Clinical grade manufacturing of human alloantigen-reactive regulatory T cells for use in transplantation.

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Public Summary:
Regulatory T cell (Treg) therapy has the potential to induce transplantation tolerance so that immunosuppression and associated morbidity can be minimized. Alloantigen-reactive Tregs (arTregs) are more effective at preventing graft rejection than polyclonally expanded Tregs (PolyTregs) in murine models. We have developed a manufacturing process to expand human arTregs in short-term cultures using good manufacturing practice-compliant reagents. The donor-specific-expanded Tregs have a diverse TCR repertoire and are more potent than PolyTregs in vitro and more effective at controlling allograft injuries in vivo in a humanized mouse model. These cells have the potential to be used to control ES cell or iPS cell-derived tissue in humans.

Scientific Abstract:
Regulatory T cell (Treg) therapy has the potential to induce transplantation tolerance so that immunosuppression and associated morbidity can be minimized. Alloantigen-reactive Tregs (arTregs) are more effective at preventing graft rejection than polyclonally expanded Tregs (PolyTregs) in murine models. We have developed a manufacturing process to expand human arTregs in short-term cultures using good manufacturing practice-compliant reagents. This process uses CD40L-activated allogeneic B cells to selectively expand arTregs followed by polyclonal restimulation to increase yield. Tregs expanded 100- to 1600-fold were highly alloantigen reactive and expressed the phenotype of stable Tregs. The alloantigen-expanded Tregs had a diverse TCR repertoire. They were more potent than PolyTregs in vitro and more effective at controlling allograft injuries in vivo in a humanized mouse model.

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