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INSIGHTS IN IMMUNOLOGY

Regulatory roles of protein phosphatases in the apical-basal polarity and their impact on lung stem cell behavior and protection against lung fibrosis

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Abstract

The balance between cell gain (self-renewal) and cell loss (apoptosis and differentiation) governs the size of the progenitors' compartment. Molecular programs regulating the balance between the self-renewal and differentiation and the balance of apoptosis versus self-renewal/differentiation 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 (mediated by Par- polarity protein complex) 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 RhoGTases. Thus, Eya1 phosphatase regulates 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. Conversely, none-receptor PTPs control Par complex by regulation of the activity of RhoGTases. 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 activation of the caspase-3 apoptotic cascade that results in increased apoptosis, but decreased cell proliferation/differentiation. Most importantly, we find that these mechanisms are recapitulated during fibrosis in alveolar epithelia undergoing apoptosis, which is a crucial early step in the development of lung fibrosis.

Key Words: Protein Phosphatase, Stem Cell, Lung Fibrosis

Biography

Professor Ahmed Hashash has completed his PhD from Manchester University, UK. He is a fellow of the California Institute of Regenerative Medicine (CIRM) and New York University Medical School (MSSM), USA. Prof. Ahmed Hashash worked as a senior biomedical research scientist 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 Keck School of Medicine and Ostrow School of Dentistry of The University of Southern California, USA. In 2016, Prof. Hashash has joined The University of Edinburgh, Edinburgh Medical School-Zhejiang International Campus, (ZJU) as Tenure-Track Associate Professor and Senior Principal Investigator of Biomedicine, Stem Cell & Regenerative Medicine. He is also adjunct Professor at the School of Basic Medical Science and School of Medicine, Zhejiang University. Prof. Hashash has several breakthrough discoveries in genes/enzymes that control stem cell behavior and regenerative medicine. He has published more than 25 papers in reputed international journals and serving as an editorial board member of repute. Prof. El-Hashash acts as a discussion leader at the prestigious Gordon Research Seminar/Conference in USA, and a Peer Reviewer/ International Extramural Review for The Medical Research Council (MRC) grant applications, London, UK. He is invited to speak at several international conferences in USA, Spain, Greece, Egypt and China. He is the editor or author of several books on stem cell and regenerative medicine.

Publications

1. Cell-based therapy for idiopathic pulmonary fibrosis, August 2019Stem Cell Investigation 6:22-22, DOI: 10.21037/sci.2019.06.09
2. Brief Overview of the Human Respiratory System Structure and Development, September 2018, DOI: 10.1007/978-3-319-95279-6_1
3. Stem Cell-Based Organoid Models in Lung Development and Diseases, September 2018, DOI: 10.1007/978-3-319-95279-6_8

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