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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 projection neurons regulate specific behavioral responses to rewarding and aversive stimuli, including drugs of abuse. However, the molecular profiles of these VP circuits remain unknown. Using Cre-dependent retrograde labeling and Ribotag-transgenic mice, we characterized the translatome of distinct mouse VP-projection cells. Retrograde Cre virus was infused into either the Lateral Hypothalamus (LH), Ventral Tegmental Area (VTA), Lateral Habenula (LHb) or Medial Dorsal Thalamus (MDT) of floxed-Ribotag male mice. Following viral expression, ventral pallidum tissue was extracted and ribosome-associated mRNA was isolated to prepare libraries for RNA-sequencing. From our bioinformatic analyses, we first identified genes and gene networks enriched within a specific VP projection cell-type. Additionally, using gene ontology analysis, we detected biological processes specific to each VP-projecting cell type. In an effort to uncover potential drivers of VP-circuit specific molecular signatures, we found upstream predicted transcription factors and their associated regulatory motifs for genes enriched within a specific VP-circuit. Through assessing the molecular signatures within VP cells of distinct circuits, our datasets provide novel gene targets to study in regards to VP function and drug use disorders.