Feiyan Mo, PhD
Graduate Student
TBMM program

Engineering T-cell Therapies for Alloimmune Diseases

After obtaining her bachelor's degree in Biological Sciences at Shanghai Jiao Tong University (China), Feiyan Mo enrolled in the Translational Biology and Molecular Medicine (TBMM) graduate program at Baylor College of Medicine. She later joined Dr. Maksim Mamonkin's laboratory at Center for Cell and Gene Therapy to conduct her thesis research, co-mentored by Drs. Malcolm Brenner and Helen Heslop. Her research interest is to develop effective and affordable cancer immunotherapies using genetically engineered T cells, with the ultimate goal of translation to the bedside.

Abstract: Adoptive chimeric antigen receptor (CAR) T cell therapies produce remarkable clinical benefit in patients with certain tumors, yet their application to non-malignant diseases is less explored. We hypothesized targeted elimination of activated pathogenic T cells by engineered T cells would prevent or reverse the onset of alloimmune diseases, such as immune rejection. We then we developed a T-cell alloimmune defense receptor (ADR) that recognizes 4-1BB, a costimulatory molecule transiently expressed on activated T- and NK-cells, enabling targeted elimination of these pathogenic lymphocytes. Our proof-of-concept study has demonstrated that expression of a 4-1BB-specific ADR protects allogeneic CAR T cells from host rejection while preserving their anti-tumor activity in preclinical models of human cancer.

Robust and specific activity of ADR-armed T cells against pathogenic T cells enabled extending this platform to other alloimmune conditions. One of them is acute graft-versus-host disease (GvHD) – a devastating complication of hematopoietic stem cell transplantation (HSCT) produced by systemic activation of host-reactive donor T cells. Using a mouse model of xenogeneic GvHD, we demonstrated that T cells expressing an OX40-specific ADR prevented GvHD by eliminating pathogenic T cells that mediate tissue damage. T cells co-expressing both an ADR and a CAR protected from GvHD and cleared systemic leukemia in vivo. This strategy can be used clinically to prevent both GvHD and tumor relapse, which are the two major causes of morbidity and mortality following allogeneic HSCT.