



Dr. Jack Parent, MD



Dr. Lori Isom, PhD



Dr. Miriam Meisler, PhD

Dravet Syndrome Foundation 2011 Research Grant Recipients ***Readthrough Treatment of Dravet Syndrome Caused by Nonsense SCN1A Mutations***

The Dravet Syndrome Foundation is pleased to announce that it has agreed to fund a very important two-year research project to be led by Dr. Jack Parent of the University of Michigan. His project, “Readthrough Treatment of Dravet Syndrome Caused by Nonsense SCN1A Mutations,” will begin January 1, 2011.

Dr. Parent, along with collaborators Dr. Lori Isom and Dr. Miriam Meisler, will investigate whether readthrough genetic therapy improves the abnormal neuronal function that results from premature termination codon (stop codon or “nonsense”) mutations in the SCN1A gene that causes Dravet syndrome. With a new technique known as the induced pluripotent stem cell (iPSC) method, they have a unique opportunity to study the effects of mutations in neural cells by deriving neurons from patients’ own fibroblasts (skin cells). In addition, they have developed a collaboration with Dr. Richard Gatti, a Professor of Human Genetics at UCLA, who is developing new and improved readthrough compounds. Parent and colleagues will test these new drugs on patient-derived neurons as well as on mice carrying a human SCN1A nonsense mutation that causes Dravet syndrome.

During their two-year study, they will complete the following two objectives:

- 1) Use the iPSC method to derive neurons from fibroblasts of one or more subjects with Dravet syndrome caused by premature termination (stop) codon nonsense mutations, and test whether readthrough therapy with gentamicin, PTC124, or newer compounds will increase normal sodium channel levels and restore channel function.
- 2) Examine whether mice with a Dravet Syndrome knockin premature termination (stop) codon nonsense mutation will respond to readthrough therapy with a decrease in seizures and normalization of sodium channel function.

These critical pre-clinical studies will allow them to determine whether readthrough therapy is a clinically viable treatment for Dravet syndrome patients that carry stop codon nonsense mutations.