



The Chinese University of Hong Kong
Department of Biomedical Engineering



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Venue: Rm. 222, Ho Sin Hang Engineering Building, CUHK

Mechanical regulation of cancer cell tumorigenicity

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Abstract

It is known that genetic and biochemical factors regulate various cellular functions and become dysfunctional in pathologic conditions. The significance of mechanical forces in biology has been well documented. However, their roles in tumorigenesis remain unclear. We recently developed a mechanical strategy for selecting tumorigenic cancer stem cells (CSCs) from a pool of cancer cells by culturing single cancer cells in 3D soft fibrin matrices. The selected cells expressed stem cell genes, resisted chemotherapy, and exhibited low stiffness and non-stiffening responses on substrates with increasing rigidity. Remarkably, as few as 10 such cells were able to survive and form tumors at the site of injection or at the lungs of wild-type mice. We further explored the mechanisms underlying the high tumorigenicity of these selected CSCs. When re-plated back to rigid substrates, the selected CSCs exhibited plasticity in Cdc42-mediated mechanical stiffening, histone 3 lysine residue 9 (H3K9) methylation, Sox2 expression, and self-renewal capability. In contrast to stiff matrices, soft fibrin matrices decreased focal adhesion kinase activity, H3K9 methylation, and promoted Sox2 expression. Mechanistically, H3K9 methylation at the Sox2 promoter region inhibited Sox2 expression that was essential in maintaining self-renewal capability of CSCs both in vitro and in vivo. In summary, we have demonstrated that 3D soft fibrin matrices can select and grow tumorigenic CSCs and that their self-renewal property is regulated by H3K9 demethylation and Sox2 upregulation mediated by matrix softness. These findings indicate that mechanical forces may significantly influence the plasticity of cancer cells and regulate tumor progression.

Biography

Dr Youhua Tan obtained his bachelor degree in Mechanical Engineering from University of Science and Technology of China in 2005 and PhD degree from City University of Hong Kong in 2010. He completed his postdoctoral fellowship in University of Illinois at Urbana-Champaign from 2011 to 2015. From 2015, Dr Tan joined PolyU as Assistant Professor in the Department of Biomedical Engineering.

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