Clinical-grade manufacturing of CD40-AIR-Treg cells as cellular therapeutics for Graft-versus-Host Disease

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Allogeneic stem cell transplantation offers a potential cure for many patients with congenital or acquired blood disorders, as well as for those with otherwise incurable leukemia and lymphoma. The success of this transplantation method is partly based on immunotherapeutic mechanisms, as immune cells from a healthy donor recognize and destroy the patient's blood cells as foreign, thus helping to eliminate leukemia or lymphoma cells. One risk of this treatment is graft-versus-host disease (GvHD), in which the immune response also targets other organs and can cause severe organ damage. Researchers have shown that so-called regulatory T-cells (Treg) from the donor can prevent this transplantation complication and are also therapeutically effective in existing GvHD.

The goal of the research consortium is to make this therapy more effective in chronic GvHD. Building on prior work, donor Treg cells are genetically modified so that they become activated in inflamed tissues and exert their immunosuppressive and tissue-healing effects locally. For this purpose, a biosensor containing the molecule CD40 is genetically introduced into the Treg cells, which interacts with its partner molecule on activated lymphocytes (CD40L), thereby activating the Treg cells and inhibiting the function of other immune cells. The aim is to further develop this therapy so that it can be tested in clinical trials for safety and efficacy.