CANCER SCIENCE INSTITUTE OF SINGAPORE

IN THE SPOTLIGHT

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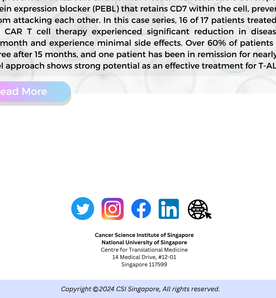

Research Highlights

Super Enhancer Acquisition Drives Expression of Oncogenic PPP1R15B that Regulates Protein Homeostasis in Multiple Myeloma (Nature Communications, Aug 2024)

Multiple myeloma (MM), a common blood cancer, begins in antibody-secreting plasma cells. Through comprehensive transcriptomic and phenomic analyses, Professor Chng Wee Joo, Senior Principal Investigator at Cancer Science Institute of Singapore (CSI Singapore), and his team compiled a list of candidate genes driven by Super Enhancers (SE) which have key implications in MM. SE are a dense cluster of mediator and transcription regulating proteins, which induces the target gene to be expressed at a substantially higher level than a single enhancer. They discovered that myeloma cells often acquire SE which transcriptionally activates an oncogene, PPP1R15B which regulates translation initiation factor eIF2α. Their research shows that inhibition of PPP1R15B has potential anti-myeloma effects as myeloma cells are vulnerable to disruption of PPP1R15B-dependent protein homeostasis. This suggests that PPP1R15B and/or eIF2α can be promising new therapeutic targets in the treatment of MM.

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Fratricide-resistant CD7-CAR T cells in T-ALL (Nature Medicine, Sep 2024)

Researchers at the National University of Singapore, led by **Professor Dario Campana**, a **Senior Principal Investigator** from the Cancer Science Institute of Singapore (CSI Singapore), have made significant advancements in treating T cell acute lymphoblastic leukaemia (T-ALL). This disease is notoriously difficult to treat, with poor outcomes, particularly when it relapses or resists standard chemotherapy. The team focused on improving chimeric antigen receptor (CAR) T cell therapy by targeting CD7, a protein present on T-ALL cells and normal T cells. The researchers developed an anti-CD7 protein expression blocker (PEBL) that retains CD7 within the cell, preventing CAR T cells from attacking each other. In this case series, 16 of 17 patients treated with this modified CAR T cell therapy experienced significant reduction in disease burden within a month and experience minimal side effects. Over 60% of patients remained relapse-free after 15 months, and one patient has been in remission for nearly six years. This novel approach shows strong potential as an effective treatment for T-ALL.

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