

## Current Studies

### Current Studies Seeking Patient Enrollment

#### Placebo-controlled trial of Dextromethorphan in Rett Syndrome

Location: Kennedy Krieger Institute, John's Hopkins School of Medicine, Baltimore, MD

Dr. Sakkubai Naidu, Principal Investigator, is initiating a double blinded placebo controlled clinical drug trial using dextromethorphan (DM) in Rett Syndrome (RTT), at the Pediatric Clinical Research Unit (PCRU) of the Johns Hopkins Hospital/Kennedy Krieger Institute, that is sponsored by the FDA and Johns Hopkins Institute for Clinical and Translational Research (ICTR).

It has been shown that receptors for a certain brain chemical called glutamate, in particular the NMDA type, are increased in the brain of young RTT patients (<10 years of age). This chemical and its receptors, when in excess, cause harmful over-stimulation of nerve cells in the brain, contributing in part to the seizures, behavioral problems, and learning disabilities in RTT.

We propose to initiate a specific treatment using DM to counter/block the effects of this brain chemical and its excessive receptors because of DM's identified ability to block NMDA receptors. DM is available for human consumption. Infants and children with respiratory infections and cough, as well as non-ketotic hyperglycinemia, are treated with DM, which has been well tolerated.

The study will last for 3 months and will be limited to MECP2 mutation-positive children, 2 years – 9.99 years of age. This clinical trial, which is a placebo-controlled study, will randomize patients to the drug or placebo to determine the benefits of DM vs placebo on cognition, behavior, or seizures if present.

Your child will stay twice in the Pediatric Clinical Research Unit (PCRU) at Johns Hopkins ICTR, for 3 days during each admission. The first hospital stay will be for 3 days, before she starts the DM or placebo. The follow-up 3-day hospital stay will be 3 months after she starts taking DM or placebo. There will also be two interim follow up evaluations at 2 weeks and 1 month after she starts taking the DM or placebo consisting of a neurological evaluation, EKG, and blood work, which can take place at your local doctor's office or at Johns Hopkins, and will be paid for by this study. Our research nurse or research associate will contact you at least weekly during the first month, and at least monthly thereafter until the end of the 3-month study. There is no financial compensation for participating in this research study.

#### How to Participate:

If you would like more information regarding the study's Procedures, Risks, Benefits, or other details, please contact our study coordinator, Barbara Ann Bradford, in the Neurogenetics Unit at the Kennedy Krieger Institute ([bradford@kennedykrieger.org](mailto:bradford@kennedykrieger.org)) or at phone # 443-923-2778 or # 1-800-873-3377.

## Treatment of Rett Syndrome With rhIGF-1 (Mecasermin [rDNA]Injection)

Location: Children's Hospital Boston

Collaborators: International Rett Syndrome Foundation, Autism Speaks

Letter from Dr. Scott Pomeroy 378.33 Kb

### Summary:

The investigators are recruiting children for a research study using a medication known as IGF-1 (mecasermin or INCRELEX) to see if it improves the health of children with Rett syndrome (RTT). To participate in the study your child must be female, between the ages of 2 to 12 and have a genetic diagnosis (MECP2 deletion or mutation) of Rett Syndrome. As you may know, there is no treatment for this illness. Currently, the standard management of Rett syndrome is supportive, which means attempting to prevent complications and treatment of symptoms.

This study involves testing an investigational drug, which means that even though IGF-1 is approved by the Food and Drug Administration (FDA) for use in children, it has not been used before to treat Rett syndrome specifically. Information from this research will help determine whether the drug should be approved by the FDA in the future for the treatment of Rett Syndrome.

There are three goals to this study:

- As one of the features of Rett Syndrome is unstable vital signs, the investigators are trying to determine if IGF-1 has any effect on normalizing your child's pulse, blood pressure and breathing pattern. During PHASE 2, a device called BioRadio® will be used to monitor vital signs in a non-invasive way. This information will be recorded and stored on the accompanying laptop. Before starting PHASE 2, the investigators would like to "beta-test" the BioRadio® in PHASE 1. As such, the investigators may ask you to try using the BioRadio® with your child to test the fit and the performance of the equipment. Should you choose to enroll your child in PHASE 2, the investigators will then ask that your child wear the BioRadio® for two hours, on two consecutive days every four weeks.

- The safety of IGF-1 in children with Rett syndrome. The study personnel will ask you to complete a medication diary and side effect reporting form on a regular basis. They will assist you in completing this by telephone interviews. Your child will undergo 2 lumbar punctures performed at the bedside in the clinical research facility. In addition, laboratory tests will be performed throughout the study to evaluate the safety of IGF-1. These will be blood tests similar to those provided in routine clinical care. Your child will undergo regular non-invasive comprehensive physical examinations including neurological and eye examination, tonsil evaluation, electrocardiograms (ECG), measurement of height, weight and head circumference.

- IGF-1 may improve your child's behavior, communication and speech. In order to measure this, the investigators will evaluate your child once during each month of treatment with neurodevelopmental assessments and a neurological exam. All of the tests used during these evaluations are non-invasive. the investigators will also ask you what your impressions are about her behavior and day-to-day activities through a structured parental interview and various questionnaires.

## Rett Syndrome Natural History Study

Location: Various (see list below)

Status: Recruiting

#### Summary:

The purpose of this natural history study is to establish a phenotype-genotype correlation over a broad spectrum of Rett syndrome phenotypes including the longitudinal pattern of progression of clinical features, quality of life, and longevity across this cohort.

#### Published Results to Date:

Pubs JCN North American Database (82.11 kB)

JCN Ret Research Update (1.07 MB)

Pubs NeuNeuro Revise Final (175.68 kB)

Ann Neurol 2010 Lessons on Criteria 91.85 Kb

Ann Neurol 2010 Updated Criteria 161.24 Kb

Glaze seizure paper Neurology 2010 481.25 Kb

J Peds 2009 Kirby et al Rett longevity 241.84 Kb

JB Lane QOL paper Neurology 306.47 Kb

JCN North American Database 81.47 Kb

Motil JPGNVitamin D deficiency 97.66 Kb

Motil 143.68 Kb

Profiling Scoliosis in Rett Syndrome 2010 Ped Res 204.12 Kb

#### Target Enrollment:

Individuals fulfilling consensus clinical criteria for Classic or Variant Rett Syndrome or individuals with MECP2 mutations who do not meet the clinical criteria. All ages will be eligible. Patients must be able to travel to study sites for annual evaluations (for those 6 years or older) or bi-annual evaluation (for those through age 5).

#### The data collection sites include:

- Birmingham, AL
- Oakland, CA – travel site
- Tampa/Miami (alternating), FL - travel site
- Chicago, IL - travel site
- Boston, MA

- New Brunswick, NJ – travel site
- Greenwood, SC
- Houston, TX

2012 Site Visit Schedule 272.70 Kb

#### How to Participate:

In order to participate in a study, you must personally contact the study coordinator of any of the participating institutions by phone or by e-mail. Please use the information below to inquire about participation.

- The Blue Bird Circle Rett Center, Texas Children's Hospital and Baylor College of Medicine

Coordinator: Judy Barrish, RN, BSN

E-mail: [jobarris@texaschildrenshospital.org](mailto:jobarris@texaschildrenshospital.org)

Telephone: 832-822-1781

- Boston Children's Hospital Rett Center

Boston, MA

Coordinator: Kate Barnes, BSc

Email: [Katherine.Barnes@childrens.harvard.edu](mailto:Katherine.Barnes@childrens.harvard.edu)

Ph: 617-355-5230

- University of Alabama at Birmingham, Birmingham, AL

Coordinator: Jane Lane, RN, BSN

E-mail: [jlane@uab.edu](mailto:jlane@uab.edu)

Telephone: 205-934-1130

- Greenwood Genetic Center, Greenwood, SC

Coordinator: Fran Annese, LMSW

E-mail: [fran@ggc.org](mailto:fran@ggc.org)

Telephone: 864-941-8100

#### Autonomic Dysfunction and Seizures in Rett Syndrome

Location: Albert Einstein College of Medicine, Bronx NY

Dr. Solomon Moshé, Vice-Chairman of the Department of Neurology at the Albert Einstein College of Medicine in NYC, is interested in studying the relationship of autonomic dysfunction and seizures in children with Rett Syndrome.

Rett Syndrome results in abnormal regulation of vital functions such as breathing, heart rate and blood pressure. RTT is also often associated with seizures and epilepsy. Even in the absence of RTT, seizures can impact on the control of vital functions. Vital functions are regulated automatically by specialized circuits and brain regions in the nervous system known collectively as the autonomic nervous system. Seizures can disrupt normal function in the autonomic nervous system. In fact, sudden unexpected death in epileptic patients (SUDEP) is strongly suspected to result from seizure induced disruption of vital functions by disrupting activity of the autonomic nervous system.

Dr. Moshé suspects that the underlying abnormality of autonomic function associated with RTT results in an increased susceptibility to seizure-induced disruptions of vital functions, and increased risk of death or impairment in children with RTT.

Children with Rett Syndrome (positive MECP2 testing is not necessary) who have seizures or suspected seizures will be studied in the epilepsy monitoring unit of Montefiore Children's Hospital in the Bronx, NY.

The usual set of scalp electrodes used in video-EEG monitoring are applied. In addition, patients will wear a vest with respiration sensors woven into it, additional EKG leads and a pulse oximeter.

#### How to Participate:

If your child is 12 years of age contact Dr. Moshé: 718-405-8140 for an appointment to assess the child for inclusion in the study.

If your child is 13 years of age or older contact Dr. Alex Boro: 718-920-5370.

#### The Natural History of Osteopenia in Rett Syndrome

Location: The Bluebird Circle Rett Center, Texas Children's Hospital and Baylor College of Medicine, Houston, TX

Drs. Kathleen J. Motil and Daniel Glaze from The Bluebird Circle Rett Center, Texas Children's Hospital and Baylor College of Medicine, Houston, TX, are conducting a study to characterize the development of osteopenia (bone mineral loss) in girls and women with Rett syndrome and determine if associations between bone demineralization and dietary, hormonal, physical, or inflammatory factors are present in these individuals. We are requesting permission from the parents or guardians of our Rett girls and women, 1 to 40 years of age, to allow their daughters to undergo bone density measurements, using the dual-energy absorptiometry (DXA) technique; bone age x-ray measurements; growth measurements; blood and urine collections to assess nutritional, hormonal, and inflammatory factors; 3-day food consumption records; and a review of their medical history as it relates to ambulation, bone fractures, and medication use. We hope that the information obtained from this research study will advance our understanding about osteopenia and bone fractures in Rett Syndrome, and ultimately, will lead to the development of treatment strategies for girls and

women affected with this disorder.

#### How to Participate:

If you would like to find out if your child is eligible for participation in this study please contact Judy Barrish, R.N. Toll-free: 1-888-430-7388 or Direct: 832-822-1781.

#### Biliary Tract Disease in Rett Syndrome

Location: The Bluebird Circle Rett Center, Texas Children's Hospital and Baylor College of Medicine, Houston, TX

Drs. Kathleen J. Motil and Daniel Glaze from The Bluebird Circle Rett Center, Texas Children's Hospital and Baylor College of Medicine, Houston, TX, are conducting a study to characterize the pattern of biliary tract disease in girls and women with Rett Syndrome and to identify factors that may predispose these individuals to cholecystitis, gallstones, and biliary dyskinesia. We are requesting permission from the parents or guardians of our Rett girls and women who have been affected with biliary tract disease to review their daughter's medical records for symptoms, physical findings, results of diagnostic studies, and surgical outcomes associated with gall bladder disease. We hope that the information obtained from this research study will advance community understanding and promote awareness about biliary tract disease in Rett Syndrome, and ultimately, will benefit the health and well-being of the girls and women affected with this disorder.

#### How to Participate:

If you would like to find out if your child is eligible for participation in this study please contact Judy Barrish, R.N. Toll-free: 1-888-430-7388 or Direct: 832-822-1781.