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Hematopoietic stem cell-based therapy for HIV disease: 'Berlin' versus 'Essen' patients

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The goal of our work is to develop insight and understanding of the effect of deleting the chemokine receptor CCR5 in T cells, and its interplay with immune regulation of human immunodeficiency virus type - 1 (HIV-1), to enable a novel technology platform to cure HIV disease. A critical point is the use hematopoietic stem cell (HSC) transplantation of the cells resistant to HIV such as CCR5Δ32 cells, which harbor deletion in the CCR5 promoter. Such mutation confer resistance to CCR5-tropic HIV-1 in homozygous individuals and could cure HIV-1 disease based on the outcome of bone marrow engraftment in HIV+ leukemic patients using a CCR5Δ32 homozygous donor ('Berlin Patient'). However, a shift of HIV tropism to CXCR-4 tropic strains of HIV-1 might be limiting after HSC transplantation with CCR5Δ32/Δ32 mutation since it could lead to recurrence of viremia ('Essen patient'). In addition, patients receiving allogeneic bone marrow transplantation often suffer from graft- versus-host disease (GvHD), and for that reason HIV infection is not considered an indication, unless a hematologic malignancy warrants transplantation. To advance this field, it is, however, vital to search for novel determinants to HIV susceptibility using genome-wide analyses and exploit mechanisms, which play a crucial role in repression of CD4+ T conventional cells (Tcons) by naturally occurring CD4+CD25+ T regulatory cells (nTregs). In order to ameliorate GvHD, further understanding of the mechanisms of immunological self-tolerance will also provide insights into how strong immune responses such as graft rejection could be restrained and engraftment of HIV resistant cells in HIV+ leukemic patients could be augmented.

Biography

Josef Bodor received his PhD (1990) with honors from Institute of Molecular Genetics in Prague, Czech Republic. As of 2013, he is a Senior Investigator working at the Institute of Experimental Medicine in Prague, Czech Republic. He is a Senior Scientist with faculty experience from Ivy League Institutions in US hosting on sabbatical leaves around the world (Harvard University Boston, MA, Columbia University; New York, NY, Kyoto University, Kyoto, Japan, Würzburg University, Würzburg, Germany, and Johannes Gutenberg University in Mainz, Germany). He as an Associate Member of Transregio 52 published series of original reports summarized in authoritative reviews.

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