Docket #: S26-116

CD38-Directed Immune Conditioning for Type 1 Diabetes

Current immunotherapies for Type 1 diabetes (T1D), such as anti-thymocyte globulin (ATG) and anti-CD3 monoclonal antibodies, have several limitations. While these agents broadly deplete T-cell populations, they fail to completely eradicate the pathogenic autoreactive T cells attacking insulin-secreting beta cells in the islets of Langerhans, and preserve the essential regulatory T cells (Tregs) that prevent autoimmunity. Consequently, these therapies offer only a brief delay in disease progression and carry a substantial off-target toxicity. Thus, an urgent unmet need remains for targeted immune-conditioning strategies that selectively clear pathogenic T cells while preserving overall protective immunity.

The Meyer lab at Stanford has developed a novel CD38-directed strategy to selectively eliminate pathogenic autoreactive T cells. This approach leverages the high expression of CD38 on diabetogenic effector/memory T and B cells relative to naive T cells and Tregs, allowing for the selective depletion of pathogenic T cells while preserving cell populations essential for long-term immune tolerance. Furthermore, this non-genotoxic strategy leverages CD38's ectoenzyme role in modulating local NAD/adenosine signaling and T-cell activation thresholds to dampen inflammatory signaling in the pancreatic islets, thereby creating a temporary window in which other tolerance-inducing interventions can also be applied.

Stage of Research
Pre-clinical stage, *in vivo* data

Applications

- A humanized anti-CD38 monoclonal antibody formulated and dosed specifically for T1D prevention in high-risk, autoantibody-positive individuals

- An anti-CD38-based conditioning backbone for allogeneic or stem-cell-derived islet transplantation that reduces or replaces calcineurin inhibitors and ATG

Advantages

- A mechanistically selective and clinically tractable improvement over existing lymphodepleting regimens such as ATG or anti-CD3 antibodies
- Results in lower toxicity, while enhancing long-term graft survival and immune tolerance
- Broad commercial potential

Publications

- Pathak S, Ahmed R, Nagy N, Lee S, Bader CS, Regmi S, Iliopoulou BP, Chen PI, Gupta B, Villar-Prados A, Kim YB, Hussein N, SooHoo E, Twoy A, Thakor AS, Jensen KP, Utz PJ, Davis MM, Annes JP, Meyer EH. CD38 defines a therapeutically targetable pathogenic T cell population for precision immunotherapy in autoimmune diabetes. **bioRxiv [Preprint]**. 2026 Jul 3:2026.06.27.734105. doi: 10.64898/2026.06.27.734105. PMID: 42427724; PMCID: PMC13345075.

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