

Biomarkers to Enable Therapeutics Development in Neurodevelopmental Disorders

*Crystal Gateway Marriott
1700 Jefferson Davis Highway, Arlington, VA
Salons 1 & 2*

December 7 – 9, 2017

AGENDA

Thursday, December 7, 2017

7:00 AM – 5:30 PM	Registration
8:00 – 8:15 AM	Welcome and Opening Remarks – <i>Walter Koroshetz, NINDS Director</i>
8:15 – 8:30 AM	Workshop Goals – <i>Laura Mamounas, NINDS</i>
8:30 – 9:00 AM	Session I: Setting the Stage Session Chair: <i>Laura Mamounas, NINDS</i> The Need for Translational Biomarkers in Neurodevelopmental Disorders (NDDs) – <i>Mustafa Sahin, Boston Children’s Hospital</i> FDA Biomarker Qualification Program for Pediatric NDDs – <i>Susan McCune, FDA</i> Neuroscience Biomarkers: A View from Industry – <i>Hartmuth Kolb, Janssen R&D, LLC</i> Linking Macroscale Biomarkers to Microscale Circuit Mechanisms: A Basic Science Perspective – <i>Stephanie Jones, Brown University</i>
9:00 – 9:30 AM	
9:30 – 10:00 AM	
10:00 – 10:30 AM	
10:30 – 10:50 AM	Break
10:50 – 10:55 AM	Session II: Basic Cortical Mechanisms and the EEG Session Chair: <i>David McCormick, University of Oregon</i> Overview of Session: <i>David McCormick</i> Translational Studies Aimed at the Neuronal Generators of Critical EEG/ERP Biomarkers – <i>Charles Schroeder, Columbia University</i> From Cells and Circuits to ERPs and EEGs – <i>Barry Connors, Brown University</i> Potential Mechanisms Underlying Altered Resting Gamma EEG in FMR1 KO Mice – <i>Jay Gibson, University of Texas Southwestern Medical Center</i> Cortical Dysfunction in Rett Syndrome – <i>David Katz, Case Western Reserve University School of Medicine</i> Discussion
10:55 – 11:15 AM	
11:15 – 11:35 AM	
11:35 – 11:55 AM	
11:55 AM – 12:15 PM	
12:15 – 12:40 PM	

12:40 – 1:40 PM	Lunch (on your own)
	Session III: Applied Research in Clinical Electrophysiology Session Chair: <i>Sara Webb, University of Washington</i>
1:40 – 1:45 PM	Overview of Session: <i>Sara Webb</i>
1:45 – 2:05 PM	Signal Processing Methods in EEG-Based Biomarkers – <i>Joshua Ewen, Kennedy Krieger Institute</i>
2:05 – 2:25 PM	Auditory ERPs in Fragile X Syndrome: A Translational Tool for Development of Novel Therapeutics – <i>Lauren Ethridge, University of Oklahoma</i>
2:25 – 2:45 PM	M100 and Gamma Oscillations in 16p11.2, 47,XYY and ASD: Identifying Mechanisms of Neural Dysfunction – <i>Timothy Roberts, Children’s Hospital of Philadelphia</i>
2:45 – 3:05 PM	Beta Oscillations in Dup15q Syndrome: Biomarker Development and Implications for Clinical Trials – <i>Shafali Jeste, University of California Los Angeles</i>
3:05 – 3:30 PM	Discussion
3:30 – 3:50 PM	Break
	Session IV: Imaging Biomarkers Session Chair: <i>Darcy Krueger, Cincinnati Children’s Hospital Medical Center</i>
3:50 – 3:55 PM	Overview of Session: <i>Darcy Krueger</i>
3:55 – 4:15 PM	Predictive fcMRI Biomarkers for ASD – <i>John Pruett, Washington University Medical School</i>
4:15 – 4:35 PM	Imaging Biomarkers for ASD in Tuberous Sclerosis Complex – <i>Simon Warfield, Boston Children’s Hospital</i>
4:35 – 4:55 PM	White Matter Morphology as a Possible Biomarker in Angelman Syndrome – <i>Heather Hazlett, University of North Carolina, Chapel Hill</i>
4:55 – 5:40 PM	Discussion: integrating all approaches discussed in Day 1 <ul style="list-style-type: none"> • Discussion Leaders: <i>Darcy Krueger, David McCormick, Sara Webb</i>

Friday, December 8, 2017

	Session V: Developmental Considerations for Clinical Biomarkers in Pediatric Disorders Session Chair: <i>Daniel Tarquinio, Emory University</i>
8:00 – 8:20 AM	Brain Imaging Biomarkers in Early Childhood: Developmental Considerations – <i>Joseph Piven, University of North Carolina, Chapel Hill</i>
8:20 – 8:40 AM	A Tale of Two Functional Connectivity-Based ASD Biomarkers – <i>Tal Kenet, Massachusetts General Hospital</i>
8:40 – 9:00 AM	Potential Biomarkers and their Expression during Adolescent Neurocognitive Development – <i>Beatriz Luna, University of Pittsburgh</i>
9:00 – 9:20 AM	The Use of EEG and Evoked Potentials as Biomarkers in NDDs – <i>Charles Nelson, Boston Children’s Hospital</i>
9:20 – 9:40 AM	Discussion

9:40 – 10:00 AM	Break
10:00 – 10:20 AM	<p>Session VI: From the Clinic to Development of Translatable Biomarkers in Models Session Chair: <i>Eric Marsh, Children’s Hospital of Philadelphia</i></p> <p>Visual Circuit Dysfunction in Rett Syndrome and CDKL5 Disorder: Development of Translatable Markers from the Clinic to Mouse Models – Michela Fagiolini, Boston Children’s Hospital</p> <p>Abnormal Auditory Processing in Fragile X Syndrome: Mechanisms and Biomarkers – Khaleel Razak, University of California, Riverside</p> <p>Using MEG-measures of Task-Based Oscillatory Dynamics and Resting-State Connectivity as New Translational Markers of Disease, Trait, and Genetic Risk – Krish Singh, Cardiff University</p> <p>Preclinical and Clinical EEG Biomarkers in Angelman Syndrome – Benjamin Philpot, University of North Carolina, Chapel Hill</p> <p>Anatomical MRI as a Translatable Tool to Study NDDs – Jason Lerch, Toronto Hospital for Sick Children</p> <p>Discussion</p>
10:20 – 10:40 AM	
10:40 – 11:00 AM	
11:00 – 11:20 AM	
11:20 – 11:40 AM	
11:40 AM – 12:00 PM	
12:00 – 1:30 PM	<p>Lunch (on your own)</p> <ul style="list-style-type: none"> Working Group members meet and finalize group presentations. (<i>Boxed lunches are available for pre-order</i>)
1:30 – 1:50 PM	<p>Panel I: Current Biomarker Development Programs: Moving from Biology to Clinical Trials Session Chair: <i>William Potter, NIMH</i></p> <p>Brief History of Role and Rationale for Biomarkers in CNS Drug Development – William Potter, NIMH</p> <p>Biomarkers for Speeding Drug Discovery in NDDs: An Academic Perspective – John Sweeney, University of Cincinnati</p> <p>European Autism Interventions – A Multicentre Study for Developing New Medications (EU AIMS) – Declan Murphy, King’s College London</p> <p>The Autism Biomarkers Consortium for Clinical Trials (ABC-CT) – James McPartland, Yale Child Study Center</p> <p>Introducing the Healthy Brain Network: An Open Resource for Transdiagnostic Research in Pediatric Mental Health and Learning Disorders – Michael Milham, Child Mind Institute</p> <p>The Development of Clinical Trials Tools for ASD – Results from the Janssen Autism Knowledge Engine (JAKE) System – Gahan Pandina, Janssen R&D, LLC</p> <p>Discussion</p>
1:50 – 2:10 PM	
2:10 – 2:25 PM	
2:25 – 2:40 PM	
2:40 – 2:55 PM	
2:55 – 3:10 PM	
3:10 – 3:50 PM	
3:50 – 4:10 PM	Break

4:10 – 5:40 PM	<p>Panel II: Real World Challenges of Taking Biomarkers from the Lab to Clinical Trials Session Chair: <i>Adam Hartman, NINDS</i></p> <p>Panel & Discussion Leaders</p> <ul style="list-style-type: none"> • <i>Martina Bebin, University of Alabama, Birmingham</i> • <i>Elizabeth Berry-Kravis, Rush University Medical Center</i> • <i>Craig Erickson, Cincinnati Children’s Hospital Medical Center</i> • <i>Debra Moritz, mother of a son with Tuberous Sclerosis Complex</i> • <i>Dominique Pichard, mother of a daughter with Rett Syndrome</i>
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Saturday, December 9, 2017

	<p>Session VII: Emerging Strategies and other ‘Hot Topics’ in Biomarker Development Session Chair: <i>Elizabeth Berry-Kravis, Rush University Medical Center</i></p>
8:00 – 8:10 AM	<p>Summary of pre-meeting Emerging Strategies Working Group (WG) deliberations:</p> <ul style="list-style-type: none"> • <i>Elizabeth Berry-Kravis (WG Chair)</i> <p>Specific examples of emerging functional biomarker measures</p>
8:10 – 8:25 AM	<p>TMS Metrics of Cortical Excitation, Inhibition, and Plasticity – <i>Lindsay Oberman, Uniformed Services University of the Health Sciences, and Alex Rotenberg, Boston Children’s Hospital</i></p>
8:25 – 8:35 AM	<p>Development and Validation of Eye-Tracking Based Measures for Evaluating Autism Risk – <i>Thomas Frazier, Autism Speaks</i></p>
8:35 – 8:45 AM	<p>Using Pupillometry to Monitor Variations in Brain State – <i>David McCormick, University of Oregon</i></p>
8:45 – 9:00 AM	<p>Respiratory Dysfunction in Rett Syndrome: Evolution of Biometrics Through Clinical Trials – <i>Daniel Tarquinio, Center for Rare Neurological Diseases</i></p>
9:00 – 9:15 AM	<p>Early Insights from Wearable Multimodal Sensors in the Neurodegenerative Diseases – <i>Art Combs, MC10 Inc.</i></p> <p>Molecular/cellular measures</p>
9:15 – 9:25 AM	<p>Non-targeted Approaches to Molecular Biomarkers in NDDs – <i>Jeffrey Neul, Vanderbilt University Medical Center</i></p>
9:25 – 9:35 AM	<p>Peripheral Molecular Pathway Marker Use in NDD Trials – <i>Craig Erickson, University of Cincinnati College of Medicine</i></p> <p>Model for bidirectional translation of cognitive markers</p>
9:35 – 9:50 AM	<p>Probabilistic Learning as a Cognitive Marker for Use in Mouse Models of Autism and Clinical Trials – <i>Mike Ragozzino, University of Illinois at Chicago</i></p> <p>Directions for future work</p>
9:50 – 10:00 AM	<p>Biomarker Taxonomy – <i>Alex Rotenberg and Meera Modi, Boston Children’s Hospital</i></p>
10:00 – 10:10 AM	<p>An Eye Tracking Measure of Social Gaze in Fragile X: An Example of Development and Implementation in Clinical Trials – <i>David Hessl, University of California Davis MIND Institute</i></p>

10:10 – 10:20 AM	Discussion Prompter: What Are the Strategies and Guidelines for Biomarker Development and Validation? – <i>David Hessl, University of California Davis MIND Institute</i>
10:20 – 10:35 AM	Discussion
10:35 – 10:55 AM	Break
10:55 – 11:10 AM	<p>Key Challenges in Biomarker Development and the Path to Clinical Trials Remaining WG co-Chairs summarize pre-meeting deliberations</p> <p>Electrophysiology I (data/acquisition standards, rigor, reproducibility in clinical measures)</p> <ul style="list-style-type: none"> • <i>Joshua Ewen, Kennedy Krieger Institute</i> • <i>William Potter, NIMH</i> <p>Electrophysiology II (basic biology underlying signals, translatable models, and demonstrating clinical relevance of signals)</p> <ul style="list-style-type: none"> • <i>April Levin, Boston Children’s Hospital</i> • <i>Barry Connors, Brown University</i> <p>Imaging Biomarkers in Clinical Trials</p> <ul style="list-style-type: none"> • <i>Mustafa Sahin, Boston Children’s Hospital</i>
11:10 – 11:25 AM	
11:25 – 11:40 AM	
11:40 AM – 1:10 PM	<p>Discussion: Recommendations for Future Directions & White Paper Outline Session Chairs: <i>Mustafa Sahin, John Sweeney, Stephanie Jones, NIH Program Staff</i></p> <p>Topics Include</p> <ul style="list-style-type: none"> • Data/acquisition standards, rigor, test-retest reliability, reproducibility across sites, common data elements • Basic and clinical research collaborations in biomarker development • Linking biomarkers to clinical outcomes • Development of translatable biomarkers in models • Across-disease collaborations that allow comparative studies • Pathways for including biomarkers in clinical trials, and collaborations with the FDA • Practical challenges of using biomarkers in multi-site protocols and in pediatric populations • Pre-competitive consortia to validate biomarkers (industry-academic collaborations) • What is needed from NIH and the foundation to spur progress in this area?
1:10 – 1:30 PM	Closing Remarks