Beginnings

The UCSD Suramin Autism Study began with a new idea about the origins and treatment of autism in 2008. This new idea emerged from 20 years of clinical experience caring for children with genetic forms of mitochondrial disease, combined with new observations of a different kind of mitochondrial dysfunction in autism, and Dr. Naviaux’s long-standing interest in the connection between genes, environment, and metabolism in human health and disease. Dr. Naviaux published the first descriptions of these new ideas in 2012-3. Research in the lab led to the discovery that a drug called suramin, used for 100 years to treat African sleeping sickness, corrected the symptoms of autism in two classical mouse models. The mouse models have many of the same troubles with social behavior, learning, attention, fear of novelty, anxiety, brain circuits and connections, muscle coordination, GI motility, gut microbiome, immune system, and metabolism as children with ASD. Dr. Naviaux’s team published these results in 2013-20154-6.
What is suramin?

Suramin is unique in all of medicine. It is the oldest man-made drug still in active medical use. It was first synthesized by Bayer scientists in 1916, and has been used for nearly 100 years for the treatment of African sleeping sickness in both children and adults. Because of this long history, we have extensive information about its risks and how to use the drug safely. In addition to its long-known anti-parasitic properties, in 1988, suramin was discovered to bind to cellular receptors that sense and respond to danger. Working in this way, suramin calms the cell danger response (CDR) and reverses the metabolic syndrome that is ultimately caused by the special kind of mitochondrial dysfunction seen in autism. Suramin is the first of a new class of medicines called antipurinergic drugs. These new medicines work by inhibiting the cell danger signals sent by extracellular ATP. Dr. Naviaux’s pioneering work was honored with a Trailblazer award in 2011.

What is the cell danger response (CDR) and how is it related to autism?

When cells are threatened, they activate an ancient and deeply embedded code—a subroutine in our genetics—that protects us from danger. Like nations at war, one of the first responses of cells to environmental danger is to harden their borders, and to limit communication with neighboring cells. Dr. Naviaux calls this the Cell Danger Response (CDR). It is a natural
and universal cellular response to any kind of acute injury, toxin, or infection. Even certain DNA mutations like Fragile X and copy number variations (CNVs) like the one that causes Angelman syndrome can activate the CDR. Healing normally shuts down the CDR after the threat is gone in a few days or weeks. This allows cellular resources spent for defense, to be redirected back toward normal growth and development. But sometimes the CDR persists abnormally—gets stuck. Because the CDR is a normal and universal response to injury or threat, the question relevant to autism treatment is not “Why does the CDR turn on?” Instead, the important question is “Why doesn’t the CDR turn off when it should?” And for treatment, the the most important question is, “How can we turn off the CDR when it persists too long?” Dr. Naviaux’s research has shown that the CDR is maintained by abnormal purinergic signaling. When the CDR persists during times of rapid brain growth, it usurps cellular resources for defense, and creates roadblocks to normal developmental progress. This can lead to autism spectrum disorders¹-⁶, and many other disorders³. Suramin helps to normalize purinergic signaling, removes the roadblocks, and allows cells to return to normal metabolism and development.

The Clinical Trial—The First Study of Suramin in Autism

The UCSD Suramin Autism Treatment trial opened in May 2015 and clinical studies were completed in March 2016. This first study was small. We studied 10 subjects divided into 5 pairs, and matched for age and autism severity. Half of the children received a single intravenous infusion of suramin, and the other half received a single dose of saline as a placebo. The results were very promising. All of the children who pre-enrolled will have first preference for the follow-up studies. The researchers plan to submit their results for publication in this summer. If accepted for publication, the research results could be published in the scientific literature before the end of 2016. The next studies (studies #2, 3 and 4) are now being planned.

Locations and Contact Information

The infusions and routine blood and urine tests took place at the UCSD Clinical Translational Research Institute (CTRI) in La Jolla, California. All the behavioral studies took place at the UCSD RAD (Research on Autism and Development) Lab, La Jolla. For more information about the trial you can click on the link at clinicaltrials.gov: https://www.clinicaltrials.gov/ct2/show/NCT02508259.

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Funding for this trial was entirely supported by private donors and foundations. If you would like to help support this trial and future autism treatment studies, please feel free to contact Dr. Naviaux by email (naviaux@ucsd.edu) or cell phone (619-993-2904).
References
(Available upon request as PDF files from: naviaux@ucsd.edu)


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- The Rodakis Family

UCSD Trailblazers—The 2011 Team that started this work. Front row (left to right): Lin Wang, MD, PhD; Zuela Zolkipli, MD; Laura Dugan, MD; Jane Naviaux, MD, PhD; Susan Powell, PhD; Tomohiro Nakayama, MD, PhD; Thuy Le, PhD; Back row (left to right): Mihael Rogac, MD, PhD; Michael Schuchbauer; Robert K. Naviaux, MD, PhD; Other team members (not pictured): Qingbo Tang, PhD.