T-cells in stem cell transplants: dissecting the good, the bad and the ugly

Wolfl M\textsuperscript{1,2}, Eyrich M\textsuperscript{2}, Schlegel PG\textsuperscript{2}, and Greenberg PD\textsuperscript{1}

\textsuperscript{1}Fred Hutchinson Cancer Research Center, Seattle, USA
\textsuperscript{2}Pediatric Stem Cell Program, Children’s University Hospital, Wurzburg, Germany

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Allogeneic stem cell transplantation for patients with hematologic malignancies has proved to be one of the most powerful forms of immunotherapy. Studies comparing T-cell depleted versus undepleted grafts convincingly demonstrated the role of T-cells in the graft-versus-leukaemia effect at the cost of increased graft-versus-host-disease. It has been an elusive goal of research to prevent GVHD without dramatically increasing the chance of relapse or major transplant complications. New insights in the regulatory mechanisms and dynamics of various T-cell subsets now open avenues for dissecting the T-cell response adapted to the patient’s requirements: 1) supportive antigen-specific T-cell therapy provides protection against viral and fungal antigens; 2) regulatory T-cells may be used to modulate GVHD; 3) T-cells against minor histocompatibility antigens and leukaemia-associated antigens can provide targeted immunotherapy with a reduced risk of increased GVHD. We have developed methods to prime and expand antigen-specific cells from the naive T-cell repertoire and to specifically select for these T-cells on the basis of their CD137 expression upon stimulation. In consequence various epitopes of the leukaemia-associated transcription factor Wilms Tumor antigen 1 have been described that will be of further use for leukaemia-specific T-cell therapy. Furthermore the use of novel cytokine combinations in vitro results in a T-cell phenotype with a favourable CD28 expression, which increases the chances that adoptively transferred T-cells persist in vivo.