

**Inflammatory Brain Disorders CME Series Syllabus**  
**Hosted by Neuroimmune Foundation and accredited in collaboration with**  
**The Wisconsin Medical Society**

**Contents**

The Inflammatory Brain Disorders Series 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.

**Target Audience**

The intended audience is pediatric and adult physicians. Both generalists as well as specialists will find the conference valuable to their practices. The conference is designed for pediatricians, family physicians, psychiatrists, rheumatologists, immunologists, neurologists, and infectious disease physicians. Though the conference is designed for physicians, physician assistants and nurse practitioners will find the series valuable to their practices as well.

Though all content is geared towards providers, patients and families are welcome to view the recorded lectures. Additional follow up support will be provided through monthly Case-Based Q&A webinars for providers featuring experts in the field.

**Statement of Need**

Immune-mediated causes of neuropsychiatric deteriorations are frequently misdiagnosed. There is a pressing need for medical knowledge in this area to advance. The need is increasing due to post-COVID-19 sequelae. Failure to utilize immunomodulatory therapies can lead to a dramatic worsening in symptoms and even permanent neurologic impairment as well as dramatically reduced quality of life for patients with these conditions, and physicians are not adequately educated in these areas.

**Additional Information**

Neuroimmune Foundation 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 [cme@neuroimmune.org](mailto:cme@neuroimmune.org) or 608-381-0367. Requests should be made as early as possible to allow time to arrange the accommodation.

North Carolina physicians wishing to view this activity will be able to do so free of charge. Once your credentials have been verified, you will be provided access to the materials.

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**Date of release:** January 1, 2023

**Date of expiration:** December 31, 2024

### **Instructions to Receive Credit**

This continuing medical education enduring material is in a video format. References are linked to online resources. In order to receive credit for this activity, the participant must view the video presentations and complete the post-test and evaluation. Upon completing this activity as designed, participants should complete the post-test on the website. After achieving a passing score on the post-test (80%), participants will submit their signed evaluation and registration form on the website below and will receive their CME certificates via email. Multiple attempts of the post-test are allowed.

### **List of references from the literature for future reading**

- [Exploratory analysis of the potential for advanced diagnostic testing to reduce healthcare expenditures of patients hospitalized with meningitis or encephalitis](#), Fulton BD et al, PLoS One. 2020 Jan 15
- [Clinical Metagenomic Sequencing for Diagnosis of Meningitis and Encephalitis](#), Wilson MR et al, N Engl J Med. 2019 Jun 13
- [Pan-viral serology implicates enteroviruses in acute flaccid myelitis](#), Schubert RD et al, Nat Med. 2019 Nov
- [Kelch-like Protein II Antibodies in Seminoma-Associated Paraneoplastic Encephalitis](#), Mandel-Brehm C et al, N Engl J Med. 2019
- PANS Research Consortium Treatment Recommendations 2017: *JCAP Volume: 27 Issue 7: September 1, 2017*, Clinical Management of Pediatric Acute-Onset Neuropsychiatric Syndrome:
  - [Part I—Psychiatric and Behavioral Interventions](#). Thienemann M et al.
  - [Part II—Use of Immunomodulatory Therapies](#). Frankovich J et al.
  - [Part III—Treatment and Prevention of Infections](#). Cooperstock MS et al.
- BiteSized Immunology: <https://www.immunology.org/public-information/bitesized-immunology>
- Neuroscientifically Challenged: <https://www.neuroscientificallychallenged.com>
- CDC page on Group A Strep <https://www.cdc.gov/groupastrep/diseases-hcp/index.html>

### **Activity Director:**

Anna Conkey

Executive Director and Founder, 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 member:**

Amy Malik, MD

*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.*

**Hosts/Moderators:**

**Anna Conkey**

Executive Director and Founder, Neuroimmune Foundation

**Lawrence Steinman, MD**

Professor of Neurology and Pediatrics, Stanford University School of Medicine

Dr. Lawrence Steinman is 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 senior author on 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 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. Dr. Steinman is a member of the National Academy of Sciences, and the National Academy of Medicine. Dr. Steinman cofounded several biotech companies, including Neurocrine, Atreca, 180 Life Sciences, 5 Integrin 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. All of the relevant financial relationships for this individual have been mitigated.*

**Samuel Pleasure, MD, PhD**

Glenn W. Johnson, Jr. Memorial Endowed Chair Professor, Department of Neurology, University of California, San Francisco (UCSF) Director Neuroscience Graduate Program, UCSF

Dr. Samuel Pleasure 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. He 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. Dr. 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.

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### **Eyal Muscal, MD**

Section Chief, Pediatric Rheumatology, Baylor College of Medicine

Dr. Eyal Muscal is a pediatric rheumatologist with a MS Degree in Clinical Research whose activities include patient care, fellowship education, quality improvement, and clinical research. His research, quality improvement, and clinical interests include neurologic manifestations of systemic autoimmune disorders (primarily autoimmune encephalitis, NPSLE, APS, and CNS vasculitis), systemic vasculitides, and patient-powered research in rare diseases. Dr. Muscal is the Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry PI and co-director of the CARRA autoimmune encephalitis work group. An increased portion of his clinical effort is spent on standardizing and enhancing care of children with inflammatory brain disorders. As part of this effort, he obtained additional training in advanced QI. During the COVID-19 pandemic Dr. Muscal has been one of his section's champions on the pathophysiology and treatment of MIS-C. This has included providing educational sessions at his institution and also to international audiences. He has coordinated evidence-based guidelines for MIS-C at his institution and has insured timely, rational, and multi-disciplinary MIS-C care in both general floor and critical care areas. He is also the rheumatology lead for a joint cardiology-rheumatology clinic that follows MIS-C patients after hospital discharge. Dr. Muscal is well suited to support institutional efforts regarding COVID-19 and MIS-C care and specifically the Artificial Intelligence COVID-19 Risk Assessment for Kids (AICORE-kids) program.

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## Learning and Outcome Objectives

- Learn how to effectively treat inflammatory brain conditions as well as the circumstances in which each treatment is appropriate.
- Learn the clinical work up required to accurately diagnose immune mediated causes of neurologic and psychiatric deteriorations.
- Recognize that neuropsychiatric sequelae can result from infections, autoimmune, and inflammatory conditions.
- Accurately diagnose various inflammatory brain conditions.
- Describe appropriate treatments for patients with inflammatory brain conditions.
- Identify the various immune and inflammatory markers that can present in patients with inflammatory brain conditions.
- Report the cognitive and psychiatric effects seen in some patients following COVID-19.

## 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 Wisconsin Medical Society and Neuroimmune Foundation. The Wisconsin Medical Society is accredited by the ACCME to provide continuing medical education for physicians.

The Wisconsin Medical Society designates this enduring material activity for a maximum of 20 *AMA PRA Category 1 Credit(s)*<sup>™</sup>. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

This activity has been produced with no commercial support. **We are very grateful to the State of North Carolina for the educational grant that allowed us to offer this series.**

## Faculty, Agenda, and Syllabus

### **Samuel Pleasure, MD, PhD**

Glenn W. Johnson, Jr. Memorial Endowed Chair  
Professor, Department of Neurology, University of California, San Francisco (UCSF) Director  
Neuroscience Graduate Program, UCSF

### **Joined by Claire Johns, MD, second year medical resident at UCSF**

*Neuropsychiatric Presentation in Pediatric COVID-19 Patients Associated with Anti-neural Autoantibodies*

Maximum of 1.0 *AMA PRA Category 1 Credit(s)*<sup>™</sup>

### **Speaker Biographies**

Dr. Samuel Pleasure 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. He 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. Dr. 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. Claire Johns is currently a second-year Pediatric Resident at University of California, San Francisco Benioff Children's Hospital. She obtained her medical degree from University of California, San Francisco and attended undergraduate at University of California, Berkeley. In between undergraduate and medical school she spent 3 years conducting research at the Salk Institute and University of California, San Diego.

**Learning Objectives:**

- Primary objective: Describe the association between anti-neural autoantibodies and neuropsychiatric dysfunction in pediatric COVID-19 patients.
- Cases: Three cases of teenage COVID-19 patients who presented with primarily neuropsychiatric manifestations, and had their CSF interrogated for anti-SARS-CoV-2 and autoreactive antibodies.
- Findings: Anti-SARS-CoV-2 and anti-neural antibodies were detected in the cerebrospinal fluid (CSF) of two of three pediatric COVID-19 patients with neuropsychiatric dysfunction.
- Conclusions: A subset of pediatric COVID-19 patients with neuropsychiatric symptoms have detectable anti-neural autoantibodies in their CSF.

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*Dr. Johns 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.*

**Jennifer Frankovich, MD**

Clinical Professor of Pediatrics, Rheumatology; Director of PANS Research Program  
Stanford University School of Medicine  
*Rheumatology & Psychiatry - What We Can Learn From Overlapping Conditions*

Maximum of 0.75 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Jennifer Frankovich's primary research and clinical interest is in the intersection between mental health and systemic inflammation. She co-founded the Stanford PANS 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.

### **Learning Objectives:**

- Recognize rheumatic conditions that overlap with psychiatric disease
- Describe a few clinical evaluation pearls or clues that the child has rheumatic conditions
- Understand general approach to treatment

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### **Hrissanthi (Chris) Ikonomidou, MD, PhD**

Chief, Section of Pediatric Neurology, University of Wisconsin American Family Children's Hospital Faculty, University of Wisconsin School of Medicine and Public Health

*A Neurologist's Perspective on PANS: Case Studies*

Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Hrissanthi (Chris) Ikonomidou is a Child Neurologist and physician researcher with expertise in neurodegenerative and neurodevelopmental disorders. She is the Division Chief of Pediatric Neurology at the University of Wisconsin Madison and American Family Children's Hospital. She received her MD and PhD degrees from the University of Goettingen in Germany. She completed her residency and Pediatric Neurology fellowship at Washington University in St Louis and holds board certification in Neurology with Special Qualification in Child Neurology and UCNS certification in Headache. Dr Ikonomidou and her team discovered that imbalance between excitatory and inhibitory signals in the developing brain can lead to brain injuries and subsequent neurologic, cognitive, and mental disabilities. Several pediatric drugs, including sedatives, anesthetics and anticonvulsants, utilize these mechanisms to elicit their therapeutic effects and bear the potential to cause brain injury during critical periods of brain development. Her current research aims to investigate ways to prevent neurotoxicity of these classes of medications in infants and children. Her second research focus entails adverse effects of cancer chemotherapy agents on the developing central nervous system. She has authored over 140 peer reviewed publications and book chapters and serves on several editorial boards of scientific journals.

**Learning Objectives:**

- Review severe presentations of PANDAS/PANS in children
- Review treatments and therapeutic responses in severe cases of PANDAS/PANS

*Dr. Ikonomidou receives stocks from Solvay Stocks. All of the relevant financial relationships for this individual have been mitigated.*

**Christopher Pittenger, MD, PhD**

Professor of Psychiatry in Yale Child Study Center

*Antibodies in Children With PANDAS Bind To And Inhibit Specific Interneurons In The Basal Ganglia*

Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>

**Speaker Biography**

Dr. Christopher Pittenger earned his MD and PhD degrees from Columbia University where his graduate work was done with Nobel Prize recipient Eric Kandel. He returned to Yale University, his undergraduate alma mater, for residency and research training in psychiatry in 2003. He joined the faculty as an Assistant Professor in 2007 and is now a tenured Professor and Assistant Chair for Translational Research in the Department of Psychiatry.

**Learning Objectives:**

- To appreciate recent data suggesting that antibodies from children with PANDAS can bind to and inhibit specific interneurons in the basal ganglia
- To appreciate how dysregulation of interneurons in the basal ganglia may contribute to the development of symptoms in PANDAS

*Dr. Pittenger provides research support for Biohaven Pharmaceuticals. He is a consultant for Biohaven Pharmaceuticals, Ceruvia, and Lundbeck Pharmaceuticals. He is author for Oxford University Press. All of the relevant financial relationships for this individual have been mitigated.*

**Cynthia Kappahn, MD, MPH**

Medical Director, Eating Disorders Program, Lucile Packard Children's Hospital, Stanford  
Clinical Professor, Division of Adolescent Medicine, Stanford University School of Medicine  
Disordered Eating in PANS

Maximum of 0.25 AMA PRA Category 1 Credit(s)<sup>™</sup>

**Speaker Biography**

Dr. Cynthia Kappahn is a Clinical Professor in the Division of Adolescent Medicine at Stanford University School of Medicine. She is Medical Director, Eating Disorders Program of Lucile Packard Children's Hospital, Stanford, which specializes in the treatment of adolescents and young adults with eating disorders. She completed medical training at Yale Medical School, a pediatric residency at the Johns Hopkins Hospital, and an adolescent medicine fellowship at the

University of California, San Francisco. She received a master's degree in Public Health and Policy from Johns Hopkins University. In addition to her clinical and administrative responsibilities, she is involved in research regarding eating disorders, medical complications, and care outcomes, and has a special interest in Avoidant Restrictive Food Intake Disorder (ARFID). She is a member of the National Eating Disorders Quality Improvement Research Collaborative, and has served as Chairman of the Society for Adolescent Health and Medicine's Eating Disorder Clinical Committee.

**Learning Objectives:**

- Recognize that eating restriction is common in PANS/PANDAS
- Identify the common reasons children and adolescents with PAN/PANDAS restrict intake
- List four factors associated with increased risk of medical instability from restricted intake in PANS/PANDAS the approach to managing eating issues in children and adolescents with PANS/PANDAS

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**Elizabeth Mellins, MD**

Professor of Pediatrics, Pediatric Rheumatologist and Molecular Immunologist, Stanford University School of Medicine  
*Monocyte Research in PANS*  
Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>

**Speaker Biography**

Dr. Elizabeth Mellins is a Pediatric Rheumatologist and a Molecular Immunologist at Stanford University School of Medicine. She has focused her career on laboratory-based research on normal and disease-causing immune responses, including those in PANS. She received her MD degree at Harvard Medical School and completed a pediatric residency at the University of Colorado and the University of Washington. She did a fellowship in Pediatric Rheumatology followed by a research fellowship in Immunology, both at the University of Washington. She holds board certifications in General Pediatrics and Pediatric Rheumatology. After being an Assistant Professor at the University of Pennsylvania, she moved to Stanford, where she is now a full Professor. She has served on the NIH Cellular and Molecular Immunology study section and has received research funding from the NIH, the Arthritis Foundation and other foundations, and several pharmaceutical companies. She has authored over 165 peer-reviewed publications and is an editor of the premier textbook in Pediatric Rheumatology. She was the founder and first Chairperson of the Childhood Arthritis and Rheumatology Research Alliance, an organization that now includes almost all Pediatric Rheumatology Divisions in the US and Canada. She is a Distinguished Fellow of the American Association of Immunologists. Dr. Mellins is committed to training young investigators and has received several mentoring awards.

**Learning Objectives:**

- To be aware of the heterogeneity of human monocytes, particularly during chronic inflammation
- To become familiar with the monocyte subsets associated with PANS
- To appreciate the differences in monocyte subset frequencies in different PANS clinical subgroups

*Dr. Mellins provides research support for GlaxoSmithKline, Codexis, Inc. and Genentech. All of the relevant financial relationships for this individual have been mitigated.*

### **Theresa Willett, MD, PhD**

Clinical Assistant Professor, Pediatrics – Immunology and Allergy  
 Medical Director, SCH Immune Behavioral Health Clinic, Stanford University School of Medicine  
*Clues from the Clinical Exam and PANS/PANDAS for the Busy Primary Care Provider*  
 Maximum of 1.75 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Theresa Willett is a general pediatrician and current medical director of the Stanford PANS/Immune Behavioral Health Clinic. She pursued her MD-PhD at Tufts University in Boston, where she completed her thesis work on t-cell mediated autoimmunity in treatment resistant Lyme arthritis, and antigenic mimicry in OspA. She then trained and worked as a primary care pediatrician. After returning to California, she found her cross-specialized people in the Stanford PANS clinic.

### **Learning Objectives:**

- Utilize exam findings to support PANS/PANDAS diagnosis or support alternative diagnoses
- Recognize choreiform movements vs chorea
- Identify skin findings for alternative diagnosis (rheumatic fever) and comorbidity (psoriasis)
- Identify findings on joint exam that indicate need for rheumatology evaluation

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### **Margo Thienemann, MD**

Clinical Professor of Psychiatry, Stanford University School of Medicine  
*Psychiatric Medication Management in Inflammatory Psychiatric Disease With a Focus on PANS*  
 Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Margo Thienemann is a clinical professor of psychiatry and behavioral sciences at Stanford. She is the lead psychiatrist of the Packard Children's PANS clinic, the first in the country exclusively devoted to PANS. She developed an interest in PANS after directing the Obsessive

Compulsive Disorder Clinic at Stanford in the Division of Child and Adolescent Psychiatry. Dr. Thienemann has enjoyed, over the course of her career, watching the field of psychiatry search more and more into the biological underpinnings of mental health disorders in hopes that we can address their causes, in addition to their symptoms.

**Learning Objectives:**

- Participants will appreciate indications for psychiatric medication treatment in children and adolescents with inflammatory brain disorders.
- Participants will appreciate the level of evidence currently available for psychiatric medication treatment in children and adolescents with inflammatory brain disorders.
- Participants will appreciate possible psychiatric medication treatment in children and adolescents with inflammatory brain disorders.

*Dr. Thienemann 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, Keynote speaker  
*Topic: Does Molecular Mimicry Explain Epidemiology Linking EBV & MS? Oligoclonal Antibody in MS Cerebrospinal Fluid Binds EBNA-1 and GlialCAM*  
Maximum of 0.75 AMA PRA Category 1 Credit(s)<sup>™</sup>

**Speaker Biography**

Dr. Lawrence Steinman is 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.

Dr. Steinman was senior author on 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 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. He is a member of the National Academy of Sciences and the National Academy of Medicine.

Dr. Steinman cofounded several biotech companies, including Neurocrine, Atreca, 180 Life Sciences, 5 Integrin 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.

### **Presentation Synopsis**

Dr. Steinman's presentation will integrate new papers linking multiple sclerosis to viral infection and autoimmunity. How to capture the molecular characteristics of the immune response in the brain will be described, using technologies that allow clarity at a single cell level.

*Dr. Steinman is a consultant for BristolMeyersSquibb. All of the relevant financial relationships for this individual have been mitigated.*

### **Jennifer Frankovich, MD**

Clinical Professor of Pediatrics, Rheumatology; Director of PANS Research Program  
Stanford University School of Medicine

### **Elizabeth Mellins, MD**

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

*Topic: Evidence for PANS as an Inflammatory Brain Disorder*  
Maximum of 1.25 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biographies**

Dr. Jennifer Frankovich's primary research and clinical interest is in the intersection between mental health and systemic inflammation. She co-founded the Stanford PANS 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. Elizabeth Mellins is a Pediatric Rheumatologist and a Molecular Immunologist at Stanford University School of Medicine. She has focused her career on laboratory-based research on normal and disease-causing immune responses, including those in PANS. She received her MD degree at Harvard Medical School and completed a Pediatric residency at the University of Colorado and the University of Washington. She did a fellowship in Pediatric Rheumatology followed by a research fellowship in Immunology, both at the University of Washington. She holds board certifications in General Pediatrics and Pediatric Rheumatology. After being an Assistant Professor at the University of Pennsylvania, she moved to Stanford, where she is now a full Professor. She has served on the NIH Cellular and Molecular Immunology study section and has received research funding from the NIH, the Arthritis Foundation and other foundations, and several pharmaceutical companies. She has authored over 165 peer-reviewed publications and is an editor of the premier textbook in Pediatric Rheumatology. She was the founder and first Chairperson of the Childhood Arthritis and Rheumatology Research Alliance, an organization that now includes almost all Pediatric Rheumatology Divisions in the US and

Canada. She is a Distinguished Fellow of the American Association of Immunologists. Dr. Mellins is committed to training young investigators and has received several mentoring awards.

### **Presentation Synopsis**

Dr. Frankovich and Dr. Mellins will cover objective findings that point to PANS/PANDAS as an organic brain disease, discuss the epidemiological studies that have evaluated the links between autoimmunity/inflammation, infection, and OCD, and discuss evidence for autoimmunity and inflammation in PANS/PANDAS and briefly outline management strategies.

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### **Jonas Bergquist, MD, PhD**

Professor in Analytical Chemistry and Neurochemistry in the Department of Chemistry at Uppsala University, Sweden; Adjunct Professor in Pathology at the University of Utah School of Medicine; Distinguished Professor in Precision Medicine at Binzhou Medical University in Yantai, China

*Topic: Chronic Fatigue Syndrome/Myalgic Encephalomyelitis*  
Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Jonas Bergquist is Full Chair Professor in Analytical Chemistry and Neurochemistry at the Biomedical Centre, Department of Chemistry at Uppsala University, Sweden, Adjunct Professor in Pathology at the Department of Pathology, School of Medicine, University of Utah, USA, and Distinguished Professor in Precision Medicine, Binzhou Medical University, Yantai, China. He is also the director of the clinical collaborative research centre in Uppsala (together with Harvard Medical School, Stanford University, Montreal and Melbourne) with a focus on myalgic encephalomyelitis (ME). Dr. Bergquist's group is continuously developing general analytical tools for molecular diagnostic screening and discovery of biomarkers of pathological states. Technologies include all important links: identifying relevant clinical applications, invasive in-situ sampling of complex samples, advanced sample pretreatment, multidimensional liquid-based separation, high resolution mass spectrometry, and multivariate data analysis. Dr. Bergquist aims to explore the neuroimmunological involvement in neurodegenerative diseases by using proteomics and metabolomics with a special interest in cerebrospinal fluid and hard-to-reach tissue studies. Dr. Bergquist has currently published over 540 papers, with around 11,000 -15,000 citations (h-index of 57 in Web of Science and 69 in Google Scholar).

### **Presentation Synopsis**

The presence of autoantibodies in circulation, in peripheral body fluids and tissues, as well as in central nervous system is involved in complex neurological, neurodegenerative, and post-viral

neuroinflammatory processes that have recently been explored as part of the pathophysiological processes. This lecture will look at a few examples, including the post-viral consequences of herpes simplex encephalopathies, myalgic encephalomyelitis, and post-covid. The similarities and differences between the pathophysiological processes will also be discussed.

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**Shreyas Vasanawala, MD, PhD**

Division Chief of Pediatric Radiology, Associate Chair of Radiology  
Radiologist-in-Chief for Pediatric Radiology, Stanford University School of Medicine

**Meiqian Ma, MD**

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

*Topic: Arthritis, Enthesitis, and Development of Autoimmune/Inflammatory Disease in Patients with PANS (Presented by Dr. Jennifer Frankovich, Dr. Meiqian Ma, and Dr. Shreyas Vasanawala)*  
Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>

**Speaker Biographies**

Dr. Shreyas Vasanawala is the William R. Brody Professor of Pediatric Radiology and Child Health and serves as Radiologist-in-Chief for Stanford Children’s Health and Chief of Pediatric Radiology at Stanford University. After completing undergraduate studies in mathematics at the California Institute of Technology, he pursued a medical degree and doctorate in biophysics at Stanford University, where his studies led to a resurgence of signal efficient methods in magnetic resonance imaging. After a surgical internship, a residency in radiology, and a fellowship in pediatric radiology, Dr. Vasanawala joined the faculty at Stanford University. He then focused on building the MRI programs at Lucile Packard Children’s Hospital and at Stanford Hospital and Clinics, and building the Division of Body MRI.

He leads a multidisciplinary research group focused on developing fast and quantitative pediatric medical imaging methods. The group’s efforts include development of new medical imaging hardware, new pediatric-friendly image acquisition methods, novel image reconstruction approaches, and unique strategies to image analysis. These endeavors have led to the first routine clinical translational deployment of high density pediatric specific MRI receiver coils, the first routine clinical use of innovative compressive sensing and deep learning medical image reconstruction methods, and the routine ability to obtain high resolution pediatric images with reduced anesthesia. Together, these efforts, and those of other pediatric radiology faculty, have contributed to Lucile Packard Children's Hospital at Stanford becoming a leading pediatric MRI program internationally. With over 150 peer-reviewed publications and 25 patents, he has developed a deep collaborative network within Stanford and beyond.

Dr. Ma is an Assistant Clinical Professor in the Department of Pediatrics, Division of Allergy, Immunology Rheumatology (AIR) at Stanford University/Lucile Packard Children's Hospital. She completed her medical training at the Medical College of Wisconsin. She then went to Cohen Children's Medical Center/Northwell Health to complete her training in pediatrics and pediatric rheumatology. Her research in fellowship focused on the validation of the 2019 European League Against Rheumatism/American College of Rheumatology Criteria Compared to the 1997 American College of Rheumatology Criteria and the 2012 Systemic Lupus International Collaborating Clinics Criteria in Pediatric Systemic Lupus Erythematosus . She joined the Stanford PANS Program in July 2020.

### **Presentation Synopsis**

Drs. Frankovich, Vasanaawala, and Ma will present on the increased incidence of enthesitis/arthritis among patients meeting criteria for PANS, the three types of arthritis found in patients with PANS, including clinical features. Participants will learn to recognize that children with PANS have severe psychiatric symptoms and sensory dysregulation which may interfere with normal perception of pain (under or over report of pain) and thus prompting clinicians to use objective tools for evaluating arthritis.

*Dr. Vasanaawala is a consultant for Heart Vista and InkSpace, a founder of Arterys, Inc, and research collaborator for GE Healthcare. All of the relevant financial relationships for this individual have been mitigated.*

*Dr. Ma 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.*

### **Sean Pittock, MD**

Director, Neuroimmunology Laboratory and the Center for Multiple Sclerosis and Autoimmune Neurology, Mayo Clinic

*Topic: GAD65 Neurological Autoimmunity*

*Maximum of 1.0 AMA PRA Category 1 Credit(s)<sup>™</sup>*

### **Speaker Biography**

Dr. Sean Pittock is Professor of Neurology, Director of the Neuroimmunology Laboratory and the Center for MS and Autoimmune Neurology at the Mayo Clinic. His expertise is in the laboratory and clinic-based diagnosis and management of immune mediated neurological disorders. In 2006, he set up the Autoimmune Neurology Clinic at the Mayo Clinic, the first dedicated clinic of its type in the USA. This clinic provides a multidisciplinary approach to the evaluation and treatment of patients with a broad range of autoimmune neurological disorders. He is the co-founder of the Autoimmune Neurology Section at the American Academy of Neurology and currently serves as its Chair. His research is translational and is focused on 1) the identification of novel biomarkers of autoimmune neurological diseases. His group discovered antibodies targeting AQP4, GFAP, MAP1B-IgG, KELCH11, NIF, PDE10 and CRMP5; 2) the clinical application of laboratory-based tests in diagnosis and outcome prediction for patients with

autoimmune and paraneoplastic neurological disorders; 3) optimizing the clinical management of autoimmune and paraneoplastic neurological disorders. He has published 325 peer reviewed papers.

The Neuroimmunology Laboratory tests sera and CSF from approximately 200,000 patients for comprehensive neural antibody profiles (CAP and New York State certified) pertinent to encephalopathy, epilepsy, myasthenia gravis, and CNS inflammatory demyelinating disorders including neuromyelitis optica. His recent work has focused on Phase 3 immunotherapy trials for patients with autoimmune epilepsies and CNS demyelinating disorders (targets include LGI1 and AQP4). This unique translational practice, extending the laboratory's serologic findings directly to the bedside, has allowed the creation of diagnostic decision trees which will optimize triaging of such patients for further phenotype analysis and biomarker discovery.

### **Presentation Synopsis**

In 1956, Moersch and Woltman identified a syndrome they termed stiff-man (now termed person) syndrome (SPS). In 1988, Solimena and colleagues recognized that SMS was an autoimmune disorder associated with antibodies to glutamic acid decarboxylase-65 (GAD65). Antibodies targeting GAD65 are a biomarker of type 1 diabetes mellitus (T1DM), but at low titers they lack clinical specificity for autoimmune neurological disease. In contrast, high-titer GAD65 antibodies, over 1000-fold higher than the upper limit of normal, confer high clinical specificity for GAD65 neurological autoimmunity. SPS was determined to be a prototypical presentation of GAD65 neurological autoimmunity, however it is now recognized that nearly half of patients lack an SPS phenotype. SPS, cerebellar ataxia, epilepsy, and limbic encephalitis may all occur in isolation, and these are considered the primary disease manifestations of GAD65-neurological autoimmunity. Many patients have overlapping phenotypes with multifocal manifestations that also can include cognitive impairment, brainstem dysfunction, and myelopathy. Psychiatric symptoms, especially anxiety, are common. SPS is the most immunotherapy-responsive presentation, while epilepsy is least immunotherapy-responsive. Complete response to immunotherapy is rare.

*Dr. Pittock is a consultant for Sage Therapeutics, Astellas and Genentech. He is also on the advisory board for Genentech and F. Hoffman-LaRoche AG; UCB. He also provides research support for Alexion; Grifols; NIH; Viela Bio/MedImmune. All of the relevant financial relationships for this individual have been mitigated.*

### **Sameer Sheth, MD, PhD**

Associate Professor of Neurosurgery, Psychiatry & Behavioral Sciences, and Neuroscience  
Cullen Foundation Endowed Chair, Baylor College of Medicine

*Topic: Neuromodulation for Psychiatric Disorders*

*Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>*

### **Speaker Biography**

Dr. Sameer Sheth is currently Associate Professor, Cullen Foundation Endowed Chair, Vice-Chair of Research, and McNair Scholar in the Department of Neurosurgery, Baylor College of Medicine, Houston, TX. He also holds joint appointments in the Department of Neuroscience and Department of Psychiatry & Behavioral Sciences at Baylor, and is an Adjunct Associate Professor in the Department of Electrical and Computer Engineering at Rice University. Dr. Sheth received his bachelor's degree in Physics and Astronomy at Harvard University Summa Cum Laude before earning his MD and PhD from the University of California Los Angeles.

Dr. Sheth completed his residency and a fellowship in stereotactic and functional neurosurgery at the Massachusetts General Hospital and Harvard Medical School. Clinically, Dr. Sheth specializes in stereotactic/functional neurosurgery, including the surgical treatment of movement disorders, epilepsy, and psychiatric disorders. He employs a combination of stereotactic and traditional open surgical techniques, including deep brain stimulation (DBS), neuromodulation, laser ablation, radiosurgery, and microsurgery.

Dr. Sheth's research focuses on cognitive neurophysiology, often using opportunities derived from his clinical work. He studies higher order human cognitive processes, including decision-making and emotional regulation, using intracranial electrophysiological recordings and advanced imaging techniques. His lab also strives to improve neuromodulatory treatments for neurological and psychiatric disorders, including depression and dementias, using innovative surgical techniques.

### **Presentation Synopsis**

Dr. Sheth will review the history and development of neurosurgery for psychiatric disorders, focusing on neuromodulation therapies like DBS. In particular, he will discuss DBS for severe, treatment-resistant depression and will cover the current state of this therapy and future directions of research.

*Dr. Sheth is a consultant for Boston Scientific Corporation, Zimmer Biomet, Neuropace, and Abbott. All of the relevant financial relationships for this individual have been mitigated.*

### **Charles Raison, MD**

Professor of Psychiatry, University of Wisconsin

*Topic: Inflammation in the Development and Treatment of Depression*

Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Charles Raison is the Mary Sue and Mike Shannon Distinguished Chair for Healthy Minds, Children & Families; Professor, Human Development and Family Studies, School of Human Ecology; Professor, Department of Psychiatry, School of Medicine and Public Health, University of Wisconsin-Madison; and the Director of Clinical and Translational Research for Usona Institute. Web of Science named him one of the world's most influential researchers, with nearly 11,000 citations in the decade preceding 2019 and 137 publications.

Prior to his appointment in the School of Human Ecology, he was Professor in the Department of Psychiatry, College of Medicine, and the Barry and Janet Lang Professor of Integrative Mental Health at the Norton School of Family and Consumer Sciences, College of Agriculture and Life Sciences, University of Arizona. Dr. Raison serves as the founding Director of the Center for Compassion Studies in the College of Social and Behavioral Sciences at the University of Arizona. Dr. Raison is internationally recognized for his studies examining novel mechanisms involved in the development and treatment of major depression and other stress-related emotional and physical conditions, as well as for his work examining the physical and behavioral effects of compassion training. The recipient of several teaching awards, Dr. Raison has received research funding from the National Institute of Mental Health, National Center for Complementary and Alternative Medicine, and the Centers for Disease Control and Prevention. Dr. Raison has received a NARSAD Independent Investigator Award and has received the Raymond Pearl Memorial Award from the Human Biology Association “in recognition of his contributions to our understanding of evolutionary biocultural origins of mental health and illness.”

In addition to his academic activities, Dr. Raison is the mental health expert for CNN.com.

### **Presentation Synopsis**

Dr. Raison will discuss how increased inflammation is associated with a unique type of major depressive disorder, how to utilize inflammatory biomarkers to help guide psychopharmacologic treatment decisions, and how to identify which patients are likely to benefit from and which are likely to be harmed by treatment with anti-inflammatory agents

*Dr. Raison is a consultant for Usona Institute, Alfasigma, Novartis, and Otsuka. All of the relevant financial relationships for this individual have been mitigated.*

### **Michael Wilson, MD**

Distinguished Professor of Neurology at University of California, San Francisco (UCSF); Neurologist, UCSF Weill Institute for Neurosciences, Department of Neurology

*Topic: Autoimmune and Infectious Encephalitis*

*Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>*

### **Speaker Biography**

Dr. Michael Wilson is a Debbie and Andy Rachleff Distinguished Professor of Neurology and an Associate Professor in the UCSF Department of Neurology and Weill Institute of Neurosciences. He is a neurologist specializing in infectious and autoimmune diseases of the central nervous system. He sees patients with autoimmune diseases like multiple sclerosis as well as patients with a wide array of infectious diseases that impact the nervous system like HIV, neurocysticercosis, neurosyphilis, viral encephalitis and fungal infections like coccidiomycosis (valley fever). His laboratory uses metagenomic and immune repertoire sequencing techniques as well as phage display technologies to enhance understanding of the causes and

immunopathogenesis of multiple sclerosis as well as autoimmune and infectious causes of meningoencephalitis.

### **Presentation Synopsis**

Dr. Wilson will review the tools for differentiating between infectious and autoimmune causes of encephalitis and what they do to identify autoantibody targets in patients with autoimmune encephalitis.

*Dr. Wilson received honorarium for speaking for Genentech, Takeda, and Novartis. He also received honorarium for research support for Roche/Genentech. All of the relevant financial relationships for this individual have been mitigated.*

### **Sarkis Mazmanian, PhD**

Luis B. and Nelly Soux Professor of Microbiology, Caltech;  
Investigator, Heritage Medical Research Institute

*Topic: Development of Microbiome-Based Therapeutics for Autism*

*Maximum of 0.75 AMA PRA Category 1 Credit(s)<sup>™</sup>*

### **Speaker Biography**

Dr. Sarkis Mazmanian is the Luis B. and Nelly Soux Professor of Microbiology in the Division of Biology & Biological Engineering at the California Institute of Technology (Caltech). He is a Phi Beta Kappa graduate from the University of California, Los Angeles, where Dr. Mazmanian also received his doctoral training in microbiology and immunology studying the mechanism by which Gram-positive pathogens anchor surface protein adhesins during bacterial infection. He was a Helen Hay Whitney Post-doctoral Fellow at Harvard Medical School where he studied how symbiotic bacteria promote healthy maturation of the immune system. He was promoted to assistant professor at Harvard Medical School in 2006, and later that year moved to Caltech to start his independent laboratory. Dr. Mazmanian has won numerous awards including a Searle Scholar, Young Investigator of the Year at Harvard Medical School, Damon Runyon Innovation Award, was named by Discover Magazine as one of the “Best Brains in Science under 40” and recently received the MacArthur Foundation “Genius” award. His laboratory currently focuses on the study of beneficial bacterial molecules from the human gut microbiome as novel therapies for immunologic and neurologic disorders. This research has led to identification of novel drug candidates being developed for Inflammatory Bowel Disease, Autism Spectrum Disorder, and Parkinson’s disease. He is a founder of three biotech companies and serves on the Scientific Advisory Board of over a dozen companies, academic centers and not-for-profit foundations. Most importantly, Dr. Mazmanian has trained numerous students and fellows who have gone on to successful independent careers in academia, industry, and medicine.

### **Presentation Synopsis**

The gut microbiome has been associated with effects on the brain. Recently, research has shown that engineering bacteria to selectively produce microbial metabolites in the gut of mice led to changes in brain activity, functional and structural connectivity in brain regions linked to

emotional behavior, as well as gene expression signatures of altered oligodendrocyte function. Indeed, production of gut-derived molecules by the microbiome is associated with increased proportions of immature oligodendrocytes in mice and, accordingly, decreased myelination of neuronal axons in the brain. Furthermore, mice exposed to 4EPS display anxiety-like behaviors, reduced social activity and decreased vocalization. Thus, molecules from the gut microbiome can impact complex behaviors.

*Dr. Mazmanian is the cofounder and a board member of Axial Therapeutics. He receives a consulting fee and equity. All of the relevant financial relationships for this individual have been mitigated.*

### **Mark Pasternack, MD**

Chief of Infectious Disease, Massachusetts General Hospital;  
Associate Professor of Pediatrics, Massachusetts General Hospital, Harvard Medical School  
*Topic: Use of Antibiotics in Infection Associated Neuropsychiatric Syndromes Including PANS*  
Maximum of 0.75 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Mark Pasternack is Chief, 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.

### **Presentation Synopsis**

Dr. Pasternack will review the evolution in understanding the role of group A streptococci as a trigger for postinfectious neurobehavioral disorders, address the diversity of group A streptococci as a possible explanation to the challenge of “Why PANDAS? Why now?” and review the natural history of PANDAS and PANS and the challenges inherent in their diagnoses and management.

*Dr. Pasternack receives equity from Merck and author royalty from Up To Date. All of the relevant financial relationships for this individual have been mitigated.*

### **Janet Cunningham, MD**

Associate Professor in the Department of Neuroscience; Associate Professor in Experimental Psychiatry; Psychiatrist, Uppsala University, Sweden  
*Topic: Clinical and Biological Heterogeneity in An Adult Patient Cohort with Psychiatric Symptoms Enriched for Suspected Immunological Involvement*

Maximum of 0.75 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Janet Cunningham is an Associate Professor in Experimental Psychiatry at Uppsala University, is also affiliated with the Department of Neurosciences at Karolinska Institute and a board-certified specialist in Clinical Psychiatry at Uppsala University Hospital. She has an unusual background for a psychiatrist. She completed a BSc in Immunology and Microbiology with Honors at McGill University, Canada and thereafter a preclinical PhD and postdoc in Uppsala, Sweden, where she applied molecular techniques to further characterize and subgroup rare serotonin producing endocrine tumors. Dr. Cunningham shifted her focus to Psychiatry after several coinciding experiences profoundly shifted her perception of psychiatric disease and awoke her curiosity for the biological mechanisms. Dr. Cunningham leads the Immunopsychiatry team in Uppsala which aims to develop tools to differentiate adaptive from maladaptive immunological responses in treatment-resistant patients with severe psychiatric symptoms in order to identify patients for whom immunomodulation therapy will be beneficial. The hypothesis is that different types of maladaptive immunological responses include immunodeficiencies, vulnerability such as difficulty in mobilizing anti-inflammatory processes needed for inflammation resolution, and autoimmunity. To ensure relevance for clinical psychiatry, research is tightly integrated with patient care at Uppsala University Hospital. Cross-sectional and longitudinal data and samples are continuously collected from daily practice and clinical trials. The strategy is to use and compare knowledge gained by in-depth analysis of individual cases and large-scale analysis of markers related to the immune system in broad patient cohorts to identify markers with variation within the patient group with potential relevance for diagnosis and clinical prognosis. The research questions have the potential to directly impact clinical practice in psychiatry. Dr. Cunningham is the coordinator for a professional network, The Swedish Immunopsychiatry Alliance. She is a member of the Research Network, European College of Neuropsychopharmacology (ECNP) Immuno-NeuroPsychiatry work-group and is a member the Scientific and Medical Advisory Board for The European Immunopsychiatric Association (EXPAND).

### **Presentation Synopsis**

This talk will discuss the establishment of the Uppsala Immunopsychiatry Clinic which started as a pilot project in 2015 and has now been implemented into standard care. Illustrative cases and the high rates of CNS pathology but also heterogeneity in the data from the first 127 patients will be presented.

*Dr. Cunningham receives speaker honorarium from Otsuka Pharma Scand, Janseen-Lil ag AB, and H Lundbeck AB. All of the relevant financial relationships for this individual have been mitigated.*

### **Chandra Menendez, PhD**

Postdoctoral Research Fellow, Microbiology & Immunology, Madeleine Cunningham Laboratory, University of Oklahoma Health Sciences Center

*Topic: A New Look: Autoantibodies Against the Dopamine Receptors Define PANDAS and Sydenham Chorea*

Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Chandra Menendez is a Postdoctoral Fellow in the Department of Microbiology and Immunology at the University of Oklahoma Health Sciences Center in Dr. Madeleine Cunningham's Laboratory. Her primary research focus is to understand the autoimmune pathophysiology of neuropsychiatric disorders. Her neuroimmunology and infectious disease background provide a unique angle aimed at investigating the relationship between neural inflammation-mediated autoimmunity and cognitive and/or behavioral disorders in children. She is currently exploring cross-reactive humoral responses and their biological impact in neuropsychiatric disorders including Sydenham Chorea and PANDAS.

Dr. Menendez aspires to continue the legacy of Dr. Cunningham's impressive contribution to science, commitment to mentorship, and her pioneering work in autoimmune-related mechanisms in infectious disease.

### **Presentation Synopsis**

Basal ganglia encephalitis (BGE) is poorly understood and is associated with infection-related neurologic and neuropsychiatric sequelae. We provide understanding of BGE on a new level, and identify two immune subtypes of BGE as Sydenham Chorea (SC) and pediatric autoimmune neuropsychiatric disorders associated with group A streptococcal infections (PANDAS). In our study, neuropsychiatric syndromes were associated with autoantibodies that activated the dopamine D1 receptor (D1R) and choreatic movement disorders were associated with the dopamine D2 receptor (D2R). We describe a novel mechanism for behavioral dysfunction in neuropsychiatric disturbances in BGE where autoantibodies target D1R, lead to dopaminergic signaling abnormalities, and drug-like enhancement of signaling mediated by dopamine. Our findings shed a new perspective on distinguishing BGE subtypes and offer insight into alternative therapies.

*Dr. Menendez 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.*

### **Brent T. Harris, MD, PhD, FCAP**

Associate Professor of Pathology and Neurology, Director of Neuropathology, Director, Georgetown Brain Bank at Georgetown University Hospital; Director, Histopathology and Tissue Shared Resource, MedStar Health/Georgetown University Medical Center

*Topic: The Neuropathology of Autoimmune Encephalitis and PANS and Development of Specialized Brain Banks for these Disorders*

Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Brent Harris is a tenured faculty member of Georgetown University with dual appointments in Neurology and Pathology. As a neuropathologist and physician-scientist, Dr. Harris has clinical, research, and teaching interests in neurological and oncological diseases. He has active collaborations and research programs in his own lab in the areas of neurodegeneration and CNS neoplasia. His primary interest is in understanding how mechanisms of neuroinflammation and glial-neuronal communication influence the pathophysiology of neurological diseases. In addition to investigating disease processes, he also seeks to uncover targets for pharmacological intervention.

### **Presentation Synopsis**

Dr. Harris will describe the different types of neuroimmune related diseases that have been studied by neuropathological methods and what is seen on brain biopsies or post-mortem examination and discuss 21st century brain banking techniques.

*Dr. Harris 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.*

### **Agnieszka Kalinowski, MD**

Clinical Instructor, Psychiatry and Behavioral Sciences, Stanford

*Topic: C4B Gene Copy in Children With PANS*

Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Agnes Kalinowski is a physician-scientist conducting translational research in schizophrenia as an Advanced Fellow in Mental Health Research at the Palo Alto VA and Department of Psychiatry and diagnosing and treating patients with schizophrenia in the INSPIRE Early Psychosis Clinic. The overarching theme of her work is understanding the initiating and perpetuating factors that result in abnormal pathology in individuals with schizophrenia. She uses a combination of clinical samples and molecular studies in model systems.

### **Presentation Synopsis**

Dr. Kalinowski will present the results from the first analysis of experimentally determined C4 gene copy number variation in a cohort of 225 PANS/PANDAS patients compared to 248 controls. Relationships to known C4 gene variation associations will be discussed.

*Dr. Kalinowski is a consultant for Pasitheia. All of the relevant financial relationships for this individual have been mitigated.*

### **Shannon Delaney, MD**

Neuropsychiatrist, Assistant Professor of Psychiatry, Columbia University Medical Center; Director, Child and Adolescent Evaluation, Lyme & Tick-borne Disease Research Center

*Topic: Neuropsychiatric illness associated with Lyme and tick-borne illness*  
Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Shannon Delaney is a neuropsychiatrist at Columbia University Irving Medical Center who is co-director with Dr. Fallon of the Cohen Center for Health and Recovery from Lyme and Tick-borne Diseases. She completed her NIH-sponsored research fellowship at Columbia University in 2017. Her clinical research has focused on immune and infectious contributions to psychiatric disease, especially psychosis in children and young adults. She specializes in seeing children and adults with complex neuropsychiatric presentations, especially those with suspected Lyme disease or other tick-borne diseases, as well as those with PANS.

### **Presentation Synopsis**

Dr. Delaney's presentation will discuss an overview of the epidemic of Lyme disease and basics regarding EM rashes and diagnostic testing, discuss literature reviewing persistent symptoms after Lyme disease, provide case vignettes highlighting neuropsychiatric symptoms after Lyme Disease, and review other tick-borne illnesses such as *Borrelia miyamotoi*.

*Dr. Delaney 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.*

### **Emily Severance, PhD**

Assistant Professor of Pediatrics, Johns Hopkins University School of Medicine

*Topic: Autoimmune Phenotypes in Psychiatric Disorders*

Maximum of 0.75 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Emily Severance is an Assistant Professor of Pediatrics at the Johns Hopkins University School of Medicine. She is a member of the Stanley Division of Developmental Neurovirology research team and has served with the Scott-Gentle Foundation of The Brain and Behavior Research Foundation and the Johns Hopkins Silvio O. Conte Center for Schizophrenia Research. As part of her ongoing research program, Dr. Severance focuses on the major gateway of the immune system, the gastrointestinal mucosa, where inflammation, food hypersensitivities, barrier defects and immune dysregulation can cause downstream brain dysfunction in people with psychiatric disorders. She is also involved in research studies of COVID-19 and the roles of other viral, bacterial, and fungal pathogens in mental illness.

Dr. Severance earned her BS from the University of Maryland and her PhD from the University of South Florida.

### **Presentation Synopsis**

Psychiatric researchers are looking beyond the central nervous system (CNS) for novel ways that the body's peripheral cellular and molecular pathways might be harnessed into effective

treatments of brain disorders. The gastrointestinal tract and its resident microbiome serve as a critical hub regulating self and non-self-interactions, which when dysregulated can generate pathological autoimmunity peripherally and in the brain. Within a framework of the gut-brain axis, Dr. Severance will review the role of inflammation, infectious agents, food antigens, gut dysbioses, endothelial barrier instabilities, and autoantibody propagation on CNS pathologies such as neurotransmitter receptor hypofunction and complement pathway-mediated synaptic pruning. Dr. Severance will talk about the current major findings propelling the field forward and the future of translating this research to clinical application and treatments.

*Dr. Severance is receiving honorarium for speaking for American Psychiatric Association and Missouri Psychiatric Physicians Association. All of the relevant financial relationships for this individual have been mitigated.*

**Sarosh Irani, FRCP, DPhil, FEAN**

Associate Professor, University of Oxford; Head of Autoimmune Neurology Group at University of Oxford

*Topic: The Immunology Underlying Autoantibody Associated CNS Diseases*

Maximum of 1.0 AMA PRA Category 1 Credit(s)<sup>™</sup>

**Speaker Biography**

Dr. Sarosh Irani is a consultant neurologist and clinician-scientist with clinical and laboratory experiences in the field of autoantibody mediated diseases of the nervous system, in particular the central nervous system. He cares for patients with these disorders and leads a research group to learn more about the origins and treatments of these diseases. He has studied the antigenic targets of autoantibodies in patients with encephalitis and epilepsies. In particular, his research has focused on LGI1, CASPR2, and the NMDA-receptor. In addition, he has been involved with projects examining autoantibodies against the GABAA-receptor, glycine receptors, and aquaporin-4.

He has looked after more than 200 patients with these disorders and characterized their clinical responses to therapies. These findings have generated clinical features, often distinctive, which correlate well with a high likelihood of an immunotherapy-responsive condition. They have also identified novel clinical descriptions of patients with cognitive, movement, and seizure disorders, in particular faciobrachial dystonic seizures - a novel autoimmune epilepsy syndrome which often responds better to immunotherapies than conventional anti-epileptic drugs.

He leads a research group combining approximately 15 talented clinicians, clinician-scientists, and basic scientists with the aim of better understanding the causes and potential treatments of this condition. In particular, they study the role of B cell subsets in propagating autoantibody responses and the effects of antibodies in the brain. They are funded by the Wellcome Trust, Medical Research Council, British Medical Association, Association of British Neurologists and industry partners.

**Presentation Synopsis**

Dr. Irani will discuss the clinical features and emerging immunobiology underlying autoantibody-mediated CNS disease syndromes with a focus on LGI1, CASPR2, and NMDAR-antibody encephalitis and their antigen-specific B cell populations.

*Dr. Irani receives honorarium for consulting for UCB, Immunovant, MedImmune, Brain and ADC therapeutics, and Medlink Neurology. He receives royalty for being an inventor of the patent for LGI1/Caspr2 antibodies. He also provides research support as PI for CSL Behring, UCB, and ONO Pharma. All of the relevant financial relationships for this individual have been mitigated.*

### **Wei Zhao, MD, PhD**

Professor and Chief, Division of Allergy and Immunology, Virginia Commonwealth University

*Topic: Plasmapheresis in Treatment of PANS*

Maximum of 0.75 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Dr. Wei Zhao received his medical degree from Wenzhou Medical University in China. He received his PhD in Immunology from West Virginia University. He then completed his pediatric residency at West Virginia University and his fellowship in Allergy and Immunology at Virginia Commonwealth University. He has been on faculty with VCU since 2003. Currently he is a Professor in Pediatrics and Division Chief of Allergy and Immunology. Dr. Zhao is board certified with the American Board of Pediatrics and American Board of Allergy and Immunology. He is also a member of the American Academy of Allergy, Asthma, and Immunology and American College of Allergy, Asthma, and Immunology. He served as the President of the Allergy and Asthma Society of Virginia from 2012-2014. He has been named as Top-Doctor since 2012 by Richmond Magazine. His research interest has been human mast cells and their role in allergic and immunologic disorders. He has been the principal investigator of NIH sponsored projects and key member of asthma and allergic disease center in VCU.

### **Learning Objectives:**

- Discuss the role of plasma pheresis in management of PANS and PANDAS.
- Summarize the results and outcomes of patients receiving plasma pheresis in our institution.

*Dr. Zhao 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.*

### **Jill Hollenbach, PhD, MPH**

Associate Professor, Department of Neurology, University of California, San Francisco

*Topic: Immunogenetic Variation in PANS and Neuroinflammatory Disease*

Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>

### **Speaker Biography**

Jill Hollenbach is Associate Professor in the Department of Neurology and Department of Epidemiology and Biostatistics at the University of California, San Francisco. She was raised in California and completed her undergraduate studies in Physiology and Master's degree in Public Health at the University of California, Berkeley. After several years working in public health in the Caribbean and Bay Area, she returned to UC Berkeley for her doctoral studies in Immunology, with an emphasis on population genetics of the human leukocyte antigen (HLA) system. Throughout her career, Dr. Hollenbach's work has continued to focus on the HLA loci and related systems such as the killer immunoglobulin-like receptor (KIR) genes in disease association, transplantation, and evolutionary studies. She has also been deeply involved in the establishment of community standards and software development for immunogenetic data management and analysis and is a Councilor of the International HLA and Immunogenetics Council and Associate Editor for disease association studies at HLA Journal. Dr. Hollenbach's laboratory at UCSF applies study of these complex systems to advance efforts to elucidate the genetic basis of underlying immune dysregulation in neurological, autoimmune, and infectious disease.

**Learning objectives:**

- Understand the nature of variation in HLA and KIR, polymorphic genes encoding immune receptors.
- Understand the role that immunogenetic variation plays in neuroinflammatory diseases like multiple sclerosis, and implications for ongoing research in PANS.

*Dr. Hollenbach 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.*

**Kiki Chang, MD**

Adjunct Professor of Psychiatry and Behavioral Sciences, University of Texas at Houston

*Topic: Review of Expert Consensus Treatment Guidelines for Youth with PANS*

Maximum of 0.75 AMA PRA Category 1 Credit(s)<sup>™</sup>

**Speaker Biography**

Dr. Kiki Chang is a child psychiatrist with over 22 years of experience in working with younger children, adolescents, adults and families. Formerly, Dr. Chang was Professor of Psychiatry and Behavioral Sciences at Stanford University School of Medicine and co-founder of the Stanford PANS Clinic. His specialty is working with youth and young adults who have or are at risk for serious mood disorders, such as depression or bipolar disorder, as well as PANS/PANDAS and related neuropsychiatric disorders. By working with children who have these complex conditions, he has also accumulated extensive experience in working with ADHD, anxiety, behavioral disorders, OCD, tic disorders, psychotic disorders, and autism spectrum disorders. His research has focused on genetic and biological markers, particularly brain imaging, for risk for development of severe mood disorders, and interventions to prevent such disorders from occurring.

**Learning Objectives:**

- Understand the role of psychotropic medications in treating youth with PANS/PANDAS.
- Discuss the different symptoms that present in PANS and how they may overlap with typical psychiatric disorders.
- Consider appropriate psychiatric treatments and therapies for youth with PANS.

*Dr. Chang is a consultant for Sunovion, AbbVie, and Compass Pathways. All the relevant financial relationships for this individual have been mitigated.*

**Dritan Agalliu, PhD**

Associate Professor of Pathology and Cell Biology in Neurology, Columbia University  
*The Role of the Adaptive Immunity and Genetic Risk Factors in Vascular and Neuronal Dysfunction in Post Infectious Autoimmune Encephalitis*  
Maximum of 0.5 AMA PRA Category 1 Credit(s)<sup>™</sup>

**Speaker Biography**

Research in Dr. Dritan Agalliu's laboratory is focused on understanding the cellular and molecular mechanisms that regulate formation of the blood-brain barrier in the central nervous system (CNS) using genetic approaches in mice and the mechanisms of barrier breakdown in a variety of CNS diseases, such as stroke and autoimmune diseases having symptoms that include bloodbrain barrier failure, using genetic, molecular, cellular and imaging approaches. We have developed novel mouse strains that allow us to visualize changes in structural components of the blood-brain barrier, namely tight junctions and caveolae, in living animals for several CNS diseases (e.g. stroke and multiple sclerosis) in order to understand the cellular mechanisms underlying barrier impairment in these neurological disorders. In addition, we are investigating the role of Wnt/b-catenin signaling in development of the CNS vasculature and formation of the blood-brain barrier, and we are exploring the role of this pathway in repairing the barrier in diseases where its function is compromised (e.g. stroke and autoimmune disorders). Finally, we are investigating the mechanisms of immune cells' entry into the CNS in a novel animal model for a neuropsychiatric disorder caused by multiple *Streptococcus pyogenes* infections, in order to understand how immune cells induce neurovascular, synaptic, and behavioral deficits in the brain.

**Learning Objectives:**

- Describe what causes Autoimmune Encephalitis, Post-Infectious Autoimmune Encephalitis, and what are the immune mechanisms that induce the disease.
- Identify how Th17 lymphocytes induce blood-brain barrier damage, neuroinflammation, and cause neuronal impairment in animal models for post-infectious basal ganglia encephalitis.
- Describe which potential cytokines are present in sera from PANDAS/PANS patients and their effect on the blood-brain barrier in vitro.
- Understand how genetic risk factors are identified in PANDAS/PANS that predispose the children to develop the disease and discuss the main outcome of these studies.

*Dr. Agalliu 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.*

**Cheri Standing, MD**

Pediatrician, Greater Regional Health

*Topic: PANS Cases: Through the Eyes of a Pediatrician*

Maximum of 0.50 AMA PRA Category 1 Credit(s)<sup>™</sup>

**Speaker Biography**

Dr. Cheri Standing is a pediatrician at Greater Regional Health in Creston, Iowa. She completed a pediatric residency at Strong Memorial Hospital and fellowships in pediatric emergency medicine at Nationwide Children's Hospital and more recently Andrew Weil's integrative medicine fellowship program. She practices general pediatrics, pediatric emergency medicine, and has a designated interdisciplinary PANS clinic.

**Presentation Synopsis**

Dr. Standing will present case reviews from patients she has treated at Greater Regional Health in Creston, Iowa. The PANS Clinic is in a nonacademic, clinical setting. Cases are chosen to portray a general pediatrician's perspective relating to recognizing and treating post-infectious neuropsychiatric presentations in children.

*Dr. Standing 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.*