Scientific Tracks & Abstracts
September 18, 2017

Neuroimmunology 2017

4th International Conference on

NEUROLOGY AND NEUROIMMUNOLOGY

September 18-19, 2017 | Embassy Suites by Hilton,
Dallas Park Central Area, Dallas, USA

Candace J Strang, J Neurol Neurosci, 8:5
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Complement anomalies in neurodegenerative and neurodevelopmental disorders as a trackable molecular event during the pre-clinical phase of disease development

Candace J Strang
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Recent advances on the interactions of immune pathways and molecules with the cells of the central nervous system have demonstrated a striking inter-relationship. By a still poorly understood biological signal, injured neuronal cells come under the surveillance of immune systems designed for destruction and clearance of foreign cells, but not for autologous cells. This destruction of neuronal circuitry accounts for the clinical neurological deficits observed in behavior studies. Some diseases for which neuronal destruction has been shown are considered "autoimmune" diseases for the established destruction of self-designated cells, such as SLE. Other diseases are not yet considered to be "autoimmune", but indeed maybe, such as schizophrenia. In animal models, treatment with immunosuppressive agents has been shown to be beneficial for prevention of the clinical signs and symptoms of CNS decline. However, this approach cannot be considered as a prophylactic therapeutic angle, due to the profound side effects of immune suppression for normal immune defense. We have developed an analytical approach for the analysis of immune molecules in context to gain a molecular preview of the initial neuronal changes and neuroimmune interactions. We describe the application of this approach to gain early insight into the developing pathology of neuronal destruction. Our plan is to describe the point of molecular pathology that precedes tissue pathology with the aim to define a window for therapeutic intervention where CNS decline is prevented or minimized without complete immune collapse.

Speaker Biography

Candace J Strang has done her PhD from UCLA, USA. She is affiliated as CSO at IPPIN Biomarkers USA. She is a Neuroscientist with extensive experience in translational biochemistry, neuroscience, immunology, protein design and research "at the edge" with an interdisciplinary approach to disease pathogenesis.

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Estrogens downregulate cyclo-oxygenase -2 *(COX-2)* gene expression

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Inflammation plays a role in neurodegenerative illnesses such as Alzheimer's disease (AD). As a distinct fact, AD predominates in post-menopausal women as compared to aged men. Together, these observations suggest that sex steroids regulate neuro-inflammatory processes. Specifically, in the premenopausal state, estrogens could have a protective effect that would be lost after the menopause. To determine whether estrogens could down-regulate an inflammatory process, an amygdalar cell line was used to determine the effect of estradiol (E2) on cyclooxygenase–2 *(COX-2)* gene expression. Estradiol (E2) reduced *COX-2* mRNA and pre-mRNA levels. Given that E2 exerts most of its known genomic effects by binding to two estrogen receptors (ERs), ER-alpha (ER-a) and ER-beta (ER-b), ER-a and -b selective ligands were used to determine the relative contributions of the two receptors. ER-b accounted for all the E2 repressive effect on *COX-2* RNA expression. Ligand-bound ERs exert activating effects by binding to palindromic estrogen response elements (EREs); however, repression may occur via a different mechanism. The proximal *COX-2* gene promoter of the *COX-2* gene lacks an ERE, and E2 treatment leads to decreased recruitment of the transcription factor NF-kB to the promoter. E2 also leads to recruitment of histone deacetylase 1 and Sin3A, members of a repressive complex. Lastly, E2 leads to increased methylation of the *COX-2* proximal promoter. ER-b accounts for some but not all of these effects. These data suggest that E2 has a neuroprotective effect by decreasing an inflammatory response through pathways that are in part regulated by ER-b.

Speaker Biography

Rosalie M Uht was awarded her MD and PhD from the State University of New York at Stony Brook in 1990. She did a combined Anatomic Pathology Residency and Neuropathology Fellowship at the University of California, San Francisco (UCSF). This was followed by Post-doctoral work as an NIH Clinical Investigator, also at UCSF. She established her first independent laboratory at the University of Virginia at Charlottesville in 2000. In 2008, she moved to UNTHSC where she established a second independent lab and helped found the CANDR Brain Bank.

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Ann M Stowe, J Neurol Neurosci, 8:5
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Adaptive lymphocyte profiles correlate to brain Aβ burden in patients with mild cognitive impairment

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Background: We previously found that subjects with amnestic mild cognitive impairment exhibit a pro-inflammatory immune profile in the cerebrospinal fluid similar to multiple sclerosis, a central nervous system autoimmune disease. We therefore hypothesized that early neuroinflammation would reflect increases in brain amyloid burden during amnestic mild cognitive impairment.

Methods: Cerebrospinal fluid and blood samples were collected from 24 participants with amnestic mild cognitive impairment (12 men, 12 women; 66±6y; 0.5 Clinical Dementia Rating) enrolled in the AETMCI study. Analyses of cerebrospinal fluid and blood included immune profiling by multi-parameter flow cytometry, genotyping for apolipoprotein (APO)ε, and quantification of cytokine and immunoglobin levels. Amyloid (A)β42 deposition was determined by 18F-florbetapir positron emission tomography. Spearman rank order correlations were performed to assess simple linear correlation for parameters including amyloid imaging, central and peripheral immune cell populations, and protein cytokine levels.

Results: There was a significant decline in solube Aβ42 in the cerebrospinal fluid as mean brain Aβ42 deposition, as well as amyloid burden in the precuneus and posterior cingulate cortices, increased. Lymphocyte profiling revealed a significant decline in T cell populations in the cerebrospinal fluid, specifically CD4+ T cells, as Aβ42 deposition in the posterior cingulate cortex increased. In contrast, increased Aβ42 burden correlated positively with increased memory B cells in the cerebrospinal fluid, which was exacerbated in APOε4 carriers. For peripheral circulating lymphocytes, only B cell populations decreased with Aβ42 deposition in the precuneus cortex, as peripheral T cell populations did not correlate with changes in brain amyloid burden.

Conclusions: Elevations in brain Aβ42 burden associate with a shift from T cells to memory B cells in the cerebrospinal fluid of subjects with amnestic mild cognitive impairment in this exploratory cohort. These data suggest the presence of cellular adaptive immune responses during Aβ accumulation, but further study needs to determine whether lymphocyte populations contribute to, or result from, Aβ dysregulation during memory decline on a larger cohort collected at multiple centers.

Speaker Biography

Ann M Stowe has completed her PhD in Molecular & Intergrative Physiology from the University of Kansas, and a Post-dotoral Fellowship fromWashington University in St. Louis. She is currently an Assistant Professor in the Dept. of Neurology at UT Southwestern Medical Center in Dallas. Her research focuses on the role of neuroinflammation in CNS injury and repair in both preclinical mouse models of stroke, as well as clinical studies involving patients with either stroke or amnestic mild cognitive impairment (aMCI).

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Victor V Uteshev, J Neurol Neurosci, 8:5
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Modulation of endogenous cholinergic cytoprotection in Ischemic stroke

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The cholinergic system is essential for maintenance of cognitive, autonomic and immune homeostasis in mammals. Pre-clinical studies utilizing rodent models of ischemic stroke suggest that endogenous cholinergic tone elevated by injury, infection and/or inflammation serves as a combination therapy aiming at multiple cellular and molecular pathways with converging anti-inflammatory cytoprotective efficacies. These hardwired endogenous protective mechanisms can be augmented by cholinergic treatments including nicotinic acetylcholine receptor (nAChR) agonists, positive allosteric modulation and vagus nerve stimulation. Strategies that augment endogenous cholinergic protective mechanisms are expected to selectively target ischemic brain injury with high spatiotemporal precision. The α7 subtype of nAChRs is uniquely positioned as a promising therapeutic target in ischemic stroke because of the high anti-inflammatory cytoprotective efficacy of α7 nAChR activation and the ubiquitous expression of α7 nAChRs in mammalian neuronal, glial and immune tissues. The injury-induced endogenous α7-dependent auto-therapy may act as an important physiological function of these receptors. Selective cholinergic agents that enhance endogenous protective mechanisms may hold significant translational potential.

Speaker Biography

Victor V Uteshev has made the long-term goal of his laboratory to help develop clinically useful drug therapies that will ameliorate or even restore cognitive and autonomic functions in patients with age-, disease- and trauma-related impairments. His research concentrates on the positive effects chemicals such as nicotine may have on the brain – as in enhancing cognitive performance and resistance to brain injury, particularly in aging patients and people who have high risk for stroke and traumatic brain injury. He is focusing on compounds that are similar to nicotine but can bring mostly positive effects. In many diseases and pathological conditions, the brain doesn't create enough nicotine receptors and natural compounds that activate these receptors. In diseases and conditions such as schizophrenia, Alzheimer's and traumatic brain injury, the level of activation of nicotine receptors is deficient and cannot support normal brain function. His team's goal is to develop clinically tested drug therapies that can compensate for these deficits and improve or restore cognitive and autonomic functions in patients with age-, disease- and trauma-related impairments. He also serves as an Adjunct Associate Professor in the Department of Pharmacology of Southern Illinois University School of Medicine at Springfield, Ill., where he previously served as an Assistant Professor.

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Dmitriy Labunskiy, J Neurol Neurosci, 8:5
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Neurological complications of Gluten Fibromyalgia

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University of Northern California, USA

Fibromyalgia (FM) is a complex chronic pain syndrome that affects about 2% of the population, mainly women, from all over the world, and is characterized by widespread pain in soft tissues, generalized sensory points, pathological fatigue and sleep disturbances. Celiac disease is a multisystem autoimmune disease that occurs as a result of gluten intolerance and affects 1-2% of the population, mostly women. The relationship of individual parameters with the presence of FM in patients of the main group and the comparison group was characterized by the presence of similar traits and differences. In particular, there was a coincidence of the fact and direction of the relationship of FM and parameters such as RLS, depression, anxiety. The relationship of FM with polyneuropathy of thin and thick fibers was noted only in patients with celiac disease, and the relationship of FM with migraine only in the comparison group. The study showed that the prevalence of FM in patients with celiac disease is three times higher than in the population. The typical form of celiac disease and the age of patients 40-59 years are prognostic unfavorable signs of the development of FM in patients with celiac disease. Qualitative signs of FM in patients with celiac disease did not have any specific features: *statistically significant* differences in both groups by such features as the number of sensitive points, the duration of FM in months, the number of points on the FM questionnaire were absent ($p > 0.05$). Both FM and celiac disease are often undiagnosed diseases, typical of any gender and age. FM is often combined with diseases of the gastrointestinal tract. In this study, the frequent occurrence of FM in patients with celiac disease was identified. It is necessary to exclude FM in patients with celiac disease. The dependence of FM on polyneuropathy of fine fibers, restless leg syndrome, depression, anxiety in the group of patients with celiac disease was revealed. One of the modern methods for diagnosing polyneuropathy of fine fibers in patients with FM is the immune-histochemical study of skin biopsy specimens on C-fibers by means of antibodies to the protein gene product 9.5.

Speaker Biography

Dmitriy Labunskiy graduated wish M.D. from the Medical School of the Moscow State University in 2002. After his graduation he worked at the Research Center of Neurology in Moscow working upon project on Neuroimmunology in Neurodegenerative Diseases. He have got his Ph.D. upon defending his thesis of Immune State, Neurospecific Proteins and Antibodies in Hereditary Spino-Cerebellar Ataxias. From 2008 he works at the University of Northern California in Petaluma, CA on a number of research project in Neuroimmunology.

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Maria Anagnostouli, J Neurol Neurosci, 8:5
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HLA-immunogenetics in multiple sclerosis: On clinical applications and personalized therapeutics

Maria Anagnostouli
National and Kapodistrian University of Athens, Greece

Multiple sclerosis (MS) is a multi-factorial disease of the central nervous system, with a neuroinflammatory and a neurodegenerative component, from its initiation and further on. Many factors have been described to play a role in the initiation and clinical course of the disease and in the response to medication. These factors include age at onset, gender, viral infections, human leucocyte antigen ()-genotype, non-*HLA* genes, vitamin D levels, body-mass-index(BMI) and smoking. *HLA* genetic profile is considered the most important, as it not only influences every aspect of the disease, the cognitive status included, but it also modifies the effect of the other factors. *HLA-DRB1*15:01* is the best established allele, both increasing the risk of MS, 2-3 times and influencing response to first line medication (including interferon-beta and glatiramer acetate), but neutralizing antibodies' formation against natalizumab, as well. Cognitive decline is a well recognized manifestation of MS and some new drugs are now available having a direct or indirect effect on this neurodegenerative feature. Only *HLA-DRB1*15:01* has been proved to deteriorate cognitive function measured by neuropsychological tests. Other Class I and Class II *HLA* alleles have either a detrimental *(DRB1*08:01, 03:01, 13:03, 15:03, 04:05)* or a protective *(DRB1*14:01, *07*11, A*02:01)* effect on MS. Genome wide association studies (GWAS) provide evidence concerning the role of non-*HLA* genes, which have a well established, but much weaker than *HLA* genes, effect on MS risk. Although, taking into account their epistatic interactions, we conclude that *HLA*-genotyping, having the core role may lead to an individualized approach of MS patients, in different ethnic groups.

Speaker Biography

Maria Anagnostouli has completed her PhD from 1st Dept. of Neurology, of Medical Scool of NKUOA and Post-doctoral studies from Neuro-ICU, Harvard University School of Medicine. Her Phd was on Biotin Determination in Neurological Disorders and especialy MS. Based on her results and suggestions, recently a patent was established concerning therapeutic use of biotin in Primary Progressive MS, which is in progress. Her main interest is MS of adults, children and adolescents and she is the Director of Immunogenetics Laboratory, at 1st Dept. of Neurology, Aeginition Hospital, Athens, Greece. She has published more than 40 papers in reputed journals and has been serving as an Editorial Board Member of repute. She is Member of scientific societies on neurology, neuroimmunology and MS. She has also written a book on Neuroaesthetics and a chapter on Neuroimmunology/Neuroinflammation.

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Aage R Møller, J Neurol Neurosci, 8:5
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Aage R Møller

The University of Texas at Dallas, USA

Similarities between severe tinnitus and chronic pain

Chronic neuropathic pain and severe tinnitus have many similarities. Activation of maladaptive neuroplasticity plays important roles in the creation of the symptoms of both diseases and they are both plasticity diseases. The symptoms are generated in the central nervous system. Acute pain that is caused by tissue injury is often a precursor to chronic neuropathic pain with stress as a co-factor. While less severe tinnitus may be generated in the ear, it is believed that severe tinnitus is caused by changes in the nervous system that occurs as a result of activation of neuroplasticity. The changes in the nervous system that produce the symptoms of these two diseases are altered synaptic efficacy causing a change in the excitability and functional connections in many related neural circuits of the brain. These components of the pathology cannot be detected by the methods currently available for diagnostic purposes.

Speaker Biography

Aage R Møller is known internationally for his innovative research on sensory systems and neural plasticity and for developing methods for reducing the risk of neurological deficits in neurosurgical operations. His work has helped establish UT Dallas as a leader in tinnitus-related research. His lengthy research career has focused on four primary areas: The basic function of the ear, sound transmission in the middle ear and cochlea, the neural code of complex sounds and neural plasticity. He eventually moved on to research in humans aimed at studying disorders of the year and the nervous system, such as tinnitus. He began his research career at the famed Karolinska Institut in Sweden. In 1978, he was invited to join the University of Pittsburgh. There he did innovative research in the area of neurosurgery and intraoperative neurophysiology; he developed methods for reducing the risks of serious neurological deficits after neurosurgical operations. He was one of the founders of a new specialty; intraoperative neurophysiological monitoring and he did innovative research that lead to better understanding of several neurological diseases. When he joined UT Dallas in 1997, he became interested in abnormalities in the nervous system function among individuals with autism. He developed teaching programs in the biology of pain; sensory systems, neuroplasticity and he established the first university program in teaching IONM in a graduate program. During his time at UT Dallas, he was named the university's "President's Teaching Excellence Award," won Teacher of the Year for the School of Behavioral and Brain Sciences, and was named distinguished Lecturer in Cognition and Neuroscience. He earned his PhD in Medical Science at the Karolinska Institut in Stockholm, Sweden.

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Diana R. Kerwin, J Neurol Neurosci, 8:5
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Update on alzheimer's disease and related-dementias: Amyloid and tau immunotherapy developments and alzheimer's prevention trials

Diana R Kerwin
University of Texas Southwestern Medical Center, USA

Drug development in Alzheimer's disease has moved to development of disease-modifying therapies in early stage and pre-clinical disease. With the growing body of literature in the association of several mid-life risk factors that have been identified, several large scale, preventive studies are underway for the prevention of the memory and cognitive impairments due to Alzheimer's disease neuropathology and neurodegeneration. In this presentation, several current and ongoing Phase 1,2 and 3 studies will be discussed, including safety and tolerability data of anti-amyloid and anti-tau monoclonal antibody therapies. There will also be a review of the current risk factors for development of AD and current state of understanding of the potential prevention of AD and related dementias.

Speaker Biography

Diana R Kerwin completed internal medicine residency and geriatric medicine fellowship training at Northwestern University Feinberg School of Medicine in Chicago, Ill, and specializes in cognitive disorders. Dr. Kerwin is the Director of the Texas Alzheimer's and Memory Disorders program at Texas Health Presbyterian Hospital-Dallas and Assistant professor in the Department of Neurology and Neuro-therapeutics at University of Texas Southwestern Medical Center in Dallas. Prior to founding the program in July 2013, she was Assistant Professor of Medicine-Geriatrics at Northwestern and faculty in the Northwestern University Cognitive Neurology and Alzheimer's Disease Center (CNADC). Dr. Kerwin is the principal investigator on several Phase 1, 2 and 3 clinical trials for the development of therapeutics in Alzheimer's and other dementias such as Progressive Supranuclear Palsy. She is the PI for several NIA funded studies on the prevention of Alzheimer's disease, and collaborative studies for patients with frontotemporal lobe dementia syndromes. Dr. Kerwin's areas of research and clinical interests include the prevention of cognitive decline and dementia.

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Video Presentaions
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Zoran M Pavlovic, J Neurol Neurosci, 8:5
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Correlation link between immune system abnormalities and cannabinoid receptors 2 (CB2) signal dysregulation in autism: novel approach in autism research and treatment

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Neuroscience and Mental Health Services Belgrade, Serbia

Various types of immune system abnormalities were detected in children with autism, such as higher expression of plasma pro-inflammatory cytokines and increased levels of antibodies against brain, central nervous system and maternal proteins. These findings confirm the role of endocannabinoid (EC) system in orchestrating the peripheral and central neuro-immunologically mediated effects in autism. Current pharmacological approaches for autism are directed at symptoms, rather than the underlying pathogenesis. The newest studies suggest that pharmacological modulation of the EC system could represent a novel approach for autism treatment. Among the potential EC system targets, modulation of cannabinoid 2 (CB2) receptor signalling, could offer a promising therapeutic target with minimal psychotropic effects. In the first part of the lecture, history of cannabis use for medicinal purposes, along with details regarding discovery, and functional role of EC system are described. In a second part of the lecture, special attention will be given to CB2 receptor, its expression pattern in human and animal tissues, and the signalling pathways induced by its activation. The role of CB2 receptors in neurodevelopment and immunomodulation will be considered in the third part. The last part of the presentation will review current pharmacological strategies in targeting CB2 receptors in patients with autism.

Speaker Biography

Zoran M Pavlovic MD, got his medical degree at the age of 25, completed his residency and obtained board certification in Psychiatry, from School of Medicine in Belgrade, Serbia. He has published numerous articles in the US (Journal of Neuropsychiatry and Clinical Neurosciences, Primary Care Companion to the Journal of Clinical Psychatry, Journal of Clinical Psychopharmacology) and European neuropsychopharmacology journals (International Journal of Neuropsychopharmacology and European Psychiatry). He serves as National Advisor at the European College of Neuropsychopharmacology (ECNP) and is a Member of the International College of Neuropsychopharmacology (CINP). He is currently working as Medical Director Psychiatry with PRA International in Germany.

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