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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

- Published Application: 20210177899
- Issued: 11,903,969 (USA)

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