

Next generation CAR-T cell therapy against hematological malignancies

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Chimeric Antigen Receptor (CAR) is an artificial receptor, in which a tumor antigen-binding antibody is fused with signaling domains of T cells. When the CAR gene is introduced to peripheral blood T cells from tumor patients, a large number of tumor-specific T cells which express CAR molecules (CAR-T cells) are able to be generated in a short period of time. These CAR T cells are infused back to the patient for T cell-mediated tumor eradication. The CAR-T cell therapy had a great success in treatment of the refractory and relapsing acute lymphoblastic leukemia leading to commercial development of several CAR-T cell drugs in the US. However, this remarkable therapeutic efficacy of the CAR-T cells is restricted to some blood tumors such as CD19(+) leukemias. The hurdles in this field include low therapeutic efficacy due to immunosuppressive tumor microenvironment and on-target off-tumor toxicity of CAR-T cells due to low-level expression of tumor antigens in normal tissues.

In this talk, I will introduce our recent experimental models to overcome those hurdles in CAR-T cell therapy on hematological malignancies.