



2011 Canavan Research Summit Synopsis

This year marked the second Canavan Research Summit, where 40 world's top scientists gathered to share data addressing Canavan disease pathology, diagnosis and potential treatments. The 2011 Canavan Research Summit was chaired by Paola Leone, PhD, and Darryl De Vivo, MD and took place in Harrison, New York on June 3-5, 2011. One key difference from the initial conference in 2008 was that this year's conference was also a family conference, with dozens of children with Canavan disease and their relatives attending from as far away as Norway and Poland. Also this year's conference was significant for a number of important new collaborations and sponsorships. Most notably, the Starker family generously sponsored a new post-doctoral fellowship in white matter research which was announced at the conference banquet.

There have been a number of developments in Canavan disease research since the last meeting. Highlights of this year's conference included a discussion of the role of histones and complex genetic regulation by a number of investigators. Dr. John Moffett was the initial discussant who focused on histone hyperacetylation in Canavan disease. Dr. Patrizia Casaccia and Dr. Jean deVellis presented data on the differentiation program of oligodendrocytes in Canavan disease models, including effects of histone acetylation and epigenetic regulation.

Another important theme was the role of NAA in energetics, cell growth, and differentiation. Dr. Klaus Armin Nave discussed the energetics of NAA in the axon and myelin-producing cells. This topic is related to the translational project of the 2011 Starker Fellow, Dr. Vladimir Markov, who will be working on anapleurotic therapy for Canavan disease with triheptanoin. Dr. Maria Traka presented data on cell cultures derived from Dr. Brian Popko's *nur7* mouse model of Canavan disease, with a focus on possible effects of NAA on the maturation program of oligodendrocytes. Dr. Emile Van Schaftingen discussed the role of biosynthetic enzymes for NAA and NAAG. Dr. Morris Baslow presented an elaboration of his hypothesis on multi-compartmental effects of NAA in the neuronal, astrocytic, and oligodendrocyte compartments.

In terms of therapeutics, Dr. Paola Leone presented preliminary results of her collaboration with Geron Corporation on progenitor cell transplantation in the *nur7* mouse model of Canavan's disease, with a view toward future clinical trials. Dr. Dolan Sondhi presented results from the Cornell gene therapy study of late infantile neuronal ceroid lipofuscinosis. Dr. Maria Escolar presented very compelling data on the effects of timing of cord blood transplantation for Krabbe disease and mucopolysaccharidosis,

demonstrating that early treatment in the first week of life provided vastly superior results. She pointed out that this timing issue may also apply to Canavan's disease or other neurometabolic diseases. Dr. Darryl DeVivo, conference co-chair, pointed out that this fact was a compelling reason to implement broader screening for neurometabolic diseases, with a goal of early diagnosis and treatment. Dr. Lidia DeFilippis presented preclinical data from Dr. Angelo Vescovi's stem cell lines with applications to lysosomal storage disease. Dr. Evan Snyder presented his vision of stem cells as a pharmacological screening tool.

Dr. Ronald Viola and Dr. Ruben Matalon advocated enzyme replacement therapy for Canavan disease, which they claim may access the brain without any kind of blood-brain-barrier disruption. This claim was challenged by Dr. Christopher Janson, who is currently working on new microcatheter techniques of blood-brain-barrier disruption in neurometabolic diseases. The question was raised whether the blood-brain-barrier was defective in Dr. Matalon's mouse model. Dr. Guangping Gao presented comparative data on gene transfer with AAV9 and AAV10 vectors in Dr. Matalon's mouse model, and Dr. Paola Leone questioned the extent of phenotypic variation existing among the models, given the very short life span of the reported mouse variant. The differences in lifespan among mouse models suggests that a variety of different animal models should be tested before drawing firm conclusions on efficacy.

Several industry presenters had interesting preclinical data, including Dr. Ed Wirth from Geron who presented an overview of their human embryonic stem cell lines and clinical applications under development. Dr. Bryan Delaney from DuPont presented toxicological data showing that NAA is rather ubiquitous and yet harmless in the low amounts encountered in the typical diet. Poster presenters had included Dr. Alessandro Burlina who presented an update on NAA/NAAG quantification as biomarkers, and Dr. Jeremy Francis who presented new findings on ASPA expression as a function of glutamatergic signalling. We thank all the researchers for their hard work and determination in pursuing research on rare diseases, and especially thank Dr. Danilo Tagle from NIH who attended and spoke about NIH support mechanisms for advancing preclinical and translational research.