Press Release:
RSRT Marks Two-Year Anniversary with Launch of Gene Therapy Projects

September 29, 2010

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The Rett Syndrome Research Trust (RSRT) is pleased to initiate two new gene therapy projects in the fight against Rett Syndrome. Both projects are aimed toward the goal of normalizing levels of *MECP2*, the protein mutated in Rett Syndrome. Since its inception two years ago, **RSRT has committed $4.2 million** in support of a sole purpose: to heal children and adults who will otherwise suffer from Rett Syndrome and related *MECP2* related disorders for the rest of their lives.

Rett Syndrome strikes little girls almost exclusively, with first symptoms usually appearing before the age of 18 months. These children lose speech, motor control and functional hand use, and many suffer from seizures, orthopedic and severe digestive problems, breathing and other autonomic impairments. Although some victims of Rett Syndrome do not survive childhood, most live to become adults who require total, round-the-clock care.

Despite the complex and horrific constellation of symptoms, Rett Syndrome has been reversed in pre-clinical models of the disease. Based on this 2007 breakthrough, the Trust has identified three broad approaches for the treatment and cure of Rett Syndrome: increase levels of the protein mutated in Rett (MeCP2); ameliorate individual symptoms via existing drugs; target modifier genes which act to diminish or cancel the effects of *MECP2* mutations. The Trust **supports projects** in each of these three areas.

Our two new gene therapy projects pair experienced basic scientists who have deep knowledge of the Rett animal models with elite researchers in the world of gene therapy. In both projects, healthy versions of the *MECP2* gene will be delivered via a vector (similar to a Trojan horse) to Rett mice.

Kaspar/Mandel Gene Therapy Collaboration

The first team is comprised of **Brian Kaspar** of Ohio State University and Nationwide Children's Hospital in Columbus, OH and **Gail Mandel** of Oregon Health Science University in Portland, OR. Kaspar is currently working on gene therapy approaches for spinal muscular atrophy, muscular dystrophy, and ALS. Mandel has been actively working in the Rett field for the last five years and recently published a landmark paper showing that the MeCP2 protein is present in glia as well as neurons.

"We are very pleased to partner with the Rett Syndrome Research Trust on developing gene therapy approaches for *Rett Syndrome. A strength of this partnership is our collaboration with Dr. Mandel's laboratory, bringing together the expertise to carry out some difficult experiments for a difficult disease. The gene delivery systems we are working with have demonstrated significant promise in other disorders to target the central nervous system, so we are determined to design and test vector systems in the Rett model for developing a therapy for Rett Syndrome"* - Brian Kaspar

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Crystal/Bird Gene Therapy Collaboration

The second team consists of Ronald Crystal of Weill Cornell Medical Center in New York City and Adrian Bird of the University of Edinburgh. Crystal is one of the few pioneering researchers to have brought gene therapy from laboratory work into actual clinical trials for a neurological disease. He is currently leading a gene therapy trial for Batten Disease, a fatal childhood neurological disorder. Bird needs no introduction to anyone familiar with Rett Syndrome; he discovered the MeCP2 protein in the early 1990's, developed several animal disease models and published the seminal reversal experiments in 2007. The catalyst for this collaboration was sparked at a scientific meeting organized by RSRT this past May in Tarrytown, NY.

"Gene therapy is the most direct strategy to cure this disease. By combining forces with Adrian Bird, we are bringing together expertise in gene therapy with expertise in the basic mechanisms of Rett Syndrome, a strategy that will tell us in a few years whether gene therapy will work." - Ronald Crystal

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RSRT's scientific advisors believe it is crucial at this early stage to explore different vector delivery systems in parallel. The Crystal lab works with AAV10, a new generation vector with an increased distribution profile in the brain. The Kaspar/ Mandel team will utilize the AAV9 vector, which can be delivered to the central nervous system via injections into the bloodstream rather than invasive injections into the brain.

"While gene therapy intuitively makes sense for a single gene disorder there are inherent challenges - some related to the field of gene therapy and others unique to Rett Syndrome. When the risks and potential rewards are this high there is one crucial criterion: Alignment with the best people in the field. If anyone can get to the clinic with a gene therapy approach for Rett Syndrome, it's the teams that we are funding. To our donors, my message is: This is your money at work. Stay tuned." - **Monica Coenraads**, Executive Director of RSRT

UPDATE: SEE GENE THERAPY CONSORTIUM

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About Rett Syndrome

Rett Syndrome is a genetic neurological disorder that almost exclusively affects girls. It strikes randomly, typically at the age of 12 to 18 months, and is caused by random mutations of the MECP2 gene on the X chromosome. Rett Syndrome is devastating as it deprives young girls of speech, hand use, normal movement often including the ability to walk. As the girls enter childhood the disorder brings anxiety, seizures, tremors, breathing difficulties, severe gastrointestinal issues. While their bodies suffer, it is believed that their cognitive abilities remain largely intact. Although most children survive to adulthood, they require total round-the-clock care.

About the Rett Syndrome Research Trust

The Rett Syndrome Research Trust (RSRT) is a non-profit organization with a highly personal and urgent mission: a cure for Rett Syndrome and related MECP2 disorders. In search of a cure and effective treatment options, RSRT operates at the nexus of global scientific activity. We enable advances in knowledge and drive innovative research through constant engagement with academic scientists, clinicians, industry, investors and affected families. These relationships catalyze the development and execution of a research agenda that neither academia nor industry could achieve alone. RSRT refutes the conventional practice of labs working in isolation, instead seeking out, promoting and funding collaborations and consortia in which scientists work across multiple disciplines. Since 2008, RSRT has awarded $34 million to research projects. To learn more about the Trust, please visit **www.ReverseRett.org**.