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Application of organoid technology for prostate luminal progenitor culture, tumour modelling and drug screening

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Abstract

Historically, prostate luminal epithelial progenitors and cancer cells have been difficult to culture, thus hampering the generation of representative models for the study of prostate homeostasis, epithelial lineage hierarchy relationship and cancer drug efficacy assessment. In this presentation, we describe a newly developed culture methodology that can efficiently grow prostate luminal epithelial progenitors and cancer cells as organoids. Notably, the organoid assay favours prostate luminal cell growth, thus overcoming the basal cell dominance issue upon the establishment and continuous propagation of prostate epithelial cells. Importantly, prostate epithelial organoids cultured under this condition have demonstrated preservation of androgen responsiveness and intact androgen receptor signalling, providing a representative system to study castration resistance and androgen receptor independence. Under the identical culture medium, we are capable to establish primary adherent cell lines from single prostate luminal progenitors in a clonal manner. By combining rat embryonic urogenital mesenchyme and the established prostate epithelial organoids, we have discovered that the primitive stromal cells are capable to differentiate into mature smooth muscle cells in vitro. More recently, we have extended the use of this assay to grow primary cancer specimens from patients, including prostate, bladder, ovarian and triple negative breast tumours. Taken together, our results highlight the potential use of the organoid assay for the study of reciprocal stromal-epithelial interaction as well as genomic landscape and drug response assessment in cancer patients, thus paving the way for personalized medicine.

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Biography

Chee Wai Chua was awarded with PhD in Cancer Biology in 2009 and then joined as Professor Michael Shen's group at the Columbia University Medical Center as a Postdoctoral Research Scientist and was later promoted to an Associate Research Scientist position at the Department of Urology and Medicine at Columbia University in October 2014. In the Shen Lab, he has pursued studies of genetically engineered mouse models of prostate cancer and prostate stem cell biology, focusing on the role of androgen receptor in prostate epithelial stem cells and organogenesis. In 2011. He is currently a Principal Investigator at the Clinical Research Stem Cell Center, State Key Laboratory of Oncogenes and Related Genes as well as well an Adjunct Professor at the Department of Urology, Shanghai Jiao Tong University School of Medicine affiliated Renji Hospital. He is also appointed as a Professor of Special Appointment, which carries the title "Eastern Scholar" by Shanghai Institutions of Higher Learning from 2017 to 2019, and is selected for the Shanghai Jiao Tong University School of Medicine "Double Hundred" Talent Program. Dr. Chua group is currently focusing on the investigation of intrinsic and extrinsic regulation of castration-resistance in the prostate using the state-of-the-art genetically engineered mouse models, tissue recombination assay as well as the newly developed organoid technology.