**Genomic mosaicism and the Alzheimer's disease brain**

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The human brain contains hundreds of billions of cells that have been widely assumed to have identical genomes amongst all cells from the same individual. This assumption is incorrect, as evidenced by neurons whose genomes appear to be unique despite being derived from a single zygote. Genomic mosaicism[1], arising somatically, accounts for most of this variation, and can take many forms, ranging from aneuploidies and aneusomies[2] – gains/losses of chromosomes – to smaller copy number variations (**CNVs**)[3] to single nucleotide variations, with combinations of these forms commonly existing in individual neurons. In addition to sequence differences, the sum total of these changes within a single nucleus can be detected by DNA content flow cytometry, which revealed robust heterogeneity of DNA content variation[4] amongst neurons of the human brain, producing a complex genomic mosaic of cells within the brain. Notably, these increases can be accentuated in sporadic Alzheimer's disease (**SAD**)[5], the most common form of AD. Some of this increase has been attributed to CNVs in the amyloid precursor protein (*APP*) gene, a causal gene in rare families and in Down syndrome, but produced somatically and mosaically within SAD neurons[5]. New data on mechanisms producing genomic mosaicism along with implications for the normal and SAD brain will be presented.

**REFERENCES**

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