. Bowen co-directs the core pharmacology course for the molecular pharmacology and physiology (MPP) graduate program at Brown. In addition, he contributes to endocrinology and neuroscience courses for Brown University undergraduates. He has served as chair of the department of molecular pharmacology, physiology and biotechnology since 2007.

Dr. Bowen is a member of the Society for Neuroscience, the International Brain Research Organization/World Federation of Neuroscientists and the American Association for Cancer Research. He is the recipient of numerous awards and honors and has performed service on NIMH and NIDA Study Sections. Dr. Bowen's research has been funded by NIDA, NINDS, NIDDK, the Rhode Island Science and Technology Advisory Council and a Salomon Award from Brown University.







Michael A. Cahill, Ph.D. Lecturer in Biochemistry and Cell Biology Charles Sturt University New South Wales, Australia

Michael Cahill, Ph.D. joined Charles Sturt University in 2008 and serves as a lecturer in biochemistry and molecular cell biology at the School of Biomedical Sciences. In 2016, Dr. Cahill was elected to the CSU Academic Senate, the university's highest level of academic decision making and quality assurance.

Prior to his academic appointment in Australia, Dr. Cahill spent 18 years in Germany where in 2000 he co-founded a proteomics-based biotechnology company with the goal of developing and commercializing a platform for improved protein detection. In 2001, the firm underwent a corporate merger to form ProteoSys AG, where he served on the managerial board and as chief research officer. At ProteoSys, Dr. Cahill directed the team that discovered differential PGRMC1 phosphorylation in cancer, a discovery that led to several patent applications. Dr. Cahill returned to his native Australia to pursue the characterization of PGRMC1 in a university environment and has advanced this research during his academic tenure. At CSU, his research interests revolve around the role of the PGRMC1 protein in cell biology and cellular metabolic regulation.

In addition to his research responsibilities, Dr. Cahill is a member of the Australian Society for Biochemistry and Molecular Biology (ASBMS) and a member of the Cognition Therapeutics, Inc. scientific advisory board. He is currently a development grant commercial expert reviewer and a project grant reviewer for the National Health and Medical Research Council (NHMRC), Australia's premier funding body for medical research.





**Susan Catalano, Ph.D.** Chief Science Officer and Founder Cognition Therapeutics, Inc.

Susan Catalano, Ph.D. is the founder of Cognition Therapeutics and architect of its discovery, preclinical and clinical science. Leveraging her 15 years of industry experience, she and her team discovered and developed the company's drug candidate, CT1812, and advanced it into clinical testing for the treatment of patients with mild-to-moderate Alzheimer's disease.

Prior to founding Cognition Therapeutics, Dr. Catalano was director of discovery biology for Acumen Pharmaceuticals, leading the team that discovered some of the industry's first drug candidates targeting A $\beta$  oligomers. Prior to this, at Rigel Pharmaceuticals, she led the team that pioneered the use of phenotypic screening to discover the Aurora kinase inhibitor R763, which was later licensed to Serono for use against solid tumors. While a scientist at Roche Palo Alto, she led the neurophysiology and neuroimaging groups along with an exploratory program in psychiatric disorders.

Dr. Catalano received her B.A. from Barnard College and Ph.D. from U.C. Irvine, with postdoctoral training at U.C. Berkeley and Caltech. She also holds an adjunct appointment at the University of Pittsburgh School of Medicine. She is an EY Entrepreneurial Winning Women class of 2015 recipient.





**Nicholas J. Izzo, Ph.D.** Principal Scientist and Director of Screening Cognition Therapeutics, Inc.

Nicholas Izzo, Ph.D. is a research biologist with expertise in cell-based assay development and drug discovery. He joined Cognition Therapeutics, Inc. in 2009, where he now leads the company's efforts to develop small molecule drug candidates for the treatment of mild-to-moderate Alzheimer's and other neurodegenerative disorders.

Together with Dr. Susan Catalano and colleagues, Dr. Izzo authored the two seminal papers elucidating the role of the sigma-2/PGRMC1 receptor complex in A $\beta$  42 oligomer binding and synaptotoxicity, and the identification of small molecule antagonists to this receptor complex that displace A $\beta$  42 oligomers, improving cognitive deficits.

Dr. Izzo is a member of the Society for Neuroscience. He earned a B.S. in chemistry from Georgetown University and a Ph.D. in pharmacology from the University of Virginia. He conducted post-doctoral training at Brigham and Women's Hospital and Harvard Medical School.



### Timothy E. Kennedy, Ph.D.



co-Director, McGill Program in Neuroengineering Professor, Department of Neurology and Neurosurgery Professor, Department of Anatomy and Cell Biology Montreal Neurological Institute McGill University, Montreal, Quebec, Canada

Timothy Kennedy, Ph.D. joined McGill University in 1996, where he is a full professor in the departments of neurology and neurosurgery and anatomy and cell biology, and co-director of the McGill Program in NeuroEngineering.

Dr. Kennedy's laboratory at the Montreal Neurological Institute investigates the molecular mechanisms that regulate cell movement and cell-cell interactions in the mammalian central nervous system. Ongoing studies are investigating the biochemical mechanisms that regulate synaptogenesis, synapse maintenance and plasticity, and myelination. A major focus addresses the function of netrins, a family of secreted proteins critical for normal neural development, in which mutations in humans are correlated with the susceptibility to develop Parkinson's disease, amyotrophic lateral sclerosis and Alzheimer's disease. Active projects targeting demyelinating diseases, including multiple sclerosis, aim to promote myelin maintenance and enhance remyelination by addressing the mechanisms that regulate axonal-oligodendroglial interactions. In Neuroengineering, ongoing projects aim to manipulate cell-cell interactions to enhance regeneration and to form stable synthetic synaptic connections onto engineered surfaces to extend the function of the damaged or degenerating nervous system.

Dr. Kennedy is a recipient of research grants from the Canadian Institutes of Health Research (CIHR), the Natural Sciences and Engineering Research Council (NSERC), the Alzheimer Society of Canada and the Multiple Sclerosis Society of Canada. In addition, he has received a Fonds de la Recherche en Santé du Québec (FRSQ) Chercheur Nationaux Award and is a Killam Foundation Scholar.





**Robert H. Mach, Ph.D.** Britton Chance Professor of Radiology University of Pennsylvania

Robert Mach, Ph.D. is currently the Britton Chance Professor of Radiology and the director of the positron emission tomography (PET) radiochemistry program at the University of Pennsylvania. His research interests include the development of radiotracers for imaging CNS receptors, oxidative stress, aggregated alpha-synuclein and mechanisms of cellular death. Dr. Mach pioneered the concept of using the sigma-2 receptor as a biomarker for imaging the proliferative status of solid tumors with PET and it was his group that reported the association of the sigma-2 receptor with the PGRMC1 protein complex.

Previously Dr. Mach was a member of the Washington University School of Medicine Division of Radiological Sciences, where he served as a professor in the departments of radiology, cell biology & physiology and biochemistry & molecular biophysics. Dr. Mach was also the director of the Washington University cyclotron facility and chief of the radiological chemistry lab of the Mallinckrodt Institute of Radiology, an academic radiology center associated with the Washington University School of Medicine.

Dr. Mach has served as president of the Radiopharmaceutical Sciences Council of the Society of Nuclear Medicine and Molecular Imaging and on the board of directors of the Society of Radiopharmaceutical Sciences. He recently received the Michael J. Welch Award from the Society of Nuclear Medicine for his outstanding contributions to the field of Radiopharmaceutical Chemistry. He is a scientific advisor to Cognition Therapeutics, Inc. and a founder of Accuronix Therapeutics, an oncology-focused biotechnology company developing small molecule drug conjugates that target the sigma-2 receptor.





Stephen F. Martin, Ph.D. M. June and J. Virgil Waggoner Regents Chair in Chemistry University of Texas at Austin

Stephen Martin, Ph.D. joined the faculty at The University of Texas at Austin in 1974, where he currently holds the M. June and J. Virgil Waggoner Regents Chair in Chemistry. His research interests lie broadly in organic and bioorganic chemistry and chemical biology. His work currently focuses on the design and synthesis of small molecules that may be used as molecular probes to study biological function and as potential leads to treat various diseases, including cancer, neurodegeneration and neurological disorders.

Dr. Martin has received a number of awards, including the NIH Career Development Award, an American Cyanamid Academic Award, the Alexander von Humboldt Prize, an Arthur C. Cope Scholar Award, a Japanese Society for the Promotion of Science Award, a Wyeth Research Award, the International Society of Heterocyclic Chemistry Senior Award, and most recently the Ernest Guenther Award in the Chemistry of Natural Products. He is a Fellow of the American Association for the Advancement of Science and was recently designated as a Fellow of the American Chemical Society. He is an editor of Tetrahedron and has published over 320 scientific papers in primary journals together with several patents, reviews and book articles. He is also co-author of the popular undergraduate laboratory book Experimental Organic Chemistry: A Miniscale and Microscale Approach.





Aladdin A. Riad, Ph.D. Postdoctoral Fellow University of Pennsylvania

Aladdin Riad, Ph.D. received his Ph.D. in biomedical sciences from the University of Central Florida Burnett School of Biomedical Sciences in 2018. He is currently conducting postdoctoral research at the University of Pennsylvania in the laboratory of Dr. Robert H. Mach in the department of radiology/nuclear medicine. Dr. Riad's research is focused on lipoprotein trafficking, imaging and characterization of sigma receptors utilized in treatment of cancer and neurodegenerative diseases.





#### Meharvan "Sonny" Singh, Ph.D.

Professor, Department of Pharmacology and Neuroscience Interim Executive Director, Institute for Healthy Aging University of North Texas Health Science Center

Sonny Singh, Ph.D. is professor in the department of pharmacology and neuroscience, and interim executive director for the Institute for Healthy Aging, a multi-disciplinary research- and education-focused institute. The Institute for Healthy Aging is home to faculty at UNT Health Science Center conducting basic biomedical research, translational research and clinical studies into the early diagnosis, prevention and treatment of age-related conditions that include neurodegenerative diseases such as Alzheimer's disease. In addition, Dr. Singh is the director of a NIH-sponsored T32 training grant, which supports predoctoral training in the neurobiology of aging.

Dr. Singh has spent his career focusing on how hormones, like estrogen, progesterone and testosterone affect the brain, particularly within the context of "normal" brain aging and such degenerative diseases as Alzheimer's disease. As such, his research addresses the potential role of these hormones and their associated signaling pathways in the observed sex differences in the prevalence and/or risk for age-associated diseases.

In addition, Dr. Singh serves on the board of directors of the North Central Texas chapter of the Alzheimer Association. He also serves on national grant review panels, including that of the NIH, the American Heart Association and the Alzheimer's Association.





**Tara L. Spires-Jones, DPhil** Professor of Neurodegeneration UK Dementia Research Institute Programme Lead Deputy Director of the Centre for Discovery Brain Sciences University of Edinburgh, Scotland

Tara Spires-Jones, DPhil joined the University of Edinburgh in 2013, where she runs a research group studying the mechanisms and reversibility of synapse degeneration in ageing and neurodegenerative diseases including Alzheimer's disease. Her laboratory studies the synaptic connections between neurons, which facilitate learning and memory in healthy brains. Her work has shown that soluble forms of both of the proteins involved in the neuropathological lesions in Alzheimer's (amyloid beta and tau) contribute to synapse degeneration, and further that reducing the levels of these can prevent and even reverse degeneration. These findings indicate that the plasticity of the brain will allow recovery after treatment, giving hope for some functional recovery in patients.

In addition to conducting her own research, Professor Spires-Jones works to improve the field through engaging with colleagues, the public, and policymakers. She is a FENS-KAVLI Network of Excellence Scholar, working to foster the careers of early career scientists through scientific exchanges, influencing science policy and facilitating exchange between science and society. She is on editorial boards of multiple journals including membership on the Board of Reviewing Editors at Science. She is a member of the Scottish Science Advisory Council, in which role she advises the Scottish Government on science policy.

Professor Spires-Jones received her DPhil from the University of Oxford and was an assistant professor at Massachusetts General Hospital and Harvard Medical School, where she led a team studying Alzheimer's disease pathogenesis with an emphasis on synaptic pathology.



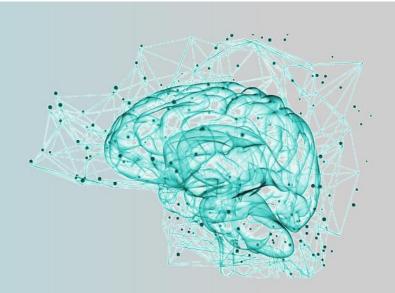


**Chenbo Zeng, Ph.D.** Research Assistant Professor of Radiology University of Pennsylvania

Chenbo Zeng, Ph.D. is currently a research assistant professor of radiology at the University of Pennsylvania. In collaboration with Dr. Robert Mach, Dr. Zeng is exploring the biological functions of the sigma-2 receptor in breast cancer and in the central nervous system.

In 1996, Dr. Zeng received her Ph.D. in biochemistry from Iowa State University and conducted postdoctoral training at Washington University School of Medicine. Before joining the faculty of the University of Pennsylvania, she was a research instructor at the Mallinckrodt Institute of Radiology.

Dr. Zeng is a member of the American Association for Cancer Research and the Society for Neuroscience.



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