Single cell genomics: cell type definition, monitoring and genetic access

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Single-cell genomics has fundamentally changed the way we define cell types and assess changes in their states or identity. One of the major team efforts at the Allen Institute for Brain Science is to define all cell types in young adult mouse brain by single-cell/single-nucleus RNA-sequencing (sc/snRNA-seq) and spatial transcriptomics. The main output of this project will be a public resource that defines cell types, their taxonomy, and their distribution across the whole brain in healthy young adult male and female mice[1,2,3]. In parallel to this comprehensive effort in healthy young adults, we are pursuing a variety of projects to define cell type changes with age or organismal state and their correlates with changes in chromatin. Chromatin profiling at the single cell level (for example, by snATAC-seq) provides complementary cell type definition, illuminates mechanistic links between chromatin and gene expression changes, and defines enhancer elements that can be used to build the next generation of cell-type specific genetic tools[4,5]. These compact enhancer elements can be introduced into recombinant adeno-associated viruses (AAVs) which can be delivered to the whole mouse brain to specifically label, monitor, perturb, or treat a cell class or type. The new viral genetic tools perform well across rodents and primates[4,5] and have the potential to be the next generation of highly specific neural circuit therapeutics.

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