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Proper Establishment of Epithelial Polarity as a New Mechanism for Lung Stem Cell Behavior

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The balance between cell gain (self-renewal) and cell loss (apoptosis/differentiation) governs the size of the progenitors' compartment. Molecular programs regulating the balance between different fates of endogenous organ-specific stem/progenitor cells are likely critical both to development and to regenerating diseased and damaged tissues in different organs, including the lung. Recent studies demonstrated the importance of disruption of epithelial apical-basal polarity in epithelial cell apoptosis and proliferation. However, how epithelial polarity regulation is coupled to apoptosis and proliferation is not well understood. We find that Asp-based PTPs such as Eya1 and none-receptor PTPs are essential for balancing differentiation and proliferation and apoptosis versus self-renewal/differentiation, respectively by controlling the activity and localization of Par polarity complex in lung distal epithelial progenitors during pre- and postnatal development. The difference of the effect of these different PTPs possibly reflects the facts they regulate the activity and localization of Par polarity complex by targeting the activity of different upstream signaling events: Eya1 controls Par polarity complex by binding to and controlling aPKCζ activity, while none receptor PTPs controls Par complex by controlling the activity of GTPases. Thus, Eya1 phosphates regulate cell polarity and mitotic spindle orientation by controlling aPKCζ phosphorylation levels. Loss of apical-basal polarity in Eya1-/- distal lung progenitors results in loss of asymmetric cell division, leading to increased symmetric differentiation and hence lack of stem/progenitor cell self-renewal. Conditional deletion of none-receptor PTPs in lung epithelial progenitors results in disruption of Par polarity complex and consequently inhibition of PI3K pathway leading to increased apoptosis, but decreased cell proliferation/differentiation.

Biography:

Dr. Ahmed Hashash has completed his PhD from Manchester University, UK. He is a fellow of the California Institute of Regenerative Medicine and New York University Medical School. Prof. Hashash worked at Mount Sinai School of Medicine of New York University and Children's Hospital Los Angeles. He was Assistant Professor and Principal Investigator of Stem Cell & Regenerative Medicine at School of Medicine, University of Southern California, USA. In 2016, Prof. Hashash has joined The University of Edinburgh, as Tenure-Track Associate Professor of Biomedicine, Stem Cell & Regenerative Medicine. Prof. Hashash has several breakthrough discoveries in genes/enzymes that control stem cell behavior and regenerative medicine. He acts as a discussion leader at the Gordon Research Seminar/Conference in USA and a Peer Reviewer at the MRC, UK. He is invited to speak at several international conferences in USA, Spain and Greece. He is the editor or author of three books on stem cell and regenerative medicine.