THE REGULATION OF SHANK3 IN THE ABSENCE AND PRESENCE OF DIFFERENT DELETIONS

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Shank3 is a complex gene found on chromosome 22 that is disrupted in cases of neurodevelopmental disorders such as Phelan McDermid Syndrome (PMDS) and Autism Spectrum Disorder (ASD). PMDS is a rare genetic disorder linked to autism that comes with a suite of phenotypes, including decreased muscle tone, developmental delays, and intellectual disabilities. Shank3 codes for a protein found in the postsynaptic density that coordinates synaptic function. To study the genetic underpinnings of PMDS and ASD, we utilized induced pluripotent stem cells (iPSCs) to grow genetically identical neurons and employed a CRISPR/Cas9 system to introduce two deletions that recapitulate those seen in PMDS and ASD (Table 1). The hypothesis was that the regulation of Shank3 would change in the presence of deletions. To test this, we designed promoter-specific primer sets to target each of the sites that can produce unique isoforms of Shank3. PCR and gel electrophoresis were then run to identify the resulting isoform lengths. Preliminary results showed possible deletion-dependent regulation of Shank3. Understanding the regulation of Shank3 when it contains deletions will contribute to overall knowledge of how genetic mutations create a plethora of observed phenotypes.

Table 1. The four engineered cell lines and their unique deletions. The EYQ2-20 cell line is intended to mimic the genotype found in all human patients with ASD/ PMDS. Partial homozygotic deletions are not found in humans but can be replicated in mouse models.

Cell Line:	**Deletion:**
H9	Control-no deletions
EYQ2-20	Complete heterozygous deletion
2242	Control-no deletions
EP2-15	Partial homozygous deletion