August 15th, 2025

Caregiver Session

12:15PM PDT | 9:15PM CEST

Davis Ehrler

“Supporting Sound Sleep”

1:00PM PDT | 10:00PM CEST

Parent-Lead Stories

Whitnie Strauss

Bio

Whitnie Strauss is a wife, mom of three, and relentless problem solver. After her son Reid was diagnosed with Creatine Transporter Deficiency, she jumped into action—serving as Vice President and President of the Association for Creatine Deficiencies from 2013 to 2020. Today, she channels her energy into marketing for Mend Services, her family’s plumbing, electrical, and HVAC company, and into storytelling as managing editor of Dripping Springs City Lifestyle, a community magazine that spotlights local businesses through editorial features and events. You’ll often find her in the kitchen or chicken coop, juggling dinner, deadlines, and connecting with friends and family.

Maaike Roefs

Bio

Maaike Roefs lives in the Netherlands with her partner Desmond and their 3-year old son Oscar. Oscar was diagnosed with CTD just after his 2nd birthday. Maaike has a background in technical medicine and communication science, and is currently working as a data analyst in healthcare.

Jeff Allen

Bio

Jeff has nearly 20 years of experience as a sales and business development leader in the healthcare industry. From medical devices to medtech, Jeff has always been attracted to sectors that are in need of new technologies to solve old problems. A native of Ohio and graduate from Ohio University, he now lives in Northern California with his wife, Jennifer, and their sons Jack and Lucas. Lucas was diagnosed with Creatine Transporter Deficiency in 2019.

August 22nd, 2025

General Session Day 1

8:00AM PDT | 5:00PM CEST

Sangeetha Iyer, | Phd - Opening Remarks

Scientific Advisor, ACD

8:15AM PDT | 5:15PM CEST

Maaike Roefs - Patient Spotlight

Patient Caregiver

Bio

Maaike Roefs lives in the Netherlands with her partner Desmond and their 3-year old son Oscar. Oscar was diagnosed with CTD just after his 2nd birthday. Maaike has a background in technical medicine and communication science, and is currently working as a data analyst in healthcare.

August 22nd, 2025

General Session Day 1

8:25AM PDT | 5:25PM CEST

Amanda Thomas - Wilson | PhD, FACMG

Clinical Genome Resource Cerebral Creatine Deficiency Syndromes Variant Curation Expert Panel

Bio

Amanda Thomas-Wilson, PhD, FACMG is a director of Molecular Diagnostics at the New York Genome Center and is Board Certified by the American Board of Medical Genetics and Genomics in Clinical Biochemical Genetics and Laboratory Genetics and Genomics. She was trained under the direction of Dr. Marzia Pasquali at the University of Utah for her Clinical Biochemical Genetics fellowship, and Dr. Vimla Aggarwal at Columbia University for her Laboratory Genetics and Genomics fellowship. Amanda has been involved in the Clinical Genome Resource (ClinGen) since 2014 and the Cerebral Creatine Deficiencies Variant Expert Curation Panel (CCDS VCEP) since its inception. She is particularly interested in biochemical genetics disorders, newborn screening, and prenatal and pediatric genetic diagnostics.

Abstract

"Collaboration Update: The Association for Creatine Deficiencies and the Clinical Genome resource; re-defining SLC6A8 variant classification specifications"

Understanding the clinical significance of variants in genes causing cerebral creatine deficiency syndromes (CCDS) is important to ensure timely diagnosis and initiation of treatment for these disorders. The Association for Creatine Deficiencies (ACD), a patient advocacy organization, collaborates with the NIH-funded Clinical Genome resource (ClinGen) to share biochemical and genetic data to assist in variant classification and increase knowledge of the molecular etiology of the CCDSs.
The ClinGen CCDS Variant Curation Expert Panel (VCEP) has developed guidelines for classification of variants in the CCDS genes (GAMT, GATM, SLC6A8) and is actively working on curation of variants in these genes as well as reassessing Variants of Uncertain Significance submitted to public repository ClinVar.
The CCDS VCEP was honored to speak at the ACD conference in 2024, where we presented planned updates to variant interpretation specifications for SLC6A8. From feedback we received, additional granularity was added to these specifications enabling more consistent classification of variants. Updates include more specific guidance on use of population databases, additional guidance on counting segregation evidence in families, updated functional evidence, and increased sensitivity for phenotype specificity in females with CTD allowing for more accurate variant interpretation. We also transitioned scoring of SLC6A8 variant evidence to a Bayesian framework in preparation for a field-wide update expected by the end of 2025.
Updates of these guidelines will provide additional strength and power to classify SLC6A8 variants accurately and consistently and provide guidance for clinical labs curating CCDS variants worldwide. Collaboration with the ACD allows leveraging biochemical and variant information from registry participants for classification and ongoing reclassification efforts of variants. Cooperation between the ACD and ClinGen enhances the understanding of the clinical significance of variants in genes causing CCDS and serves as a model for collaboration between other ClinGen VCEPs and patient advocacy organizations.

8:50AM PDT | 5:50PM CEST

Filippo Ingoglia | PhD

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 the ARUP Laboratories. Dr. Ingoglia was born and raised in Italy, where he completed all his higher education, receiving BA, MA, and PhD degrees from the University of Parma. During his PhD training, he spent four months at the University of Utah as a visiting fellow, and the lab's research was focused on rare inherited metabolic disorders. That experience piqued his interest in biochemical genetics, and to apply to the Clinical Biochemical Genetics Fellowship with the Department of Pathology two years later. In 2021 he graduated and obtained the American Board of Medical Genetics and Genomics (ABMGG) certification in Clinical Biochemical Genetics. Since he stepped into the biochemical genetics field, he has focused on creatine metabolism in patients with urea cycle disorders and, ultimately, on the development of methods to determine the effectiveness of potential therapeutic agents for the treatment of guanidinoacetate methyltransferase (GAMT) deficiency. In 2023 Dr. Ingoglia joined the Creatine Deficiency Research Center, Funded by ACD and launched at the University of Utah. He will contribute with his expertise in cellular transport studies by developing a functional test to confirm the diagnosis of creatine transporter deficiency (CTD), to determine whether there is residual creatine transport activity in CTD patients, and to define the function of variants of uncertain significance.

ACD
ASSOCIATION FOR CREATINE DEFICIENCIES

August 22nd, 2025

General Session Day 1

Abstract

"Immortalized Fibroblasts from Patients with CTD Retain Minimal Creatine Transport"

Ipsum LoremMeasurement of creatine transporter activity is essential in establishing a diagnosis and possible response to therapy in creatine transporter deficiency (CTD). We developed a non-radioactive, stable isotope creatine transport assay (measuring intracellular creatine levels by UPLC-MS/MS) to evaluate the activity of the creatine transporter in fibroblasts from patients with CTD. In normal controls, kinetic analysis showed that net creatine uptake was linear for up to 2 hours with a Km value of 22.3±6.1 µM. CTD fibroblasts carrying premature termination codons had 1% or less of the normal creatine transport activity, confirming CTD and demonstrating the assay's clinical utility. To determine how novel missense SLC6A8 variants affected creatine transport, we created SV40-immortalized CTD fibroblast cell lines that can be transfected with normal and mutant SLC6A8 transporters. After SV40 transformation, normal fibroblasts exhibited an approximately 5-fold increase in creatine transport, whereas those from CTD patients retained absent creatine transport. Initial attempts to permanently transfect SV40-CTD fibroblasts with wild-type and mutant SLC6A8 constructs resulted in elevated cell mortality and are being optimized. By contrast, transient transfection of SV40-CTD fibroblasts with wild-type SLC6A8 cDNA restored supra-normal creatine transport, while missense variants abolishing activity in fibroblasts failed to cause any increase. Importantly, transient transfection of the P455L variant, which retains residual transport activity, generated a small but significant increase in creatine transport, indicating that the novel assay can distinguish between hypomorphic and functionally null variants. In conclusion, we have developed a novel non-radioactive assay to measure creatine transport and immortalized cells lacking creatine transport, which can be used together to assess the functional activity of missense variants identified in patients with CTD.

9:15AM PDT | 6:15PM CEST

Emily Reinhardt

Association for Creatine Deficiencies

Bio

Emily has almost 15 years of research experience, with particular emphasis in pre-clinical and translational neuroscience research. Through her love of science, she has grown passionate about using data to improve the lives of people within her community. Emily is a graduate of Kansas State University, earning both her BS and MS in Psychology with a focus in Behavioral Neuroscience. She currently lives in Vancouver, Washington, with her husband, Andrew.

9:55AM PDT | 6:55PM CEST

Laura Baroncelli | PhD

Neuroscience Institute, CNR

Bio

Laura Baroncelli is a Senior Researcher at the Neuroscience Institute of the Italian National Research Council (CNR) in Pisa and is affiliated with IRCCS Fondazione Stella Maris. She earned her PhD in Neurobiology from the Scuola Normale Superiore, where she developed a strong background in sensory system plasticity. Over the past decade, her research has focused on understanding the neurobiological mechanisms underlying neurodevelopmental disorders and rare diseases, with a particular emphasis on genetic disorders such as Creatine Transporter Deficiency, Angelman and Rett syndromes.
Her expertise lies in translational neuroscience, including the development of functional biomarkers and therapeutic strategies using gene therapy and antisense oligonucleotides. She has extensive experience with preclinical animal models, in vivo brain imaging, electrophysiology, and behavioral neuroscience. She actively leads and participates in multidisciplinary projects aimed at advancing novel treatments and diagnostic tools, often in collaboration with national and international institutions.
Dr. Baroncelli also coordinates initiatives focused on bridging basic and clinical research, with the aim of accelerating the transfer of scientific discoveries into clinical applications. She has secured competitive funding from national and international bodies, including Telethon, the Italian Ministry of Health, and EU programs. She is an author of numerous peer-reviewed publications and serves as a scientific advisor for various academic and patient-centered networks.
Driven by a strong commitment to scientific rigor and innovation, her research aims to improve the quality of life of individuals affected by severe neurological conditions through targeted and personalized approaches.

ACD
ASSOCIATION FOR CREATINE DEFICIENCIES

August 22nd, 2025

General Session Day 1

Abstract

"Progress Toward a Gene Therapy for Creatine Transporter Deficiency"

Creatine Transporter Deficiency (CTD) is an X-linked neurodevelopmental disorder caused by mutations in the SLC6A8 gene, leading to severely reduced brain creatine levels. This metabolic disruption results in intellectual disability, language and motor impairments, seizures, and autistic-like features. At present, no effective treatments exist for CTD. Our research explores gene therapy as a potential disease-modifying strategy. Using an AAV9-based vector to deliver the human SLC6A8 gene, we achieved broad expression of the creatine transporter (CRT) in the brains of CTD model mice following early intracerebroventricular administration. This intervention significantly restored cerebral creatine levels and improved multiple clinically relevant outcomes, including increase of body weight, enhancement of brain connectivity, and reduction in repetitive and social behaviors. Memory functions also improved, although working memory deficits remained. Notably, when administered to wild-type mice, the therapy unexpectedly impaired certain memory domains, suggesting possible risks associated with CRT overexpression in healthy brain circuits. These findings underscore the potential of gene therapy to address core deficits in CTD while also highlighting the need for refined strategies with improved cell-type targeting and safety. In this presentation, I will summarize the progress of our preclinical work, discuss its implications for clinical translation, and outline the next steps toward safer and more effective gene therapy approaches for individuals living with CTD.

10:20AM PDT | 7:20PM CEST

Chiara Sawilla

Queen's University

Bio

My name is Chiara Sawilla and I am a masters student in the Walia lab at Queen's University. I have been working on this dosage study project for our vector aimed to treat CTD for the past two years. I am excited to share these results and how they will contribute to ongoing research of CTD.

Abstract

"Delivery of scAAV9.SLC6A8 for Restoration of Creatine Transporter Function in a Creatine Transporter Deficient Mouse Model: A Dosage Study"

Creatine deficiency syndromes are inborn errors of creatine metabolism, which result in impaired synthesis and transport of creatine. Under normal physiological conditions creatine is synthesized and released into the blood stream to provide cellular energy. Creatine transporters facilitate the movement of creatine against large concentration gradients to ensure cellular energy supply to tissues. Creatine transporter deficiency (CTD) is an X-linked disorder caused by mutations in the SLC6A8 gene, leading to impairments in these transporters. Clinically, CTD presents as developmental delays, speech and motor impairments, behavioural abnormalities, and intellectual disability. There are currently no effective treatments for CTD. We hypothesized that the delivery of a codon optimized SLC6A8 transgene via self-complementary adeno-associated virus 9 (scAAV9.SLC6A8) can correct this disorder. This study investigates the dose-response of scAAV9.SLC6A8 in a Slc6a8Y/- murine model. At 6 weeks of age, five cohorts of 6 mice per cohort received intrathecal lumbar injections of either vehicle or varying vector doses (1.22+e10, 2.45+e10, or 3.59+e11 vg/mouse). Short term (13 weeks) and long term (24 weeks) outcomes, which included weight, grip strength testing, and biochemical analysis were assessed. Long term cohorts were additionally assessed for hyperactivity phenotype using digitally ventilated cages (DVC). Results demonstrated a dose-dependent increase in weight and grip strength evident at 13 weeks and sustained to 24 weeks. Mass spectrometry confirmed elevated creatine levels in both peripheral and central organs of treated mice. Additionally, all treated cohorts tested in DVC exhibited reduced hyperactivity compared to untreated knockout mice. Overall, these findings provide critical insight for the use of scAAV9.SLC6A8 in the treatment of CTD patients. Further investigation into safety and dose optimization will provide greater translation for clinical use.

August 22nd, 2025

General Session Day 1

10:45AM PDT | 7:45PM CEST

Robyn Binsfield | PhD

Queen's university

Bio

Dr. Robyn Binsfeld recently completed her PhD at Queen's University working with Dr. Jagdeep Walia on developing a gene therapy approach to treating GAMT creatine deficiency. She is currently working with Dr. Walia to help transition several investigational gene therapies for rare disease, including GAMT-D and CTD, to clinical trial. She was also accepted into the prestigious Pre-Amp Fellowship program working alongside Amplitude Ventures to explore the intersection between business and life sciences for therapeutic development.

Abstract

"Intrathecal scAAV9.hGAMT effectively restores creatine and GAA levels and is well tolerated in mouse models of GAMT creatine deficiency Intrathecal scAAV9.hGAMT effectively restores creatine and GAA levels and is well tolerated in mouse models of GAMT creatine deficiency"

Guanidinoacetate methyltransferase (GAMT) is an essential enzyme in the biosynthesis of creatine, a small molecule that plays an important role in energy metabolism. The family of rare inborn errors of metabolism deemed creatine deficiency syndromes lead to several neurological impairments including developmental delay, intellectual disability, and epilepsy, emphasizing the importance of creatine's role in the brain. Creatine biosynthesis takes place through the enzymatic function of arginine:glycine amidinotransferase (AGAT) to form guanidinoacetate (GAA) which is then converted to creatine by the GAMT enzyme. GAMT-deficiency is an autosomal recessive disorder resulting in little to no available intracellular creatine accompanied by an accumulation of the neurotoxic metabolite, GAA. We have recently completed an extensive pre-clinical investigation for a CNS-directed adeno-associated virus-based gene therapy for the treatment of GAMT-D. A proof-of concept study demonstrated that the scAAV9.hGAMT vector had the potential to restore expression and function of GAMT in cellular and murine models of GAMT-D following intrathecal administration. To follow up, various doses of the vector were tested, and durability was assessed. A dose-dependent increase in creatine and decrease in GAA accumulation was detected in the brain and periphery of treated animals. The vector established improvements that were detectable at 5-months post-treatment and stable long-term expression in the liver. Finally, we characterized the immunogenic profile of the GAMT transgene determining it was well-tolerated in mice regardless of immunosuppression. Additionally, we determined the use of immunosuppression can improve short-term biochemical outcomes and recommend its use in further pre-clinical and clinical studies. Overall, we have shown that scAAV9.hGAMT represents a promising therapeutic for the treatment of GAMT creatine deficiency and upon determining a full toxicological profile, it warrants translation to clinical investigation for use in human patients.

11:50AM PDT | 8:50PM CEST

Amy Perry - Patient Spotlight

Patient Caregiver

Bio

Amy Perry lives in Powell, Ohio with her husband, Jeff, and their two sons — Ben (12) and Will (14)— plus two dogs, Ace and Leia, and a cat named Lucy. Her youngest son, Ben, has Creatine Transporter Deficiency (CTD). Sharing their story and participating in research is one way Amy and her family hope to raise awareness, support the CTD community, and help drive progress toward a treatment or cure. Professionally, Amy leads a cybersecurity awareness and technology communications team at Nationwide Insurance. She's passionate about using communication to help people understand complex topics and connect with what matters most.

August 22nd, 2025

General Session Day 1

12:00PM PDT | 9:00PM CEST

Emanuele Bartolini

IRCCS Foundation Stella Maris, Pisa

Bio

Clinical neurologist and researcher with special interest in epileptology. Since 2010 to 2017 he had been working in United Kingdom (London) and Italy (Pisa and Florence). Experienced in emergency neurology and in management of chronic neurological disorders of children and adults.
Currently head of the Epilepsy and Clinical Neurophysiology Lab, IRCCS Foundation Stella Maris, Pisa, Italy. Chair of the Study Group on Climate Change and member of the Neuroimaging Commission of the Italian League Against Epilepsy. Research focus is on advanced neuroimaging, neurophysiology and treatment of children with epilepsy.

Abstract

"Dynamic electro-clinical features in Guanidinoacetate N-methyltransferase deficiency: a familial case series"

Guanidinoacetate N-methyltransferase deficiency is an inborn error of creatine metabolism, responsible for the absent conversion of guanidinoacetic acid into creatine, resulting in cerebral creatine deficit. It could present a variety of symptoms such as neurodevelopmental delay, epilepsy, movement disorder (ataxia, dystonia, chorea) and behavioral disturbances. After intellectual disability, epilepsy is the second most frequent expression of the disorder, usually arising during infancy with febrile seizures that are typically followed by generalized seizures and electroencephalographic anomalies. Herein we describe three siblings with the same homozygous truncating variant in GAMT, all of whom showed significant global developmental delay during early infancy. The eldest two developed initially neglected atypical absences, preceded by focal motor seizures in the older brother, with complete remission with antiseizure medications and dietary treatment. Despite seizure freedom, during follow-up both developed overt focal epileptiform discharges that have persisted after two years of creatine supplementation. Neither seizures or electroencephalographic abnormalities were noted in the youngest brother who took advantage of an earlier diagnosis and treatment.
The dynamic electroclinical pattern we observed has never been reported beforehand. Further studies are needed to assess the long-term prognosis of epilepsy in patients who have introduced dietary treatment after the seizure onset.

12:15PM PDT | 9:15PM CEST

Maria Borrell-Pichot

Hospital de la Santa Creu i Sant Pau, Barcelona

Bio

Resident in Neurology with special interest in rare diseases and movement disorders. During residency I have collaborated with the Epilepsy Unit at Hospital de Sant Pau, publishing a research article on refractory epilepsy in a patient with creatine transporter deficiency.

Abstract

"Positive Response to CBD and CLB in a Case of Creatine Transporter Deficiency with Refractory Epilepsy"

INTRODUCTION
Creatine deficiency disorders are a group of rare genetically determined diseases that affect neurodevelopment and behavior. Patients with creatine transporter deficiency (CTD) frequently develop epilepsy. Currently, there is no evidence regarding which anti-seizure medications (ASM) are most appropriate for these patients.
MATERIALS AND METHODS
A 29-year-old male diagnosed with CTD, with severe psychomotor developmental delay and severe intellectual disability. At 2.5 years of age, he began experiencing frequent seizures, initially bilateral tonic-clonic seizures (including two episodes of status epilepticus requiring barbiturate coma), and currently focal seizures with impaired awareness, manual automatisms, and tonic posturing of the left hand.Brain MRI showed biparietal subcortical hypomyelination and low creatine levels on spectroscopy. Genetic testing revealed a deletion in the SLC6A8 gene (c.942_944delCTT) on the X chromosome.After trying numerous ASM combinations, supplements of arginine, creatine, and glycine, and a ketogenic diet—being treated at that point with BRV + LTG + PHT—seizures continued at a frequency of 10–20 per month.
RESULTS
CBD and CLB were added to his treatment (5 mg/kg/day and 20 mg/day respectively). Over a 2 year follow-up period, the patient has not experienced any seizures and has also shown improvement in cooperation and attention, with good tolerability.
CONCLUSIONS
This case illustrates complete seizure remission in a CTD patient with the combination of CBD and CLB, which could represent an individualized therapy option in this type of developmental and epileptic encephalopathy.

August 22nd, 2025

General Session Day 1

12:45PM PDT | 9:45PM CEST

Aloïse Mabondzo (Presented by Clémence Disdier)

Paris Saclay University, CEA, LENIT/SPI/DMTS/Frédéric Joliot Institute, Gif sur Yvette, France

Bio

Dr Aloïse Mabondzo, research director is a head of Neurovascular Unit Research & Therapeutic Innovation Laboratory at CEA Saclay in France. He joined the CEA, the Life Science Division, in May of 1998 as the leader of a neurovascular pharmacology Lab with a strong focus on in vitro blood-brain barrier (BBB) modeling and pathophysiology of the brain. His Lab has developed fully characterised in vitro screening tools allowing the optimisation of the molecules under development for brain penetration. His innovative research has made possible the development of research programs in the neuroscience field : Alzheimer's disease, nanotoxicology, ischemic hypoxia encephalopathy, X-linked creatine transporter deficiency disease. Dr Aloïse Mabondzo is author or co-author of 77 articles in peer reviewed journals, ten patents, gave lectures as lecturer and as well as guest speaker, poster presentation in the scientific congress, and he often reviews articles for scientific journals. He has directed more than twenty PhD students, and several postdoctoral positions have been part of his team. As a Neuroscientist, Dr Mabondzo aims to bridge the gap between experimental research and clinical therapy for brain diseases. He is a cofounder of CERES BRAIN THERAPEUTICS, a spin-off from the French Alternative Energies and Atomic Energy Commission (CEA), committed to focus its resources to the preclinical development of advance drug over coming years in order to provide CTD patients with a therapeutic solution to deliver creatine in the brain.

Abstract

"Toward Identification of Creatine Transporter Deficiency circulating Biomarkers Associated with Brain Dysfunction for Therapeutic Efficacy Drug Monitoring"

Creatine transporter deficiency (CTD) is a devastating neurological disorder that results in intellectual disability, epilepsy, and a lack of language development. Knowledge of the molecular and cellular brain mechanisms affected by creatine deficiency in CTD patients remains very limited. There is a need to expand studies to biomarker discovery in order to enhance drug candidate development.
In this context, we cross integrate several relevant proteomic databases describing protein expression in CTD context. Shotgun proteomics analysis was performed first in Slc6a8-/y mice brain. Comparison of the protein abundance between wild-type, Slc6a8-/y mice with or without dodecyl creatine ester (DCE) treatment identified several tissue biomarkers. We generated another proteomic database using our model of cerebral organoids from three male CTD patients. The biomarkers identified remain to be measured in the brain tissue and cannot be easily used during clinical trials. To check their clinical relevance, we analyzed plasma from CTD male patients using the same methodology to describes modulation of protein abundances in an accessible body fluid. The analysis across the different proteomic databases highlighted 4 very promising markers. The consistency of modulation of those proteins in all 3 databases support their relevance in the context of CTD as well as the validity of the in brain organoids and in KO mice. The restauration of these markers after DCE treatment in the KO mice model also support their interest as markers to monitor therapeutic efficacy. While promising, there is still much work to be done to demonstrate clinical efficacy of DCE treatment in patients. We will develop an innovative model of choroid plexus organoids producing cerebro-spinal fluid (CSF). allowing us to correlates between choroid plexus, in vitro CSF, Slc6a8-/y mice and plasma clinical samples. We expect to provide an innovative tool for monitoring DCE treatment efficacy in CTD males and females patients.

1:10PM PDT | 10:10PM CEST

Israel Abebe Admasu | MD, MSc

Boston Children's Hospital/Harvard Medical School

Bio

Dr. Israel Abebe Admasu is a postdoctoral researcher with a background primary care and specialization in basic and translational neuroscience. His research focuses on severe neurodevelopmental disorders, with particular interest in identifying functional brain signatures that inform diagnosis and objectively track therapeutic response. He is currently an ACD fellow working on a project investigating cortical visual responses in creatine deficiency syndromes (CCDS), using functional near-infrared spectroscopy (fNIRS) to develop physiologically grounded biomarkers that reflect treatment-related changes in neural dynamics.His other work includes the study of Gamma Entrainment Using Sensory Stimulation (GENUS), a noninvasive neuromodulation approach leveraging rhythmic light flicker to restore neural network synchrony in Autism related disorders. Across projects, his research combines circuit-level insights with in vivo and ex vivo imaging, functional near infrared spectroscopy(fNIRS) and computational analysis. Dr. Admasu's broader interests lie in brain development, gene–environment interactions, and the systems-level mechanisms that link disrupted neural activity to clinical outcomes in early-onset brain disorders.

August 22nd, 2025

General Session Day 1

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. To address this gap, we aim to establish functional near-infrared spectroscopy (fNIRS) as a reliable and broadly applicable tool to monitor brain function in individuals with rare neurometabolic disorders such as CCDS. In this study, we enrolled 40 children diagnosed with CCDS—including the GAMT and CTD subtypes—and 18 age-matched, typically developing controls to assess group-level differences in cortical responses. Of these, 28 participants from the CCDS group and 16 from the control group underwent fNIRS recording during visual stimulation involving alternating mock and checkerboard stimuli. Consistent with previous findings, our results demonstrate that individuals with CCDS exhibit elevated hemodynamic responses compared to controls. Additionally, the CTD subgroup exhibited an earlier onset and steeper rise in hemodynamic responses compared to the GAMT subgroup. These results reveal a characteristic hemodynamic pattern associated with CCDS. The normalization of these response dynamics—from an abnormally early and amplified pattern to one resembling that of typically developing children—may serve as an indicator of restored cortical physiology and could be used as a functional biomarker for effective treatment or potential cure. Our study further demonstrates the feasibility of using fNIRS to detect functional cortical differences in CCDS, with a protocol that is well-tolerated by both typically developing children and those with neurodevelopmental challenges. These findings support the clinical translation of fNIRS as a practical and scalable tool for validating new therapies and monitoring brain function in rare neurometabolic disorders. We gratefully acknowledge the support of the Association for Creatine Deficiencies (ACD) and Boston Children's Hospital, whose contributions made this research possible.

1:35PM PDT | 10:35PM CEST

Gerry Lipshutz | MD

UCLA School of Medicine

Bio

Gerry Lipshutz MD received his medical degree from the University of California Los Angeles (UCLA) School of Medicine and completed his postgraduate training at the University of California San Francisco. Dr. Lipshutz is a Professor within the Department of Surgery and the Department of Molecular and Medical Pharmacology at UCLA. He is also a member of the Intellectual and Developmental Disabilities Research Center at UCLA along with the Broad Center. As a physician-scientist, his laboratory has focused on developing an improved understanding of the underlying neuropathophysiology of specific rare metabolic and neurodevelopmental disorders and in developing gene therapy approaches in pursuit of genetic-based therapies.

Abstract

"Positron Emission Tomography Reporters are Brain Biomarkers for the Creatine Transporter Slc6a8 Loss of Function Mutation: Changes and Gene Therapy"

Pathogenic variants in the creatine transporter gene SLC6A8, reported to represent 2% of all intellectual disabilities in males, result in a spectrum of behavioral abnormalities including developmental delay, intellectual disability, and deficit in speech. While at present there are no effective treatments available, preclinical development and testing of gene therapy and other approaches to increase brain creatine are being actively pursued. In studying a mouse model of the disorder, [18F]-fluorodeoxyglucose ([18F]-FDG)-based positron emission tomography (PET)/computed tomography (CT) was performed to assess brain glucose metabolism in wild type and creatine transporter mutant mice (Slc6a8-/y). The findings demonstrate marked differences in glucose metabolism in the brains of wild type and Slc6a8-/y mice. Restoring creatine transporter activity in the brain reversed these metabolic changes as detected by PET/CT. In conducting behavioral phenotyping studies, notable abnormalities in behavior in a the murine model led to additional studies in serotonin-mediated activity. Serotonergic signaling differences were detected between wild type and Slc6a8-/y mice using 4-(2'-methoxyphenyl)-1-[2'-(N-2"-pyridinyl)-p-[18F]fluorobenzamido]ethylpiperazine ([18F]-MPPF). These data demonstrate that [18F]-FDG-PET and 18F-MPPF-PET may serve as appropriate and sensitive biomarkers that could be used to assess the efficacy of not only new approaches in treating mutations of the creatine transporter SLC6A8 and their effectiveness in normalizing brain metabolism but also in enhancing our understanding of the mechanism of brain dysfunction that occurs in this complex brain disorder.

2:15PM PDT | 11:15PM CEST

Heidi Wallis - Closing Remarks

Executive Director, ACD

August 23rd, 2025

General Session Day 2

8:00AM PDT | 5:00PM CEST

Sangeetha Iyer | Phd - Opening Remarks

Scientific Advisor, ACD

8:15AM PDT | 5:15PM CEST

Carmon Phillips - Patient Spotlight

Patient Caregiver

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 30. They are hopeful their daughter's story will give hope to other families struggling to find answers.

8:25AM PDT | 5:25PM CEST

Alex Edwin

Stanford School of Medicine

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. He is a current ACD fellow, and his ongoing work is aimed at further characterizing hit prodrugs and advancing them toward in vivo testing and preclinical development.

Abstract

"Development of a Small Molecule Therapeutic for Creatine Transporter Deficiency"

Effective delivery of creatine or a creatine mimetic has been the goal of numerous therapeutic approaches for the treatment of Creatine Transporter Deficiency. To date, the most advanced approaches utilize ester and amide prodrug linkages for delivery of creatine across the blood brain barrier and neuronal membranes. However, these approaches are limited by poor bioavailability and stability: both creatine amides and esters are unsuitable for use in an oral therapeutic due to peripheral enzymatic degradation. In addition, creatine esters are chemically unstable and rapidly convert to creatinine. Therefore, our research aims to identify a refined series of creatine prodrugs with improved brain delivery. Thus far, we have synthesized 78 creatine prodrugs and developed an in vitro assay alongside a novel fluorometric detection method to quantify intracellular creatine levels following prodrug treatment. Preliminary findings have identified several prodrugs that significantly increase intracellular creatine levels in SLC6A8 knockout cells. Subsequent research will focus on advancing these candidate prodrugs toward in vivo studies.

August 23rd, 2025

General Session Day 2

8:50AM PDT | 5:50PM CEST

Jonathan Schlebach

Purdue University

Bio

Jonathan Schlebach is a researcher whose work centers on the biochemical and biophysical processes governing the biosynthesis, folding, and misfolding of integral membrane proteins within cells. As head of the Schlebach Lab, he leads an interdisciplinary team that integrates biochemical, cellular, and computational approaches to uncover the mechanistic details that regulate protein homeostasis and their roles in evolution and disease. His research also applies these insights to the development of precision therapeutics for genetic disorders, including cystic fibrosis, retinitis pigmentosa, and cerebral creatine deficiency syndrome.

Dr. Schlebach earned his BS in Biochemistry from the University of Illinois at Urbana–Champaign, a PhD in Biophysics through Purdue University's PULSe program, and completed his postdoctoral training in Biophysics and Structural Biology at Vanderbilt University Medical Center.

Title

"Towards the Optimization of Pharmacological Chaperones for SLC6A8 Creatine Transporter Deficiency Syndrome"

9:15AM PDT | 6:15PM CEST

Sara Biagotti

Dept. Biomolecular Sciences, University of Urbino

Bio

University of Urbino and owns a module in the course "Advanced Therapies" at the Biomolecular and Health Sciences in the PhD program at the same university. She started working on RBCs as a drug delivery system more than 10 years ago, and more recently, she moved on to using RBC-derived extracellular vesicles to deliver RNA molecules. During her career, she worked on several rare genetic diseases (e.g., ataxia telangiectasia, phenylketonuria, and GAMT deficiency). She is the principal investigator of a NextGeneration EU-funded project named "RNA-based therapy by RBCEVs for the treatment of Guanidinoacetate methyltransferase deficiency." She is the author of 22 publications in international journals and a presenter at more than 30 international congresses. In particular, she has been selected for talks at more than six international conferences. She is also very engaged in the rare disease community, being the volunteer president of the Italian Association for Ataxia Telangiectasia since 2016.

Abstract

"RNA-based therapy by RBCEVs for the treatment of Guanidinoacetate methyltransferase deficiency"

Guanidinoacetate methyltransferase (GAMT) deficiency is an autosomal recessive inborn error of creatine (Cr) synthesis causing severe developmental epileptic encephalopathy leading to severe intellectual disability, drug-unresponsive seizures, and movement disorders. Both brain Cr depletion and neurotoxic guanidinoacetate (GAA) accumulation contribute to the pathogenesis of severe encephalopathy.
Red blood cell-derived extracellular vesicles (RBCEVs) are being explored as a novel platform for RNA-based therapies due to their safety, biocompatibility, and efficient RNA delivery.
Here, we show the application of RBCEVs loaded with synthetic messenger RNA to treat a murine model of GAMT deficiency.
We produced a synthetic mRNA coding for the GAMT enzyme, using all the tricks to increase its stability and improve translation. For the first time, we loaded this long mRNA into human RBCs with excellent efficiency. Moreover, it was efficiently retained in the EVs, reaching up to 50 copies per EV. The obtained RBCEV population was very homogenous, with a size mode of 140 nm and a good production yield. RBCEVs showed perfect integrity in the membrane bilayer and high expression of common RBC surface markers (i.e., GPA and CD47). In contrast, phosphatidylserine exposure was lower than 4%, suggesting a long circulation time. The plasma pharmacokinetics was longer than expected, with an estimated half-life of about 15 minutes, and 10% was still in circulation after 2 hours. Moreover, the cargo mRNA efficiently reached the liver, and immunofluorescence imaging demonstrated hepatocyte uptake. Biodistribution analyses in other organs are ongoing. Preliminary results showed that a single administration of GAMT mRNA-loaded RBCEVs was effective and reduced GAA levels for up to 5 days. Repeated administration experiments are ongoing.
In conclusion, we set up a platform to obtain RBCEVs loaded with long RNAs to gain lacking functions and treat several genetic diseases. The process has already been scaled and can be further scaled up.

ACD ASSOCIATION FOR CREATINE DEFICIENCIES

August 23rd, 2025

General Session Day 2

10:00AM PDT | 7:00PM CEST

Aurore Curie | MD, PhD

French National Reference Center for Rare Diseases with Intellectual Disability, Department of Child Neurology, Woman Mother and Child Hospital, Lyon University Hospital, Lyon Neuroscience Research Center, CNRS UMR 5292, Inserm U1028, Bron, France

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).

Abstract

"CREAT_criteria : a prospective study in 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.To determine these relevant endpoints and describe clinical/cognitive profile in CTD, using both existing neuropsychological tests, and new outcome measures specifically developed for CTD, we performed a prospective study on 24 French Male CTD patients, 24 chronological age-matched healthy controls, and 24 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 (kinematic task, Purdue-Pegboard), Social assessment (ADOS, eye-tracking analysis of social visual scenes), 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 the 24 CTD patients included in the study (mean age 16.9 years, [6.7 to 26.9]). Mean non verbal IQ was 54.4 [30-75]. 96% of the CTD patients could perform the first level of simple reasoning tasks (match-to-sample), 96% the second level (categorization), 75% the SimpleMatrices task, and 71% could perform the implicit rules learning task. Tasks on tablets could be easily performed at home under remote supervision through visioconference. All patients were able to perform eye-tracking analysis. The mean average steps per day was 12677. 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 CTD patients despite their cognitive deficit.

10:25AM PDT | 7:25PM CEST

Olivier Braissant | PhD

Service of Clinical Chemistry, University of Lausanne and Lausanne University Hospital, Lausanne, Switzerland

Bio

Prof Olivier Braissant, biologist, obtained his PhD thesis at the University of Lausanne, Switzerland, in 1994. After a post-doc on nuclear receptors and their expression in CNS, he moved in 1997 to the University Hospital of Lausanne (CHUV) in the Service of Clinical Chemistry. There, he developed his line of research on various inherited metabolic diseases affecting brain development, in particular creatine deficiency syndromes (CDS), urea cycle diseases and organic acidurias. Olivier Braissant has become one renowned expert in the field of creatine metabolism and transport in the brain, and the way CDS affect them. He is author of about 100 papers published in international journals and conference proceedings, as well as invited book chapters.

Abstract

"Creatine deficiency disorders: a Swiss cohort study showing diagnostic delay"

Patients with creatine deficiency disorders (CDD), caused by defects in L-arginine:glycine amidinotransferase (AGAT), guanidinoacetate-N-methyltransferase (GAMT) or the creatine transporter (CRTR), develop many different unspecific symptoms such as developmental delay, intellectual disability, speech disorder, behavioral troubles and seizures. Early diagnosis and treatment start are essential for a favorable outcome, in particular for AGAT and GAMT deficiencies. We present a CDD patient cohort from a single Swiss center, as well as how the measure of the biomarkers guanidinoacetate and creatine were referred to two Swiss metabolic centers (Lausanne and Zurich) between 2015 and 2023.
Our cohort comprised 6 CDD patients (2 GAMT, 4 CRTR) who were initially seen by different subspecialties depending on first symptoms. The diagnostic and therapeutic delays were comprised between 3 and 32 months (mean 13.8). Creatine and guanidinoacetate annual requests constantly increased during the study period, with a majority of tests performed in urine. Most samples (93.3%) were sent in by large hospitals (mainly from neurology, pediatrics and metabolism) while only few (5.2%) were addressed by pediatricians in private practice, although those usually see the patients first.
Our data demonstrate a relevant delay in the diagnosis of CDD, with specific biomarkers essentially prescribed from specialized pediatric units involved in patient management, most often long after the first symptoms. To decrease diagnostic delay and ameliorate the outcome of patients, the current practice of sample referral should be reevaluated, while first-contact healthcare providers should be encouraged to initiate selective screening.

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10:50AM PDT | 7:50PM CEST

Terrance Dolan, MD | Sophie Scharner, MD

Massachusetts General Hospital, Boston, USA

Bio

Terrance M. Dolan, MD is an attending child, adolescent, & adult psychiatrist at McLean Hospital where he currently serves as an Instructor of Psychiatry at Harvard Medical School. He completed his child and adolescent psychiatry fellowship at Massachusetts General Hospital and McLean Hospital. Dr. Dolan received his adult psychiatry training at the VA Boston Healthcare System – Harvard South Shore training program. Dr. Dolan has also received training in psychotherapy through the completion of the one-year fellowship at the Boston Psychoanalytic Society & Institute. Dr. Dolan enjoys role-playing games, the beach, video games, hiking, gardening, and relaxing with his wife in their backyard Adirondack chairs.

Sophie Scharner, MD is a child psychiatrist in training at Massachusetts General Hospital.

Abstract

"Case report of catatonia and psychosis in a person with AGAT deficiency"

In the below case report, we describe the development of psychotic and catatonic symptoms in an individual with Arginine-Glycine-Amindinotransferase (AGAT) deficiency, requiring creatine supplementation.
We have conducted a literature review and to our knowledge this is the first documented instance of psychiatric symptoms of this kind developing in an individual with AGAT deficiency.
This case provides clinical support for the role of brain creatine metabolism in the development of psychotic and catatonic symptoms.

11:45AM PDT | 8:45PM CEST

Andrea Johnson - Patient Spotlight

Patient Caregiver

Bio

Siobhan (Bonnie) is a 19 year old young woman living with CTD. She loves playing tennis and works hard to develop her skills and live life well.

Her mum Andrea is privileged to share the CTD journey as a parent. She is also a teacher and mum and step mum to two older girls, both of whom have uniquely complex health profiles. Professional and family life sees her always continuing to learn more about health and disability. She believes that every child has a right to quality health and education outcomes and meaningful life as part of their community.

August 23rd, 2025

General Session Day 2

12:00PM PDT | 9:00PM CEST

Aleks Bogoniewski

UCLA

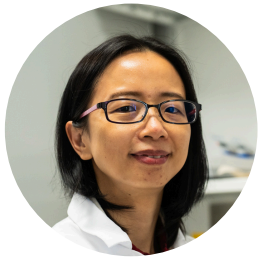
Bio

Aleks is an ACD Fellow at UCLA where he studies the neurodevelopmental consequences of SLC6A8 and GAMT deficiencies using humanized model systems. By leveraging brain organoids (“mini-brains”), stem cells and 2D neuronal cultures, he investigates how these mutations affect brain development and evaluates adeno-associated virus (AAV)-mediated gene therapies as potential treatments. His work aims to refine current clinical approaches and advance new therapeutic strategies for cerebral creatine deficiency syndromes (CCDS). In parallel, he is assessing the efficacy of the current treatment regimen of creatine, L-ornithine, and sodium benzoate supplementation, while comprehensively characterizing patient mutations.
Outside the lab, Aleks enjoys hiking, going to the gym, and spending time with his siblings.

Abstract

“Stem Cell-Based Models of SLC6A8 Deficiency Reveal Cellular Mechanisms of Neurodevelopmental Delay”

Creatine is a high-energy compound that is crucial for various metabolic processes throughout the body. While it is predominantly utilized in muscle, the liver, kidneys, and pancreas, it is also important in normal brain function.The SLC6A8 gene encodes the sodium and chloride-dependent creatine transporter 1 (CRT1), a transmembrane protein responsible for facilitating creatine uptake into tissue. Loss-of-function mutations in SLC6A8 disrupt creatine import into the brain, resulting in creatine transporter deficiency (CTD): a rare but severe X-linked neurodevelopmental disorder characterized by global developmental delay, intellectual disability, epilepsy, and behavioral disturbances. Current therapeutic strategies, including oral supplementation with creatine, L-arginine, and sodium benzoate, fail to restore cerebral creatine levels in CTD patients due to the intrinsic transport defect, leaving a critical therapeutic deficit. Despite its clinical significance, the molecular and cellular mechanisms by which SLC6A8 mutations impair human brain development remain incompletely understood. To address these limitations, our research employs human-derived model systems using induced neurogenin-2 cortical neurons and cerebral organoids from patient-derived induced pluripotent stem cells (iPSCs). Our data reveal significant differences in neuronal maturation and synaptic pruning in mutant 2D cortical neuron cultures. Additionally, while 3D cerebral organoids display neurodevelopmental delays, they do not display differences in growth rate, raising questions about the metabolic compensatory mechanisms at play. By integrating stem cell biology with neurodevelopmental and functional assays, our work aims to elucidate the neurodevelopmental consequences of CTD and ultimately inform the development of more effective therapeutic strategies for individuals affected by SLC6A8 mutations.



12:15PM PDT | 9:15PM CEST

Chin-Yi Chen

Fralin Biomedical Research Institute (FBRI) at Virginia Tech

Bio

I am a molecular neuroscientist committed to uncovering the mechanisms underlying rare neurological and neuromuscular diseases. My early research focused on mitochondrial DNA mutations, rare genetic inherited diseases, and the molecular mechanism in disorders such as MERRF/MELAS syndrome, PRRT2-related conditions and Machado-Joseph disease (MJD; SCA3) and multiple sclerosis (MS). Currently, my work centers on applying focused ultrasound (FUS) to treat rare neurological conditions. I am exploring how FUS can safely and temporarily open the blood-brain barrier to enhance creatine delivery in creatine transporter deficiency (CTD), a disease with no effective brain-targeted therapies. My research goal is to translate these findings into preclinical strategies that accelerate the development of treatments for rare brain disorders, ultimately improving patient outcomes through personalized, precision medicine.

Abstract

“Focused Ultrasound-Enabled Creatine Delivery to the Brain in Creatine Transporter Deficiency”

Creatine transporter deficiency (CTD) is a rare genetic disorder that prevents creatine from reaching the brain, leading to severe neurological symptoms such as intellectual disability, speech delays, seizures, and autistic-like behaviors. While creatine supplements can help muscles, they do not improve brain function in CTD due to the brain’s protective barrier, the blood-brain barrier (BBB), blocking creatine from entering. A promising new approach involves using focused ultrasound (FUS), a non-invasive technology, to temporarily open the BBB. When used with microbubbles, FUS creates gentle vibrations that loosen the connections between cells surrounding brain blood vessels. This allows therapeutic substances, like creatine, to pass into the brain more easily. FUS has already been tested in clinical trials for adults with Alzheimer’s disease, Parkinson’s disease, epilepsy, and glioblastoma, as well as for children with brainstem tumors. Early clinical trials involving FUS have been approved by the FDA and NIH, demonstrating its safe use in pediatric populations. We are currently using this non-invasive technique to deliver creatine directly into the brain in animal models of CTD. By combining FUS with BBB opening, our goal is to restore brain creatine levels and improve neurological outcomes in preclinical studies. Our animal research will provide critical insights into how FUS can be translated into future clinical trials for children with CTD.

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General Session Day 2

12:30PM PDT | 9:30PM CEST

Tesla Peretti

Centre for Neuroscience Studies, Queen's University, Kingston, ON

Bio

I am a PhD Candidate and ACD 2025 Fellow at Queen's University researching AGAT deficiency. I have been working on developing a novel gene replacement therapy for AGAT deficiency since 2021.

Abstract

"Correction of Arginine:Glycine Amidinotransferase (AGAT) Deficiency through Gene Replacement Therapy"

Gene therapy(GT) functions through the manipulation of cells at the genetic level by delivering nucleic acids. Viral vectors are employed for GT, primarily due to the manipulation of the host cells' machinery to produce foreign gene products. Adeno-associated viruses(AAV) can transduce several cell types, have stable transgene expression, and low risk of insertional mutagenesis without a large immune response. 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 gene therapies 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 proof-of-concept study with a novel sc.AAV9hGATM construct administered intravenously to an AGAT-D murine model. Mice entered the study at 5 weeks of age and underwent baseline serum collection and began an oral immunosuppression regimen. One week later, mice were intravenously injected with a control substance or sc.AAV9hGATM vector via the tail vein. The mice performed strength tests and had serum collected every 2 weeks. 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. The increase in creatine production overtime is represented through the various serum collection timepoints. With no concerning levels of GAA present in the organs of the treated mice. Biodistribution of the vector demonstrated appreciable copies of vector in the brain, while the liver maintained a relatively low number of copies. The myopathy and weight phenotypes of the treated mice closer resembled the untreated heterozygotes. This proves the intravenous administration of sc.AAV9hGATM construct can efficiently cross the BBB to correct the biochemical aspects of AGAT-D in mice.

1:00PM PDT | 10:00PM CEST

Kim Cecil | PhD

Cincinnati Children's Hospital Medical Center

Bio

Kim M. Cecil, PhD is an MR Spectroscopist, and Professor of Radiology, Pediatrics, Neuroscience, Environmental and Public Health Sciences at Cincinnati Children's and the University of Cincinnati College of Medicine. She noted the absence of creatine in the brain on the proton MR spectrum of a six-year-old male patient. This finding and subsequent work with Drs. Ton deGrauw and Gaija Salomons resulted in the discovery of creatine transporter deficiency syndrome. Dr. Cecil and her colleagues have published several articles describing the disease characteristics observed in patients and their families. Dr. Cecil is part of the research leadership team within the Imaging Research Center and Department of Radiology at Cincinnati Children's. With community-based environmental cohorts, Dr. Cecil is funded by the National Institutes of Environmental Health Sciences as a multiple principal investigator to study the effects of ubiquitous exposures in typically developing populations to air pollution, heavy metals (lead), flame-retardants and perfluorinated chemicals. The multidisciplinary teams employ neurobehavioral and neuroimaging methods to assess effects from exposure to known and potential neurotoxicants. The objective of these studies is to improve our understanding of the effects environmental toxicants exert on the human brain during childhood, adolescence and eventually, into adulthood. She also currently supports other NIH funded efforts of her colleagues in psychiatry, neurology, genetics, adolescent medicine and gastroenterology.

Abstract

"Brain Creatine Concentrations Measured by Proton Magnetic Resonance Spectroscopy"

Creatine deficiency syndromes were initially recognized by the absence of brain creatine upon performing proton magnetic resonance spectroscopy (MRS). However, biochemical testing of plasma and urine are typically the first line of diagnostics to point clinicians toward a diagnosis. Genetic testing is used to confirm the diagnosis. Now, proton MRS continues to play a role as a functional test to link the recognition of a genetic variant with the presentation of the patient's symptoms. MRS is uniquely positioned to measure in vivo brain creatine and phosphocreatine concentrations as it is noninvasive and can safely be performed longitudinally. It could address scientific questions by correlating brain creatine concentrations with urine and blood biomarkers along with exploring genotype and phenotype associations. While the potential benefits are known, barriers have limited the usage of MRS. Recent technical innovations and collaborations in the field of MRS have addressed differences in implementation across MRI scanner vendors. The next step is defining a standard protocol across imaging sites. Upon protocol acceptance, quantification methods are available but need adaption to become automatic steps in practice. While the need for anesthesia and high expense of MRI/MRS remain fixed for the foreseeable future, these have not been the major barriers towards progress in the field of creatine deficiency syndromes. This talk outlines steps towards achieving a standardized MRS approach available to advance the field. Besides the diagnostic benefit to the individual patient, and the scientific discoveries possible to the field towards understanding the significance of brain creatine concentrations towards cognitive and neurobehavioral skills, seizure control, gastrointestinal functioning and other roles in the body, there is a role for MRS in clinical trials of potential therapeutics.

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1:20PM PDT | 10:20PM CEST

Audrey Thurm, PhD | Judith Miller, PhD, MS

Bio

Audrey Thurm, PhD, is a psychologist and formerly the Director of the Neurodevelopmental and Behavioral Phenotyping Service in the Intramural Research Program of the NIMH. Her research focuses on conducting systematic developmental and behavioral evaluations on individuals with a variety of neurodevelopmental disorders and studying both the longitudinal trajectory of these conditions and clinical trial readiness.

Judith S. Miller, PhD, MS, is a psychologist in the Department of Child and Adolescent Psychiatry and Behavioral Sciences and a senior scientist and training director in the Center for Autism Research at CHOP. Her areas of expertise include diagnosis and classification issues in ASD and how they relate to clinical practice and studies of etiology, autism spectrum, neurodevelopmental conditions and quality improvement.

Abstract

"Moving from Natural History to Clinical Trial Readiness in the CCDS"

Simultaneously over the last several years, two efforts have produced priority domains and data for clinical trial outcomes in Creatine Transport Deficiency: a parent-led project producing a core outcome set (COS) and a natural history study. The current talk will be divided into two parts to bridge findings from these efforts.
The first part will be led by Dr. Judith Miller, PI of the Vigilan natural history study, and will include detailed examples of several measures administered in the longitudinal study, to illustrate challenges to either administration or interpretation based on limited validation in the population (e.g. measures of cognition, fine motor skills and emotion regulation).
The second part will be led by Dr. Audrey Thurm, co-lead of "Parents Advancing REsearch NeTworkS 2.0: Expand Community, Tools, & Engagement" ACD's currently funded PCORI grant focused on caregiver input for optimal characteristics of outcome measures. This portion will provide discussion points based on work of the project thus far on the five neurodevelopmental-focused core outcome domains, which includes methods for capturing meaningful change within them in the context of clinical trials. Results of a recent scoping review will be presented, illustrating how measures in these domains have been used in related clinical trials.
The session will close with ideas on how to utilize data from both of these projects in the context of the FDA's Patient Focused Drug Development process, which requires outcome measures be "fit for purpose," so validated not only within the context of the condition being tested, but also the timeframe of the trial and for the purpose of being an outcome in relation to the treatment being tested. The importance of patient and family involvement in all aspects of this process will be emphasized.

1:45PM PDT | 10:45PM CEST

Carien Basson

Bio

Carien Basson is the mother of 4-year-old Mias, who was diagnosed with GAMT deficiency at 1 year and 9 months. She has a strong scientific background, holding a PhD in Wine Science (Dr. Carien Coetzee), with extensive experience in analytical chemistry, particularly with techniques such as gas chromatography. Carien's career includes experience at Stellenbosch University and a commercial wine laboratory in South Africa. She currently serves as a consultant in the wine industry, collaborating with producers to enhance the quality of their wines. She has applied her scientific expertise to support Mias' health and development, using her analytical skills to better understand and manage Mias's condition.

Title

"Plasma GAA: Considerations for Measuring in Clinical Trials and for Clinical Care"

August 23rd, 2025

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1:45PM PDT | 10:45PM CEST

Anthony Tedesco | MD

ACD Australia

Bio

Tony is a medical doctor working in general practice in Australia. He has a twelve year old daughter diagnosed with GAMT deficiency when she was 5 years old. He helped establish the charity ACD Australia in 2023.

Abstract

"Plasma GAA: Considerations for Measuring in Clinical Trials and for Clinical Care"

In GAMT deficiency, plasma levels of GAA vary during the day. There are multiple factors which could influence GAA levels and this then affects the choice for when GAA levels should be measured.

1:45PM PDT | 10:45PM CEST

Marzia Pasquali | PhD, FACMG

ARUP

Bio

Dr. Pasquali is a professor of Pathology at the University of Utah School of Medicine, and Medical Director of Biochemical Genetics and Newborn Screening at ARUP Laboratories. Dr. Pasquali earned her degrees of doctor in pharmaceutical chemistry and technology and pharmacy doctor at the University of Parma School of Pharmacy in Italy. She trained in clinical biochemical genetics at Emory University, in Atlanta, Georgia where later served as the co-director of the Biochemical Genetics Laboratory. Dr. Pasquali is board certified in Clinical Biochemical Genetics. She is a member of the Society for Inherited Metabolic Disorders, the American College of Medical Genetics and Genomics, and several other professional societies. Her research interests are newborn screening, disorders of carnitine and creatine metabolism and transport, and lysosomal storage disorders.

Abstract

"Plasma GAA: Considerations for Measuring in Clinical Trials and for Clinical Care"

Background: Guanidinoacetate (GAA) is a key biomarker for evaluating treatment efficacy in patients with Guanidinoacetate Methyltransferase (GAMT) deficiency. High levels of GAA can have significant neurotoxic effect on the brain. Persistent high levels can aggravate the neurological symptoms seen in GAMT deficiency, such as movement disorders, seizures, and cognitive impairment. Treatment adjustments are made based on the GAA blood level. However, it is unknown whether GAA blood level varies throughout the day, and whether its level is the same before and after taking medications and before and after having a meal. A single measurement of GAA in clinic may not represent the levels of GAA throughout the day.
Objectives: In this study we want to measure the GAA blood levels in GAMT deficiency patients at multiple time points during the day, to determine whether there is a circadian change and whether a meal or medication affects GAA concentration in blood. Understanding potential circadian fluctuations may help optimize treatment plan for GAMT deficiency patients, improve outcomes and improve the patients' quality of life. Methods: Study design Ten (10) GAMT deficiency patients will be enrolled in this study with the help of the Association of Creatine Deficiencies (ACD). Blood spots will be collected at home via finger pricks, 5-6 times per day on four days over a two-week period (weeks A and B). The families can decide which weekday and which weekend day works best for them. However, the same weekday and weekend day will be selected for both week A and week B.

August 23rd, 2025

General Session Day 2

2:20PM PDT | 11:20PM CEST

The Road to Rare: Innovating and Delivering Therapies - A Panel Discussion

Andrew Steinsapir

Deerfield Management | Apertura Gene Therapy

Andrew Steinsapir is the Acting Chief Technology Officer of Apertura Gene Therapy and a Director, Gene Therapy Program Lead of Deerfield Management's Discovery and Development team. Prior to Deerfield, Mr. Steinsapir was a Consultant for over three years at Dark Horse Consulting Group, where he provided strategic and tactical support for more than 30 cell and gene therapy firms, pharma, and investment firms. Previous to Dark Horse, Mr. Steinsapir worked at 4D Molecular Therapeutics, in several research and process development roles. Mr. Steinsapir holds a B.S. in Chemical Engineering with an emphasis on Biotechnology and an MBA from the University of California, Berkeley. Andrew is on the scientific advisory board for Jack's Tomorrow, a foundation whose mission is to fund research to develop a treatment - and ultimately a cure - for PURA Syndrome.

Clayton Beard

BridgeBio Gene Therapy

Clayton Beard is the Chief Scientific Officer and Site Head of BridgeBio Gene Therapy. Dr. Beard's scientific and management experience has spanned academia, government, biotech, and pharmaceutical organizations. These have included positions at Novartis Vaccines, Precision Biosciences, Global Vaccines, the USDA, the University of North Carolina, and Maxygen. Prior to joining BridgeBio, Dr. Beard was the vice president of therapeutic discovery at Precision Biosciences where he oversaw the buildout and expansion of the gene editing/therapy programs. As head of viral vector R&D at Novartis, he led a team that developed novel RNA virus-based vaccines and RNA vaccines. Dr Beard later built and led the Novartis technical development team responsible for synthetic virus and RNA vaccine production process development and scale up. His R&D expertise includes discovery and development of RNA and DNA-based viral vectors for vaccines and gene therapy, molecular virology, analytical development, and large-scale RNA production. Dr. Beard received his Ph.D. in viral genetics from The University of Georgia, and a B.S. in microbiology from The University of Georgia.

Dave Jacoby | MD, PhD

Ultragenyx

David is Senior Vice President, Head of Global Clinical Development at Ultragenyx Corporation for the past year, responsible for the clinical advancement of the portfolio from research through approval. He is responsible for clinical development plans of programs in preclinical stages. Prior to this position, he held leadership positions in development at BioMarin, and was involved in the approval of 5 medicines for rare diseases, nomination of INDs and nominations for new therapeutic areas. He has been a drug developer for 25 years, before that he was a faculty member of the Neurology department at Massachusetts General Hospital and Harvard, as a member of the Molecular Neurogenetics Unit.

2:50PM PDT | 11:50PM CEST

Sangeetha Iyer | Phd - Closing Remarks

Scientific Advisor, ACD