Our lab has extensive experience in the comprehensive analysis of cell regulation and communication networks in brain tissue. We have successfully identified sets of differentially expressed genes from PsychENCODE single-cell RNA seq data using the standardized ENCODE pipeline [1]. Building upon this, we used snATAC-seq and snRNA-seq data from healthy individuals to predict regulatory links between TFs and their target genes, employing SCENIC and

scGRNom pipelines to construct cell-typespecific GRNs that captured both proximal and distal regulatory interactions across brain cell types [2]. In addition, we developed an intercellular communication network by integrating publicly accessible ligand-receptor pair data with snRNA-seq. Distinct broad communication patterns were identified among excitatory, inhibitory, and glial cell types, with significant alterations in these patterns observed in patients with neuropsychiatric disorders such as schizophrenia and bipolar disorder. Figure 1 presents the construction of cell-type-specific gene regulatory networks through the integration of snRNA-seq, snATAC-seq, and scQTL datasets from the brain tissues of healthy individuals [3].

Figure 2 illustrates the construction of intercellular communication networks in our recent publication through systematic mapping of co-expressed ligand-receptor pairs, with a circos plot visualizing the signaling interactions between distinct brain cell populations [3].





- 1. Wang, D., et al., *Comprehensive functional genomic resource and integrative model for the human brain.* Science, 2018. **362**(6420).
- 2. Emani, P.S., et al., *Single-cell genomics and regulatory networks for 388 human brains*. Science, 2024. **384**(6698): p. eadi5199.
- 3. Emani, P.S., et al., *Single-cell genomics and regulatory networks for 388 human brains*. bioRxiv, 2024.