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Molecular Profiling of Mouse Ventral Pallidum Projection Neurons

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The ventral pallidum (VP) is a critical brain region for drug-seeking behaviors, as it is a primary output to the several regions within the reward system. Further, this region is unique because it receives dense input from both ventral striatal (nucleus accumbens) projection neuron subtypes compared to other brain regions that display more segregated input. Recent circuitry mapping revealed that distinct VP cell types and projections regulate specific behavioral responses to rewarding and aversive stimuli, including drugs of abuse. However, a comprehensive molecular characterization of these cell types and circuits have not been performed. Here, we generated several sequencing data sets to examine the molecular architecture of the VP. First, using Cre-dependent retrograde labeling and Ribotag-transgenic mice, we characterized the translatome of VP neurons projecting to the following downstream regions using bulk RNA-Sequencing: Lateral Hypothalamus (LH), Ventral Tegmental Area (VTA), Lateral Habenula (LHb) or Medial Dorsal Thalamus (MDT). From our bioinformatic analyses, we identified biological processes and gene networks enriched within each type of VP projection neuron. Currently, we are performing single-nucleus RNA-sequencing on VP tissue from male and female mice. Through subclustering analysis, we will identify several distinct VP neuronal populations and marker genes for each transcriptionally distinct population. In addition to this, we are using MAP-Sequencing to examine the relative strengths of VP projections to each of the above downstream regions. Altogether, these investigations aim to detect the cellular populations present within the VP and identify novel gene makers to study in VP function and drug use disorders.