



Areas of Excellence Scheme cum Departmental Lecture

## Developing New Cancer Cellular Immunotherapies



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Adoptive cell therapy (ACT) is a particularly promising area of cancer immunotherapy. ACT therapy uses both T cells and NK cells. Unlike T cells, natural killer (NK) cells play an important role in immune surveillance by targeting tumor cells that downregulate HLA class I molecules or express stress markers. Engineered T and NK cells that express chimeric antigen receptors (CARs) with PD-1 ablation have been successfully used to treat hematopoietic malignancies but exhibit limited clinical benefits for solid tumor patients. One of the obstacles for treating solid tumors is the tumor microenvironment (TME), which contains immune suppressive molecules, including PD-L1, CTLA-4, and TGF $\beta$ , and anti-inflammatory cells such as regulatory T cells and myeloid derived suppressor cells. TGF $\beta$  represses the antitumor effects of T cells directly and indirectly. TGF $\beta$  directly inhibits the development, proliferation, and function of cells in both the innate and adaptive arms of the immune system, including T cells and NK cells. I am leading a team to study tumor immunology in three aspects: 1) Design new CAR-T cells to disrupt the TME; 2) Derive new types of anti-cancer immune cells as sources of ACT; 3) Establish humanized mouse models for evaluating efficacy of ACT. In the presentation, I will show recent progress in these three initiatives. Briefly, we have designed new CAR-T cells with improved killing and tumor penetration capacities and CAR molecules that rewire immune suppressive signals in the TME. Preliminary clinical trial results of these CAR-T cells will be discussed. In addition, preclinical and clinical data on a new type of tumor killing cells derived from T cells will be presented. Finally, I will show a liver humanized mouse model that mimics the initiation and progression of human hepatocellular carcinoma with genetically defined factors.

~ All are Welcome ~

Date : 9 November 2021 (Tuesday)

Time : 17:00-18:00

Venue : Kai Chong Tong Communication Resources Centre (KCTCRC),  
1/F, Postgraduate Education Centre, Prince of Wales Hospital



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