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Authors: A E Hegab, V L Ha, J L Gilbert, K X Zhang, S P Malkoski, A T Chon, D O Darmawan, B Bisht, A T Ooi, M Pellegrini, D W Nickerson, B N Gomperts
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Public Summary:
Our large airways are directly in contact with the environment and therefore at risk for injury. Basal cells have been shown previously to be involved in repair of the large airway epithelium, but the possible contribution of other stem cell populations to airway epithelial repair has not been identified. Here, we describe the identification and characterization of a novel population of stem cells in the ducts of the mucus producing glands in the airway. These ducts are located under the surface lining of the airway in a relatively protected site and are capable of giving rise to cells of the mucus glands and the surface epithelium. The identification of this novel stem cell population in the airways has direct implications for furthering our understanding of airway diseases such as cystic fibrosis, COPD and asthma.

Scientific Abstract:
The airway epithelium is in direct contact with the environment and therefore constantly at risk for injury. Basal cells have been found to repair the surface epithelium, but the contribution of other stem cell populations to airway epithelial repair have not been identified. We demonstrated that airway submucosal gland duct cells, in addition to basal cells, survived severe hypoxic-ischemic injury. We developed a method to isolate duct cells from the airway. In vitro and in vivo models were used to compare the self-renewal and differentiation potential of duct cells and basal cells. We found that only duct cells were capable of regenerating submucosal gland tubules and ducts, as well as the surface epithelium overlying the submucosal glands. Submucosal gland duct cells are therefore a multipotent stem cell for airway epithelial repair. This is of importance to the field of lung regeneration as determining the repairing cell populations could lead to the identification of novel therapeutic targets and cell-based therapies for patients with airway diseases.