

PHARMACY

Modeling *SCN2A* Deficiency in Mice

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Encoded by the gene *SCN2A* (*Scn2a* in mice), Nav1.2 sodium channels propagate action potentials as the main form of communication in the brain, especially during development. When the *SCN2A* gene becomes disrupted by mutation, the phenotypic results range from epilepsy to autism in humans. A mouse was selected to model the effects of *SCN2A*-related neurodevelopmental disorders and examine the efficacy of potential therapies. A gene trap reduced *Scn2a* gene expression and increased survivability past the perinatal state, unlike a complete *Scn2a* knockout. A functional *Scn2a* transcript was produced at levels of $29 \pm 4\%$ in homozygous (HOM) gene-trap mice, compared to 100% expression in wild-type (WT) mice. HOM mice did not mate, so heterozygous (HET) mice had to be used for breeding. Mendelian genetics dictates crossing two HETs gives a 1:2:1 probability that offspring could be either HOM, HET, or WT. Therefore, each mouse pup was genotyped

with PCR, and a final Mendelian ratio was calculated to determine if the litters followed the theoretical 1:2:1 pattern. A chi-square goodness of fit test was performed and concluded the results were not significant ($p = 0.0676$), showing the data followed the theoretical 1:2:1 ratio at a >95% confidence interval. Only litters with at least one HOM were included to reduce bias from inconsistent genotyping. The most frequent genotyping issues were maintaining consistent DNA/elution buffer concentrations during extraction and streaking on the electrophoresis gel. Overall, the HOM gene-trap mice will continue to serve as a model for testing new therapies for *SCN2A*-related neurodevelopmental disorders.

Research advisor Muriel Eaton writes: "Jacobs's research in the lab is essential to study the use of a preclinical mouse model to model neurodevelopmental disorders of the gene SCN2A. His critical work involves genotyping all the mice for the study, which he performs in a timely manner with quality work. He works with his peers to troubleshoot and optimize the protocol. The data he collects is valuable in the development of this preclinical model. Jacob is also familiar with the most recent literature regarding the use of mouse models in studying neurodevelopmental disorders."