

Title: Multi Modal Atlas of Cellular Diversification in the Mouse Cerebral Cortex

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The mammalian cerebral cortex contains an unparalleled diversity of cell types, which are generated during development through a sequence of temporally orchestrated events that are under tight evolutionary constraint and are critical for proper cortical assembly and function. However, the molecular logic that governs the establishment and topographic organization of cortical cell types remains elusive. This is largely due to the need for investigation of a vast numbers of cell types through dynamic cell-state transitions, and over developmental time. Through single-cell RNA-seq and single-cell ATAC-seq, we have generated a molecular atlas, of the developing mouse neocortex, sampled every day through the duration of embryonic corticogenesis and complemented with a spatial transcriptomics time-course. We were able to identify the full array of known cortical cell types and computationally infer developmental trajectories across the diversity of cortical cell classes. From this we infer their spatial organization and unveil gene regulatory programs that accompany fate specification and diversification. The data provides a global picture of the regulatory mechanisms governing cellular diversification in the neocortex. We are now functionally testing the candidate genes identified through multiplexed in vivo studies, with the goal to uncover novel mechanisms underlying neuronal specification.