DKMS Stiftung Leben Spenden

Project Summary

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Systematic identification of minor histocompatibility antigens to inform GvHD outcomes

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Despite major advances achieved in the field of allogeneic hematopoietic cell transplantation, Graft-versus-Host-Disease (GvHD) remains one of the main sources of its failure. Minor histocompatibility antigens (mHAgs), arising from single-nucleotide differences between donor and recipient, have been long-acknowledged as the molecular basis of beneficial (graft-versus-leukemia, or GvL) and detrimental GvHD immune effects following transplantation from an HLA-matched donor. Conversely, non-identity at major HLA loci is considered the main reservoir for alloreactivity in the context of partially matched transplants. I have recently created a computational tool that makes it possible to comprehensively predict the full complement of mHAgs for any donor-recipient pair based on analysis and comparison of whole-coding DNA sequences from the donor versus the recipient. The availability of this analytic tool now opens the opportunity for us to gain knowledge of the individualized mHAg landscape, as I hypothesize that genome-wide alloantigen load is associated with the risk of developing GvHD and could potentially help refine current donor selection algorithms and enable personalized tailoring of post-transplant immunosuppression. I propose to undertake a large-scale collaborative sequencing effort of thousands of samples from donor-recipient pairs across different transplant platforms to determine if an immunogenomic-based GvHD prognostic tool can be created.