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Department of Biomedical Sciences

Special Departmental Seminar

Deregulated lineage-specific transcriptional program and signaling in lung cancer metastasis

By

Dr William Ka-Chun CHEUNG

Department of Pathology,
Yale University School of Medicine

Date: 21 August 2015 (Friday)

Time: 10:00 am-12:00 noon

Venue: Benjamin Kwok Lecture Theatre (LT-16)
4/F, AC1
City University of Hong Kong
Tat Chee Avenue, Kowloon Tong

For abstract, please refer to the attachment.

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~ All are Welcome ~

Deregulated lineage-specific transcriptional program and signaling in lung cancer metastasis

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Abstract

Lung cancer is the leading cause of cancer-related deaths worldwide. This poor prognosis is due to the heterogeneous nature and rapid metastatic progression of this disease. Following tumor initiation from specific cell types, lung cancers can adopt various aberrant differentiation states that typically correlate with poor survival, yet the mechanistic link between such phenotypic plasticity and metastatic competence is unclear. By analyzing the transcriptomic profile of lung adenocarcinoma (LUAD), the most frequently diagnosed subtype of lung cancer, we uncovered an alveolar lineage-selective gene signature that stratifies LUAD into molecular subtypes of distinct differentiation states and metastatic propensity. This transcriptional program is in part driven by the suppression of two alveolar cell fate transcription factors, GATA6 and HOPX, whose low levels correlate with poor differentiation state and patient prognosis. Functionally, suppression of GATA6 and HOPX in LUAD cells cooperatively enhances metastatic colonization *in vivo*, and promotes organoid outgrowth and invasion *in vitro*. RNA sequencing revealed that suppression of GATA6/HOPX pathway causes LUAD to transdifferentiate from alveolar to basal lineage. This switch in epithelial lineage is functionally required for LUAD metastasis. Collectively, these findings suggest that the acquisition of phenotypic plasticity through disrupting the alveolar differentiation program confers LUAD with metastatic competence.