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2. Title
   Uncovering the Molecular Mechanisms of Connecting Club Cell Fate Conversion to Precancerous Change

3. Period
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4. Summary
   Differentiated airway epithelial cells retain plasticity that supports tissue repair after injury, yet the role of this plasticity in precancerous lesion formation remains poorly understood. In this study, we combined single-cell transcriptomic analysis, RNA velocity analysis, and airway injury and carcinogenesis models using Scgb1a1-positive club cell lineage-tracing mice to investigate the fate and function of club cell-derived dedifferentiated cells. Hes1 inactivation induced dedifferentiation of club cell lineage cells into induced basal (iB) cells and further promoted differentiation into Krt13-positive Hillock cells. RNA velocity analysis predicted a continuous state transition from iB cells to Hillock cells. In a naphthalene-induced airway injury model, iB cells generated Hillock cells during tissue repair and exhibited reserve stem cell-like properties. Furthermore, in an NTCU-induced squamous metaplasia model, iB cells differentiated into squamous-like epithelial cells, suggesting that they may serve as candidate cells of origin for precancerous lesions. These findings suggest that club cell-derived dedifferentiated basal cells represent a cellular state linking tissue regeneration and precancerous lesion formation. Moreover, this study supports the existence of a shared epithelial plasticity program underlying tissue repair and early tumorigenesis.