

Enhancing Hematopoietic Stem Cell Transplantation with Genetically Modified Donor T Cells

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is an efficacious therapy for patients with life-threatening leukemias, but its use has been hindered by the limited availability of donors with matching HLA. Graft manipulation by removing T cells and B cells can reduce the risk for graft-versus-host disease (GvHD), but leukemia relapse still occurs in 25% of pediatric patients. A novel approach to improving stem cell transplantation is to engineer the donor T cells removed from graft to express chimeric antigen receptors (CARs) targeting CD19, while simultaneously inactivating the T cell receptor (TCR). The modified T cells, with >90% loss of TCR expression and >75% expressing CD19-CAR, enabled robust suppression of leukemia without causing GvHD in xenograft animal model. Thus, deploying TCR- CAR+ T cells can enhance the efficacy of T cell-depleted allo-HSCT.

Applications

- Hematopoietic stem cell transplant with engineered CAR T cell therapy for patients with refractory or relapsed leukemias
 - Combinations of this treatment regimen with other drugs
 - Overcome dose-limiting toxicities

Advantages

- Enhanced allo-HSCT with no increased risk of GvHD
- Manufacturing from healthy donor cells (avoiding unhealthy or impaired autologous cells)

- Bidirectional immune compatibility as the T cells are derived from same donor as the source of the graft

Publications

- Wiebking, V., et al. [Genome editing of donor-derived T-cells to generate allogenic chimeric antigen receptor-modified T cells: optimizing ?? T cell-depleted haploidentical hematopoietic stem cell transplantation](#). *Haematologica* 2020

Patents

- Issued: [11,903,969 \(USA\)](#)

Innovators

- Matthew Porteus
- Alice Bertaina
- Volker Wiebking

Licensing Contact

Eileen Lee

[Email](#)