THE HARTWELL FOUNDATION

2013 Individual Biomedical Research Award

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Therapeutic Strategy for Maternal Autoantibody-Related Autism

Autism spectrum disorders (ASD) are a set of neurodevelopmental disorders diagnosed in early childhood and are classified by a loss of abilities in social interaction, social communication, and presence of repetitive behaviors and restricted interests. Currently, ASD affects about 1 in 88 children in the United States (US), with an estimated cost to society at a staggering $126 billion per year. Current therapeutic interventions available for ASD are behaviorally directed or symptom-based pharmacological treatments applicable only after diagnosis. Little is known about the causes of ASD and while certain therapeutic approaches applied following early diagnosis have shown promise, no preventive alternatives currently exist. What is known is that activation of the maternal immune system during early fetal growth can have a negative effect on fetal brain development. For reasons that are not clear, the immune system in some pregnant women produces autoantibodies (proteins produced by the immune system in response to a constituent of one's own tissues) that mistakenly identify parts of the fetal brain as foreign substances. Judy hypothesizes that fetal exposure to these maternal autoantibodies could lead to alterations in neurodevelopment resulting in ASD. In 2013, she reported that 23% of mothers who gave birth to children with ASD have circulating autoantibodies against seven proteins highly expressed in the developing brain, in contrast to only 1% of mothers that deliver otherwise normal children. Each of the proteins is known to play an important role in neurodevelopment; interference with the level or function of more than one of them could act synergistically to change the trajectory of brain development. There is clearly a compelling need to address the causes and treatment of this maternal autoantibody related (MAR) form of ASD and not just the associated symptoms. The innovation Judy proposes is to block the autoantibodies to fetal brain proteins in MAR autism with synthesized short segments of the proteins, called peptides. Her approach will be to develop a mouse model of MAR autism to test the effectiveness of the peptides in blocking fetal exposure to the antibodies while maintaining desired (normal) behavior in offspring. If she is successful, early identification of these autoantibodies in the affected mother could allow for medical interventions to limit fetal exposure and the consequent risk of a child developing ASD. The availability of this therapeutic strategy to block maternal autoantibodies in MAR autism would reduce the prevalence of ASD, improving the quality of life for otherwise affected children and their families. In addition, a preventive measure for MAR autism would have the potential to eliminate nearly 1 in 4 cases of autism and result in a significant reduction of the economic impact on society incurred through support of therapies for ASD.