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Lymphodepletion by Selective Apoptosis Induction in T Cells for Safe and Effective Immune Tolerance in Immunotherapy, Transplantation, and Autoimmunity

Stanford researchers have developed a novel inhibitor-based conditioning regimen that safely and effectively induces immune tolerance. This technology enables improved lymphodepletion for transplantation, autoimmune diseases, and cell-based therapies without chemotherapy-related toxicities.

Cell-based therapies, including hematopoietic stem cell transplantation and CAR-T cell treatments, require effective lymphodepletion to ensure successful engraftment and therapeutic outcomes. Current conditioning regimens typically rely on chemotherapy or radiation, which can cause severe toxicities and life-threatening complications, limiting their use, especially in autoimmune or non-cancerous conditions. Existing antibody-based lymphodepletion methods, such as anti-CD3 antibodies or anti-thymocyte globulin, often trigger dangerous inflammatory responses like cytokine release syndrome (CRS). There is a critical unmet need for safer, more precise, and less inflammatory conditioning strategies.

Stanford researchers have developed a novel conditioning regimen combining anti-CD3 antibodies and BCL2 inhibitors to safely and effectively achieve lymphodepletion and immune tolerance. Unlike current chemotherapy or radiation-based approaches, this method avoids severe toxicities and life-threatening inflammatory complications by using an anti-CD3 antibody, thereby preventing CRS. This innovative combination enhances lymphodepletion, resulting in improved long-term graft survival and immune tolerance. Preclinical transplantation models

demonstrate reduced irradiation requirements, decreased inflammation, and superior engraftment compared to existing standard-of-care regimens.

Stage of Development
Proof of concept – in vivo data in mice

Applications

- Hematopoietic stem cell transplantation and CAR-T cell therapies
- Solid organ transplantation
- Treatment of autoimmune diseases

Advantages

- **Safer lymphodepletion** without chemotherapy toxicity or cytokine release syndrome risks
- **Enhanced immune tolerance induction**
- **Reduced irradiation requirement** compared to standard total lymphoid irradiation/anti-thymocyte serum regimens
- **Improved long-term graft survival** in transplantation models

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