Single nuclei sequencing of brain regions from healthy and Parkinson's Disease individuals

Dataset Description: We performed single nuclei RNA sequencing of post-mortem PD and control brain tissue of four different brain regions (substantia nigra, putamen, amygdala, and prefrontal cortex). Briefly, 8500 nuclei were FACS sorted from approximately 2 mm3 of tissue. Single nuclei RNAseq libraries were prepared using 10X genomics platform for single cell 3' sequencing. Sequencing libraries are prepared by fragmentation, end repair and a tailing followed by sample index PCR. To process the data, FASTQ files were processed using Cell Ranger, aligning and quantifying for hg38. Intronic reads were also quantified.

ASAP Team: Team Jakobsson:

> *Project:* **Activation of transposable elements as a trigger of neuroinflammation in Parkinson's disease**:A range of genetic clinical and pathological studies have established that inflammation is a central component of neurodegenerative disorders including Parkinson's disease (PD). However what still remains unclear is the underlying cause for this inflammation. Here we propose a novel hypothesis involving the aberrant activation of transposable elements (TEs) as the trigger for neuroinflammation in PD. TEs are viral-like mobile genetic elements that comprise nearly 50% of the human genome. We propose that the combination of age and the underlying pathogenic processes in PD result in their aberrant activation and with this the expression of viral-like sequences in the brain which in turn activates an immune response (as would be the case for any viral infection in the brain) and then drives further neurodegeneration. This theory by invoking an entirely new pathogenic mechanism will open up a number of new avenues of PD-research with clear clinical relevance. This includes novel diagnostic biomarkers that could be developed based on the presence of TE-derived transcripts or peptides as well as new drug targets that could be exploited for example by targeting viral-like mechanisms or viral-induced inflammation. In summary this project has the potential to identify a novel disease-contributing mechanism in PD with a high clinical potential for development of much needed diagnostics and therapies for this condition.

ASAP CRN Cloud Dataset Name: jakobsson-pmdbs-sn-rnaseq