

Tumor Adaptation and Re-sensitization to Immune Checkpoint Therapy

13 April (Thursday) · 3pm (SGT, GMT+8)

In-person @ GIS Seminar Room (L2)



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Therapy-induced tumor microenvironment (TME) remodelling poses a major hurdle for cancer cure. As the majority of patients with hepatocellular carcinoma (HCC) exhibits primary or acquired resistance to immunotherapies, we aim at unravelling the mechanisms underlying tumor adaptation to immune-checkpoint targeting. By serial orthotopic implantation of HCC cells through anti-PD-(L)1-treated syngeneic, immunocompetent mice, we have established adaptive resistance models that recapitulate the immune landscape of human 'cold' HCC and enable identification of actionable targets to improve response. Corroborated with single-cell analysis of HCC tumor biopsies from a pembrolizumab clinical study, we have uncovered adaptive transcriptional and epigenetic programs by which tumor cells acquire immune evasion capacities via a T cell-excluded and immunosuppressive TME, thus providing new strategies for counteracting immunotherapeutic resistance in HCC.

Alfred Cheng is a Professor and Assistant Dean in Research of the Faculty of Medicine at The Chinese University of Hong Kong (CUHK). He completed his Ph.D. under the mentorship of Prof. Joseph Sung at CUHK and his postdoctoral training in the laboratory of Prof. Tim Huang at The Ohio State University. His research aims at advancing the basic understanding and precision immunotherapy of hepatocellular carcinoma. His multi-disciplinary collaborative team has employed the cutting-edge single-cell multi-omics and AI innovation to understand tumor adaptation to immune-checkpoint blockade and identify the cellular and molecular mechanisms of immunotherapeutic resistance. His recent works on the development of effective and durable combination immunotherapies have been published and highlighted in top journals of the field such as *Gut*, *Journal of Hepatology*, and *Science Translational Medicine*. He is the recipient of the Most Promising Young Investigator Award by the HK Government (2014) and CUHK (2015, 2019), and the 10th HMRF Anniversary Award in Breakthrough Research by the Food and Health Bureau of HK Government (2021).