27-2006-382 | Novel Treatment of Mitochondrial Disorders using Enzyme Replacement Therapy
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Background

DNA mutations in mitochondrial proteins/enzymes (nuclear encoded) that may lead to disease are present in approximately 1 in 8,000 individuals.

Any treatment for mitochondrial diseases must be capable of targeting and crossing the cellular and the two mitochondrial membranes, as well as crossing the blood-brain barrier (BBB).

Our Innovation

- Novel concept for treating mitochondrial diseases through enzyme replacement therapy (ERT) using a fusion protein made up of a protein transduction domain fused to a functional component of a mitochondrial enzyme. The innovation enable to replaces the mutated endogenous enzyme and restores the activity of the essential mitochondrial multi-component enzymatic complex (pyruvate dehydrogenase complex (PDHC)) to near normal enzymatic function.

Application

- Major opportunities in the many different mitochondrial diseases and other metabolic diseases
- Many other diseases including Alzheimer's, dementia, Parkinson's, diabetes, hypertension, heart disease that are only just being understood to involve damaged mitochondrial enzymes

Highlights

Novel fusion proteins enable ERT for the first time:

- Novel approach to treating mitochondrial disease involves replacing mutated enzymes within the mitochondria in general, and in the context of replacing one mutated component to restore the activity of an immense multi-component enzymatic complex
- No current known treatments or cures for mitochondrial disease.
- The Lipoamide dehydrogenase (LAD) subunit was fused with the transactivator of transcription (TAT) peptide, which can rapidly cross the membranes. There are results also for Friedrich Ataxia as well as additional indications.
- For the first time, demonstration of both introduction and functioning of a normal mitochondrial enzyme to replace a damaged enzyme, as well as replacement of one mutated component to restore the activity of an essential mitochondrial multicomponent enzymatic complex

Key Features

- TAT capable of rapid crossing of biological membranes, enabling the TAT-LAD fusion protein to be delivered into cells and their mitochondria.
- Concept proven in LAD deficiency and in Friedrich Ataxia; already applied to other mitochondrial and metabolic disorders
- Development Milestones
- Seeking investment and cooperation for production of the protein in large quantities, toxicity studies and clinical trails. Enlarge the scope of molecules for additional mitochondrial diseases and other metabolic disorders

Patent Status
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