JEET PATEL

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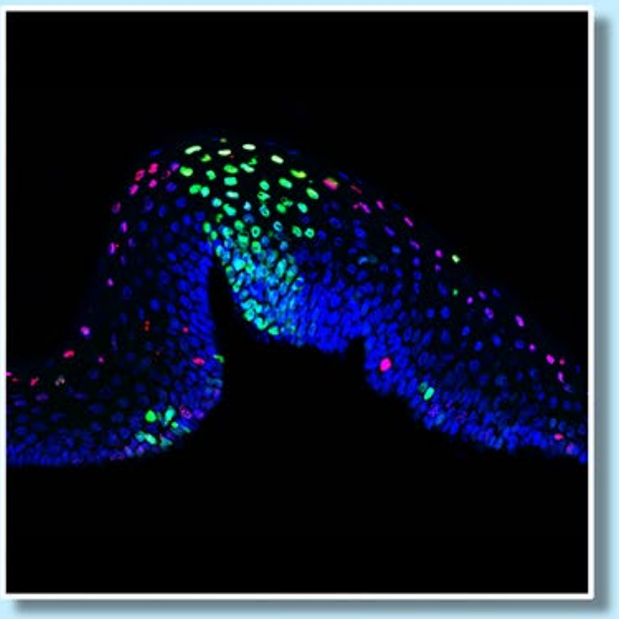

Sagittal View of Epithelia in the Roof of the Mouth from an Adult Mouse
(green: candidate stem cells, red: dividing cells, blue: nuclei)

Rare Label Retaining Cells in Palatal Epithelia Display Characteristics of Reserve Stem Cells

The oral mucosa consists of diverse and understudied epithelia that all exhibit remarkable capacity for repair. It is thought that reserve populations of stem cells are responsible for replenishing epithelia following injury, though no markers for reserve stem cells have been identified in the oral epithelia. Previous studies in epithelial tissues such as the epidermis and intestine have found that regenerative stem-like cell populations generally reside in the basal layer of these multilaminar epithelia. Here, we attempt to identify candidate reserve stem cells through an unbiased genetic "pulse-chase" strategy. We use transgenic mice that express GFP fused to a histone protein, under the control of the promoters for basal keratins 5 and 14, labeling the highly proliferative basal cells during the "pulse" period. Upon administration of a drug (doxycycline; via the food), new translation of H2B-GFP ceases and existing GFP signal is diluted during mitosis. Thus, after a prolonged "chase" period, the only GFP+ cells remaining are those that have divided infrequently or not at all, a behavior indicative of reserve cells. We successfully identified such "label-retaining cells" (LRCs), which are candidate stem cells, after 28- and 56-day chases. We sorted cells to isolate those with high levels of GPF (the LRCs), and found that they highly express the transcription factors Sox9 and TAp63, known markers of quiescence. This expression profile may be used in the future to uniquely mark LRCs in this tissue for further study. Furthermore, we identified patterned enrichment of LRCs in certain regions along the axes of the palate and around the palatal ridges, known as rugae. Understanding the spatial patterning of palatal cell niches gives us insight into the tissue level coordination of epithelial regeneration and wound closure.