Ground Breaking Discovery into the Causes of Amyotrophic Lateral Sclerosis (ALS). Opportunity for the Development of new Therapeutic Strategies for Neurodegenerative Diseases

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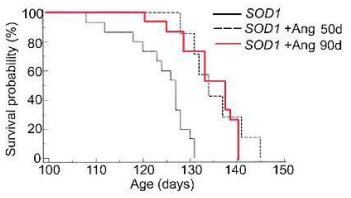
Introduction

Amyotrophic lateral sclerosis (ALS) is the most common neurodegenerative disorder of young and middle aged adults that is incurable and invariably fatal. Novel disease - specific mutations in a particular gene have recently been identified in ALS patients. This gene has not previously been associated with ALS, thereby opening up a whole new avenue of possible treatments to slow down or even reverse the process of cell degeneration in this condition and potentially other neurodegenerative disorders. Our novel technology is a therapy of pre - formulation sterile, recombinant preparations of human angiogenin protein that can be delivered systemically to treat patients with ALS. This technology is a therapeutic treatment paradigm that could potentially delay disease progression and increase survival in ALS patients.
The angiogenin is based on the identification of loss - of - function mutations of the angiogenin gene in ALS patients. Our proof of concept research demonstrates the neuroprotective and disease - delaying effect of systemic angiogenin protein delivery in a mouse model of ALS (Figure 1).

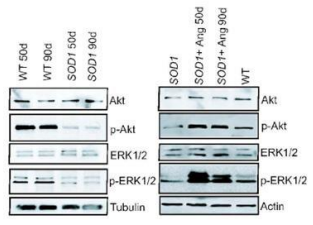
- Angiogenin is enriched in motorneurons and a potent protective factor against neuronal cell death
- Angiogenin protein delivery significantly increased life - span and improved motor function in an established mouse model of ALS
- Angiogenin can be administered systemically with effect in mouse models of ALS

Applications

Dr Orla Hardiman and
Prof Jochen Prehn of the RCSI have carried out key studies building on these findings showing that angiogenin is expressed preferentially in the spinal cord and is neuroprotective to motorneurons, both in cultures and in a mouse model of ALS (Greenway et al., Nat Genetics, 2006; Kieran et al., J Neurosci, 2008.). Angiogenin delivery also led to a functional improvement and increased life span when applied after disease onset in this mouse model. Currently both protein delivery - based and viral delivery - based therapeutic approaches are being developed by the team.



Increased life span



Increased anti-apoptotic signaling

Advantages

- This New opportunity points to the development of new therapeutic products for ALS, an incurable and invariably fatal disease where only one disease - modifying therapy currently exists. Given that ALS is a relatively rare disease there is the potential that new agents will be given "orphan drug" status
  - The new approach is based on breakthrough work on a gene not previously associated with ALS
  - There is the potential that disease - modifying drugs in ALS may have therapeutic effects in other more common neurodegenerative diseases

Feature	Benefit
Use of Angiogenin treatment for ALS	Potentially delay disease progression & increase survival in ALS patients
Costs/difficulty in administration route	Angiogenin can be applied systemically with success
Existing solutions for ALS not effective	Angiogenin can compete for an unmet market demand in ALS drug therapies

A patent application has been filed under the title "Treatment of CNS Disease", relating to the use of angiogenin in the treatment, prevention and/or diagnosis of ALS and other neurodegenerative diseases (PCT/IE2005/00131).

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