June 25, 2026

Outcome Measurements Session

ALIGNMENT JAM **9:00am - 10:20am MT**

Abstract

"PAReNts 2.0 Alignment Jam - Integrating Expert Recommendations and Caregiver Input for CCDS Outcome Measurement Tools "

This afternoon-long session of the symposium will feature the culmination of the PAReNts 2.0 project, which explored how to best measure the outcomes included in the CTD & GAMT Core Outcome Set. A Core Outcome Set (COS) is a small set of important outcomes that should be measured and reported in all research studies for a disease. In November of 2023, ACD completed a study to establish a Core Outcome Set for CTD & GAMT, with recommended outcomes including brain creatine measured by magnetic resonance spectroscopy (MRS), plasma guanidinoacetate measurements (applicable to GAMT only), seizures, and neurodevelopmental outcomes including adaptive functioning, cognitive functioning, fine motor function, expressive communication, and emotional dysregulation.

During the Alignment Jam subject matter experts in each of the core outcomes will present their recommendations applicable to the CCDS community. A literature review will also be presented, describing the current tools available to measure neurodevelopmental outcomes. The audience will be invited to provide feedback on the suitability of these tools for their own children or patients, as applicable, and their desired smallest meaningful differences in neurocognitive behavior in the context of a clinical trial. Attendees at this session will be invited to take a research survey as part of the PAReNts 2.0 study.

Heidi Wallis, ACD

Bio

Heidi holds a Bachelor of Science in Business Management and previously worked in the Utah Newborn Screening Informatics program. She serves on the Utah Newborn Screening Advisory Committee, ClinGen DAPC Working Group, and ClinGen CCDS Variant Curation Expert Panel. Passionate about early detection and treatment, she envisions universal newborn screening for creatine deficiencies and safe, effective therapies for each disorder. Heidi lives in Salt Lake City with her husband, Trey, and their four children. Her daughter, Samantha, was diagnosed with GAMT deficiency at 5½ years old, while her son, Louis, was diagnosed and treated shortly after birth.

Andreas Schulze, University of Toronto/SickKids

Bio

Dr. Andreas Schulze is Professor of Paediatrics and Biochemistry at the University of Toronto. He is Medical Director of the Newborn Screening Program and Senior Associate Scientist in the Research Institute at the Hospital for Sick Children. He is board certified in Physiological Biochemistry and Pediatrics. After graduating from Med School with medical diploma and doctorate at the University of Leipzig, Dr. Schulze completed a PhD program in Physiological Biochemistry with summa cum laude. At Ruprecht-Karls University Heidelberg, he received training in Pediatrics, wrote a Professorial Thesis (Habilitation), and received the Venia Legendi.
Since 2007, Dr. Schulze has worked as Clinician Scientist at SickKids in Toronto and established a research program at the SickKids Research Institute. His research encompasses creatine deficiency syndromes, creatine homeostasis, arginine-, ornithine-, and guanidino compound metabolism, and drug discovery.

ACD ASSOCIATION FOR CREATINE DEFICIENCIES

June 25, 2026

Outcome Measurements Session

Jamie Capal, Cincinnati Children's Hospital Medical Center

Bio

Dr. Capal is a Professor of Pediatrics and Neurology at Cincinnati Children's Hospital Medical Center. She has a background in neurodevelopmental disabilities and leads several clinical and research efforts in neurodevelopmental disorders across the lifespan. Dr. Capal is co-Director of the Vinaya Rett Syndrome and Related Spectrum Disorders clinic Center of Excellence, Director of the TSC-Associated Neuropsychiatric Disorders Clinic (TAND) within the TSC Center of Excellence, and Director of the Moving to Adult Care Clinic in the Division of Developmental and Behavioral Pediatrics.

Beth Potter, University of Ottowa; Audrey Thurm, Boston Children's Hospital

Bio

Beth Potter is a Professor of Epidemiology and Public Health at the University of Ottawa and an Affiliate Investigator at the Children's Hospital of Eastern Ontario Research Institute. Her research aims to produce evidence to improve health care and outcomes for children with rare genetic diseases. She is Principal Investigator for the INFORM RARE research network, which brings together patients and caregivers, clinical providers, and methodologists in the design of patient registries and clinical trials for specific inherited metabolic and neurologic diseases. She also leads the Registry sub-platform for the RareKids-CAN Pediatric Rare Disease Clinical Trials and Treatment Network.

Jill Henley, BrainWise

Bio

Dr. Henley is a pediatric neuropsychologist and the founder of BrainWise, a multidisciplinary private practice established in September 2025. She earned her undergraduate degree in psychology from Cornell University, a master's degree in math education from Brooklyn College, and her doctorate in psychology from Widener University, where she completed specializations in neuropsychology and school psychology. She completed dual APA-accredited clinical internships in Philadelphia at Thomas Jefferson Hospital and Clinical Neuropsychology Associates, a private practice specializing in medical-legal evaluation. She then went on to complete her postdoctoral fellowship at the UPMC Sports Medicine Concussion Program in Pittsburgh, one of the top academic, clinical, and sports-related concussion programs in the world. She gained extensive experience evaluating and treating concussions across all levels, from youth sports through professional NFL and NHL athletes. Dr. Henley's clinical work encompasses comprehensive neuropsychological assessment, diagnosis, and evidence-based treatment of neurodevelopmental disorders as well as helping students recover from concussion. Dr. Henley is experienced in translating complex neuropsychological findings into clear, actionable guidance for multidisciplinary teams and is available for expert consultation and neuropsychological evaluation.

June 25, 2026

Outcome Measurements Session

Audrey Thurm, Boston Children's Hospital

Bio

Dr. Audrey Thurm is a clinical scientist and a child clinical psychologist focused on phenotyping and outcome measures for genetic conditions associated with neurodevelopmental disorders (GCAND). She is an investigator on the Rare Disease Clinical Research Network (RDCRN) Developmental Synaptopathies Consortium, as well as on several other collaborative studies focused on understanding phenotypes of specific conditions and harmonization of data across natural history and clinical trial studies. Dr. Thurm leverages her expertise in understanding developmental trajectories of neurodevelopmental disorders to study measures for use in clinical trials to establish meaningful change, in partnership with scientific collaborators and the patient and family community. Dr. Thurm is board certified in clinical child and adolescent psychology from the American Board of Professional Psychology. She received her Ph.D. in clinical psychology from DePaul University after completing her year of internship at Boston Children's Hospital/Harvard Medical School. She subsequently completed a post-doctoral fellowship at Johns Hopkins University/Kennedy Krieger Institute. Dr. Thurm spent over two decades working at the National Institute of Mental Health, serving various roles in both extramural and intramural programs, including initiating and directing a Neurodevelopmental and Behavioral Phenotyping Service that has provided her with extensive experience in conducting research regarding the assessment and diagnosis of children with rare genetic disorders.

Celeste Graham, ACD

Bio

Celeste has a background in special education with an undergraduate degree from the University of North Carolina at Charlotte in Child and Family Development and a master's degree from Western Carolina University in Special Education. Celeste is passionate about education and empowering parents. Celeste, her husband, Phil, and their four children, Gabriel, Blaine, Paisley, and Levi, live in North Carolina. Levi was diagnosed with CTD at 5 years old.

Emily Reinhardt, ACD

Bio

Emily currently serves as ACD's Patient Registry Coordinator, which affords her the privilege of collaborating directly with CCDS patients, caregivers, researchers, and other rare disease partners. Emily is a graduate of Kansas State University, earning both her BS and MS in Psychology with a focus in Behavioral Neuroscience. She has over 15 years of research experience, with particular emphasis in pre-clinical and translational neuroscience. Through her love of science, Emily is passionate about using data to improve the lives of people in her community.

ACD
ASSOCIATION FOR CREATINE DEFICIENCIES

June 25, 2026

Outcome Measurements Session

Judi Miller, CHOP; Jill Henley, BrainWise

Bio

Judith Miller, PhD, is a clinical psychologist with 25+ years' experience in developmental disorders. She has a joint appointment as Associate Professor in both the Psychiatry and Pediatrics departments at the Children's Hospital of Philadelphia (CHOP), which is affiliated with the Perelman School of Medicine at the University of Pennsylvania. She is also the Clinical Training Director at the Center for Autism Research, and the Associate Director for the Leadership in Education in Neurodevelopmental Disorders (LEND) program at CHOP. She has been studying Creatine Transporter Deficiency since 2015, and served as the coordinating Principal Investigator for the Vigilan Observational Study.

SESSION1: OVERVIEW OF CCDS AND TREATMENT TOOLS — 9:00am - 10:20am MT

Brittney & Kevin McKittrick, PAReNts 2.0 Spotlight

Bio

Brittney and Kevin McKittrick are parents to Sonny (CTD, 6 yo m). Sonny also has a 14 mo old sister, Murphy and a dog, named Mabel. Sonny lives in Minneapolis, MN with his family and just finished kindergarten. Sonny was diagnosed with CTD at 20 months old after an explosive onset of tonic clonic seizures through genetic testing. Through his diagnosis, we also learned that Sonny has a heart condition, prolonged QT. Sonny is the happiest, most present boy we know. He has an incredible sense of human and is very curious and social. Sonny loves connecting with people and will love you forever if you engage with him!

Nicola Longo, UCLA

Bio

Dr. Longo is a Professor and Vice Chair of Human Genetics, the Dr. Allen and Charlotte Ginsburg Chair in Precision Genomic Medicine, and the Chief of the Division of Clinical Genetics at the David Geffen School of Medicine at University of California Los Angeles (UCLA). Dr. Longo earned his M.D. and Ph.D. in Molecular Biology at the University of Parma School of Medicine in Italy. He received residency and fellowship training in Pediatrics, Medical Genetics, and Clinical Biochemical Genetics at Emory University in Atlanta, Georgia. He was then at the University of Utah from 2001 to 2024 where he served as Professor of Pediatrics and Chief of the Division of Medical Genetics. He is passionate in advancing treatments for genetic and inherited metabolic diseases. His basic and clinic research cover disorders of fatty acid oxidation, carnitine metabolism, brain creatine deficiencies, and the development of novel treatments for metabolic disorders.

June 26, 2026

Scientific Sessions Day 1

Nicola Longo Abstract

"Overview of Cerebral Creatine Deficiency Syndromes"
Creatine shuttles high-energy phosphate groups from the site of production in mitochondria to the sites of utilization in the cytosol. There are two autosomal recessive defects of creatine biosynthesis, arginine:glycine amidinotransferase (AGAT) deficiency (OMIM 602360) and guanidinoacetate methyltransferase (GAMT) deficiency (OMIM 601240) and an X-linked defect of creatine transport, SLC6A8 creatine transporter deficiency (OMIM 300036). These disorders cause cerebral creatine deficiency detectable by magnetic resonance spectroscopy. Patients can present with delays in development, hypotonia, autism spectrum disorder, behavioral abnormalities, seizures, and in many cases failure to thrive early in life. Diagnosis relies on measuring plasma and urine creatine and guanidinoacetate. In AGAT and GAMT deficiencies, plasma creatine is reduced; guanidinoacetate is low in AGAT deficiency and elevated in GAMT deficiency. In contrast, creatine transporter deficiency is characterized by an increased urine creatine/creatinine ratio with normal plasma creatine and guanidinoacetate. GAMT deficiency can be detected by newborn screening where available. Levels of creatinine, the breakdown product of creatine, can be low in patients with all creatine deficiency syndromes. Definitive diagnosis for all three disorders requires molecular confirmation or functional studies. Treatment for AGAT and GAMT deficiencies includes oral creatine supplementation, with GAMT deficiency also requiring ornithine supplementation and dietary arginine restriction. When initiated early, these therapies can prevent intellectual disability and seizures. No consistently effective treatment exists for creatine transporter deficiency, although many patients receive creatine and precursor amino acids such as arginine and glycine. All patients benefit from supportive therapies such as physical, occupational and speech therapy that should be initiated as soon as possible.

Kim Cecil, Cincinnati Children's Hospital Medical Center

Bio

Dr. Kim M. Cecil serves as a Professor of Radiology, Pediatrics, Neuroscience, Public and Environmental Health Sciences at Cincinnati Children's Hospital Medical Center and the University of Cincinnati College of Medicine. Her research efforts focus on the application of magnetic resonance spectroscopy and imaging in pediatric brain disorders and evaluating the effects of known and potential environmental neurotoxicants on brain development. Her recognition of the near absence of creatine on brain magnetic resonance spectroscopy led to the recognition of the first patient with creatine transporter deficiency.

Abstract

"Pediatric Magnetic Resonance Spectroscopy Harmonization"
There is a pressing demand to implement a standard acquisition and post-processing approach for proton magnetic resonance spectroscopy performed in children within the clinical setting. Clinical magnetic resonance spectroscopy data is needed to characterize and understand phenotypes especially in rare genetic disorders with distinct metabolite signatures. For instance, infants and children with cerebral creatine deficiency syndromes are too often misdiagnosed, which leads to delay in life-changing supplementation especially for those with synthesis deficiencies. Quantitative information about brain creatine concentrations is useful in characterizing these syndromes, tracking treatment response and guiding future clinical trial designs for patients. Our paper is a call for the usage and a recommendation of a minimum standard single voxel proton magnetic resonance spectroscopy approach that can be implemented for rapidly evaluating pediatric patients with neurodevelopmental delays consistent with genetic etiologies.

June 26, 2026

Scientific Sessions Day 1

SESSION 2: MODELS OF CEREBRAL CREATINE DEFICIENCIES

10:30am - 1:45pm MT

Laura Baroncelli, Neuroscience Institute CNR

Bio

Laura Baroncelli, PhD, is a researcher at the Istituto di Neuroscienze del CNR in Pisa, Italy, and is affiliated with IRCCS Fondazione Stella Maris. Her research focuses on neurodevelopmental disorders, rare diseases, epilepsy, and translational neuroscience, with particular expertise in preclinical animal models, functional biomarkers, and gene therapy approaches. Her work is centered on the development of innovative therapeutic strategies and translational biomarkers for rare neurological disorders, including Angelman syndrome and Creatine Transporter Deficiency (CTD). She has extensive experience in functional brain imaging techniques, including intrinsic optical signal imaging and functional near-infrared spectroscopy (fNIRS), and in the characterization of neurophysiological and behavioral phenotypes in rodent models. Dr. Baroncelli is currently coordinating and participating in several national and international research projects focused on rare neurodevelopmental disorders and translational biomarker development.

Abstract

“Preclinical models of Creatine Transporter Deficiency: strengths, limitations and translational opportunities”
Creatine Transporter Deficiency (CTD) is a rare X-linked neurometabolic disorder characterized by intellectual disability, epilepsy, behavioral abnormalities, and impaired brain energetics. Despite increasing efforts toward therapeutic development, effective treatments remain unavailable, highlighting the need for robust preclinical models capable of reproducing the key molecular, metabolic, and neurofunctional features of the disease. This overview talk will provide a comparative analysis of currently available preclinical models of CTD, with a primary focus on rodent systems. The presentation will discuss the strengths and limitations of the different mouse models in reproducing disease-relevant phenotypes, including brain creatine deficiency, epilepsy, cognitive dysfunction, altered synaptic activity, and network-level abnormalities. Particular attention will be devoted to the translational relevance of these models for therapeutic testing, biomarker development, and mechanistic studies. In addition, emerging complementary approaches, including cellular and organoid-based models, will be briefly discussed as tools to investigate specific molecular and developmental aspects of CTD biology. Finally, the talk will highlight how the integration of behavioral, electrophysiological, imaging, and molecular readouts across models may accelerate the development of translational biomarkers and novel therapeutic strategies, including gene therapy approaches, for CTD.

Aleksander Bogoniewski, UCLA

Bio

Aleks is a fourth-year PhD candidate at UCLA, where he studies the neurodevelopmental consequences of SLC6A8 and GAMT deficiencies using humanized model systems. By leveraging pluripotent stem cells, he generates cortical neurons and cerebral organoids ("mini-brains") to investigate their impact on brain development. Using a series of automated assays, he is evaluating the efficacy of the current treatment regimen of creatine, L-ornithine, and sodium benzoate supplementation on neurogenesis and neuronal function. He is also exploring adeno-associated virus (AAV)-mediated gene therapy as a potential treatment for these disorders. His work aims to refine current clinical approaches and advance new therapeutic strategies for cerebral creatine deficiency syndromes (CCDS).
Outside the lab, Aleks enjoys hiking, going to the gym, and spending time with his siblings.

June 26, 2026

Scientific Sessions Day 1

Aleksander Bogoniewski Abstract

“Elucidating the Neurodevelopmental and Metabolic Mechanisms of GAMT Deficiency Using Stem Cell-Derived Model Systems”
With their unique ability to differentiate into most tissue types, including those that have historically been difficult to model in vitro, stem cells may offer transformative insights into human physiology,. Leveraging this model system, our research utilizes human induced pluripotent stem cells (hiPSCs) to investigate the neurodevelopmental consequences of Guanidinoacetate N-Methyltransferase (GAMT) deficiency. Using GAMT-deficient patient derived stem cells, we modeled GAMT deficiency utilizing cerebral organoids. At day 50, cerebral organoids demonstrated no alterations in expression of NeuN (post mitotic neurons) and PAX6 (neural progenitor cells) by RT qPCR; however, organoid growth rates demonstrated inconsistent results compared to a wild type control. At day 100, these same organoids exhibited decreased GFAP (astrocytes) and OLIG2 (oligodendrocyte) markers by immunocytochemistry and decreased CTIP2 (deep layer V, VI neurons), suggestive of delayed cerebral maturation. To further characterize these differences, we generated a GAMT knockout hiPSC line and compared gene expression by RT-qPCR to the isogenic control; findings here revealed significant alterations in pluripotency-associated stem cell markers consistent with an increased cellular stress state, along with downregulation of the creatine pathway and downstream metabolic processes. Notably, transcriptional abnormalities in SLC6A8 expression were rescued following 72 hours of 100 μM creatine supplementation in the KO cell line. These cell lines are currently being differentiated into cortical neurons to evaluate for the presence of neuronal alterations and whether they are rescued by creatine supplementation. Together, this work aims to elucidate the molecular and cellular mechanisms underlying GAMT deficiency in human brain development and inform the design of more effective, and potentially earlier, therapeutic interventions for affected individuals.

Emil Alexov, Clemson University

Bio

Emil Alexov is a professor of biophysics and bioinformatics in the Department of Physics and Astronomy; Clemson University and he is a Fellow of the American Institute for Medical and Biological Engineering (AIMBE). He is also Editor-in-Chief of the Journal of Computational Biophysics and Chemistry, and editor for Genes, PLOS Computational Biology and many others. His research focuses on understanding the molecular mechanisms underlying various biological processes, including protein-protein interactions, ion channels, and the effects of mutations on protein stability and function, and their association with diseases. He carries out in-silico drug discovery to identify small molecules, potential drugs, that mitigate or eliminate the disease-causing effects.

Abstract

“Cracking the code: Mapping the full translocation pathway of creatine across the creatine transporter”
Maintaining energy in the brain and heart requires the constant import of creatine via the SLC6A8 transporter (CRT). Despite its clinical importance, the large-scale conformational "alternating access" of CRT has never been fully captured. Here, we bridge this gap, utilizing a hybrid computational approach to simulate the full transport cycle at atomistic resolution. Our results reveal a conserved intracellular release sequence (Na2+, Creatine, and Na1+) driven by a distinct "water-assisted destabilization" mechanism. By providing the first continuous molecular description of creatine transport, this study clarifies the biophysical basis of CRT function and offers a vital lens through which to interpret pathogenic mutations in SLC6A8.

Hana Young, PAReNts 2.0 GAMT Spotlight

Bio

Hana Young - GAMT parent to Tilly (13) and NHS midwife from Portsmouth UK

June 26, 2026

Scientific Sessions Day 1

Hanna Polari, Revvity

Bio

Hanna Polari, M.Sc., is MSMS Business Lead at Revvity with over 11 years of experience in global newborn screening. She works closely with NBS laboratories worldwide to translate their needs into practical solutions, supporting improved screening workflows and outcomes. Her work also supports the development of robust, reliable screening tools aimed at improving early detection and health outcomes for newborns and their families.

Abstract

"Plenary Talk: Towards Expanded Newborn Screening for GAMT Deficiency"
Revvity is developing the next-generation NeoBase 3 MSMS kit for newborn screening, enabling the measurement of more than 50 analytes from a single dried blood spot in one analysis. The panel includes guanidinoacetate and creatine, key biomarkers utilized for Guanidinoacetate Methyltransferase (GAMT) deficiency screening. The NeoBase 3 assay is designed to meet high-throughput newborn screening laboratory needs for ease of use, minimal hands-on time, and streamlined sample preparation. Preliminary analytical performance was evaluated on the QSight® 225 MD UHPLC Screening System and SCIEX Triple Quad™ 4500MD LC-MS/MS System including precision, linearity, sensitivity, and carry-over. Method comparison with the existing NeoBase 2 MSMS kit was performed across a wide concentration range including de-identified newborn specimens. Results demonstrated robust analytical performance and good correlation with the NeoBase MSMS 2 kit. No clinical outcome data is available at this stage. NeoBase 3 is under development and aims to support expanded newborn screening, including detection of GAMT deficiency, to enable earlier diagnosis and timely intervention.

SESSION 3: ADVANCES IN THERAPEUTIC DEVELOPMENT FOR CCDS – I

1:45pm - 3:20 MT

Preeti Vyas, Johns Hopkins University

Bio

Preeti Vyas, MS., PhD, has a broad background in pharmacology, drug discovery, and neuroscience, particularly in neurodevelopmental and epilepsy research. Her initial research at Daiichi Sankyo included the high-throughput screening of new chemical compounds using translationally sound cell-free and cell-based models. She has received rigorous pre- and postdoctoral training in interpreting behavioral and quantitative video-electroencephalographic changes associated with various models of epilepsy, neurodevelopmental, and sleep disorders. Her foundational expertise was further refined during her initial post-doc at the Michael V. Johnston Center for Developmental Neuroscience at the Kennedy Krieger Institute and Johns Hopkins Neurology, where she broadened her focus to include other models of neurodevelopmental disorders frequently associated with seizures, like Syngap1 haploinsufficiency, CDKL5 deficiency disorders, hypoxic ischemic encephalopathy, etc. Currently, at Kannan lab, she evaluates the translational value of clinically relevant dendrimer nanotherapies using diverse in vitro and in vivo models, including mouse models of Creatine transporter deficiency disorder, Rett syndrome, cerebral palsy, pediatric brain injury, temporal lobe epilepsy, and other rodent models of neuropathic pain. As she embarks on a career in translational neuroscience, her primary focus is on drug discovery and development strategies for these disorders. Her goal is to expand her understanding of disease mechanisms in neurological conditions and work towards developing effective interventions, particularly for neurodevelopmental disorders and epilepsy

June 26, 2026

Scientific Sessions Day 1

Preeti Vyas Abstract

"Novel glucose dendrimer creatine conjugates for intracellular delivery of creatine in Creatine Transporter Deficiency disorder"
Creatine transporter deficiency (CTD) is an X-linked inborn error of metabolism caused by pathogenic variants in SLC6A8, which encodes Cr transporters (CrT). There are currently no FDA-approved treatments for this devastating disorder. CTD treatment requires increasing brain creatine (Cr) and phosphocreatine (P-Cr) levels; however, bypassing defective or absent Cr transporters at the blood-brain barrier and on neuronal cell membranes to deliver Cr intracellularly, thereby restoring the Cr-P-Cr shuttle, remains a major challenge. Developing a transporter-independent delivery strategy to provide adequate creatine within neurons and glia would be the most effective approach. For this purpose, we have conjugated novel glucose dendrimers with creatine (GD-Cr) using click chemistry via an esterase-sensitive bond, with a 10.3 wt% drug payload and sustained drug release profile over 14 days under intracellular conditions. Once within the target cells, the Cr molecules are released from the GD, enabling their entry into the Cr-P-Cr shuttle in a CrT-independent manner. In vitro studies using creatine transporter inhibitors demonstrated CrT-independent delivery of creatine intracellularly in neuronal cell lines. For in vivo studies, we used CrT−/y (CrT-null, KOs) that lack CrT, show global cognitive deficits, small size, and low brain Cr as seen in patients. Our early pilot studies show that systemic treatment with GD-Cr increased Cr levels in the brain, as demonstrated by tissue MALDI. Pilot studies also showed that GD-Cr improved the phenotype, with increases in grip strength and body weight compared with pre-treatment levels. Detailed in vitro and in vivo studies are currently ongoing. Glucose dendrimers have the potential to deliver creatine intracellularly by bypassing creatine transporters and could serve as an effective nanotherapy for the treatment of creatine transporter deficiency.

Alex Edwin, Stanford University

Bio

Alex Edwin graduated with a B.S. in neuroscience from Santa Clara University in 2023. Since 2021, he has worked as a Life Science Research Professional in the Montine Lab at Stanford School of Medicine, where he focuses on developing a small molecule therapeutic for Creatine Transporter Deficiency. Alex has used molecular modeling to design novel creatine prodrugs with targeted enzymatic release mechanisms and has developed a high-throughput in vitro assay using fluorometric quantification to assess intracellular creatine delivery. Building on this foundation, he has since expanded his work to include in vivo pharmacokinetic and behavioral studies in a Slc6a8 knockout mouse model, evaluating the CNS delivery efficacy of prodrugs identified through in vitro screening. Alex is a current ACD fellow and a recipient of the Race for A Cure grant, which supports his ongoing efforts to characterize effective creatine delivery strategies and advance lead candidates toward preclinical development.

Abstract

"Beyond the Transporter: Developing Small Molecule Creatine Delivery Strategies for CTD"
Effective delivery of creatine across the blood-brain barrier and neuronal membranes has been the goal of numerous therapeutic approaches for Creatine Transporter Deficiency. To date, the most advanced approaches utilize ester and amide prodrug linkages, but are limited by poor bioavailability and stability, rendering them unsuitable for oral administration. Our research aims to identify a refined series of creatine prodrugs with improved brain delivery. Building on a linear amide prodrug scaffold with the greatest in vitro efficacy in our creatine delivery assays, we synthesized a cyclic derivative and evaluated both compounds in a Slc6a8 knockout mouse model. Both were administered via intraperitoneal and intravenous dosing, with creatine distribution quantified across brain, plasma, and skeletal muscle by LC-MS/MS. Following intraperitoneal dosing, the cyclic prodrug delivered roughly 17-fold more creatine to the brain than the linear amide, with substantially lower plasma and muscle levels, suggesting improved peripheral stability. Intravenous dosing further underscored this CNS selectivity: the cyclic prodrug delivered substantial creatine to the brain with minimal peripheral distribution, while the linear amide failed to deliver quantifiable brain creatine entirely. Behavioral assessment of cyclic prodrug-treated CrT KO mice revealed mild attenuation of hyperactivity and transient rescue of short-term memory impairment, while body weight and muscle strength were not rescued. These outcomes are consistent with the CNS-selective creatine distribution observed in pharmacokinetic studies.These findings suggest that cyclization of a linear amide creatine prodrug can dramatically improve CNS selectivity and delivery independent of SLC6A8. Future mechanistic studies are warranted to enable efficient structure-activity optimization of this cyclic prodrug class.

June 26, 2026

Scientific Sessions Day 1

Chin-Yi Chen, Virginia Tech

Bio

As a molecular neuroscientist, Chin-Yi Chen is dedicated to uncovering the secrets of rare neurological disorders. Her journey began by studying the genetic roots of diseases like MERRF, MELAS, Multiple Sclerosis, PRRT2-associated disorders, and SCA3/MJD, alongside studies on hippocampal synaptic plasticity. Today her work is focused on a specific challenge: Creatine Transporter Deficiency (CTD). Her current research explores focused ultrasound (FUS) as a therapeutic approach for CTD. She is designing translational studies to investigate how FUS can safely and transiently open the blood-brain barrier (BBB) to enhance creatine delivery in CTD animal models. She uses this technology to safely and temporarily open the BBB in CTD animal models, allowing her team to deliver creatine directly where it's needed most. Through the evaluation of in vivo and ex vivo creatine levels, she is developing optimized strategies to restore brain metabolite balance. Her ultimate goal is to bridge the gap between the lab bench and the clinic. By refining these innovative preclinical strategies, she hopes to accelerate the development of effective, brain-targeted therapies for patients and families facing rare disorders with limited treatment options.

Abstract

“Focused Ultrasound-Mediated Blood-Brain Barrier Opening Enhances the Delivery of Creatine to the Brain for the Treatment of Creatine Transporter Deficiency”
IFocused ultrasound (FUS)-mediated blood-brain barrier opening (BBBO) enables the noninvasive, targeted delivery of therapeutics and creatine to the brain. Here, we evaluated the safety and efficacy of repeated FUS-BBBO combined with daily creatine supplements in a mouse model of creatine transporter deficiency (Slc6a8^{-}/y). Animals underwent multiple FUS-BBBO sessions over several weeks, demonstrating that repeated, noninvasive, partial-brain BBBO is well tolerated. MRI confirmed that gross brain structure remained normal following repeated treatments, supporting overall safety, with the exception of a few severely ill animals. We employed an innovative application of in vivo magnetic resonance spectroscopy (MRS) to noninvasively quantify brain creatine levels and used ex vivo liquid chromatography-mass spectrometry (LC-MS) to validate intracellular creatine uptake. MRS revealed reproducible increases in creatine following FUS-BBBO across sessions, providing in vivo evidence of enhanced delivery across the blood-brain barrier. These findings were validated by ex vivo LC-MS, which provided direct, highly sensitive quantification of significantly elevated brain creatine and confirmed increased uptake in brain. Notably, LC-MS results correlated with the in vivo MRS measurements obtained from the same animals, establishing successful cross-platform integration between imaging and biochemical quantification. In vitro studies using patient-derived fibroblasts demonstrated increased creatine uptake via FUS-induced sonoporation, supporting a transporter-independent mechanism. Collectively, these results establish the safety and feasibility of repeated FUS-BBBO and highlight the integration of in vivo MRS with ex vivo LC-MS as a measurable method for monitoring therapeutic delivery and response, supporting its translational potential for treating creatine transporter deficiency.

Carmon Phillips, PAReNts 2.0 GAMT Spotlight

Bio

Carmon and her husband Warren live in Upstate NY. They have 3 children, Elisabeth, Daniel & Stephen. Their daughter Elisabeth was diagnosed with GAMT in December of 2023 at the age of 29. They are hopeful their daughter’s story will give hope to other families struggling to find answers.

June 26, 2026

Scientific Sessions Day 1

KEYNOTE TALK

3:30pm - 4:30pm MT

Emil Kakkis, Ultragenyx

Bio

Dr. Kakkis is best known for his work developing novel treatments for rare diseases and working on policy issues affecting rare and ultrarare disease treatment. He is Chief Executive Officer, President and Founder of Ultragenyx, a company with four approved therapies for five rare diseases and multiple late-stage clinical programs. Dr. Kakkis has received numerous awards including the Life Science Leadership Pantheon award from California Life Sciences, a Lifetime Achievement Award from the National MPS Society, the Roscoe O. Brady Award for innovation from the WORLDSymposium and BIO's Henri Termeer Visionary Leadership award for his transformative work in rare diseases.

Abstract

"The Development of Rare Disease Therapies for Neurologic Genetic Diseases"
Until the last few years, the development of disease specific treatments that impact the underlying cause of diseases has been the most difficult for diseases that affect the brain. Getting the treatments to the brain has been a challenge but also finding the technical way to solve the underlying genetic problem has also been a challenge. It could be something missing, or too much of something bad, and the impact might be on specific sites in the brain. Even if the technical challenge of treating is solved, then there is the challenge of conducting clinical trials and demonstrating benefit in diseases with high degrees of variability in disease symptoms and response. The advent of advanced genetic technologies like antisense oligonucleotides, gene therapy and gene editing is opening the door to treating complex diseases of the brain. At times, even traditional drugs that can designed to penetrate the brain and are highly specific in their action can be powerful. I will review the development of treatments for diseases of the brain and how the creation of a novel prodrug to creatine is one step away from being tested in creatine transporter deficiency. Finally, we will talk about how to assess a brain disease to be sure that we are having an effect that is meaningful to patients and also sufficient for regulators so the treatment can become widely available.

POSTER PRESENTATION

5:30pm - 6:30pm MT

Alex Edwin, Stanford University

Bio

See Above

June 26, 2026

Scientific Sessions Day 1

Alex Edwin Abstract

"A Simple Fluorometric Assay for Distinguishing Creatine from Creatine Prodrugs"
Creatine Transporter Deficiency (CTD) is a rare metabolic disorder characterized, in part, by impaired transport of creatine into and throughout the brain, motivating the development of creatine prodrug therapeutics designed to enable transporter-independent cellular uptake. Accurate, high-throughput analytic methods capable of distinguishing creatine from structurally related prodrugs are therefore critical for therapeutic evaluation. Commercially available colorimetric and fluorometric creatine detection kits, while simple and sensitive, broadly detect creatine-containing molecules, limiting their utility in prodrug development. Ninhydrin-based creatine detection, originally developed in the late 1950s and recently introduced to the CTD field by the Schulze Lab, may offer greater specificity. Here, we investigated the ability of the ninhydrin assay to distinguish creatine from creatine prodrugs and other guanidine-containing metabolites. Assay linearity and sensitivity were established using a two-fold serial dilution creatine standard curve. Reaction kinetics were characterized across multiple timepoints to define optimal incubation conditions. Compound specificity was assessed across a panel of guanidine-containing molecules, and quantum mechanical calculations of partial charge on guanidine nitrogen atoms were used to rationalize differential ninhydrin reactivity. The assay was then used to quantify intracellular creatine in HAP1 wild-type and SLC6A8 knockout cells treated with creatine or prodrug candidates, with fluorescence normalized to protein content. The assay demonstrates robust linearity, predictable reaction kinetics, and clear discrimination between creatine and structurally related guanidine-containing metabolites, confirming its suitability as a practical screening tool for creatine prodrug development.

Audrey Thurm, Boston Children's Hospital

Bio

See Above

Abstract

"CTD & GAMT Outcome Measurement Tools in Pediatric Clinical Trials"
The Association for Creatine Deficiencies received two grants from the Patient-Centered Outcomes Research Institute (PCORI). The first grant developed Core Outcome Sets (COS) for Creatine Transporter (CTD) and Guanidinoacetate methyltransferase (GAMT) deficiencies. The second grant investigated properties of measures within each COS outcome domain that were acceptable to stakeholders. To explore these measures, we completed a scoping review of outcome measures reported in clinical trials for genetic conditions associated with intellectual disability, beyond CTD and GAMT deficiency.
Methods: A specialist librarian developed a search strategy to identify pediatric trials for intellectual disability published since 2019. The MEDLINE strategy was peer reviewed prior to its translation and execution in MEDLINE, Embase, and CENTRAL. Two reviewers independently screened each retrieved citation against inclusion criteria in two stages. One reviewer extracted and a second reviewer verified each measure assessing one of our domains of interest: Cognitive Functioning, Adaptive Functioning, Expressive Communication, Fine Motor Functioning, and Emotion Dysregulation.
Results: We identified 79 eligible trials with measures assessing one or more domains of interest, with 25 trials including primary outcome measures. The most frequently reported measures were the VABS (assessing adaptive functioning, fine motor and expressive communication), the BSID (cognition) the WISC (cognition), and the ABC (emotion dysregulation). We also examined verbatim classifications of outcome measure domains and encountered variability in terminologies used.
Discussion: We identified wide variability in measures and terminology, providing data for studying measurement properties and indicating the need for standardization of language regarding concepts of interest in clinical trial reporting.

June 26, 2026

Scientific Sessions Day 1

Emily Reinhardt, Association for Creatine Deficiencies

Bio

See Above

Abstract

“Elevating patient and caregiver voices: How CCDS families are taking a patient-centered approach to prepare for clinical trials”
Individuals with cerebral creatine deficiency syndromes (CCDS) creatine transporter deficiency (CTD) and guanidinoacetate methyltransferase (GAMT) deficiency lack creatine in their brains, which affects their ability to develop typically. There is currently no FDA-approved treatment for CTD or GAMT. Caregivers have frequently expressed a desire for a better long-term solution, ideally an FDA treatment that leads to improved symptoms and quality of life. In order to increase the likelihood of a successful clinical trial, the Association for Creatine Deficiencies (ACD) set out to identify which outcomes are most important to the CCDS community. ACD partnered with caregivers of CTD and GAMT patients, along with researchers and clinicians, to develop a patient-centered core outcome set (COS) which specifies which outcomes are important to patients and families and should be measured in every clinical trial. While identifying which outcomes to measure is an important first step, it is just as important to consider the tools used to measure these outcomes and their sensitivity to capture subtle but meaningful changes in patients. Therefore, ACD is again partnering with caregivers, researchers, and clinicians to develop a set of patient-centered considerations for researchers as they select tools to measure the outcomes in the COS during clinical trials. These two projects have elevated and engaged patients and caregivers, allowing us to incorporate their priorities and ensure that CTD and GAMT patients were not left behind as we get closer to clinical trials.

Sarah Young, Duke University School of Medicine

Bio

Sarah Young is Co-Director of the Duke Biochemical Genetics Laboratory and Professor in the Division of Medical Genetics within the Department of Pediatrics at Duke University School of Medicine. She has been at Duke since 1999, where she completed postdoctoral training and a fellowship in Clinical Biochemical Genetics in 2005. Prior to this, she earned undergraduate and graduate degrees in Biochemistry from the University of Manchester and the Institute of Child Health, University College London. Her research focuses on the development and clinical implementation of biomarker assays for inherited metabolic disorders.

Abstract

“The Diagnostic Experience of Cerebral Creatine Deficiency Syndromes: Insights from a Case Series Emphasizing Biochemical Clues, Diagnostic Delay, and Newborn Findings”
Background: Cerebral creatine deficiency syndromes (CCDS) frequently present with nonspecific neurodevelopmental features, resulting in delayed diagnosis. Biochemical analysis of creatine, guanidinoacetate, and creatinine (CGA) in urine and plasma is central to the diagnostic process, but infrequently performed in the metabolic work-up of individuals presenting with neurological signs and symptoms of these disorders.
Methods: We retrospectively reviewed clinical, biochemical, and molecular data from individuals diagnosed with creatine transporter deficiency (CTD) or guanidinoacetate methyltransferase (GAMT) deficiency followed at Duke University Hospital. Diagnostic trajectories, biochemical findings, and clinical outcomes following diagnosis were examined. Performance characteristics of CGA analysis in plasma and urine by UPLC-MS/MS are described.

June 26, 2026

Scientific Sessions Day 1

Sarah Young Abstract Cont.

Results: Seven patients followed at our institution were diagnosed with a CCDS, with CGA or genetic testing as the first-tier test. These include 6 with CTD and one with GAMT deficiency. For the patient with CTD, diagnosis was significantly delayed in affected probands, and younger siblings identified earlier continued to demonstrate classic disease manifestations despite early biochemical and molecular diagnosis. In contrast, the patient with GAMT deficiency showed clear biochemical abnormalities, rapid diagnostic confirmation, and substantial clinical improvement following targeted therapy. Conclusions: This case series highlights the real world diagnostic challenges of CCDS and underscores the importance of incorporating CGA analysis into routine metabolic evaluations for children with unexplained neurodevelopmental disorders. Early biochemical identification enables diagnosis; however, effective treatment outcomes differ markedly between CCDS subtypes, emphasizing the need for improved therapies, particularly for CTD.

Katie Pulsipher, Association for Creatine Deficiencies

Bio

Katie has over 5 years of experience in the biopharmaceutical industry, mostly in late-stage development of protein-based drugs and tissue diagnostic products. She received her PhD in chemistry from the University of Pennsylvania focused on understanding and developing applications for thermophilic ferritin self-assembly, and completed a postdoc in bioengineering developing protein-stabilized microbubbles for use as ultrasound contrast agents. She has been with ACD since 2024 as a scientific advisor and loves being able to use her scientific background to contribute to the CCDS community.

Abstract

“Current Landscape of Enzyme Replacement Therapy and Considerations for GAMT Deficiency”
This poster will provide an overview of the current landscape in approved enzyme replacement therapies and considerations for the development of an enzyme replacement therapy (ERT) for GAMT deficiency. Enzyme replacement therapy provides functioning recombinant enzymes to patients with an enzyme-based disorder. ERTs are typically administered at least once every two weeks, either by intravenous infusion or subcutaneous or intramuscular injection. Most currently available ERTs are approved for lysosomal disorders, due to the difficulty of endosomal escape once an enzyme is introduced into the bloodstream. This presents a challenge for GAMT, which needs to localize to the cytosol to be effective in creatine synthesis. Considerations for how to deliver active GAMT to its proper intracellular location will be important in the development of an effective ERT for GAMT deficiency. Other factors to consider include potential enzyme modifications to enable manufacturing feasibility, ensure enzymatic stability, and explore passage through the blood-brain barrier.

Katherine Matthew, University of Toronto

Bio

Katherine is a master’s student in the biochemistry department at the University of Toronto. She is completing her project in the Schulze lab in SickKids Hospital, looking at identifying creatine sensing sites and mechanisms. She obtained her BSc (hons.) in biochemistry from McMaster University.

June 26, 2026

Scientific Sessions Day 1

Katherine Matthew Abstract

"Identifying Intracellular Creatine Sensing Sites and Mechanisms"
Creatine plays an important role in energy homeostasis in the cell and is obtained through both diet and endogenous synthesis. The endogenous synthesis of creatine involves a two-step enzymatic reaction. The first enzyme, L-arginine:glycine amidinotransferase (AGAT), uses arginine and glycine to synthesize guanidinoacetate (GAA). Then the second enzyme, guanidinoacetate methyltransferase, methylates GAA to form creatine. However, some people are born with impaired ability to synthesize or transport creatine leading to creatine deficiency syndromes (CDS). Creatine regulates its own synthesis in a negative feedback loop by downregulating AGAT expression; however, the exact mechanism of this regulation is unknown. Our lab had previously identified a portion of the N-terminus of AGAT (nAGp) which is sufficient for creatine-mediated downregulation and that this process likely occurs via ribosomal stalling. This led to our hypothesis that creatine binds the nascent nAGp in the ribosomal exit tunnel, causing translation to halt and the translation complex to disassociate. To investigate this hypothesis, I wanted to test whether the nAGp or the ribosome could interact with creatine on their own. I started by testing whether nAGp interacts with creatine without other factors using nuclear magnetic resonance spectroscopy. Using this technique, I determined that the nAGp does not interact with creatine without other factors present. The next step in this project is to investigate whether the ribosome can interact with creatine without other factors present. This work will help narrow down the mechanism of creatine-mediated AGAT downregulation which will ultimately help develop new treatment strategies for CDS patients.

Jenny Goldstein, University of North Carolina at Chapel Hill

Bio

Jenny Goldstein received her PhD in medical genetics from the University of Aberdeen, Scotland. She then moved to the University of California - Berkeley, to carry out post-doctoral studies in Molecular and Cell Biology and went on to complete a master's program in Genetic Counseling at Virginia Commonwealth University. Jenny worked as a pediatric genetic counselor at Duke University Medical Center, seeing patients and conducting research on glycogen storage diseases and creatine deficiency syndromes. Now, as an associate professor of Genetics at the University of North Carolina at Chapel Hill, Jenny works with the Clinical Genome Resource (ClinGen), a NIH-funded effort to create a publicly available resource on gene-disease clinical validity and the pathogenicity of genetic variants. Jenny is a member of various ClinGen gene and variant curation expert panels, focusing on inborn errors of metabolism and ocular disorders.

Abstract

"Annual update on the NIH-funded ClinGen Cerebral Creatine Deficiency Syndrome Variant Curation Expert Panel"
Understanding the clinical significance of variants within the genes causing cerebral creatine deficiency syndromes (CCDS) is important to ensure timely diagnosis and initiation of treatment for these disorders. In 2022, the NIH-funded ClinGen CCDS Variant Curation Expert Panel (VCEP) developed guidelines to classify the clinical significance of variants in GATM, GAMT, and SLC6A8. To date, the ClinGen CCDS VCEP has classified 55 variants in GATM, 121 variants in GAMT, and 171 variants in SLC6A8. Variant classifications are submitted quarterly to ClinVar, a public variant database. The guidelines and classifications can help genetic testing laboratories to provide accurate information to families, inform studies on the prevalence of these disorders, and contribute to the overall understanding of the genetic causes of the CCDS. We will discuss the current status of the ClinGen CCDS VCEP including 1) the impact of the CCDS VCEP's updated guidance for the classification of variants in SLC6A8 which, among other updates, allows for increased sensitivity and scoring for phenotype specificity that can be observed in females with creatine transporter deficiency (CTD), and 2) our collaboration with the ACD's patient registry, CreatineINFO, to obtain biochemical and genetic data that is critical for the VCEP to accurately assess the clinical impact of variants in genes causing CCDS. Collaboration between the ACD and ClinGen increases understanding of the clinical significance of variants in the genes causing CCDS and may serve as a model for collaboration between other ClinGen VCEPs and patient advocacy organizations.

June 26, 2026

Scientific Sessions Day 1

Filippo Ingoglia, Department of Pathology and ARUP Laboratories, University of Utah

Bio

Dr. Filippo Ingoglia, PhD, is a biochemical geneticist, Assistant Professor in the Department of Pathology at the University of Utah, and Medical Director at ARUP Laboratories. Born and raised in Italy, Dr. Ingoglia completed his higher education at the University of Parma, where he earned his BA, MA, and PhD degrees.
During his PhD training, he spent four months as a visiting fellow at the University of Utah, working in a laboratory focused on rare inherited metabolic disorders. This experience sparked his interest in biochemical genetics and ultimately led him to apply to the Clinical Biochemical Genetics Fellowship within the Department of Pathology two years later. He completed the fellowship in 2021 and obtained board certification in Clinical Biochemical Genetics from the American Board of Medical Genetics and Genomics (ABMGG).
Since entering the field of biochemical genetics, Dr. Ingoglia's research has focused on creatine metabolism in patients with urea cycle disorders and on the development of methodologies to assess the efficacy of potential therapeutic agents for the treatment of guanidinoacetate methyltransferase (GAMT) deficiency. In 2023, he joined the Creatine Deficiency Research Center, funded by the Association for Creatine Deficiencies (ACD) and launched at the University of Utah.
Within this role, Dr. Ingoglia has contributed his expertise in cellular transport studies by developing a functional assay to confirm the diagnosis of creatine transporter deficiency (CTD). This test allows for the assessment of residual creatine transport activity in CTD patients and supports the functional characterization of variants of uncertain significance.

Abstract

"Monocyte Derived Macrophages as an Alternative Cell Model for the Functional Diagnosis of Creatine Transporter Deficiency"
Measurement of creatine transporter activity is essential for establishing the diagnosis of creatine transporter deficiency (CTD) and to determine whether there is residual activity that might affect therapeutic responses. Primary skin fibroblasts are currently considered the gold standard cell type for functional assays. However, the minimally invasive nature of skin biopsy and the prolonged time required for fibroblast isolation and expansion limit their practical accessibility. To overcome these limitations, we investigated peripheral blood–derived cells as an alternative cellular model for the functional diagnosis of CTD. Peripheral blood cell fractions were isolated from apheresis cones of healthy donors using density gradient centrifugation. Based on isolation simplicity, consistency, and adherence properties, monocytes were identified as the most suitable cell type for further evaluation. Creatine transport and expression of the creatine transporter CT1 (SLC6A8) were assessed in monocytes and monocyte derived macrophages (MDM). Monocytes exhibited minimal creatine uptake (≈29 pmol/mg protein/h), whereas MDM showed a marked increase in saturable creatine uptake (≈517 pmol/mg protein/h), comparable to that observed in primary fibroblasts (≈607 pmol/mg protein/h). Consistent with these findings, SLC6A8 mRNA expression was increased approximately nine fold in MDM compared with monocytes. Kinetic analysis demonstrated that creatine uptake in MDM was linear for up to two hours and exhibited a Km of 44.7 ± 8.2 μM, closely matching fibroblast kinetic properties. In conclusion, monocyte derived macrophages represent a promising, faster, and less invasive cell system as compared to skin fibroblasts for the functional diagnosis of CTD.

Tesla Peretti, Queen's University, Centre for Neuroscience Studies

Bio

Tesla Peretti is a PhD Candidate and ACD 2026 Fellow at Queen's University researching AGAT deficiency. She has been working on developing a novel gene replacement therapy for AGAT deficiency since 2021.

June 26, 2026

Scientific Sessions Day 1

Tesla Peretti Abstract

"Route of administration investigation of a novel AAV9GATM construct in a AGAT deficiency murine model"
Gene therapy(GT) delivers nucleic acids to cells through viral vectors that manipulate the host cells' machinery to produce foreign gene products. Adeno-associated viruses(AAV) are used extensively in this field. The rate-limiting step of AAV is the second strand synthesis, this is overcome by using self-complimentary AAV(scAAV). AAV serotype 9(AAV9) is preferred for central nervous system(CNS)-related GT as it can bypass the blood brain barrier(BBB). AGAT deficiency(AGAT-D) is a recessive monogenic disease making it good candidate for gene replacement therapy. We have performed a route of administration study with a novel sc.AAV9hGATM construct administered either intravenously(IV) or intrathecally(IT) to an AGAT-D murine model at 6 weeks of age with a baseline serum collection and an oral immunosuppression regimen. The IT dose was 10 times lower than the IV dose. At the 13-week endpoint, serum, gross organs and the CNS were collected for analysis. The results demonstrate restoration of AGAT protein through western blotting and restoration of creatine production through mass spectrometry analysis in various organs in the IV treated mice. Conversely, the IT treated mice only saw a partial restoration in AGAT protein. The discrepancy in the results of these routes of administrations could be attributed to the 10-fold lower dose in IT injections due to injection volume and vector constrains. This study demonstrates that there is a threshold of AGAT activity that must be reached to produce creatine, while the IV treated mice saw full restoration of the biochemical phenotype, the dosage of the vector was inadequate for the IT treated mice. Ultimately, this proves the IV administration of sc.AAV9hGATM construct can efficiently cross the BBB to correct the biochemical aspects of AGAT-D, with future directions aimed at a minimal effective dose finding study.

Sylvia Stockler-Ipsiroglu, BC Children's Hospital Research Institute

Bio

Dr. Sylvia Stockler-Ipsiroglu is a biochemical geneticist with extensive clinical and research expertise in creatine deficiency syndromes (CDS), focusing on the development of treatment strategies and improvement of outcomes for affected individuals. She leads a collaborative team of trainees and research scientists engaged in drug repurposing approaches for cerebral creatine transporter deficiency (CTD). Building on prior work by Dr. Peter Axerio Cilies evaluating candidate compounds in SLC6A8-deficient experimental cell lines, her group, in collaboration with ACD, has established a translational platform using SLC6A8-deficient human fibroblasts, more closely recapitulating physiological conditions for the evaluation of potential treatment strategies.
Through this poster presentation at the ACD conference, we aim to share our experience in developing an LC–MS/MS-based creatine uptake assay and to explore opportunities for collaboration.

Abstract

"Development of a Creatine Uptake Assay to Evaluate Repurposable Drugs in SLC6A8-Deficient Fibroblasts"
Introduction: Therapeutic strategies for cerebral creatine transporter deficiency (CTD) include gene therapy, creatine analogues, and small molecules to restore transporter function. Previous Work: We focused on small-molecule approaches. Using an AI-based screening tool, we identified eight repurposable drug candidates that enhanced SLC6A8 activity in ΔF408-transfected HEK cells, measured by single-cell patch-clamp analysis (reported previously). Aim: To assess translational relevance, we developed a sensitive LC–MS/MS assay to quantify creatine uptake in human control and SLC6A8-deficient fibroblasts, including ΔF408. Methods & Results: Fibroblasts were incubated with D3-labelled creatine (50 µM) for 6 hours, and intracellular levels were quantified in lysates by LC–MS/MS. Experiments used ~9.6 cm² confluent monolayers (~400–600 µg protein per well), performed in triplicate and replicated across independent experiments, yielding robust reproducibility. Drug incubation ranged from 3–96 hours. Uptake variability correlated with passage number and growth rate but did not affect outcomes. Toxicity was minimal, with 7/8 compounds tolerated at 10–100 µM; one compound was excluded due to solubility issues. None of the drugs increased creatine uptake above baseline under any condition. Phenylbutyrate, currently in clinical evaluation, is currently under investigation. Relevance: Findings highlight a potential translational gap between overexpression systems and patient-derived cells. Although no compounds enhanced creatine uptake, this work establishes a valuable platform for preclinical evaluation of additional therapeutic candidates in SLC6A8 deficiency. The assay also supports functional validation of newly identified SLC6A8 variants.
Supported by: Association for Creatine Deficiencies; BC Children's Hospital Research Institute.

ACD
ASSOCIATION FOR CREATINE DEFICIENCIES

June 27, 2026

Scientific Sessions Day 2

SESSION 4: COGNITIVE OUTCOMES IN CLINICAL TRIALS

9:15 am - 10:20am MT

Ashlea Pfannenstiel, PAReNts 2.0 CTD Spotlight

Bio

We are a family of five from Wichita sharing our journey with CTD through our youngest son, Eddie. Eddie has two older brothers, Landon (16) and Jordan (9), and an older sister (14). Our family has been navigating life with CTD since Eddie was diagnosed at 18 months old, and we are passionate about raising awareness and supporting research for rare diseases.

Audrey Thurm, Boston Children's Hospital

Bio

See above

Abstract

"Update on Parents Advancing REsearch NeTworkS 2.0: Expand Community, Tools and Engagement"
The current talk will provide a synopsis of the Association for Creatine Deficiencies' current grant from the Patient-Centered Outcomes Research Institute (PCORI). In this grant we are working on understanding clinical outcome assessment and measurement qualities desired by the community for the Core Outcome Sets (COS) for Creatine Transporter (CTD) and Guanidinoacetate methyltransferase (GAMT) deficiencies. Given that the core outcome set contains 5 outcomes focused on neurodevelopmental concepts (e.g. expressive communication, fine motor, emotion regulation, daily living skills and cognitive functioning) we sought to investigate properties of measures within each of these domains that are acceptable to stakeholders. We will discuss results of several of the efforts we took to understand qualities of instruments that might be most feasible for clinical trials, including a scoping review of measures used with other genetic conditions associated with intellectual disability, a Research Jam, a community survey for caregivers, and engagement with parents who provided input through storytelling. Results converge on several themes for clinical outcome assessment measures, including granularity needed for variable meaningful change and ideas about specific behavioral changes sought. We will also discuss the different approaches to understanding measurement needs for seizures and for the biomarker core outcomes, including MRS brain creatine, serum/plasma guanidinoacetate.

Aurore Curie, Lyon University Hospital

Bio

Aurore Curie is a child neurologist (MD, PhD) at the Child Neurology Department of Lyon University Hospital (Assistant Professor) and the Reference Center for Intellectual Disability (ID) from rare causes (Co-Head). She is affiliated to the Lyon Neuroscience Research Center (CNRS UMR5292, Inserm U1028, Lyon, France) and also part of the DéfiScience national network for rare diseases of brain development and ID. She coordinates a French Inter University Diploma (DIU) on Neurodevelopmental Disorders. She has a strong expertise in genetics (especially in X-linked ID) and in neuroscience. She developed new outcome measure adapted to ID patients (HCL/CNRS patent). She contributed to the development of the research plateform "Cognitoscope". Her clinical and research expertise is dedicated to X-Linked ID and other ID from rare causes. She described cognitive profiles of neurodevelopmental disorders (including ARX, PQBP1, Rab-GDI, SLC6A8 mutated patients) using eye-tracking and neuroimaging analysis, and contributed to several multisite clinical trials for Fragile X syndrome. She also furthered our knowledge on placebo effect in ID patients, and the different trial plans that can be used in ID patients to test for an effect (Randomized controlled double blind Clinical Trials (RCT) but also n-of-1 trials, also called Single-Case Experimental Designs or SCEDs).

June 27, 2026

Scientific Sessions Day 2

Aurore Curie Abstract

"CREAT_criteria: a prospective study in male and female Creatine Transporter Deficiency (SLC6A8) patients to determine the most relevant outcome measures"
Creatine Transporter Deficiency (CTD) is a rare genetic disorder related to SLC6A8 pathogenic variants, leading to moderate-to-severe Intellectual Disability. As new therapeutic avenues are emerging, it is necessary to identify objective, reliable and sensitive outcome measures.We performed a prospective study on 39 French CTD patients (24 males/15 females), 39 sex-and-chronological-age-matched-healthy-controls, and 39 sex-and-mental-age-matched-healthy-controls. We precisely described CTD developmental trajectory, neurological/morphological examination, actimetry, cognitive assessment (Leiter, Simple reasoning tasks on tablet with 4 increasing difficulty levels), language (PPVT-5, EVT-3), motor assessment (Purdue-Pegboard), Social assessment (ADOS, eye-tracking analysis), as well as parental questionnaires (Vineland, ABC, PDD-MRS, CBI). Moreover, neuroimaging analysis was performed including spectroscopy with precise quantification of the creatine peak, volumetric and diffusion analysis. We present here preliminary results on 24 male (mean_age 16.9 years[6.7-26.9]) and 5 female CTD patients (mean_age 19.4 years[7.6-36.1]) included in the study. Mean nonverbal IQ was 54.4 [30-75] in boys and 73.2 [53-95] in girls. 96% of the CTD male patients could perform the first level of simple reasoning tasks (match-to-sample), 96% the second level (categorization), and 75% the SimpleMatrices task. Tasks on tablets could be easily performed at home under remote supervision through visioconference. All female CTD patients could perform the simple reasoning tasks on tablets. 17/24 CTD patients were able to perform brain MRI. We showed a significant decrease in white matter volume in CTD patients compared to chronological-age-matched-healthy-controls.
This study will contribute to define the outcome measures that could be used in future clinical trials in male and female CTD patients.

SESSION 5: ADVANCES IN THERAPEUTIC DEVELOPMENT FOR CCDS – II — 10:30am - 1:05pm MT

Gerry Lipshutz, UCLA

Bio

Gerald Lipshutz is a physician-scientist at the University of California Los Angeles focused on the development of gene therapies for rare metabolic and neurodevelopmental disorders. Our research centers on the use of adeno-associated virus (AAV) vectors to deliver therapeutic genes to the central nervous system, liver and other peripheral tissues, with a particular emphasis on disorders of arginine and creatine metabolism. Our work integrates molecular biology, translational neuroscience, and preclinical model systems to advance novel treatments toward clinical application. In our studies we hope to contribute to the understanding of how metabolic disturbances impact brain development, particularly myelination and oligodendrocyte biology. Our recent studies have explored how guanidino compounds disrupt cellular energetics and impair white matter development, providing new mechanistic insight into diseases such as arginase deficiency. In addition to my scientific work, I am actively engaged in translational efforts, including IND-enabling studies, biomarker development, and regulatory strategy, with the goal of bringing first-in-class gene therapies to patients. Our work bridges basic science and clinical application, with a focus on addressing unmet needs in rare pediatric diseases.

Abstract

"Restoring Creatine in the Brain in GAMT and Creatine Transporter Deficiencies: Recent Achievements and an FDA Path Forward"
Our laboratory has been studying the use of adeno-associated viral vectors to express GAMT or the creatine transporter CRT1 for the treatment of guanidinoacetate methyltransferase deficiency and creatine transporter deficiency (CTD), respectively. As part of these studies, we have employed imaging techniques available at UCLA and at the University of Minnesota. Using positron emission tomography with 18F-fluorodeoxyglucose, mice deficient in GAMT or functional CRT1 demonstrate characteristic abnormalities in brain metabolic activity. Following administration of viral vectors expressing CRT1 or the GAMT enzyme, these abnormalities are resolved. Magnetic resonance spectroscopy (MRS), which detects and quantifies brain metabolites, was also applied to the Shelton CTD mouse model. As expected, untreated mice demonstrate absent brain creatine peaks; however administration of an AAV vector encoding CRT1 restores detectable creatine in the brain.
The U.S. Food and Drug Administration recently established the Rare Disease Evidence Principles (RDEP) program to address a key barrier in rare disease drug development— facilitate the approval of drugs to treat rare diseases with very small patient populations with significant unmet medical need and with a known genetic defect that is the major driver of the pathophysiology. The program enables a new process that provides greater clarity as to the kinds of evidence that can be used to demonstrate substantial evidence of effectiveness. Our application for CTD to RDEP was accepted, underscoring the unmet need and supporting the development through early regulatory engagement, thereby facilitating more efficient translation of this emerging therapy. The importance of this acceptance will be discussed.

June 27, 2026

Scientific Sessions Day 2

Alanna Schepartz, UC Berkeley

Bio

Alanna Schepartz is the C.Z. and Irmgard Chu Distinguished Professor in the departments of Chemistry and Molecular and Cell Biology at the University of California, Berkeley. Her research group studies the chemistry and biology of complex cellular machines and exploits this knowledge to design or discover molecules–both small and large–with unique or useful properties. Dr. Schepartz obtained her undergraduate education in chemistry at the State University of New York, Albany. She earned a Ph.D. from Columbia University under the direction of Ronald Breslow and spent two years as an NIH Postdoctoral Fellow at Caltech working with Peter Dervan. Professor Schepartz joined the faculty at Yale in 1988 and was named a Sterling Professor, Yale's highest faculty honor, in 2017. In 2019 Professor Schepartz and her laboratory moved to the University of California, Berkeley. Her honors include a Packard Fellowship in Science and Engineering, an NSF Presidential Young Investigator Award, the Eli Lilly Award in Biological Chemistry, an ACS Cope Scholar Award, the ACS Chemical Biology Prize, the Ralph F. Hirschmann Award in Peptide Chemistry, the Ronald Breslow Award for Achievement in Biomimetic Chemistry, the Frank H. Westheimer Prize, and the Wheland Medal. She is a member of the American Academy of Arts and Sciences and the National Academy of Sciences.

Abstract

"Mini-protein guided delivery of bio-active substances"
Although it has been known for more than 35 years that certain transcription factors can activate transcription when added to cells in culture, it has proven difficult to translate this finding into a robust strategy for therapeutic macromolecule delivery. Designing molecules that enter the endocytic pathway is not the problem - the problem is endosomal escape. This lecture will describe the discovery of a well-folded mini-protein that guides proteins and enzymes into the cytosol by promoting efficient endosomal escape, a single-molecule tool that quantifies this trafficking event in live cells with accuracy and precision, and cellular, structural, and biochemical experiments that together reveal what can be delivered and why many other delivery approaches have failed. This work provides new insights into how cells can purposefully respond to unnatural endocytic cargo and how this knowledge can be exploited to improve the cytosolic delivery of diverse proteins and enzymes.

June 27, 2026

Scientific Sessions Day 2

Sara Biagiotti, University of Urbino

Bio

Dr. Sara Biagiotti is an Assistant Professor of Biochemistry at the University of Urbino, where she leads research on red blood cell–based platforms for therapeutic delivery. She began working on RBCs as drug delivery systems more than a decade ago, and her work has since evolved toward RBC-derived extracellular vesicles (RBCEVs) as carriers for RNA therapeutics. Throughout her career, Dr. Biagiotti has contributed to translational research on several rare genetic diseases, including ataxia telangiectasia, phenylketonuria, and guanidinoacetate methyltransferase (GAMT) deficiency. She is the Principal Investigator of the NextGeneration EU–funded project "RNA-based therapy by RBCEVs for the treatment of Guanidinoacetate Methyltransferase Deficiency," which established a novel mRNA-EV therapeutic platform for metabolic disorders. Dr. Biagiotti is the author of 23 peer-reviewed publications in international journals and has presented her work at more than 30 international conferences, including over six invited or selected oral presentations at major scientific meetings. Beyond her academic contributions, she is deeply engaged in the rare disease community. Since 2016, she has served as the volunteer President of the Italian Association for Ataxia Telangiectasia, where she works closely with families, clinicians, and researchers to advance advocacy, awareness, and research initiatives.

Abstract

"A preclinical assessment study of a novel therapeutic strategy for Guanidinoacetate Methyltransferase Deficiency (GAMT-D) based on RBCEVs loaded with IVT-GAMT mRNA"
Guanidinoacetate Methyltransferase Deficiency (GAMT D) is a rare inborn error of creatine metabolism characterized by pathological accumulation of guanidinoacetate (GAA) and reduced creatine (Cr), ultimately leading to severe neurological impairment. This project proposes a preclinical efficacy assessment of an innovative RNA based therapeutic strategy using red blood cell–derived extracellular vesicles (RBCEVs) loaded with IVT GAMT mRNA to restore GAMT activity in a murine model of GAMT D. Building on robust preliminary data, we have defined an optimal dosing regimen—200 ng IVT GAMT mRNA delivered via 0.5–1.0 × 10^{11} RBCEVs, administered weekly—and demonstrated hepatic persistence of GAMT protein for up to 10 days, supporting sustained biochemical correction in blood. Pilot studies confirmed feasibility, safety, and tolerability of repeated dosing. Importantly, in vivo MRS analyses revealed reduced GAA and increased Cr in both muscle and brain, indicating early metabolic rescue. Over the 12 month project period, GAMT deficient mice will receive repeated GAMT RBCEV administrations for up to three months. Therapeutic efficacy will be monitored longitudinally through dried blood spot (DBS) quantification of Cr and GAA, complemented by endpoint UPLC ESI MS/MS analyses of brain and muscle tissues. Expected outcomes include restoration of GAMT enzymatic activity, normalization of GAA levels in blood and plasma, increased creatine concentrations in target tissues, overall metabolic and functional rescue consistent with disease correction. This study will deliver essential in vivo evidence to guide deeper efficacy investigations and inform future translational development of this RBCEV mRNA therapeutic platform.

Melissa Evans, PAReNts 2.0 Spotlight

Bio

Melissa Evans CTRS, LNHA, MHSA,CDP is an award winning health care executive leading healthcare communities in Virginia, USA. Her most importantly role Is being a mom to Logan who was diagnosed with CTD after a cardiac arrest and full genome panel at the age of 10. She and her son Logan are advocates for creatine and brain health awareness. They has been featured in the Washington Post, local news and Believe Magazine. Melissa is a guest lecturer for the NIH and Genetics classrooms talking about the role of whole genome testing. She was the keynote speaker at the Childrens Ball in Washington DC in April 2026 raising 2.6 million for the hospital that saved her sons life. Melissa is an extreme sports junkie and dhe serves as co-president of the Alzheimer's Association Great Leap committee helping to fundraise for brain health treatment by jumping out of airplanes.

June 27, 2026

Scientific Sessions Day 2

SESSION 6: CCDS – DEFINING PATIENTS, MEASURING DISEASE, TRACKING OUTCOMES

10:30am - 1:05pm MT

Carole Chehowah, ACD

Bio

In addition to spending almost 25 years working in finance, Carol, the mother of a child with CTD, has been committed for nearly 20 years to supporting families impacted by this syndrome. Primarily by promoting awareness and funding research in France. She also contributes to improving visibility of the syndrome by organizing symposiums and events across France and Europe.

Abstract

"Xtraordinaire Update"

Israel Abebe Admasu, Boston Children's Hospital

Bio

Dr. Israel is a researcher in Neurology at Boston Children's Hospital whose work investigates the neurobiological foundations of neurodevelopmental disorders, with a particular focus on creatine transporter deficiency and Rett syndrome. His research focuses on the neurobiological basis of neurodevelopmental disorders, with particular attention to the development of biomarkers for tracking disease progression and supporting clinical translation. His work also incorporates fundamental studies of neurodevelopment and neuropathology, along with computational and data-driven approaches for analyzing complex neuroimaging datasets.
Dr. Israel has participated in interdisciplinary research projects involving functional neuroimaging, signal processing, and data analysis, and is especially interested in developing unbiased computational frameworks that improve the interpretation of neural data. Through his academic work, he aims to advance knowledge in rare neurodevelopmental disease while supporting the translation of computational discoveries into clinically meaningful outcomes. He values collaborative research across disciplines and approaches his work with an emphasis on rigor and practical usefulness.

Abstract

"Establishing Novel Functional Biomarkers for Creatine Deficiency Syndromes"
As the search for effective therapies for Cerebral Creatine Deficiency Syndromes (CCDS) advances, the absence of objective tools to assess neurological improvement remains a significant barrier to translating research findings into clinical success. Addressing this gap, we aim to establish functional near-infrared spectroscopy (fNIRS) as a reliable and scalable tool to monitor brain function in individuals with rare neurometabolic disorders such as CCDS.
In this study, we enrolled 47 children diagnosed with CCDS—including the GAMT and CTD subtypes—and 23 age-matched, typically developing controls to assess group-level differences in cortical responses. Of these, 44 participants from the CCDS group and 23 from the control group underwent fNIRS recording during visual stimulation involving alternating mock and checkerboard stimuli. In the CCDS group, 11 participants underwent repeat recordings.
Our results demonstrate that individuals with CCDS exhibit significantly exaggerated hemodynamic response. Notably, one patient with GAMT was recorded both prior to treatment and again two months after initiation, with the fNIRS data suggesting a potential treatment-related effect. We are now in the second year of funding, focusing on developing a machine learning–based computational framework for unbiased, data-driven analysis. This approach not only enables the detection of subtle differences that may be overlooked with biased analyses but also incorporates short-channel data to better account for systemic noise, further enhancing the quality of an already robust dataset. We gratefully acknowledge the support of the Association for Creatine Deficiencies (ACD) and Boston Children's Hospital, whose contributions made this research possible.

ACD
ASSOCIATION FOR CREATINE DEFICIENCIES

June 27, 2026

Scientific Sessions Day 2

Emily Reinhardt, ACD

Bio

See above

Abstract

“The CreatineINFO Patient Registry: A Five Year Update”
The Association for Creatine Deficiencies (ACD) launched the CreatineINFO Patient Registry & Natural History Study in 2021 as a patient- and caregiver-reported registry dedicated to understanding the natural history of the three cerebral creatine deficiency syndromes (CCDS). The registry has seen significant growth and change over the past five years, including enrollment of over 200 individuals with CCDS from around the world. Since its launch, the registry has 1) provided a path for research engagement and contribution among CCDS patients and caregivers, 2) established itself as an invaluable resource for new and existing CCDS investigators, and 3) opened new research possibilities to advance CCDS research. In this presentation, we provide an update on the registry’s growth and change over the past five years, highlight existing data currently available in the registry, and outline the registry’s goals as we look to the future of CCDS.

Sarah Donoghue, Murdoch Children's Research Institute

Bio

Sarah is a metabolic physician and paediatrician who is currently completing a PhD on treatable intellectual disability through the University of Melbourne. She obtained her medical degree from the University of Tasmania in 2006 before completing her fellowship training in metabolic genetics at the Royal Children's Hospital in Brisbane and Victorian Clinical Genetic Services. Sarah has worked in several clinical settings as a specialist at the Royal Children's Hospital in Melbourne, Queensland Children's Hospital, Women's and Children's Hospital in Adelaide and the Royal Melbourne Hospital.

Abstract

“Creatine supplementation in an adult female following diagnosis: clinical and biochemical progression”
We report the case of a 20 year old female with a mild intellectual disability, autism spectrum disorder, anxiety and childhood speech apraxia. She was diagnosed at the age of 17 with a cerebral creatine disorder following a genomic sequencing project to investigate childhood speech apraxia. She had a de novo genomic variant in SLC6A8 chrX:153688831 c.257G>A; p.(Gly86Asp), but urinary excretion of creatine was normal. Her MRI spectroscopy demonstrated reduced creatine relative to choline peaks which was consistent with the diagnosis of a cerebral creatine disorder. She was commenced on arginine, glycine and creatine supplementation. Over the course of two years of treatment there have been changes in the amount and complexity of her speech, but her MRI has remained unchanged. This case demonstrates the value of trialling supplementation in adults, but also highlights that imaging studies may not demonstrate normalisation even when there is clinical and biochemical improvement.

June 27, 2026

Scientific Sessions Day 2

Kimberly Morris, PAReNts 2.0 CTD Spotlight

Bio

Kimberly lives in Kansas City with her family, including her 26-year-old daughter, Allison, who has CTD. Since Allison's diagnosis 15 years ago, their family has learned from her and worked to advocate on her behalf. They remain hopeful for a better future for everyone affected by CCDS, thanks to this community and its dedicated researchers.

Thomas Joudinaud, Ceres Brain Therapeutics

Bio

Dr Thomas Joudinaud, MD, PhD, is the co-founder and CEO of Ceres Brain Therapeutics, a CEA spin-off developing innovative neurology drugs. A cardiac surgeon by training, he combines clinical expertise with over 11 years of strategic consulting experience, including senior roles at The Boston Consulting Group and AEC Partners, where he led major projects in CNS, cardiovascular and oncology strategy, R&D transformation, portfolio optimization and due diligences for global biopharma companies, all projects conducetd with extensive international exposure in the USA, Europe, the Middle East and Asia. At Ceres Brain Therapeutics, Thomas oversees corporate strategy, regulatory and medical activities, and has successfully raised >~€15M since the company's inception . His earlier career includes serving as Chief Resident in cardiac surgery at AP-HP Bichat, performing more than 100 open-heart procedures and authoring 24 clinical publications. He also completed a postdoctoral fellowship at the International Heart Institute of Montana, focusing on experimental models of cardiac insufficiency. Thomas has held governance roles as a Board Member Vaccine biotech company OSIVAX.

Abstract

"CBT101 - Poised to enter Phase 2 clinical trial in CTD"
Ceres Brain Therapeutics is a spin-off from the leading French research institution CEA, founded in 2019 by the CEA together with Dr. Aloïse Mabondzo (PhD), Dr. Henri Bénech (PharmD, PhD) and Dr. Thomas Joudinaud (MD, PhD). Ceres is developing CBT101, a nose-to-brain creatine prodrug designed to restore neuronal energy metabolism. After nasal administration, CBT101 is taken up by olfactory and trigeminal neurons and transported along their natural pathways to their origins, from which it diffuses across the brain. This Creatine-to-Neurons™ mechanism has demonstrated robust efficacy in wild-type mice, cynomolgus monkeys and creatine transporter–deficient mice, showing clear creatine delivery to neurons and associated biological, metabolic and cognitive improvements. CBT101 benefits from a scalable manufacturing process enabling GMP clinical batch production fully compliant with EMA/FDA requirements. Ceres is now strengthening this process to ensure full commercial readiness, with enhanced robustness, reproducibility and long-term supply reliability. In 2025, Ceres completed three-month GLP toxicology studies in rodents and non-rodents, as well as a Phase 1 clinical trial in 48 healthy volunteers, demonstrating an excellent safety and tolerability profile. The Phase 1 study also showed clear biological activity, with a significant increase in the beta power band, consistent with enhanced alertness and improved attentional control—evidence of cortical activation. These first-in-human efficacy signals provide strong confidence in CBT101's potential in Creatine Transporter Deficiency (CTD). Ceres is currently conducting a six-month juvenile toxicity study and finalizing the Phase 2 clinical protocol in CTD, with the objective to initiate the trial in early 2027, subject to financing.

June 27, 2026

Scientific Sessions Day 2

Judith Miller, Children's Hospital of Philadelphia

Bio

See above

Abstract

"Clinical Trial Development Lessons from Vigilan and Related Studies"
Introduction: A series of studies connected to the Vigilan Observational Study of Creatine Transporter Deficiency (CTD) can help us learn about clinical trial development strengths and challenges in this population. Methods: An initial study about parents' first concerns informed an observational study (NCT02931682) following males with confirmed CTD (SLC6A8 pathogenic variant) for up to 4 years. A subset participated in additional studies that involved imaging and specimen collection. Results: Twenty patients participated in the initial study; 50 participated in the observational study, of which 18 and 12 were able to participate in additional data or specimen collection, respectively. From parent history and prospective data collection we have now tracked acquisition of functional milestones (ages of walking, first words, first sentences, toileting skills), onset of a seizure disorder, and developmental trajectories from standardized developmental testing. For standardized testing, we have also modeled the trajectories seen in our CTD sample in contrast to trajectories expected for children in the general population. From other studies, we know parent priorities for outcome areas. Finally, with a variety of study procedures, methods, and measures attempted, we have gained insights into study populations, logistics, and measures to consider in a future interventional study. Conclusions: Much has been learned about how to design a potential intervention trial for CTD. Next steps should also include studies of other disorders with pre- and post-intervention clinical presentations (e.g., GAMT), to identify potential areas of improvement that could serve as primary outcome measures in a CTD intervention.

PANEL DISCUSSION **3:35pm - 4:20pm MT**

Judith Miller, Children's Hospital of Philadelphia

Bio

See above

Nicola Longo, UCLA

Bio

See above

June 27, 2026

Scientific Sessions Day 2

Andreas Schulze, University of Toronto/SickKids

Bio

See above

Thomas Joudinaud, Ceres Brain

Bio

See above

Richard Collis, Ultragenyx

Bio

Dr. Richard Collis, MD, MB BCh BAO, MRCPI, DPM, is an Executive Medical Director in Clinical Development with over 15 years of experience across clinical practice, academic medicine, and the biopharmaceutical industry. He specializes in advancing innovative therapies for people living with rare diseases. At Ultragenyx, he contributes to global development programs focused on inborn errors of metabolism, leading the development of a novel AAV gene therapy for the treatment of Glycogen Storage Disease Type Ia. Prior to this, he held clinical development roles at Freeline Therapeutics and Sanofi, where he worked on multiple rare disease programs. He trained in internal medicine and cardiology in Ireland and completed a clinical research fellowship in inherited cardiomyopathies at Barts Heart Centre in London. He earned his medical degree from the Royal College of Surgeons in Ireland and holds an MD in Cardiovascular Science from University College London, where his research focused on hypertrophic cardiomyopathy.