Developmental change of cell types in the mouse olfactory system capturing by Molecular Cartography™

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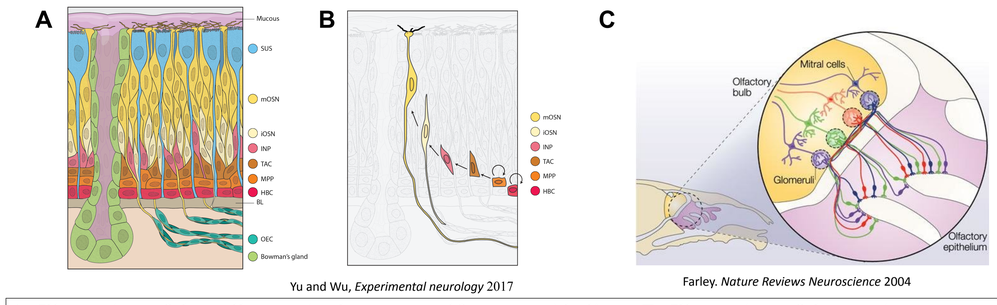
Introduction

The mouse brain undergoes significant changes during postnatal development. The mouse olfactory system matures within three weeks after birth (Yu and Wu, 2017). During this period, the olfactory bulb changes from a plastic state, that allows the remodeling of incoming axons from the sensory neurons to a less permissive state (Ma et al, 2014; Tsai and Barnea, 2014; Wu et al., 2018). It is unknown whether this process is associated with alterations in cell types, their transcriptomic profiles, or both. In this study, we have conducted single cell RNASeq studies to profile cell types in the olfactory epithelium and bulb during development. Furthermore, to further evaluate the changes in cell types and transcriptional profiles during development, we have selected a list of 100 genes, including the markers of various cell types, to perform Molecular Cartography™ (Resolve Biosciences) analysis. Using the technology, we obtain highly quantitative measurements of the mRNA expression levels and use the information to identify the various cell types, their locations, and changes during early postnatal development.

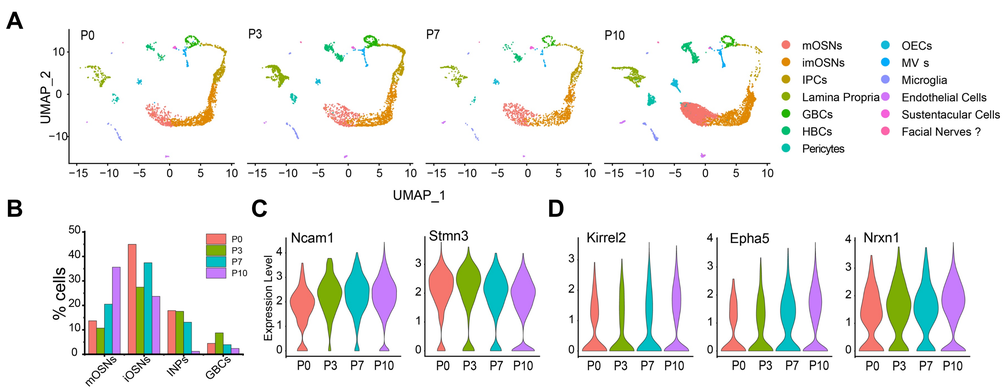


Yu and Wu, *Experimental neurology* 2017

Farley. *Nature Reviews Neuroscience* 2004

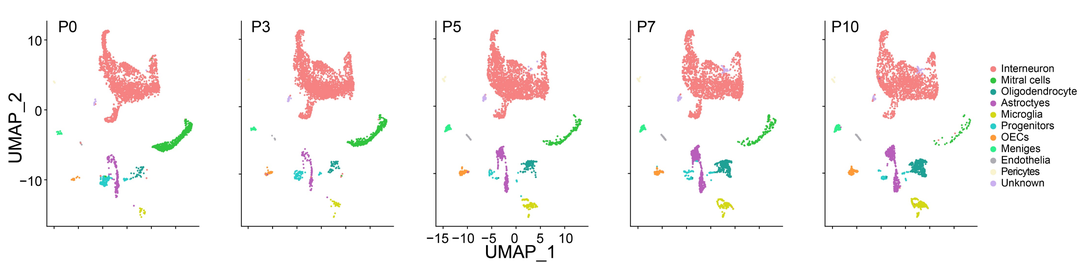
A. Illustration of the cell types in the mouse olfactory epithelium. **B**. Illustration of the continuous regeneration of the OSNs. **C**. Illustration of the convergent projection patterns in the mouse olfactory system. OSNs expressing the same odorant receptor (color coded) converge into the same glomeruli in the olfactory bulb (OB).

Transcriptomic change during olfactory epithelium development



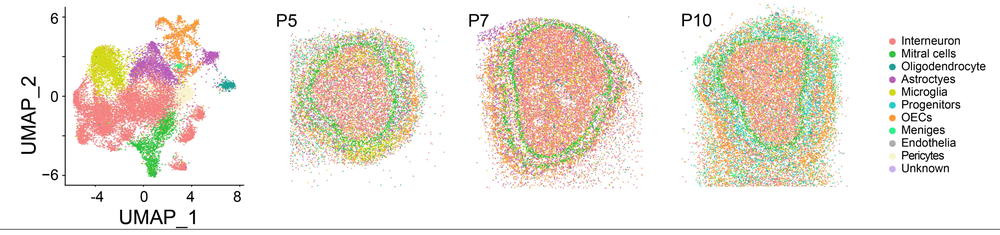
Single cell RNASeq analysis of developing olfactory epithelia **A**) UMAP plots of single cell clusters at the developmental stages. **B**) Quantification of the percentage of individual cell types during development. **C**) Sample changes in mRNA level in mOSNs.. Ncam1 and Nrxn1, two mature neuron markers, increased from P0 to P10. Two axon guidance molecules, Kirrel2 and Epha5, also increased. Lower Stmn3 level during this period is associated with less plasticity at P10. (Cutforth et al., 2003; McIntyre et al., 2010).

Cell types determined by scRNASeq in the olfactory bulb



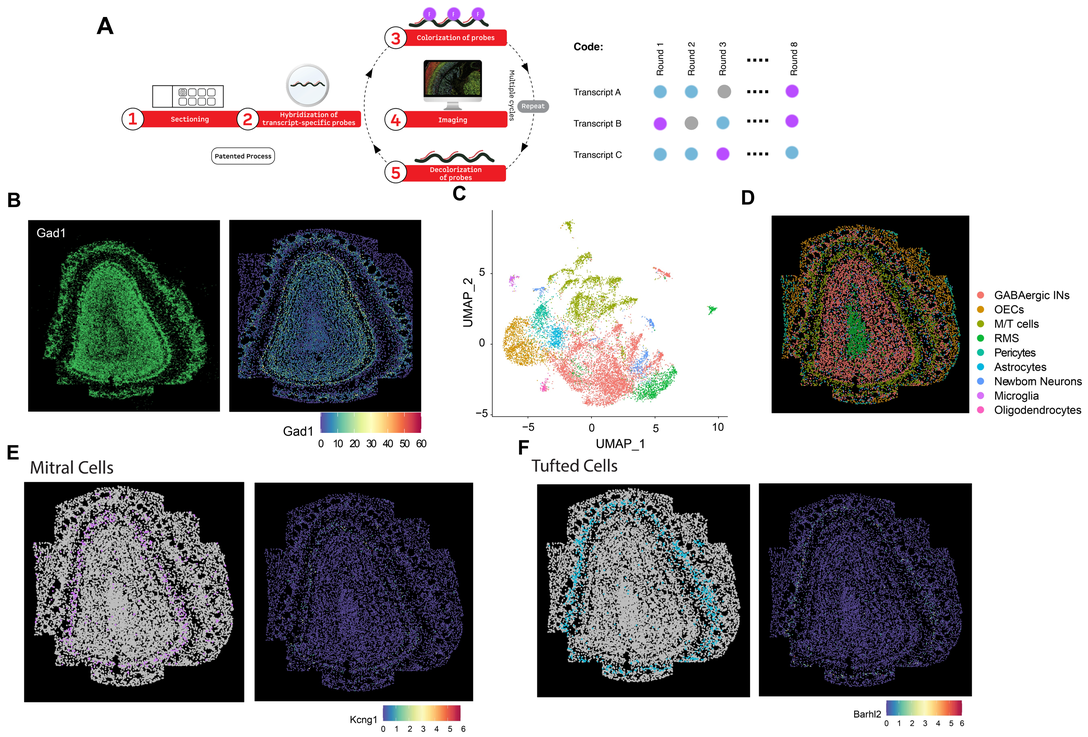
UMAP plots of single cell clusters of OB cells at various developmental stages. All major cell types are present during the period analyzed. There is significant increase in the proportion of glia cell types.

Spatial localization of cell types in the OB by SlideSeq



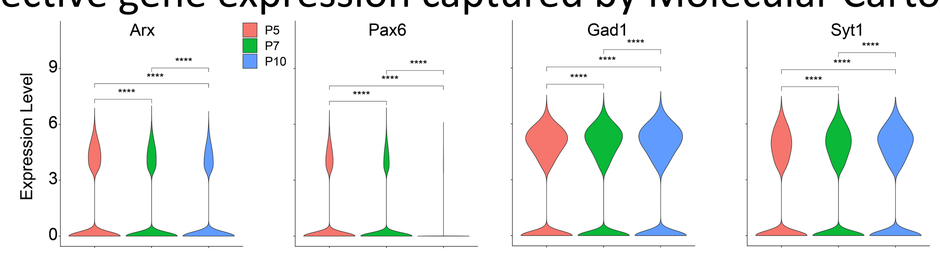
Cell types and their locations captured by SlideSeq (Stickels, R.R. et al. 2021) at various developmental stages.

Molecular Cartography clustering of cell types in the OB



A) Illustration of Molecular Cartography technology. **B**) Molecular Cartography of Gad1 expression in a P10 male mouse OB and quantification of expression in individual cells (right panel). Quantification captures the location and intensity information of cells expressing the gene. **C**) Cells are clustered based on quantified cartography data and reveal main cell types in the OB. **D**) Spatial location of individual cell types. **E-F**) Spatial location of mitral (**E**) and tufted (**F**) cells in the OB and respective marker genes.

Selective gene expression captured by Molecular Cartography



Molecular cartography captures change in gene expression from P5 to P10. Statistical results of neuroblast markers, Arx and Pax6, and mature neuronal marker, Gad1 and Syt1.

Acknowledgment

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References:

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