1158-92-136 **Joseph C Watkins*** (jwatkins@math.arizona.edu), Department of Mathematics, Tucson, AZ 85721. *The role of genetic background in the clinical outcomes of a genetic disease.*

Here we use the example of Dravet syndrome, a rare, devastating form of childhood epilepsy often associated with mutations in the voltage-gated sodium channel gene, SCN1A to consider the dependence of clinical outcomes on variants in other genes associated with brain development. We consider three possible explanations 1) a single common variant that is enriched in one of the phenotypic groups, 2) sets of common or rare variants aggregated in and around genes associated with clinical outcome, and 3) rare variants in candidate genes associated with neuronal excitability. Our population are individuals with SCN1A truncation variants, a population with a nearly identical genetic cause for Dravet syndrome. The central question for evolution – are those with poor clinical outcomes unlucky and have poor genetic background or are those with mild clinical outcome lucky and have an optimal genetic background? (Received February 27, 2020)