Identification and isolation of human striatal cell types using flow cytometry methods as part of Cerevance's NETSseq platform

Cerevance's proprietary NETSseq (Nuclear Enriched Transcript Sort sequencing) platform[1] allows for the identification and sorting of cell-type specific nuclei from human post-mortem CNS tissue, enabling deep transcriptomic comparison between disease and non-neurodegenerative disease control (NDC) tissue. This process involves isolating nuclei from small regions of flash frozen brain tissue by mechanical homogenisation and density gradient centrifugation of the tissue homogenate. Isolated nuclei are then fixed and labelled with cell-type specific antibodies or RNA probes before using fluorescence activated nuclei sorting (FANS) to analyse and sort cell-type specific populations of nuclei for downstream analysis.

In this work we used striatal tissue from age-matched Parkinson's disease (PD) and NDC donors, from which we used RNA probes to sort nuclei from dopamine D1- and D2-receptor expressing medium spiny neurons (MSNs) and antibodies to sort a range of glial cell types (microglia, astrocytes, oligodendrocytes and oligodendrocyte precursor cells). The nuclei samples were then analysed by RNAseq, generating cell-type specific transcriptomes that were used to identify differentially expressed genes between PD and NDC tissue.

The NETSseq platform enables us to measure the expression of significantly more genes, including genes expressed at lower levels, than single-cell or single-nuclei analysis. This highly sensitive approach is critical for the identification of novel therapeutic targets that may be expressed at low levels in the mature brain.

1. Xiao X, *et al.,*2018. Species and cell-type properties of classically defined human and rodent neurons and glia, eLife, 7: e37551