CD96 constrains human T cell signaling and cytotoxicity against specific tumours

Dr Chelsia Wang
Associate Staff Scientist,
Immunology
Bioprocessing Technology Institute,
A*STAR

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Seminar Abstract

Targeting immune checkpoints to cure cancer, an active area of immunotherapy, is gaining more recognition in recent times. Immune checkpoints collectively refer to the myriad of co-activating or co-inhibitory proteins expressed by immune cells, such as T cells, that serve to modulate immune activation responses. Particularly, the inhibitory mechanisms have been hijacked by various cancer cell types to prevent immune cells from mounting an attack against them. It is hoped that the inhibition of such immune checkpoints provides a permissive environment for the immune cells to kill the cancerous cells. Although the FDA approved anti-PD-1/PD-L1 and anti-CTLA-4 therapies have proven to effect dramatic responses in some patients, a significant proportion of patients still do not respond well, thus motivating the continuous search for additional immune checkpoints that can be therapeutically targeted. The aim of my current research study is to validate CD96 as a potential immune checkpoint target in cancer therapy. Using CRISPR/Cas9 knockout approach, we determined that CD96 is an inhibitory immune checkpoint in human T cells. Subsequently, we tried to identify the critical domain responsible for its inhibitory effects using a modified CAR T cell strategy. Finally, we extended our findings using an *in vivo* mouse model. In conclusion, CD96 can suppress antitumor activity of T cells, and serves as a potential target in immunotherapy.

About the Speaker

Prior to joining BTI, I was a Senior Research Scientist at the Cancer Science Institute of Singapore (CSI). From 2011 to 2017, I was a Research Fellow in the Institute of Molecular and Cell Biology, A*STAR, during which time I held an adjunct Research Fellow position with CSI. In 2015, I was awarded the IMCB Early Career Researcher project grant to establish leukemia xenograft mouse models for drug screening. I obtained my PhD in 2011 from the NUS Graduate School for Integrative Sciences and Engineering under the support of the A*STAR Graduate Scholarship.

My past research includes elucidating the role of *RUNX* family genes in leukemogenesis using cell biological approaches, *in vivo* mouse models and analysis of human cancer samples; establishing a platform for drug screening using mouse xenografts; and discovering novel leukemia genes using next-

generation-sequencing. My current work in BTI focuses on harnessing the power of the body's immune system for cancer therapy.