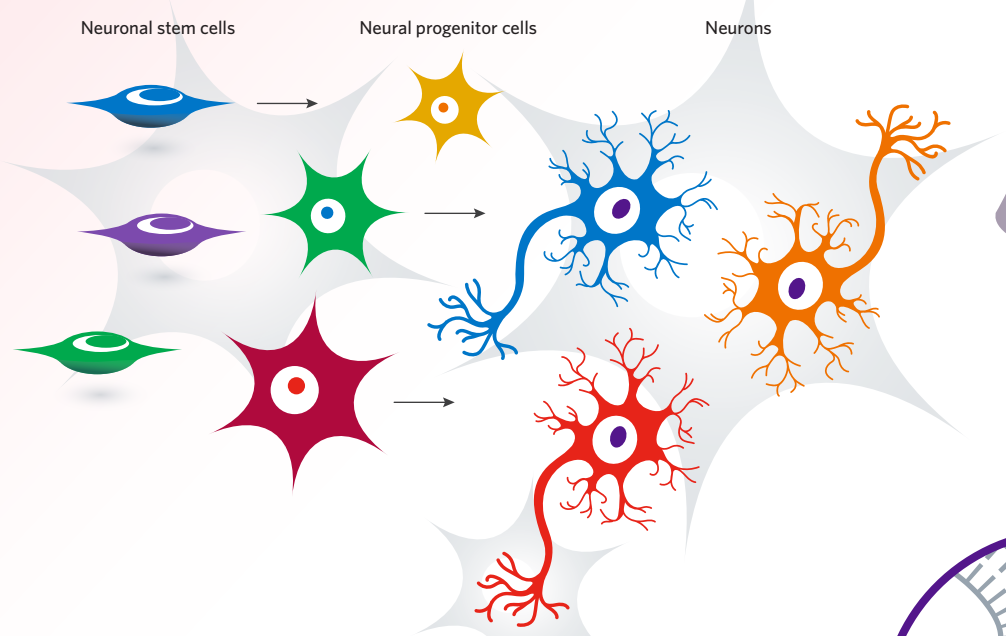
DISCOVERING DIVERSITY

Of the 100 billion or so neurons in the human brain, there may be no two that are alike. Recent advances in single-cell omics and other techniques are revealing variation at genomic, epigenomic, transcriptomic, and posttranscriptomic levels. Such diversity can arise at all stages of development and into adulthood. In the case of genetic changes that are passed on to daughter cells, the stage at which mutations occur will dictate their frequency in the brain. Researchers are now working hard to catalog every cell type within the human brain, and understand how differences among them may underlie variation in neuronal function. There are early hints that this mosaicism may contribute to personality and behavioral differences among individuals, as well as to various neurological or psychiatric disorders.



SOURCES OF DIVERSITY

GENETIC DIVERSITY

Mutations such as single nucleotide polymorphisms (SNPs) and copy number variants (CNVs) are common contributors to variation among neuronal genomes (left). Retrotransposons such as L1s that can jump around the genome can also introduce changes (above).

EPIGENETIC DIVERSITY

Beyond genomic variation, differences in histone and DNA methylation, among other epigenetic changes, can affect neurons' gene expression, leading to variation in the cells' transcriptomes.

POSTTRANSLATIONAL MODIFICATIONS

After proteins are produced, further variation can stem from the addition of sugars and other molecules that may affect stability and where the proteins go in the cell.

POSTTRANSCRIPTIONAL VARIATION

Differences in how expressed RNAs are processed into final transcripts for translation can lead to variability in protein structure and levels.

ENVIRONMENT-DRIVEN PLASTICITY

As neurons fire, they undergo molecular changes that affect their morphology, their tendency to fire again, and the amount of neurotransmitter they release. These and other responses to the local environment contribute to the overall diversity seen among individual neurons of the brain.