Mesenchymal-to-Epithelial Transition in the Oral Cavity: Highlighting Migration Dynamics During Wound Healing

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Background:
Oral cancers are particularly aggressive due to their propensity for early invasion into adjacent lymphatic and vascular structures. Consequently, a significant proportion of cases are diagnosed at advanced stages, underscoring the need to further elucidate mechanisms of metastasis. Given the established parallels between wound healing and tumor progression, we utilized a gingival injury model to investigate cellular migratory dynamics that may inform oral cancer metastatic behavior.

Methods:
K5/GFP transgenic mice were injected with Tamoxifen to induce GFP expression in Keratin 5-positive epithelial cells, followed by surgical extraction of the first molar to simulate oral tissue injury. Tissue was collected and processed for immunohistochemistry. Co-staining for Keratin 5 and GFP was used to track epithelial cell lineage, while additional co-staining with mesenchymal and microenvironmental markers was performed to further characterize cellular identity and tissue architecture.

Results:
Select regions within intact gingival epithelium lacked Tamoxifen-induced GFP signal, suggesting a non-epithelial cell lineage, with this pattern further exacerbated by tooth extraction surgery. The integrity of the basement membrane was maintained in GFP-negative regions as evidenced by ITGB1 staining. Keratin 17 expression in both GFP-positive and GFP-negative regions highlighted that GFP loss was not stress induced. Notably, Vimentin and Collagen I showed highly specific expression within GFP-negative zones, suggesting the epithelial cells present were mesenchymal in origin. Furthermore, WNT5a, known to promote the Mesenchymal-to-Epithelial Transition (MET), was prominently expressed in these GFP-negative areas, indicating its potential role in facilitating mesenchymal cell integration into the epithelium.

Conclusion:
The detection of mesenchymal markers within epithelial regions, along with the absence of GFP in these infiltrating cells, provides evidence for MET in oral mucosa. Our data indicate this cellular transition in oral mucosa may contribute to the highly metastatic nature of oral cancers by facilitating cellular plasticity and invasion processes.