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In vivo production of CAR-T cells using virus-mimetic fusogenic nanovesicles

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Seminar Abstract

Engineered T cells expressing chimeric antigen receptor (CAR) exhibit high response rates in B-cell malignancy treatments and possess therapeutic potentials against various diseases. Despite the impressive success of CAR-T cell therapy in addressing B-cell lymphoma and leukemia, the widespread clinical application has been impeded by the intricate and costly manufacturing process. To address this limitation, we provided a promising strategy that involves the direct fusion of CAR molecules, pre-expressed on fusogenic nanovesicles (FuNVs), to T cells, thereby constructing CAR-T cells *in vivo*. First, the T-cell fusogens were engineered by adding an anti-CD3 single chain variable fragment to virus-derived fusogen, which effectively induced the fusion between FuNVs and T cells both *in vitro* and *in vivo*. Subsequently, nanovesicles co-expressing anti-CD19 CAR protein and T-cell fusogen ($FuNV_{CAR}$) successfully engineered T cells to produce CAR-T cells by delivering CAR protein onto T cells *in vitro* and *in vivo*. Importantly, intravenous administration of $FuNV_{CAR}$ demonstrated significant efficacy in inhibiting the growth of B-cell lymphoma. This innovative approach effectively streamlines the manufacturing process of CAR-T cell therapy.

About the Speaker

Dr. Zhao Gui received his Ph.D. in Biomedical Engineering from the South China University of Technology in 2023. His prior research has centered on the field of nanomedicine, specifically in the delivery of biomacromolecules like nucleic acids and proteins, with a primary focus on their application in the treatment of autoimmune disorders and cancer. He is currently a Scientist in the Formulations and Deliveries for Genes team led by Dr. Yi Yan Yang in BTI.

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