Disease-modifying treatment for epilepsy

Introduction

Epilepsy is a disabling neurological disorder characterized by recurring, unprovoked seizures. It affects 65 million people worldwide. Anti-epileptic drugs (AEDs) are the primary treatment method with sales expected to increase to nearly $3.7 billion in 2016. Unfortunately, about 1 in 3 patients are either treatment-resistant or experience unacceptable side effects when treated with current AEDs. Also, current AEDs have no effect on the underlying patho-physiology. A second therapeutic gap lies in the treatment of seizures that don't stop (status epilepticus). Such seizures carry a significant risk of brain damage and are currently treated with anticonvulsant drugs such as Ativan (lorazepam), a member of the benzodiazepine class of drugs.

Technology

MicroRNAs are a novel class of small, non-coding RNAs which work by controlling protein production at the post-transcriptional level in cells. MicroRNAs have important functions in the brain and abnormal levels may contribute to both neurologic and neurodegenerative diseases. Researchers at RCSI's Department of Physiology & Medical Physics discovered that levels of microRNA-134 are abnormally high in human epilepsy and silencing microRNA-134 expression in vivo using a microRNA-134 antagomir ("AntmiR134") rendered mice refractory to both seizures and hippocampal injury caused by status epilepticus (Nature Medicine 18, 1087–1094 2012). Subsequent research by the RCSI research group has shown the antagomirs work in other seizure models and, most recently, has shown that a **single systemic injection** of AntmiR134 (30 mg/kg) resulted in: (a) a significant reduction in the total number of epileptic seizures; and (b) the total time spent in seizures.

Applications

AntmiR134 reduces brain levels of microRNA-134 providing the potential to use this inhibitory compound for:

a) the treatment or prevention of epilepsy, particularly pharmaco-resistant forms
b) the prevention of brain injury following prolonged epileptic seizures (status epilepticus)
c) other neurologic injuries without altering normal behavior
d) protection against neurodegeneration

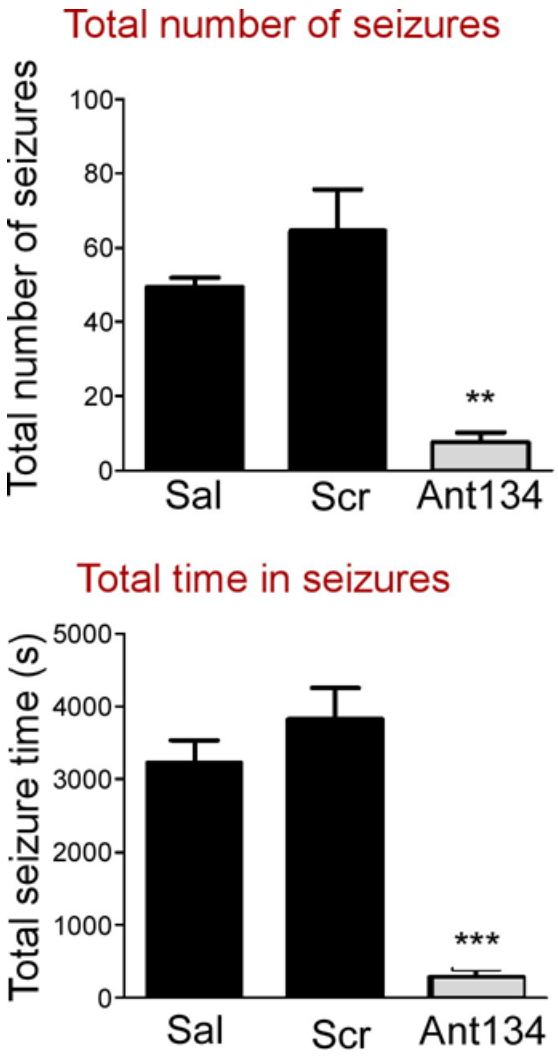

Figure 1: Seizure reduction using systemically-injected microRNA-134 antagomir, AntmiR134, in preclinical models. Data are from two-weeks of continuous video-EEG monitoring of mice treated two hours after status epilepticus.

Advantages

AntmiR134 focuses on a chemically-distinct class of drug targets to those targeted by existing AEDs. By targeting a different aspect of brain chemistry, this invention has the potential to overcome the treatment resistance and unacceptable side effects experienced by 1 in 3 patients on existing AEDs.

In addition, currently there are no AEDs available to alter/cure epilepsy. AntmiR134 has demonstrated promising disease-modifying effects with a single dose having sustained action lasting several months.

Contact:
Dr Seamus Browne,Industry Liaison Manager RCSI, 121 St Stephen's Green.
Tel: +353 1 402 8651
Email: seamusbrowne@rcsi.ie