Mapping Spatial Memory Associated Gene Expression Profiles Across the Sub-regions of the Mouse Hippocampus

The search for the memory engram is a key endeavor for the field of neuroscience. In the mammalian brain, the field has identified synaptic plasticity as a core molecular mechanism for memory, and memory-associated neuronal ensembles as the functional correlate for a memory trace. Despite these advances, the integration of the mechanistic and ensemble basis of memory remains elusive. In this study, we tackle this gap in knowledge by characterizing the gene expression topography of memory associated neuronal ensembles in the hippocampal network. We trained mice in a hippocampus function dependent active place avoidance (APA) memory task and one hour or three days after memory retention test, we collected hippocampal tissue for RNA sequencing analyses. We carried out bulk RNA-seq on microdissected hippocampal regions or single nuclei RNA-seq analyses to test for specific differences between hippocampal cells and regions associated with APA memory. Additionally, we carried out spatial transcriptomics analyses to assess the spatial distribution of gene expression profiles across the hippocampus associated with APA memory. Crucially, to define the gene expression topography of memory associated neuronal ensembles in the hippocampal network, we explored gene expression profiles identified within memory-associated, immediate-early gene tagged neuronal ensembles across the distinct sub-regions of the hippocampal network. With these data we identified and resolved the spatial organization of gene expression profiles associated with a place memory in the hippocampal network; providing a hitherto unknown gene expression map of memory.