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LIVE ON ZOOM!





XIN JIN, PHD
THE SCRIPPS RESEARCH INSTITUTE
ASSISTANT PROFESSOR, DEPT. OF NEUROSCIENCE, DORRIS NEUROSCIENCE CENTER

## "IN VIVO PERTURB-SEQ: SCALED INVESTIGATION OF GENE FUNCTIONS IN THE DEVELOPING TISSUE"

The thousands of disease risk genes and loci identified through human genetic studies far outstrip our current capacity to systematically study their functions. I will discuss our attempt to develop a scalable genetic screen approach, in vivo Perturb-seq, and apply this method to the functional evaluation of 35 autism spectrum disorder (ASD) de novo loss-of-function risk genes. Using CRISPR-Cas9, we introduced frameshift mutations in these risk genes in pools, within the developing brain in utero, and then performed single-cell RNA-seq in the postnatal brain. We identified recurrent and cell type-specific gene signatures from both neuronal and glial cell classes that are affected by genetic perturbations, and pointed at elements of both convergent and divergent cellular effects across many ASD risk genes. In addition, I will also briefly discuss the research directions in the lab in applying spatial transcriptomic approaches to study cell intrinsic and extrinsic effects of these disease risk genes. Our lab will use these systematic approaches, connecting genomic technology development with rigorous dissection of molecular mechanisms, to learn new insight about how complex inputs are integrated into the developing brain.