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Hong Kong dissects lung carcinoma at single-cell resolution uncovering new mechanism

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Better understanding of tumour microenvironment at single-cell resolution accelerates therapeutic development

Tumour formation is a multistep and complex process and the underlying mechanism behind it is still largely unclear. A new study conducted by The Chinese University of Hong Kong's (CUHK) Faculty of Medicine (CU Medicine) dissected the dynamics of lung cancer at single-cell resolution and successfully discovered a new mechanism for tumour formation via "macrophage-myofibroblast transition (MMT)". Their preclinical work demonstrated its therapeutic implication for treating lung cancer in this first study to define a pathogenic role of MMT in cancer.

The mechanism by which immune cells, "macrophages", are directly transformed into pathogenic myofibroblasts due to long-term overactivation is called MMT. This study further discovered that macrophages can also transform into protumoral Cancer-associated fibroblasts (CAFs) in the tumour microenvironment via MMT for promoting tumour growth.

In addition, the team further identified a transcription factor Smad3 as the key regulator for initiating MMT in non-small-cell lung carcinoma by gene network analysis. They demonstrated that genetic or pharmaceutical inhibition of macrophage Smad3 effectively blocks MMT leading to tumour regression in mice, representing a potential therapeutic target for precisely eliminating the "bad" CAFs.

"Our next step is to develop its precision therapeutics for clinical use", said the researchers.

Image caption- (from left) Professor Patrick Ming Kuen TANG, Assistant Professor and Dr. Philip Chiu Tsun TANG, Postdoctoral Fellow from the Department of Anatomical and Cellular Pathology, Professor Hui Yao LAN, Choh-Ming Li Research Professor of Biomedical Sciences from the Department of Medicine and Therapeutics, and Professor Ka Fai TO, Chairman of the Department of Anatomical and Cellular Pathology at CU Medicine.