DKMS Stiftung Leben Spenden

Project Summary

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Epitope Editing to Enable Next-generation Non-genotoxic Conditioning Regimens for Hematopoietic Stem Cell Transplantation

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Hematopoietic stem cell transplantation (HSCT) is a life-saving treatment for blood cancers and genetic disorders. However, the current conditioning regimens – that exploit chemotherapy or radiation to prepare the bone marrow niche – cause severe toxicity, including organ damage, infertility, and increased risk of secondary cancers. Immune-based, non-genotoxic alternatives have been proposed, but they often harm both diseased and transplanted stem cells, limiting their effectiveness. We propose a novel strategy that combines immune-based conditioning with epitope-engineered stem cells that are resistant to targeted therapies. Using advanced gene-editing techniques, we modify specific proteins on stem cells to prevent recognition by therapeutic antibodies or CAR-T cells, minimizing the risk of transplant product depletion.

To optimize this strategy, we will first investigate how anti-KIT antibodies deplete stem cells in vivo - determining whether this occurs through blocking essential growth signals or active immune-mediated killing. Next, we will develop chimeric antigen receptor (CAR) T cells targeting KIT to achieve faster and more efficient stem cell depletion, potentially doubling as an anti-cancer treatment for myeloid malignancies and KIT-expressing solid tumors. Finally, we will explore novel transplantation protocols that replace bone marrow stem cells gradually over time, reducing the risk of severe blood count suppression and potentially allowing safer outpatient transplantation procedures.

By advancing this approach, we aim to transform HSCT and gene therapies into a safer, more accessible procedure, improving patient outcomes and expanding treatment options for those previously ineligible due to conditioning-related toxicity.