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Spatiomolecular Characterization of Human D1-Islands Across the Anterior-Posterior Axis

The nucleus accumbens (NAc) is a GABAergic basal forebrain structure that is dysregulated in a variety of neuropsychiatric diseases. Recent studies have used next generation sequencing technologies to understand molecular heterogeneity and spatial topography of NAc cell types in rodents and non-human primates. These studies identified a novel cell type with high expression of dopamine receptor D1 (DRD1) and mu-opioid receptor (OPRM1), topographically organized into clusters known as D1-islands. However, no such spatial transcriptomics data exists for the human brain. To characterize the molecular heterogeneity and spatial organization of human D1-islands, we generated single cell resolution spatial transcriptomics technology from 22 sections spanning 2 donors (1M/1F) using a custom 100 gene panel designed to specifically target island cells. Sections were collected at ~500 μ m intervals, enabling systematic mapping of island cell spatial organization across the anterior-posterior, dorsal-ventral, and medial-lateral axes. This dataset identified two populations of DRD1-expressing islands that exhibit distinct transcriptional profiles. These populations differ based on their expression of OPRM1, SEMA5B, and SEMA3E. Profiling across all 3 neuroanatomical axes also identified that these populations are mixed along the dorsal-ventral and medial-lateral axes. The two populations exhibit distinct anterior-posterior topography: one is enriched in posterior sections, while the other is distributed across intermediate and posterior regions. Current efforts are focused on continued examination of these islands using a novel, near-whole transcriptome spatial transcriptomics technology.

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