Intersection of diverse neuronal genomes and neuropsychiatric disease: The Brain Somatic Mosaicism Network (Dr. Ian Burbulis)

Neuropsychiatric disorders have a complex genetic architecture. Human genetic population-based studies have identified numerous heritable sequence and structural genomic variants associated with susceptibility to neuropsychiatric disease. However, these germline variants do not fully account for disease risk.

During brain development, progenitor cells undergo billions of cell divisions to generate the ~80 billion neurons in the brain. The failure to accurately repair DNA damage arising during replication, transcription, and cellular metabolism amid this dramatic cellular expansion can lead to somatic mutations.

Somatic mutations that alter subsets of neuronal transcriptomes and proteomes can, in turn, affect cell proliferation and survival and lead to neurodevelopmental disorders. The long life span of individual neurons and the direct relationship between neural circuits and behavior suggest that somatic mutations in small populations of neurons can significantly affect individual neurodevelopment.

The Brain Somatic Mosaicism Network has been founded to study somatic mosaicism both in neurotypical human brains and inthe context of complex neuropsychiatric disorders.