

Name: Xue Pan, Ph.D.

Email: xpan@llu.edu

Spatiotemporal transcriptomic mapping of the rat brain across three developmental stages

Over the past decade, spatially resolved transcriptomics has transformed our ability to interrogate gene expression in situ, enabling precise mapping of molecular programs within intact tissue architecture. Although human and mouse spatial brain transcriptomic atlases are now available, a comprehensive spatial brain transcriptomic reference for the rat — a primary model for addiction and behavioral neuroscience—has been lacking. Given the central role of rat models in studying reward circuitry, substance exposure paradigms, and drug-seeking behaviors, this gap has limited integrative genetic, epigenetic and regulatory analyses in addiction research.

Here, we established a spatiotemporal reference transcriptome for the rat brain by integrating 10x Genomics Visium spatial transcriptomics with single-nucleus multiomics (snRNA-seq and snATAC-seq) across key developmental stages, including embryonic day 20 (E20), postnatal day 7 (P7), and adulthood (3-month). Across these stages, spatial profiling resolved 40 anatomical regions and revealed stage-dependent gene expression programs spanning early proliferative processes to later synaptic maturation and axon ensheathment, particularly within cortex and corpus callosum. Integration of single-nucleus transcriptomic and chromatin accessibility dataset enabled inference of spatial cell-type distributions, developmental trajectories, and spatially resolved regulatory landscapes. Focusing on upper-layer cortical development, we identified three gene modules exhibiting dynamic transcriptional activity coordinating with chromatin accessibility changes. Furthermore, differential accessibility analysis between E20 and 3-month revealed 23 significantly enriched transcription factor motifs, highlighting stage-specific regulatory programs, including early enrichment of zinc finger transcription factors such as Klf and Maz at E20, and later engagement of RFX, Mef2b, and Egr1 regulatory programs in adulthood. Collectively, this work provides a comprehensive spatiotemporal multiomic resource for the rat brain, fulfilling a critical gap in the field and establishes a foundational resource for mechanistic studies of neurodevelopment, substance use disorders and neuropsychiatric disease.

Authors:

Submitter: Xue Pan, Post Doc, LOMA LINDA University, Loma Linda
Wanqiu Chen, Ph.D., LOMA LINDA University
Zhong Chen, Ph.D., LOMA LINDA University
Charles Wang, Ph.D. MD, LOMA LINDA University