



INFLAMMATORY BRAIN DISORDERS CONFERENCE 2024

A live virtual event via webinar hosted by Neuroimmune Institute
in partnership with Neuroimmune Foundation and accredited
in collaboration with The Wisconsin Medical Society

JUNE 22 – 23, 2024

10:00 am – 5:30 pm Central Time

Tentative agenda, as of June 15, 2024.
Please note the agenda may be revised.



INFLAMMATORY BRAIN DISORDERS CONFERENCE 2024

A live virtual event via webinar hosted by Neuroimmune Institute
in partnership with Neuroimmune Foundation and accredited
in collaboration with The Wisconsin Medical Society

JUNE 22–23, 2024

10:00 am – 5:30 pm Central Time

The Inflammatory Brain Disorders Conference features nationally and internationally renowned experts skilled in diagnostic and therapeutic approaches who will present a diverse range of emerging clinical and research challenges, insights, and advances in the field of inflammatory brain disorders. Presentations have been carefully selected to familiarize attendees with rapidly developing research and to educate clinicians on the latest advances in the field.

Both generalists as well as specialists in pediatric and adult medicine will find the conference valuable to their practices. The intended audience is pediatricians, family physicians, psychiatrists, rheumatologists, immunologists, neurologists, and infectious disease physicians. Though the conference is designed for physicians, all are welcome to attend.



neuroimmuneinstitute.org

Neuroimmune Institute provides high-quality continuing medical education focused on autism, immunopsychiatric, neuroimmune, and inflammatory brain conditions. Neuroimmune Institute was founded with the goal of rapidly advancing clinical medicine and research.

Saturday, June 22, 2024 – Agenda

All times listed in Central Time

10:00 am – 10:45 am	Immunotherapy in Autoimmune Psychiatric Illness <i>Belinda Lennox, DM, FRCPsych</i>	4
10:45 am – 11:30 am	Optimizing Treatment in Pediatric Neuroinflammation: How Quickly and How Much <i>Ming Lim, MD, PhD</i>	4
11:30 am – 12:00 pm	Break	
12:00 pm – 12:45 pm	Immunopsychiatry From a Clinical Perspective <i>Professor Dominique Endres</i>	5
12:45 pm – 1:30 pm	Lunch	
1:30 pm – 3:45 pm	Evidence for PANS as an Inflammatory Disorder: Stanford Immune Behavioral Health Program 2024 Clinical and Research Update <i>Jenny Frankovich, MD, and PJ Utz, MD with lightning talks by multiple researchers</i>	6
3:45 pm – 4:00 pm	Break	
4:00 pm – 4:45 pm	Practical Approaches When Using Immunosuppressive Treatments Beyond Steroids and IVIg for Neuroinflammatory Diseases <i>Jeffrey Gelfand, MD, MAS, FAAN</i>	11
4:45 pm – 5:30 pm	Novel Approaches to Treating Neuroimmune Disorders Using Engineered T Cells <i>Sasha Gupta, MD</i>	12
5:30 pm	Closing	

Sunday, June 23, 2024 – Agenda

All times listed in Central Time

10:00 am – 10:45 am	Inflammation and Immunity in Depression: From Mechanism Toward New Therapeutics <i>Golam Khandaker, MBBS, MPhil, PhD, FRCPsych</i>	13
10:45 am – 11:30 am	Immuno-Genetic Risk in Major Psychiatric Disorders <i>Marion Leboyer, MD, PhD</i>	14
11:30 am – 12:00 pm	Break	
12:00 pm – 12:45 pm	IL-2 and Tregs in the Therapy of Autoimmune and Inflammatory Diseases <i>Antonios Kolios, MD, PhD</i>	15
12:45 pm – 1:30 pm	PANS/PANDAS Cases: A Neurologist's Perspective <i>Richard Morse, MD</i>	16
1:30 pm – 2:15 pm	Lunch	
2:15 pm – 3:00 pm	Pediatric Acute-Onset Neuropsychiatric Syndrome From the Perspective of an Infectious Disease Physician <i>Mark Pasternack, MD</i>	17
3:00 pm – 3:45 pm	Infections and Inflammation in Neuropsychiatric Illness: Focus on Food Antigens and Epstein Barr Virus <i>Robert Yolken, MD</i>	17
3:45 pm – 4:00 pm	Break	
4:00 pm – 4:45 pm	Novel Biomarker Approaches in Neuroinflammation – The 'Omic Era' <i>Professor Russell Dale</i>	18
4:45 pm – 5:30 pm	The Neuroimmune Axis: Clinical Implications <i>Laura Pace, MD, PhD</i>	19
5:30 pm	Closing	

June 22, 2024 – Agenda and Speaker Details

10:00 – 10:45am CT



Immunotherapy in Autoimmune Psychiatric Illness

Belinda Lennox, DM, FRCPsych

Professor and Head of the Department of Psychiatry, University of Oxford

Presentation Synopsis

There is converging evidence that some psychiatric disease has an autoimmune basis, and the discovery of neuronal cell surface antibodies in a proportion of patients with psychiatric illness offers the potential for new treatment options for patients. Dr Lennox will present the results of studies treating patients with primary psychiatric illnesses with immunotherapy, and discuss the implications of these data for patients, clinicians, and researchers.

Speaker Biography

Belinda Lennox is a Professor and the Head of the Department of Psychiatry at the University of Oxford. Her interests are in discovering the causes of and developing more effective treatments for those with severe mental illness. She leads a research program studying the possible autoimmune causes of mental illness (www.sinapps.org.uk), which includes clinical trials of immunotherapy in people with psychosis.

Dr. Lennox has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

10:45 – 11:30 am CT



Optimizing Treatment in Pediatric Neuroinflammation: How Quickly and How Much

Ming Lim, MD, PhD

HOS Children's Neuroscience, Consultant Pediatric Neurologist, Children's Neuroscience Centre, Evelina London Children's Hospital, King's Health Partners Academic Health Science Centre, Adjunct Reader in Pediatric Neurology, King's College London

Presentation Synopsis

There has been an increased recognition of the growing spectrum of childhood brain and spine inflammation. Early diagnosis is the mainstay of management. Emergent data is beginning to suggest that early initiation of corticosteroids and rapid escalation to plasma exchange mitigates against accrual of disability across a range of conditions, particularly acute attacks in antibody-mediated demyelinating disorders. For disease-modifying treatment, the availability of highly effective biologics has significantly changed treatment paradigms by adopting a much more intensive upfront treatment. How such principles are applied to an individual patient with more precision continues to be the focus of studies. In recent years, there has also been interesting work on how neurological outcomes could be further optimized by regenerative (remyelinating) or neuronal function-enhancing strategies. Advanced imaging and neurophysiologic measures are being developed as bridging biomarkers to facilitate such studies.

Speaker Biography

Dr. Ming Lim undertook his undergraduate medical training at the University of Nottingham, UK. Following completing his pediatric neurology training in South London, he began his doctoral research at the Institute of Psychiatry, Psychology and Neuroscience (London) with the award of a Royal College of Pediatrics and Child Health Research Training Fellowship. He was appointed as Consultant Pediatric Neurologist at the Evelina London Children's Hospital; and is Professor of Pediatric Neurology within Faculty of Life Sciences & Medicine, King's College London.

The Children's Neuroscience Department Brain and Spine Inflammation Service at the Evelina is one of the largest in Europe with a highly successful research portfolio; leading and participating in multi-center/multi-national investigator-led studies; contributing to industry-led studies; and collaborating in basic studies investigating the role of inflammation in neurodegeneration and immunobiology of antibody-mediated central nervous system disorders.

Ming Lim, the clinical lead of the service and research lead for children's neurosciences and Evelina Children's Hospital has generated a substantial grant income and published comprehensively on childhood neuroinflammation. His work has contributed to the important characterization and understanding of many childhood inflammatory disorders and his team is credited with leading clinical and research programs that now seek to optimize the management of severe childhood neuroinflammatory disorders. The service infrastructure and collaborative national and international networks also provide crucial clinical and research training in pediatric neuroinflammation.

Dr. Lim has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Break | 11:30 am – 12:00pm CT

12:00 – 12:45pm CT



Immunopsychiatry From a Clinical Perspective

Professor Dominique Endres

Professor, Department of Psychiatry and Psychotherapy, University Hospital of Freiburg, Germany

Presentation Synopsis

Immunopsychiatry is a transdiagnostic, multidisciplinary and translational field of research. It developed from the observation by neurologists that autoimmune encephalitides such as NMDA-R encephalitis can be associated with additional psychotic symptoms. The concept of autoimmune psychosis was developed based on these observations and international consensus criteria were suggested. However, autoimmune severe mental illnesses that go beyond this, such as autoimmune obsessive-compulsive disorder, are also discussed. The talk will provide an overview of this contemporary yet controversial field of research from a clinical perspective.

Speaker Biography

Professor Dr. Dominique Endres is a psychiatrist working in Germany at the University Medical Center Freiburg in the Department of Psychiatry and Psychotherapy. The focus of his research and clinical work is on immunopsychiatry. Therefore, in his talk, he will address "Immunopsychiatry from a clinical perspective".

Professor Endres has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Lunch Break | 12:45 – 1:30pm CT

Evidence for PANS as an Inflammatory Disorder: Stanford Immune Behavioral Health Program 2024 Clinical and Research Update

Presented by Dr. Jenny Frankovich and Dr. PJ Utz, accompanied by Stanford researchers including Dr. Tyler Prestwood, Dr. Alison Vreeland, Dr. Ayan Mondal, Dr. Claudia Macaubas, Dr. Noor Hussein, and Dr. M. Karen Newell-Rogers



Jennifer Frankovich, MD, MS

Clinical Professor, Pediatrics – Allergy, Immunology, Rheumatology; Co-Director, Stanford Children's Immune Behavioral Health Clinic; Director, Stanford Immune Behavioral Health Research Program, Stanford University School of Medicine

Presentation Synopsis

Dr. Frankovich and the Stanford Children's Immune Behavioral Health Program will briefly review past data pertaining to evidence of inflammation in their patients with PANS and related conditions and will also present new data. Topics will include arthritis & other autoimmune conditions in PANS and sub-acute deteriorations, basal ganglia signs, immunodeficiency data, vaccine response in PANS, pain, and fatigue, clinical course update (what to expect), strep prevalence in PANS (preview), clinical CSF characteristics, and they will announce their Immune-Psych Deterioration Recognition and Management paper.

Speaker Biography

Dr. Jennifer Frankovich's primary research and clinical interest is the intersection of mental health and systemic inflammation. She co-founded the Stanford PANS/Immune Behavioral Health multidisciplinary clinic and research program. Alongside other collaborators, she is building a large biorepository of patient blood samples and clinical data to share with basic scientists around the world. She collaborates with 10 basic science labs at Stanford to characterize the immunophenotypes of active PANS compared to remission samples and age-matched controls. Her ultimate goal is to understand the immunological factors contributing to mental health disturbances and to innovate effective multidisciplinary treatment regimens.

Dr. Frankovich has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.



Paul J. Utz, MD

Professor of Medicine, Immunology and Rheumatology; Stanford University School of Medicine

Presentation Synopsis

It is widely accepted that infections with specific pathogens can trigger the development of immune-mediated disorders, including psychiatric, behavioral, and movement disorders such as Sydenham's Chorea, PANS, and more recently Post Acute Sequelae of COVID-19 (PASC, also called long covid). Moreover, many children with PANS develop signs and symptoms characteristically seen with autoimmune diseases, including rashes, Raynaud's phenomenon, arthralgias, and arthritis. Dr. Utz and his team used targeted multiplexed protein microarrays to screen for IgG autoantibodies that bind connective tissue disease antigens, cytokines, chemokines, and growth factor receptors. They have identified high levels of autoantibodies directed against a small cadre of antigens in PANS patients, some of which could directly alter the biology of immune cells and neurologic systems.

Speaker Biography

P. J. Utz joined the Stanford faculty in 1999 and was promoted to Professor of Medicine in 2013. Dr. Utz earned his bachelor's degree in biology from King's College in Wilkes-Barre, PA, and his M.D. degree in 1991 from Stanford University School of Medicine, followed by internal medicine residency, rheumatology fellowship, and post-doctoral training at Brigham and Women's Hospital in Boston before joining the Harvard Medical School Faculty. Dr. Utz has expertise in the study of autoantibodies and autoantigens, apoptosis signaling pathways, animal models of autoimmunity, proteomics, and microfluidics. Members of his laboratory are developing several cutting-edge proteomics technologies for immunological applications, including multiplex autoantigen microarrays and EpiTOF. The Utz lab also studies vaccines for autoimmunity, influenza, tuberculosis, and more recently SARS-CoV-2. His work pivoted dramatically during the pandemic toward characterizing immune responses to vaccines, infection with pulmonary microbes such as SARS-CoV-2, PANS, and long COVID. Members of his lab are now actively studying the role of infection and autoimmunity in neuropsychiatric and developmental disorders, including antibodies against secreted proteins and cell surface proteins such as G-protein coupled receptors.

Dr. Utz provides sponsored research for EMD Serono, Abbott, Pfizer, and Third Rock Ventures. He serves on the SAB for 4D Molecular Therapeutics, Seranova, and Immunic. He also serves as a consultant, has stock ownership, and receives fees from 4D Molecular Therapeutics as well as consulting and stock options for Seranova. He is the co-founder of Yolo Immune and has stock options there as well. All the relevant financial relationships for this individual have been mitigated.



Imaging in PANS

Allison Vreeland, PhD

Professor of Medicine, Immunology and Rheumatology, Stanford University School of Medicine

Presentation Synopsis

Several magnetic resonance imaging (MRI) studies have identified aberrant morphology in the basal ganglia in adolescents with PANS compared to typically developing controls. Importantly, studies are mixed, likely due to differences in the subjects' stage and duration of their PANS illness. This talk reviews heterogeneous findings from the four seminal neuroimaging studies concerning PANS/PANDAS and presents new data examining macroscopic, volumetric changes during different disease stages of the PANS illness. In addition, supported by indicators of vascular inflammation in patients with PANS/PANDAS, we will also present future directions in neuroimaging including examining cerebral blood flow using other imaging methodologies (e.g., ASL, fNIRS). Neuroimaging studies examining cerebral blood flow are one important source of potential biomarkers, which offer a conceivable target for guiding diagnosis and treatment of PANS.

Speaker Biography

Allison Vreeland, Ph.D. is a Licensed Clinical Psychologist in the Department of Psychiatry and Behavioral Sciences at Stanford University. Dr. Vreeland's clinical expertise is in the assessment and treatment of anxiety disorders (e.g., obsessive-compulsive disorder), depression, and trauma and stress-related disorders. She completed her training in clinical psychology at Vanderbilt University, her pre-doctoral internship at the University of California, San Francisco, and her post-doctoral fellowship at Stanford University. Dr. Vreeland received her Ph.D. in Clinical Psychology with a minor in Quantitative Methods from Vanderbilt University in 2021. She currently provides clinical care through the Stanford Immune Behavioral Health Program. Dr. Vreeland is also actively involved in research through the PANS Research Program. Her current research is focused on identifying neurological markers of psychopathology by examining children in different stages of their PANS illness. Dr. Vreeland's ultimate career goal is to establish an independent program of clinical research aimed at better elucidating the underlying processes of psychiatric disorders and identifying neurodevelopmental and psychosocial mechanisms that compound the risk for psychopathology.

Dr. Vreeland has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.



GPCR Autoantibodies and Psychiatric Deterioration

Tyler Prestwood, MD, PhD

Postdoctoral Fellow, Department of Psychiatry and Psychology, Utz Lab, Stanford University School of Medicine

Presentation Synopsis

Autoantibodies targeting neuronal membrane proteins are known to induce a wide range of neuropsychiatric effects. The largest category of membrane proteins in mammals is G protein-coupled receptors (GPCRs). GPCRs constitute about 1 out of 3 of the known targets of FDA-approved drugs and are, therefore, of major importance in human health and disease. GPCR autoantibodies remain difficult to study due to technical limitations related to the challenges of maintaining GPCR structure during analysis. In order to study GPCR autoantibodies, we have developed a novel, high-throughput, Luminex bead-based assay that has been heavily modified to accommodate GPCR structural requirements. This method holds the potential to advance the understanding of various poorly understood neuropsychiatric diseases with suspected post-infectious etiology.

Speaker Biography

Tyler Prestwood, MD, PhD grew up in rural Northern California and earned his bachelor's degree in Bioengineering at UC San Diego. After returning from a study abroad program in Brazil, he started working in a viral immunology lab studying the dengue virus. He then completed his MD and PhD training at Stanford University School of Medicine studying cancer immunology. He is currently a research track resident at Stanford in the Psychiatry program. His interests involve investigating the serum antibody milieu in patients affected by various illnesses with post-infectious/infection-related components including PANS, schizophrenia, and post-acute sequelae of COVID.

Dr. Prestwood has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.



PANS Plasma Effects on the Blood-Brain Barrier

Ayan Mondal, PhD

Postdoctoral Researcher, Pediatrics Human Gene Therapy (Mellins Lab), Stanford University School of Medicine

Presentation Synopsis

Impaired blood-brain barrier (BBB) function is hypothesized to play a role in the pathogenesis of PANS. BBB is formed by a monolayer of tightly sealed endothelial cells (ECs) and with the cooperative interactions of astrocytes, pericytes, and microglia of the central nervous system (CNS). Dr. Mondal's research is focused on understanding whether circulatory factors alter the structural and functional properties of ECs in PANS, as ECs provide the primary restrictive feature of the barrier through a series of interactions between tight junction proteins Claudin 5, Occludin and ZO1; adherent junction proteins VE-Cadherin and beta-catenin. He has tested the effect of plasma on the transcriptional, structural, and functional changes in the ECs. The plasma Dr. Mondal used was from the PANS patients of their different clinical stages (acute, chronic, and from the same patients after improvement of symptoms) and with the healthy controls (age and sex-matched with the PANS). His results showed increased ECs monolayer permeability over time with the plasma from the individuals with PANS in active diseased states. The transcriptional analysis confirms the alteration of ECs' structural properties, such as increased expression of leukocyte adhesion molecules and decreased expression of structural proteins such as Claudins and ZO1; which are confirmed by the protein level expressions. While looking at the regulatory factors, most recently, Dr. Mondal has identified that MMP9 is induced in ECs upon exposure to PANS plasma (acute phase), which causes structural changes in the ECs and, therefore, is considered a critical regulatory factor that may lead to BBB dysfunction in PANS. Further research is underway to elucidate mechanisms of cellular changes in the BBB stimulated by PANS plasma.

Speaker Biography

Dr. Mondal is a third-year post-doctoral research fellow in Professor Elizabeth Mellins' laboratory at Dept of Pediatrics, Stanford University. He completed his graduation from the University of Calcutta, India, in 2017. He has conducted 1.5 years of research on molecular medicine following graduation and joined as a post-doctoral researcher at the Arnold School of Public Health, University of South Carolina, in the year 2019. During the training, Dr. Mondal studied neuroimmune signaling mechanisms in the gut-liver-brain axes in mouse models of metabolic disorders and military-deployment-associated disorders. His studies elucidated the mechanism of neuroinflammation, and blood-brain barrier (BBB) dysfunction mediated by specific proteins that are elevated in blood during these disease conditions. In his post-doctoral research with Prof Mellins, he is studying changes in BBB function in PANS. He is focusing on elucidating the mechanisms of action of novel modulators of BBB that are relevant to homeostatic maintenance of the BBB and other novel modulators that increase BBB permeability during flares of PANS. His proposed experimental strategies include transcriptomic and proteomic approaches in cell types of the CNS neurovascular unit.

Dr. Mondal has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.



PANS and NK cells

Claudia Macaubas, PhD

Research Scientist, Mellins Lab, Stanford University School of Medicine

Presentation Synopsis

PANS is commonly observed after infection, suggesting that an immune response, first triggered against infection, is likely involved in developing PANS. Natural Killer (NK) cells play a role in defense against infection, leading us to investigate a possible role of NK cells in PANS. The talk describes genetic findings as well as results from in vitro investigations of NK cells function and phenotype. Possible clinical implications and future directions are discussed.

Speaker Biography

Dr. Claudia Macaubas is a Research Scientist in the Department of Pediatrics, at Stanford University. Her main area of interest is the investigation of the role of innate immune cells in inflammation and autoimmunity/autoinflammation. She has a PhD in Immunology from Brazil and was previously a postdoctoral researcher in Australia before joining Stanford University.

Dr. Macaubas has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.



Treg Cells in PANS

Noor Hussein, PhD, MS, BS

Postdoctoral Fellow, Pediatrics Human Gene Therapy (Mellins Lab), Stanford Univ. School of Medicine

Presentation Synopsis

Accumulating evidence suggests that OCD is associated with inflammation, dysregulation of immune cells, and autoimmunity¹. Regulatory T cells (Tregs) are key inhibitors of autoimmunity and play an essential anti-inflammatory role². Dr. Hussein will show data which indicates a higher frequency of Tregs in the blood of patients with PANS in flare (symptom escalation) compared to healthy controls and compared to the improved state. The percentage of CD39+ cells (a marker of highly active and immunosuppressive T reg cells) was also significantly higher in PANS flare state compared to healthy controls and improved state. She will also present data on the functional stability of Tregs reflected by DNA demethylation (epigenetic analyses). Dr. Hussein will also present the functional immunosuppression activity of Tregs, by measuring the Treg-related anti-inflammatory immunosuppressive molecules (cytokines). Lastly, she will show data regarding the

immunosuppressive activity of CD39+ Treg during PANS flare-up and improvement by measuring CD39 enzymatic activity, doing sc-RNAseq to measure the transcriptional profile of good suppressor vs nonfunctional Tregs in PANS. Also, future work will evaluate the migratory capacity of Tregs in PANS by measuring expression levels of cytokine receptors that regulate Treg migration to the brain. Characterizing the role of CD39+Treg in PANS will lay the groundwork for a potential new PANS therapy, by either replacing faulty Tregs or enhancing functional ones.

References

1. Endres, D. et al. Immunological causes of obsessive-compulsive disorder: is it time for the concept of an “autoimmune OCD” subtype?. *Transl Psychiatry* 12, 5 (2022).
2. Vignali, D., et al. How regulatory T cells work. *Nat Rev Immunol* 8, 523–532 (2008).

Speaker Biography

Dr. Noor Hussein is a Pharmacologist with over 10 years of experience in the research and development of new therapeutics for human diseases, especially cancer experimental and molecular therapeutics. Dr. Hussein holds a PhD degree in Experimental Therapeutics. Her main research at Stanford aims to increase the understanding of pediatric acute-onset neuropsychiatric disorder (PANS) auto-inflammatory disease mechanism and to improve the treatment options. Her ultimate goal is to characterize the immunophenotypes of active PANS compared to remission samples and age-matched controls with a focus on regulatory T cells (Tregs), which are key inhibitors of autoimmunity and the main regulator of inflammation.

Dr. Hussein has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.



Joining for Q&A:

M. Karen Newell-Rogers, PhD

Research Professor, Texas A&M School of Medicine

Speaker Biography

Dr. M. Karen Newell-Rogers received her undergraduate degree from the University of Texas at Austin, her Ph.D. in Microbiology, and Immunology from the University of Colorado Health Science Center (UCHSC), and she performed post-doctoral work at McGill University/Montreal Neurological Institute. Dr. Newell Rogers' research broadly involves several areas of study: in the first, is studies of how an individual's immune response genes contribute to infectious and post-infectious chronic inflammatory syndromes, including Post-Traumatic Brain Injury Syndromes, Lyme Disease, Pediatric Autoimmune Neuro-psychiatric Syndromes (PANS), Multiple Sclerosis, preeclampsia, and virally induced post-infectious autoimmune syndromes. A second avenue of research involves studies of how a cell's energy strategy impacts the ability of the cell to be recognized by the immune system. By targeting selective metabolic strategies used by tumors, she and her collaborators are exploring how to limit the cells' options for energy, rendering them susceptible to cell death and/or “recognizable” by the immune system. A major arm of her research utilizes a peptide replacement strategy to reverse the effects of chronic inflammatory disease, including Rheumatoid Arthritis, MS, Lyme, and pre-eclampsia. Her work was honored in January 2011 when she was nominated as a 2011 TAMEST innovator protégé, and again in April 2011, when she received the 2011 Hope Award from the Time for Lyme Foundation, Stamford, Connecticut. A large donation to her cancer work led to a Phase I clinical trial based at the University of Texas Health Sciences Center, San Antonio, under the clinical direction of Dr. Tyler Curiel. Many of the technologies that have resulted from her research have been licensed to biotechnologies companies and are in various stages of commercialization.

Dr. Newell-Rogers is a consultant for Global Cancer Technology. She is also a scientific advisor for VG Life Sciences. All the relevant financial relationships for this individual have been mitigated.

Break | 3:45–4:00pm CT

Practical Approaches When Using Immunosuppressive Treatments Beyond Steroids and IVIg for Neuroinflammatory Diseases



Jeffrey M. Gelfand, MD, MAS, FAAN

Associate Professor of Neurology, Weill Institute for Neurosciences, Department of Neurology; Division of Neuroimmunology and Glial Biology, MS and Neuroinflammation Center, University of California, San Francisco

Presentation Synopsis

This talk will highlight practical approaches for prescribing and safety monitoring of several commonly used steroid-sparing immunosuppressive therapies. It is important to define therapy goals, whether acute, induction (some examples of which may be acute, some of which may take more time for optimal clinical effect), and maintenance (maintain remission, prevent relapse/recurrence). The goal is usually the least amount of immunosuppression, if any, for the shortest amount of time that is needed to treat the disease. This talk will review mechanisms of action (how a specific medication works biologically) and risk profiles of several agents commonly used in clinical neuroimmunology practice, including B cell depleting therapies (such as rituximab), mycophenolate mofetil, azathioprine, methotrexate, and cyclophosphamide.

Speaker Biography

Dr. Jeffrey Gelfand is a neurologist who specializes in caring for patients with autoimmune, inflammatory, and neurodegenerative neurological conditions. He serves as Medical Director of the UCSF MS and Neuroinflammation clinic and served as program director of the UCSF MS / Neuroimmunology fellowship training program for over a decade.

Gelfand received his medical degree from Harvard Medical School. At UCSF, he completed a residency in neurology, followed by fellowship training in multiple sclerosis and neuroimmunology. He also has a master's in advanced studies degree in clinical research from UCSF. He is an Associate Professor of Neurology at UCSF and is board-certified in neurology.

Dr. Gelfand is an active clinical researcher, including supervising clinical trials and other studies focused on improving care for people with neuroinflammatory conditions.

UCSF recognized his excellence in teaching in 2014 with the Robert B. Layzer Award and in 2015 with an award from the Haile T. Debas Academy of Medical Educators. In 2020, he was inducted into the Haile T. Debas Academy of Medical Educators.

Gelfand is an elected fellow of the American Academy of Neurology and serves as the elected chair of the American Academy of Neurology Autoimmune Neurology Section.

Dr. Gelfand is a consultant for Arialys. He also provides research support for Hoffman Laroche/Genentech and Vigil Neurosciences. All the relevant financial relationships for this individual have been mitigated.

Novel Approaches to Treating Neuroimmune Disorders Using Engineered T Cells



Sasha Gupta, MD

Assistant Professor, Neurology, UCSF Weill Institute for Neurosciences, School of Medicine

Presentation Synopsis

The emergence of engineered cells, such as CAR-T cells, has significantly altered the terrain of cancer treatment while prompting the neurological field to investigate their extensive clinical possibilities in autoimmune conditions. Their attractiveness lies in their demonstrated ability to penetrate deeper into tissues, including the central nervous system, surpassing that of monoclonal antibodies. Initial investigations in myasthenia gravis, NMO, and MS have displayed encouraging outcomes. Dr. Gupta will discuss her findings from animal studies and upcoming human trials, alongside providing an overview of existing data and forthcoming therapeutic prospects.

Speaker Biography

Sasha Gupta, MD is an Assistant Professor of Neurology at UCSF and Co-Director of the Neuroimmunology Cellular Diagnostics and Therapeutics Initiative. After completing neurology residency, Sasha continued at UCSF to complete a neuroimmunology fellowship under the mentorship of Drs. Michael Wilson and Scott Zamvil. She has studied CAR-T cell therapy in MS mouse models with the hope of translating this work into MS patients and is working on improved therapeutic options for progressive multifocal leukoencephalopathy (PML). Her work continues to focus on cellular therapeutics for use in neuro-autoimmune conditions.

Dr. Gupta has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Closing | 5:30pm CT

June 23, 2024 – Agenda and Speaker Details

10:00 – 10:45am CT



Inflammation and Immunity in Depression: From Mechanism Toward New Therapeutics

Golam Khandaker, MBBS, MPhil, PhD, FRCPsych

Professor of Psychiatry and Immunology, and MRC Investigator; Head, Immunopsychiatry Programme, MRC Integrative Epidemiology Unit; Co-Lead, NIHR Bristol BRC Mental Health Theme, University of Bristol

Presentation Synopsis

The immune system, particularly low-grade systemic inflammation, is implicated in the pathogenesis of depression, schizophrenia, and other psychiatric disorders. Inflammation is thought to be a clinically relevant phenotype, as immune activation is associated with poor response to psychotropic medications. Currently, several RCTs are testing the efficacy of anti-inflammatory drugs for patients with depression and schizophrenia. However, there are key unanswered questions, both mechanistic and clinical. Is inflammation a causal risk factor for depression and schizophrenia? Could anti-inflammatory drugs be used to treat these disorders? If so, which patients are likely to benefit? Prof Khandaker will present data from population-based cohort studies, genetic analysis, and clinical trials addressing some of these issues. Pitfalls of current approaches and areas for future development will be discussed.

Speaker Biography

Golam Khandaker is a Professor of Psychiatry and Immunology, and Medical Research Council (MRC, UK) Investigator at the University of Bristol Medical School, and an Honorary Consultant Psychiatrist in General Adult Psychiatry in the UK National Health Service (NHS). He leads the Immunopsychiatry Programme at the MRC Integrative Epidemiology Unit at the University of Bristol and Co-Leads the NIHR Bristol Biomedical Research Centre Mental Health Theme. His research focuses on identifying and validating novel immunological mechanisms and potential treatment targets for depression and schizophrenia using epidemiological cohort studies, genetic analysis, and early-phase clinical trials. Golam pioneered the use of population-based cohort and Mendelian randomization (a genetic causal inference method) studies for examining the role of inflammation in psychiatric conditions, particularly the issue of causality. His notable work includes cohort and Mendelian randomization studies providing evidence for a potentially causal role of the inflammatory cytokine interleukin six (IL-6) in depression and schizophrenia. These findings have led to two ongoing proof-of-concept randomized controlled trials of anti-cytokine monoclonal antibody treatment for adults with depression and schizophrenia. Golam is the Lead Editor of the Textbook of Immunopsychiatry published by Cambridge University Press (with co-editors Harrison, Bullmore, and Dantzer), and editorial board member for four journals including *Brain*, *Behavior*, and *Immunity*, the leading journal in the field of psychoneuroimmunology/immunopsychiatry.

Dr. Khandaker has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.



Immuno-Genetic Risk in Major Psychiatric Disorders

Marion Leboyer, MD, PhD

Professor and Chair of the Department of Psychiatry & Addictology, University Paris-Est Créteil;
Director, Translational Neuropsychiatry Lab; CEO, Fondation FondaMental

Presentation Synopsis

The discovery that the immune system can influence brain function and structure has profoundly changed the landscape of psychiatry. Repeated reports of the association of pro-inflammatory cytokines with major psychiatric disorders led to the exploration of the causes and consequences of this inflammatory background. This low-grade inflammation is now thought to be the consequence of the interaction between environmental factors such as infections, stress, pollution, and unhealthy lifestyles with an immune-genetic background.

Association with immune-genetic variants of Toll-Like Receptor genes (TLR, NOD), possibly explains diminished response to infections (rev in Oliveira et al, *Neuropsychopharmacol*, 2017) association while mitochondrial genes (Angrand et al, *BBI*, 2021), HLA-E and HLA-G (Boukouaci et al, *Scientific Report*, 2021) contribute to the maintenance of inflammation. Association with particular HLA haplotypes very likely explains exaggerated synaptic pruning induction, observed very early in psychotic and neurodevelopmental disorders, and later induces auto-immune reactions against brain receptors (Tamouza et al, *BBI*, 2020). In particular, association with complement genes, embedded within HLA system, can induce early abnormal pruning and excessive microglial activation thereby increasing the risk of neurodevelopmental disorders such as early-onset schizophrenia (Tamouza et al, *Acta Psy Scand*, 2019).

Systemic inflammation and persistent infections in turn activate different pathways paving the way to biomarker-guided personalized medicine. One of the best examples is the identification of “autoimmune psychosis” defined by the presence of anti-neuronal antibodies (Jezequel et al, 2017), here again highly associated with specific HLA haplotypes. Systemic inflammation induced by microbial infection and/or psychosocial factors can also be at the origin of the activation of human endogenous retrovirus (HERV-W) (Tamouza et al, *Transl Psy*, 2021). Inflammation is also known to be associated with gut dysbiosis and disturbance of the integrity of the digestive barrier leading to behavioral abnormalities. One last example can be found in the immune-metabolic abnormalities that pave the way to metabolic syndrome associated with psychiatric disorders. Although many aspects of the complex relationship between immunity and brain function are not yet fully elucidated, the findings that have accumulated so far have transformed our understanding of psychiatric disorders and favored the consideration of cellular and molecular targets for the treatment of specific subgroups.

References:

- Oliveira J, Oliveira-Maia Aj, Tamouza R, Brown As, Leboyer M. Infectious and immunogenetic factors in bipolar disorder. *Acta Psychiatr Scand*. 2017 Oct; 136 (4):409–423. doi: 10.1111/acps.12791.
- Jezequel J, Johansson EM, Dupuis JP, Rogemond V, Gréa H, Kellermayer B, Hamdani N, LeGuen E, Rabu C, Lepleux M, Spatola M, Mathias E, Bouchet D, Ramsey AJ, Yolken RH, Tamouza R, Dalmau J, Honnorat J, Leboyer M, Groc L. Dynamic desorganization of synaptic NMDA receptors triggered by autoantibodies from psychotic patients. *Nat Commun*, 2017 Nov 27, 8 (1): 1791
- Tamouza R, Krishnamoorthy R, Giegling I, Leboyer M, Rujescu D. The HLA 8.1 Ancestral Haplotype in schizophrenia: dual implication in neuro-synaptic pruning and autoimmunity? *Acta Psychiatry Scand*, 2020 Feb; 141 (2): 169–171. doi: 10.1111/acps.13125.
- Tamouza R, Krishnamoorthy R, Leboyer M. Understanding the genetic contribution of the human leukocyte antigen system to common major psychiatric disorders in a world pandemic context. *Brain Behav Immun*. 2021 Jan; 91: 731–739. doi: 10.1016/j.bbi.2020.09.033. Epub 2020 Oct 5. PMID: 33031918
- Tamouza R, Foiselle M, Richard JR, Wu CL, Boukouaci W, LeCorvoisier P, Barrau C, Lucas A, Perron H, Leboyer M. Identification of inflammatory subgroups of schizophrenia and bipolar disorder patients with HERV-W ENV antigenemia by unsupervised cluster analysis. *Transl Psychiatry*. 2021 Sept, 11, 1, 447. <https://www.nature.com/articles/s41398-021-01499-0#article-info>
- Tamouza R, Krishnamoorthy R, Leboyer M. Understanding the genetic contribution of the human leukocyte antigen system to common major psychiatric disorders in a world pandemic context. *Brain Behav Immun*. 2021 Jan; 91:731-739. doi: 10.1016/j.bbi.2020.09.033.
- Le Clerc S, ... Leboyer M, Tamouza R. HLA-DRB1 and HLA-DQB1 genetic diversity modulates response to lithium in bipolar affective disorders. *Science Rep*. 2021 Sep 8; 11 (1): 17823. doi: 10.1038/s41598-021-97140-7. PMID: 34497278
- Angrand L, Leboyer M, Tamouza R. Low peripheral mitochondrial DNA copy number during manic episodes of bipolar disorders is associated with disease severity and inflammation. *Brain Behav Immun*. 2021 Nov; 98: 349–356. doi: 10.1016/j.bbi.2021.09.003.
- Boukouaci, Wahid; Lajnef, Mohamed; Richard, Jean-Romain; et al. HLA-E circulating and genetic determinants in schizophrenia and bipolar disorder. *Scientific Reports* Volume: 11 (1); Article Number: 20260 Published: Oct 12, 2021

Speaker Biography

Marion Leboyer, M.D., Ph.D. is Professor of Psychiatry at the University of Paris Est Créteil (UPEC) in France. She is head of the DMU IMPACT (University-affiliated department of Psychiatry and Addictology (Hôpitaux Universitaires Mondor, Assistance-Publique-Hôpitaux de Paris). She also runs the laboratory “Translational NeuroPsychiatry” (<http://www.imrb.inserm.fr/equipes/m-leboyer-s-jamain/>) which is part of Mondor Institute for Biomedical research (IMRB, Inserm U955). Since 2007, she is the executive director of a non-profit foundation, “Fondation FondaMental” (www.fondation-fondamental.org) created by the French Ministry of Research. Dr. Leboyer has authored or co-authored more than nine hundred peer-reviewed international publications (H-factor = 100) and is part of the highly cited researchers (Clarivate) since 2018. In December 2021, she received the Inserm Grand Prize – <https://presse.inserm.fr/en/inserm-2021-prizes-science-more-mobilized-than-ever-to-serve-health/44300/>.

Her research efforts contributed to better identification of genetic and environmental risk factors associated with major psychiatric disorders towards a better understanding of causal mechanisms. In particular, she has contributed to the identification of associations of genetic vulnerability factors, immune dysfunctions in major mood disorders, but also of environmental risk factors as well as brain imaging abnormalities. Her goal is to develop biomarker signatures to better identify homogenous subgroups of psychiatric disorders paving the way to mechanisms-based treatments. Within the expert center network centers created and coordinated by Fondation FondaMental, several cohorts of patients have been followed allowing for the construction of shared observational databases and biobanks. These networks have enabled multiple collaborations within different national and international research programs. Dr. Leboyer is the principal investigator of several international and national research projects.

Dr. Leboyer has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Break | 11:30 am – 12:00pm CT

12:00 – 12:45 pm CT

IL-2 and Tregs in the Therapy of Autoimmune and Inflammatory Diseases



Antonios Kolios, MD, PD, Dr med. FAAD, FAAI

Senior Attending Physician, Department of Dermatology, Head of Immunodermatology Unit, University Hospital Zurich

Presentation Synopsis

Failure of regulatory T cells to properly control immune responses invariably leads to autoimmunity and organ damage. Several attempts have been made to overcome regulatory T-cell deficiencies to restore immune tolerance in many human autoimmune diseases. One example is low-dose IL-2, the main cytokine driving Treg cell survival and function. Several trials have demonstrated clinical efficacy. In this presentation, Dr. Kolios will present a timely overview of IL-2 in autoimmunity and its potential application.

Speaker Biography

Dr. Antonios Kolios is a physician-scientist, board-certified in Dermatology and Venerology as well as Clinical Immunology and Allergology. He received his medical degree at the University of Mainz, Germany, and his doctorate at the University of Zurich, Switzerland. From 2020 until 2021 he was doing a postdoc in the Department of Rheumatology and Clinical Immunology at the Beth Israel

Deaconess Medical Center, Harvard Medical School, Boston. Currently, he is a senior attending physician, and the Head of the Division of Immunodermatology at the University Hospital of Zurich, and the group leader for translational research in Immunodermatology at the University of Zurich.

His research has focused on the restoration of immune tolerance in patients with inflammatory diseases including lupus, psoriasis, hidradenitis suppurativa, and vitiligo. Additionally, his lab is using molecular profiling for disease characterization and based on that developing novel clinically meaningful and well-tolerated treatments.

Dr. Kolios is a speaker for Novartis (an independent podcast). All the relevant financial relationships for this individual have been mitigated.

12:45 – 1:30 pm CT

PANS/PANDAS Cases: A Neurologist's Perspective

Richard Morse, MD

Chief, Child Neurology, Dartmouth Children's Health; Professor of Pediatrics and Neurology, Geisel School of Medicine



Presentation Synopsis

Dr. Morse will present several cases selected from Dartmouth's Neuroimmune Psychiatry Clinic, which provides care for children, adolescents, and young adults with complex neurobehavioral disorders following an infection or illness. The cases will illustrate the current understanding of the pathophysiology of autoimmune basal ganglia encephalitis, Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS), and related conditions and the challenges of diagnosis and treatment.

Speaker Biography

Dr. Richard Morse has been a Board-certified, practicing pediatric neurologist and epileptologist for over 25 years. He is a Professor of Pediatrics and Neurology at The Geisel School of Medicine at Dartmouth, and practices at Dartmouth-Hitchcock Medical Center, Dartmouth Children's Health.

His career focus has been on epilepsy, epilepsy surgery, and the comprehensive management of children with epilepsy. In 2019, he began working in collaboration with Dr. Juliette Madan, psychiatrist, and pediatrician, to create a research-oriented, multidisciplinary clinic to address the emerging field of neuroimmune psychiatry. Dr. Morse says that caring for these patients and their families has been both rewarding and challenging and that he is thankful for the support of colleagues and organizations dedicated to this emerging field.

Dr. Morse is a Site PI for an IRB-approved IVIG Study with Octapharma. All the relevant financial relationships for this individual have been mitigated.

Lunch Break | 1:30 – 2:15pm CT

2:15 – 3:00 pm CT

Pediatric Acute-Onset Neuropsychiatric Syndrome From the Perspective of an Infectious Disease Physician



Mark Pasternack, MD

Chief of Pediatric Infectious Disease, Massachusetts General Hospital Associate, Professor of Pediatrics, Massachusetts General Hospital, Harvard

Presentation Synopsis

Dr. Pasternack will utilize a series of clinical case vignettes to explore several clinical issues relevant to the diagnosis of PANS/PANDAS including epidemiology, laboratory evaluation, natural history, and management. The use of various antibiotic therapies and non-antibiotic adjunctive measures will be addressed. Individualization of standard therapies to optimize patient tolerance will also be discussed.

Speaker Biography

Mark Pasternack, MD specializes in Pediatric Services, the Infectious Disease Unit, and is Chief of the Pediatric Infectious Disease Unit at Massachusetts General Hospital. Educated at Harvard Medical School, Dr. Pasternack completed his residency and clinical infectious disease fellowship at Massachusetts General Hospital and a research fellowship at the Center for Cancer Research, Massachusetts Institute of Technology. Author of numerous papers and articles for prestigious medical journals, Dr. Pasternack is an officer of the Massachusetts Infectious Diseases Society and a member of the Pediatric Infectious Disease Society as well as the Infectious Diseases Society of America. His broad clinical interests include Infectious Disease and Pediatric Infectious Disease. Dr. Pasternack has provided clinical care to PANS/PANDAS patients for over a decade and has participated in the PANS/ PANDAS Research Consortium to develop clinical guidelines for the management of these patients.

Dr. Pasternack has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

3:00 – 3:45 pm CT

Infections and Inflammation in Neuropsychiatric Illness: Focus on Food Antigens and Epstein Barr Virus



Robert Yolken, MD

Director, Stanley Neurovirology Laboratory, Ted and Vada Stanley Distinguished Professor of Pediatrics, Johns Hopkins School of Medicine

Presentation Synopsis

Infections and exposure to other exogenous antigens are major sources of neuroinflammation in serious psychiatric disorders terms of both diagnosis and the guidance of treatment. While the detection of inflammation within the central nervous system would be ideal, it is often difficult to accomplish in a non-invasive manner. For these reasons, we have been focusing on the measurement of antibodies in peripheral blood samples. The value of such measurement is markedly enhanced by the use of assays which are specific for different types of neuroinflammation.

We will present data on antibodies to two sources of antigen: dietary exposure to wheat gluten and infection with Epstein Barr Virus (EBV). Antibodies to dietary gluten are increased in several serious psychiatric disorders such as schizophrenia and bipolar disorder and are associated with a number of autoantibodies including those directed at the N-methyl-D-aspartate (NMDA) receptor. In the case of EBV, individuals with schizophrenia or major depressive disorder have an altered response to EBV nuclear and viral capsid proteins. High resolution studies with specific peptides indicate increased levels of antibodies to a viral encoded Z EBV replication activator protein

(ZEBRA) in individuals with schizophrenia, suggesting a role for EBV-induced gene transactivation in disease pathogenesis. The measurement of antibodies to these and other exogenous antigens may prove to be useful biomarkers for the diagnosis and management of several human brain disorders and might lead to novel immunotherapies of these disorders.

Speaker Biography

Dr. Robert H. Yolken is the Theodore and Vada Stanley Distinguished Professor of Neurovirology in the Department of Pediatrics at the Johns Hopkins University School of Medicine. He is also the chair of the Stanley Division of Pediatric Neurovirology, the nation's first pediatric research center designed to investigate links between severe mental illness (including schizophrenia and manic-depressive disorders) and early childhood viral infection. He and his research colleagues speculate that infectious agents can invade the brain and then lie dormant for years before triggering the onset of schizophrenia or manic-depressive illness in adolescence and young adulthood. Neuropathogenic microorganisms can also affect cognition and behavior through alterations in the immune system of the microbiome. They are investigating possible microbial triggers Herpesviruses, Influenza viruses, and Coronaviruses, as well as *Toxoplasma gondii* which is a protozoan that can be transmitted to humans by cats and undercooked meat from farm animals. They believe that in the future antiviral, antimicrobial, or anti-inflammatory medications might be developed to treat or prevent schizophrenia in some individuals.

The overall goal of the research laboratory is to develop a training and research program devoted to the elucidation of the role of infection and immunity in the etiology of schizophrenia and bipolar disorders as well as suicide behaviors. Interests also include elucidating the role of perinatal infections in subsequent brain development. Dr. Yolken received his M.D. from Harvard Medical School and completed his residency at Yale New Haven Hospital. He also trained at the National Institutes of Health before joining the Hopkins faculty in 1979.

He is an author or co-author of more than five hundred scientific papers as well as *Beasts of the Earth* and several editions of the *Manual of Clinical Microbiology*

<https://www.hopkinsmedicine.org/profiles/details/robert-yolken/>

Dr. Yolken has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Break | 3:45 – 4:00 pm CT

4:00 – 4:45 pm CT

Novel Biomarker Approaches in Neuroinflammation – The ‘Omic Era’

Professor Russell Dale MBChB, MRCPCH, MSc, PhD

Professor of Pediatric Neurology and Pediatric Neurology Research; Head, Kids Neuroscience Centre, Children's Hospital at Westmead, Academic Leader (Research), Specialty of Child and Adolescent Health; Faculty of Medicine and Health, University of Sydney

Presentation Synopsis

Autoimmunity defined by the presence of autoantibodies is only one disease mechanism that results in neuroinflammation. It is acknowledged that neuroinflammation can occur without defined autoimmunity (such as multiple sclerosis), as part of highly penetrant genetic auto-inflammatory disorders (such as Aicardi Goutières syndrome), and as part of infection-triggered encephalopathy syndromes with cytokine storm (such as FIRES and acute necrotizing encephalopathy). We propose a further, possibly common, immune dysregulation phenomenon which is due to an interaction of genes with environmental risk factors (termed epigenetic neuro-immunology). Combinations of vulnerability genetic factors plus environmental factors in early life (stress, infection, inflammation) can generate epigenetic dysregulation affecting the immune system and brain, which renders people vulnerable to ongoing infection/stress-mediated deteriorations or exacerbations. We propose epigenetic neuroimmune dysregulation as a putative explanation of neurodevelopmental deteriorations that may affect children, including the clinical



syndromes: autistic regression, and pediatric acute neuropsychiatric syndrome (PANS). We have developed a program of research using cerebrospinal fluid and peripheral blood, and implemented metabolomic, proteomic, and transcriptomic approaches (bulk and single-cell RNA seq), in conjunction with bioinformatic analysis.

Cerebrospinal fluid analysis of an initial cohort and then a validation cohort of autistic regression, compared to age and sex-matched controls (total 22 patients, 22 controls), demonstrated good separation of patients from controls using principal component analysis. Untargeted and then targeted metabolomics identified elevated sphingolipids, which are inflammatory metabolites, in CSF of patients with autistic regression compared to controls, and decreased butyrate.

In addition, using bulk RNA sequencing and single-cell RNA sequencing of peripheral leukocytes, we have identified evidence of epigenetic, ribosomal protein, and immune dysregulation in children with autistic regression and PANS. We have shown that this gene dysregulation is modified by anti-inflammatory therapies such as intravenous immunoglobulin and azithromycin.

Rather than 'autoimmune' disorders, we believe these findings support the concept that infection or stress-triggered neuro-regression syndromes may be due to epigenetically determined immune dysregulation, with ongoing immune-brain cross talk resulting in infection or stress-related deteriorations. Further exploration of epigenetic dysregulation of the immune system is warranted, in conjunction with anti-inflammatory and epigenetic therapeutics for children with severe and impairing neurodevelopmental disorders.

Speaker Biography

Professor Russell Dale is a Professor of Pediatric Neurology at the University of Sydney, Australia. He does clinical work at the Children's Hospital at Westmead and runs a research program on neuroimmunology at the University. His main interests are understanding disease mechanisms in rare and common neurological disorders of children, biomarkers such as autoantibodies and cellular markers, and neurotherapeutics. His main priority is to understand how environmental factors in early life interact with genetic vulnerability to create epigenetic dysfunction of the immune system and brain, and how this renders children vulnerable to neurodevelopmental disorders and neuroregression in childhood. He strongly believes that only understanding disease mechanisms will allow novel therapeutics in the future. He is the Head of the Children's Hospital at Westmead Clinical School, clinical director of the Kids Neuroscience Centre, and NHMRC Investigator fellow. He has been the chief investigator in grants totaling over AUD25M, has published 365 peer-reviewed publications, and his Google Scholar H factor is 87 with 29,380 citations.

Professor Dale has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

4:45 – 5:30 pm CT

The Neuroimmune Axis: Clinical Implications

Laura Pace, MD, PhD, FACC

Physician-Scientist, Neuroimmunogastroenterologist, Adjunct Assistant Professor, University of Utah, Department of Pediatrics, Division of Medical Genetics

Presentation Synopsis

The neuroimmune axis plays a critical role in health and disease. The gastrointestinal system is a central component of the neuroimmune axis, with its dysregulation leading to the development of many chronic illnesses. I will present a high-level overview of the neuroimmune axis, describe clinical presentations, and conclude with a call to action to leverage precision medicine for both diagnostics and advanced therapeutics for these disabling conditions.

Speaker Biography

Laura A. Pace, MD, PhD, FACC, is a physician-scientist specializing in neuroimmunogastroenterology with a focus on the diagnosis and care of people suffering from complex multisystem disorders



involving the neuroimmune axis. She is board-certified in Internal Medicine, Gastroenterology, and Autonomic Disorders. Additionally, she has formalized clinical training in Medical Genetics and a PhD in Neuroscience. She is part of the NIH Undiagnosed Diseases Network and is a former NIH BIRCWH Scholar. Her research focuses on neuroimmune axis disorders, mucosal immunology, host-microbiota interactions, and complex genetic conditions. She has over 120 publications and has received research funding from the NIH and private foundations. Dr. Pace is a fierce patient advocate and serves on the boards of numerous patient advocacy groups.

Dr. Pace has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Closing | 5:30pm CT



In Memory of Dr. Betsy Mellins

*Professor of Pediatrics, Pediatric Rheumatologist and Molecular Immunologist,
Stanford University School of Medicine*

Dr. Mellins was a pioneer in the field and a huge driver of discoveries in PANS relating to pro-inflammatory monocytes, brain-homing monocytes, Treg cells, and the blood-brain barrier. Her work brought immense understanding of PANS.

She was so kind and humble despite many incredible accomplishments throughout her career including critical research that leveraged genetic testing to predict negative and sometimes fatal outcomes of immunosuppressive medications in certain vulnerable individuals.

We will miss her presence co-hosting and presenting at the Inflammatory Brain Disorders Conference this year, but we are looking forward to hearing updates from her postdocs who will continue the important work in her lab. We are incredibly grateful for the groundwork she laid with her research at Stanford.

She will be missed.

Hosts/Moderators



Anna Conkey

Executive Director and Founder, Neuroimmune Institute and Neuroimmune Foundation

Ms. Conkey has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.



Samuel Pleasure, MD, PhD

Glenn W. Johnson, Jr. Memorial Endowed Chair; Professor, Department of Neurology, UCSF; Director Neuroscience Graduate Program, UCSF; Co-Director Center for Encephalitis and Meningitis, UCSF

Sam Pleasure, MD, PhD is the Glenn W. Johnson, Jr. Memorial Endowed Chair in Neurology at UCSF. Dr. Pleasure is a neurologist who specializes in caring for patients with multiple sclerosis. He also has expertise in caring for patients with epilepsy as well as years of experience in managing a variety of neurological conditions in both clinic and hospital settings. Dr. Pleasure has two main areas of inquiry for his research. He studies processes that regulate early brain development in both normal and diseased situations. He also studies autoimmune forms of meningoencephalitis, where inflammation in specific brain areas causes severe neurologic dysfunction. Pleasure received his medical degree and a doctorate in neuroscience from the University of Pennsylvania. He was chief resident during his neurology residency at UCSF, where he then completed a research fellowship in neuroscience Pleasure is a fellow of the American Neurological Association and a member of the American Academy of Neurology, American Epilepsy Society, Society for Neuroscience, Society for Developmental Biology and Cajal Club. He has won numerous awards for his research and has received research funding from a wide variety of private, state and federal sources. He has served in leadership roles in national organizations and in the UCSF Department of Neurology.

Dr. Pleasure has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.



Lawrence Steinman, MD

Professor of Neurology and Pediatrics, Stanford University School of Medicine

Dr. Lawrence Steinman is a Professor of Neurology, Neurological Sciences, and Pediatrics at Stanford University. He was Chair of the Stanford Program in Immunology from 2001 to 2011. His research focuses on what provokes relapses and remissions in multiple sclerosis (MS), and on the quest for antigen-specific therapy in autoimmune disease. Steinman was the senior author of the 1992 Nature article that led to the drug Tysabri, approved for MS and Crohn's disease. He is currently applying insights from Tysabri to develop new therapies for neurodegenerative diseases, aimed at blocking macrophages and microglia from eating neurons and axons "in danger." Dr. Steinman graduated from Dartmouth College, Magna Cum Laude in Physics. His MD is from Harvard Medical School. He was a post-doctoral fellow in chemical immunology fellow at the Weizmann Institute of Science. After neurology residency, he remained on the faculty in 1980. He has received numerous honors, including the John M. Dystel Prize in 2004, the Javits Neuroscience Investigator Award from the NINDS twice, the Charcot Prize in MS research, and the Cerami Prize in Translational Medicine. Steinman is a member of the National Academy of Sciences and the National Academy of Medicine. Dr. Steinman co-founded several biotech companies, including Neurocrine, Atreca, 180 Life Sciences, 5 Integriin LLC, and Pasithea. He was a Director of Centocor from 1988 until its sale to Johnson and Johnson. He is a Director of BioAtla, an immune-oncology company, co-executive Chair of 180 Life Sciences, and Executive Chair of Pasithea.

Dr. Steinman is a consultant for BristolMeyersSquibb, Atreca, Roche, and Novartis. He also serves as a board member for Pasithea Therapeutics, 180 Life Sciences, and Bio Alta. All of the relevant financial relationships for this individual have been mitigated.

ACTIVITY DIRECTOR

Anna Conkey

Executive Director and Founder, Neuroimmune Institute and Neuroimmune Foundation

Ms. Conkey has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

PLANNING COMMITTEE MEMBERS

Amy Malik, MD

Assistant Clinical Professor, Pulmonary and Critical Care Medicine, University of Wisconsin

Dr. Malik has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

Jenny Frankovich, MD

Clinical Professor of Pediatrics, Rheumatology, Stanford University School of Medicine

Dr. Frankovich has no relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.

LEARNING AND OUTCOME OBJECTIVES

- Describe how to accurately diagnose inflammatory brain conditions.
- Explain how to effectively treat inflammatory brain conditions.
- Recognize that neuropsychiatric sequelae can result from infections, autoimmune, and inflammatory conditions.
- List several immune and inflammatory markers that can be present in patients with inflammatory brain disorders.
- Report the cognitive and psychiatric effects that can occur post-infection.
- Describe appropriate treatments for patients with inflammatory brain disorders.

ACCREDITATION / CREDIT DESIGNATION STATEMENT

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Wisconsin Medical Society and Neuroimmune Institute. The Wisconsin Medical Society is accredited by the ACCME to provide continuing medical education for physicians.

The Wisconsin Medical Society designates this live activity for a maximum of 12.0 *AMA PRA Category 1 Credit(s)*[™]. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

ACCOMMODATIONS

Neuroimmune Institute subscribes to the articles of Title III of the Americans with Disabilities Act of 1990. Should you or anyone accompanying you require special assistance, please notify us by contacting conference@neuroimmuneinstitute.org or 904-599-8464. Requests should be made as early as possible to allow time to arrange the accommodation.

CME EVALUATION AND CREDIT REQUESTS

CME evaluations must be completed no later than July 1, 2024, to receive credit. CME certificates will arrive via email. Please check your spam if you do not see your certificate.

The CME evaluation is available on our website: neuroimmuneinstitute.org/ibdc-cme-evaluation

SPONSORS



Supported by Octapharma

HOSTED BY

