# 1 Use of expression studies in deciphering NDDs and the brain in general

Although the genetic etiology of NDDs is far from being completely known, significant advances have been made in the last years in understanding specific biological pathways underlying the molecular mechanisms of these illnesses.

- What is single cell and how has it been used
- in this section I will describe several studies that utilised this single cell rna-seq approach

## 1.1 Single-cell RNA-seq

Since the first paper showing the feasibility of characterizing expression profiles of individual cells was demonstrated by Tang et al, single-cell RNA sequencing has been widely accepted to dissect the cellular heterogeneity within a population of cells. From 2015 onwards over 80 papers have reported detailed characterization of brain cell types in different brain regions, and at developmental stages or disease status using scRNA-seq. In addition to the increasing number of publications, we have also observed an exponentially increasing number of sequenced cells per study in the last 5years. The technology is not only inspiring more studies in recent years, but also exponentially scaling up the number of single cells profiled in each study, which has empowered the construction of a comprehensive landscape of the cell types in the brain.

### 1.1.1 Application of scRNA-seq in the brain

The brain contains highly complex neural cell types and subtypes which are organized in specialised regions. Traditionally, neural cells were identified by morphology, excitability, connectivity and the location of the cell. However, with recent advamces, scRNA-seq approaches have become a common tool to assess and investigate the brains complexity and to identify

new subpopulations.

Table 1: Expression studies that utilised single-cell profiling technologies (Not ordered by any particular way)

| **Authors** | **Year** | **Tissues** | **Method** | **No. of Cells** | **Age** | **No. of individuals** | **Data availability** |
|---|---|---|---|---|---|---|---|
| Velmeshev et al | 2019 | PFC and ACC | snRNA-seq | 104,559 | 4-22 pm | 15 ASD; 16 controls; total 31 | |
| Late et al | 2016 | Brodmann's areas | snRNA-seq | 4488 | 51 pm | 1 healthy individual | |
| Nowakozski et al | 2017 | V1, PFC | scRNA-seq | | | | |

**single-cell nuclei technique**

Points to discuss: The first study that used it and why it was neccesary

functionally organized into regions, which are distinguised by different compositions of molecularly-defined cell types and region dependent patterns of expression. Several transcriptomic studies have thus sought to capture region specific differences in gene expression profiles. Furthermore, the brain undergoes protracted periods of development, refinement and maturation spanning the early fetail periods to adolescence.