Antisense Oligonucleotide Therapy For Scn2a Gain-of-function Epilepsies

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INTRODUCTION

- SCN2A de novo mutations cause a spectrum of neurological disorders that includes developmental and epileptic encephalopathy (DEE) and autism.
- FEER can be divided into early or late- onset based on the age that seizures start.
- Febrile seizures with early peak FEER most frequently associated with SCN2A gain of function (GOF) recombination channels leading to enhanced neuronal excitability.

METHODS

- In order to identify a mouse model exhibiting a resonant human early-onset de novo SCN2A variant (GOF) (GOF), a mouse model was generated that mimics a spatial spike pattern, as early as P1 and moves normally with normal sensory and motor function.
- A mouse strain targeting mouse Scn2a was developed to assess efficacy in this mouse model.

RESULTS

- 40 specifically demodulates Scn2a
- 40A specifically reduces Htr1, 2 expression in neocortex segment
- 40A treatment prolongs life of Scn2a+/- mouse model

CONCLUSIONS

- 40A mediated knockdown of Scn2a reduces the disease phenotype of Scn2a gain of function DEE mouse model.