Treatment for Microcephaly-Associated Neurodevelopmental Disorders, Including Rare X-Linked Christianson’s Syndrome (Case 2192)

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Technology description

Brief Description:

Intellectual and developmental disabilities (IDD) affect an estimated 4.6 million people in the US with annual costs in the range of $386BB. There are few bio-therapeutic options to improve cognitive or functional gains for children with IDD and this is an area of rapid research. Accumulating evidence indicates that a hallmark of a subset of IDD is altered axonal and dendritic growth and branching. Axonal branching phenotypes in postmortem studies in autism further support this hypothesis in common idiopathic forms of IDD.

One type of rare IDD, known as “Christianson Syndrome” is an X-linked neuro-genetic syndrome caused by one or more mutations in the endosomal Na+/H+ exchanger Nhe6 gene. The newly-characterized molecular phenotype involves development of highly acidic endosomes which leads to aberrant neuron arborization. Clinical symptoms may include postnatal microencephaly, intellectual disability, epilepsy, non-verbal status, autistic features, craniofacial dysmorphology, ataxia, brain atrophy and retinitis pigmentosa.

Researchers at Brown University have discovered methods and compounds for the rescue of mutant arborization phenotype in models of CS disease. Strategies for treating, ameliorating, reversing or slowing the progression of microcephaly-asssociated disorders, include administrating an agent that increases the level or activity of brain-derived neurotrophic factor (BDNF) and/or tyrosine-related kinase B (TrkB) receptor in the brain of the patient. The agent that increases the level or activity of BDNF or TrkB in the brain of the subject can include BDNF agonists, various forms of BDNF and mimetics, a TrkB agonists, a cell expressing recombinant BDNF, a BDNF encoding recombinant nucleic acid molecule encapsidated within a recombinant virus, and agents that decrease the acidity of endosomes.

Institution

Brown University

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