The Birth of Connections: How Embryonic Progenitor Diversity Shapes Striatal Circuitry

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The organization of synaptic connections in neural circuits is fundamental to brain function, yet the developmental processes shaping their formation remain poorly understood. Increasing evidence suggests that embryonic neural progenitor diversity influences neuronal diversity, synaptic connectivity, and circuit function. My research investigates how distinct progenitor populations in the lateral ganglionic eminence—specifically apical intermediate progenitors (aIPs) and other progenitors (OPs)—influence the synaptic architecture of the striatum, a brain region critical to movement, learning, and cognition.

Using a powerful combination of in utero electroporation, viral tracing, optogenetics, and single-cell RNA sequencing, I've mapped the input-output relationships of striatal spiny projection neurons (SPNs) derived from different progenitor lineages. My findings reveal that aIP-derived SPNs receive extensive innervation from both cortical and thalamic sources, with 32% of thalamic inputs originating specifically from the intralaminar nuclei. Functional optogenetic mapping has uncovered significant biases in connection strength based on developmental origin, with aIP-derived SPNs showing markedly reduced excitatory responses compared to OP-derived neurons when stimulating parafascicular inputs. Single-cell transcriptomics has identified LHX9 as a candidate transcription factor potentially mediating these connectivity differences. My ongoing work aims to manipulate LHX9 expression to determine its role in synaptic partner selection and dendritic architecture. This research illuminates how developmental lineage influences circuit assembly in the striatum, potentially revealing fundamental principles of circuit formation with implications for understanding both normal brain function and neurodevelopmental disorders.