Genetic sensors and targets for the treatment of spinal muscular atrophy

Technology #cu12346

Spinal muscular atrophy (SMA) is a lethal neurodegenerative disease and a leading genetic cause of infant mortality with, as of yet, no therapies directly targeting its pathogenesis. SMA is caused by a deficiency of the survival motor neuron (SMN) protein, a protein required for proper gene regulation. This technology has identified a set of genes that are dysregulated in response to SMN depletion. These genes can serve as a set of biomarkers to evaluate the efficacy of new therapies for SMA or, in some cases, serve as direct targets for drug development efforts. Adequate development of this technology could promote the development of new therapies against spinal muscular atrophy.

Identified panel of genes can serve as biomarkers for SMN activity and/or as possible therapeutic targets in SMA patients.

Currently, there are no therapies that directly target the pathogenesis of spinal muscular atrophy. Depletion of SMN leads to mis-splicing of U12 intron containing genes. About 1% of eukaryotic genes contain an U12-intron, and homologous genes are often found to be misregulated in cellular, zebrafish, drosophila or mouse models of SMN deficiency. For example, this technology identified the gene Stasimon as an U12 intron-containing gene that is misregulated in animal models of SMN. Restoration of Stasimon function reversed neuromuscular junction transmission defects and restored muscle growth in multiple animal models of SMA. The findings of this technology offer some of the first understandings of the molecular basis of SMA and could be critical to discovering and evaluating new therapies for this disease.

The relevance of the genes identified in this technology have been validated in drosophila, zebrafish, and mouse models of SMA in the Pellizzoni and McCabe labs at Columbia University.

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Applications:

- Therapeutics based on genes identified by this technology could be developed to treat SMA
- Expression of genes from this technology could be used to diagnose SMA and monitor effectiveness of treatments
- U12 SMN-dependent gene interactions could help identify ‘master regulators’ of SMA, helping to identify new therapeutic targets
- Development of therapeutics and biomarkers for other U12-splicesome defective diseases such as microcephalic osteodysplastic primordial dwarfism type I

Advantages:

- No commercially available therapy that targets the molecular pathogenesis of SMA exists
- Few validated markers for SMA exist, complicating the evaluation of therapeutic response to treatments
- The relative ubiquity of U12 intron containing genes offers multiple therapeutic avenues

Patent Information:

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Related Publications:


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