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Research interests:

Project 1

Multiple Myeloma (MM) is the second most common hematological malignancy with an incidence of 4.1/100.000 per year. Disease control can be achieved by high-dose chemotherapy followed by autologous stem transplantation but relapse occurs in over 90% of all patients. Thus novel concepts for eradication of minimal residual disease (MRD) are highly warranted. Adoptive immunotherapy represents an attractive approach for augmenting tumour immunity and may be achieved by genetically modifying T-cells with an MM-specific chimeric immunoreceptor targeting a Multiple Myeloma cell-associated antigen. Following this approach, CD4 and CD8 T cell clones are established expressing different chimeric T cell bodies and their in vitro and in vivo functions against primary Multiple Myeloma cells are assessed.

Project 2

Retargeted virotherapy with oncolytic measles specific for Multiple Myeloma cell-associated antigens, is an attractive therapeutic approach for treating Multiple Myeloma. Vaccine strain Edmonston B in an ablated variant which no longer binds the natural measles receptors CD46 and CD150 (SLAM) expressed on almost every human cell type is used and viral attachment protein (Hemagglutinine /H protein) is genetically engineered to retarget it displaying single-chain antibodies known for highly restricted binding of Myeloma cells resulting in retargeted modified measles viruses. In vitro and in vivo specific oncolytic anti-Myeloma activity is investigated.
The clinical application of retargeted measles virus is currently limited by an anti-measles humoral immune response in most of the patients. To overcome this obstacle, genetically modified T-cells as carriers for oncolytic measles virus are evaluated which may protect the virus from being destroyed in vivo allowing site directed delivery of a high viral dosis to the bone marrow as the prominent location of the viral targets, the malignant plasma cells.

Project 3

Viruses may strongly impair functions of hematopoietic stem cells. CD150, in humans a receptor for measles virus (MV), is a signal transducing protein on hematopoietic cells which is expressed in mice as differentiation marker on stem cells. Therefore, the role of CD150 as differentiation marker of human healthy and malignant hematopoietic stem cells (HSC), as well as possible CD150-dependent and –independent consequences of MV - stem cell interactions on functions of these cells will be investigated.