NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

VIRTUAL BIOLOGY COLLOQUIUM

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Hosted by A/P Ge Ruowen

Autocrine Hedgehog signaling promotes epithelial airway cell proliferation and differentiation

By **Yin Wenguang**

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About the Speaker

Wenguang Yin is a principal investigator in State Key Laboratory of Respiratory Disease at Guangzhou Medical University in China.
Yin received his PhD in biochemistry and molecular biology in 2012 from Guangzhou Institute of Biomedicine and Health, Chinese Academy of Sciences. During his PhD work, he investigated the role of Notch signaling pathway in pancreas development using zebrafish with Duanqing Pei. Subsequently, he initiated the studies on lung development using mouse models as a postdoctoral fellow with Didier Stainier at Max Planck Institute for Heart and Lung Research (Bad Nauheim).
By conducting a large-scale forward genetic screen using ethylnitrosourea mutagenesis, he developed a number of animal models for human pulmonary development and diseases, including tracheamalacia, tracheal stenosis and emphysema, and revealed the unexpected role of the potassium channel KCNJ13 and the extracellular matrix glycoprotein fibrillin-2 in tracheal formation and smooth muscle polarization. Recently, he has also investigated the role of Hedgehog signaling in airway epithelial cell formation.

Large GWAS have linked Hedgehog signaling components to COPD pathogenesis. Research on Hh signaling in the lungs focuses primarily on its paracrine function in patterning the mesenchyme and its responses. We investigated an autocrine function of Hh signaling in airway cells during development. Epithelial-specific deletion of Hh or its signal transducer, Smo decreased airway cell proliferation and interfered with secretory and ciliated cell differentiation. Key transcription factors regulating epithelial cell fates were downregulated in Smo mutant lungs. Constitutively active Smo promoted epithelial cell differentiation. Similarly, manipulations of Hh signaling components in primary human bronchial epithelial cells suggested a direct role of Hh in airway epithelial cells proliferation and differentiation. These results establish a conserved, autocrine function of Hh signaling in the lungs. Genetic alterations linked to lung disease in patients may directly compromise Hh signaling in both epithelial and mesenchymal cells.

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