Use of MAPK pathway inhibitors for the treatment of Friedreich Ataxia

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Technology description

A novel treatment for rare disease Friedreich ataxia using p38 or MK2 kinase inhibitors
Technology Overview
Background
Friedreich ataxia (FA) is an autosomal recessive, inherited neuro- and cardio-degenerative disorder characterized by progressive ataxia of all four limbs, skeletal deformities, and hypertrophic cardiomyopathy. FA is the most prevalent inherited ataxia, affecting about 1 in 50,000 people in the United States. The estimated carrier prevalence is 1:110. Onset of symptoms can vary from childhood to adulthood with most patients being confined to a wheelchair by their late 20s. Myocardial failure and/or arrhythmias are the most common cause of premature death. It is commonly believed that FA is caused by mitochondrial dysfunction caused by the decreased expression of the protein Frataxin.
Problem
Currently there are no approved drugs to treat FA and the resultant disability, prolong the life of a FA patient, or cure the disorder.
Invention
Work in the Wilson’ s lab led to a surprising discovery that p38 MAP kinase inhibitors (many of which are in clinical trials for various indications) rescue disease phenotypes of cells affected by FA. This suggests that the p38 kinase (or MK2) can be possible targets for therapeutic intervention in Friedreich ataxia.rules, are highly specific to FA, and are active in the low nanomolar range. Several optimized modifications of the lead compounds have been generated.
Reference Media
Cotticelli et al. Sci Rep 2018, 8: 5007
Keywords:therapeutic, drug discovery, orphan disease

Advantages

- A number of p38 kinase inhibitors are being tested in clinical trials for various indications
- Regulatory fast-track: FA is a FDA designated orphan disease with no approved treatment
- Access to the expertise and resources of Wilson’ s lab (see Inventor’ s Bio)

Institution

University of Pennsylvania

Inventors

Robert Wilson