Colloquium

Institute for Regenerative Medicine (IREM) in collaboration with Wyss Translational Center Zurich (Wyss Zurich), Regenerative Medicine Technologies Platform

Interdisciplinary Colloquium Regenerative Medicine I

Tuesday, 26th Sept. 2017 at 12:30 – 1:30 pm,
Kleiner Hörsaal OST,
University Hospital Zurich

PD Dr. Nina Khanna

Division of Infectious Diseases and Hospital Epidemiology, University and University Hospital Basel

T-cell Therapy for Infectious Diseases

Opportunistic infections remain a leading cause of morbidity and mortality in transplant recipients. Clinical studies using adoptive transfer of pathogen-specific T cells aim at restoring immunity and thereby preventing and treating infections.

The generation of virus-specific T-cells is currently limited due to its elaborate production requiring in-vitro expansion over at least 10 days under good manufacturing practice (GMP) conditions. Therefore, more rapid approaches without the need of long-term in vitro expansion would be desirable. The selection of IFN-γ-producing T cells following stimulation with viral antigens by the GMP-approved Miltenyi® IFN-γ Capture System for direct infusion into patients is rapid (< 48 hours) and promising for cytomegalovirus (CMV), adenovirus and Epstein-Barr virus (EBV). In the current Phase I/II study, we investigate the safety and feasibility of direct infusions of donor-derived pathogen-specific IFN-γ positive selected T-cells under GMP requirements using the clinically certified Miltenyi® cytokine capture system in recipients of hematopoietic stem cell transplantation with post-transplant adenovirus, CMV or EBV infections. So far, three patients have been treated for treatment refractory CMV infection and two patients for EBV at the University Hospital of Basel.

However, the IFN-γ Capture System is restricted to antigens with moderate to high memory T-cell frequencies in peripheral blood and can therefore not be used for the isolation of fungus-specific T cells. To increase the sensitivity for isolation of these rare pathogen-specific memory cells, other T-cell activation markers may be more suitable which enable capture of a greater number of antigen-specific T cells irrespective of cytokine production. Different T-cell surface molecules that are selectively expressed or strongly upregulated after T-cell activation such as CD25, CD69, CD71, CD134, CD137 and CD154 could be similarly useful for selection of antigen-specific T cells. CD154 and CD137 for example are transiently expressed on activated CD4+ and CD8+ T cells following antigen stimulation. We could previously show that CD154 and CD137 are promising candidates for selection of pathogen-specific T cells due to its high specificity and sensitivity.

Organiser: Prof. Dr. Dr. Simon P. Hoerstrup
Execution/Chair: Dr. Steffen M. Zeisberger
IREM & Wyss Zurich, Univ. of Zurich and ETH Zurich