DKMS Stiftung Leben Spenden

Project Summary

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Single cell phenotypes and dynamics of measurable residual disease after allogeneic hematopoietic stem cell transplantation.

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Disease relapse remains the primary clinical hurdle for achieving long-term survival after allogeneic hematopoietic stem cell transplantation. Often, this results from immune escape by leukemia cells, enabling them to evade the graft-versus-leukemia effect, the mechanism by which donor-derived cells control residual disease. Currently, our understanding of when and how exactly immune escape after stem cell transplantation arises is incomplete. Additionally, we lack diagnostic tools to monitor the development of resistance towards donor-derived immune cell surveillance at the early stages when therapeutic interventions would have the highest chance of successful salvage.

In this project, I will develop a technology for detecting residual leukemia populations and their transcriptional profiles after stem cell transplantation, using single cell RNA sequencing in combination with targeted genotyping of natural barcodes that identify leukemia cells such as somatic mutations and single nucleotide polymorphisms. This will help uncover novel insights into the trajectories of disease recurrence after stem cell transplantation at the time of residual disease. Furthermore, it will lay the foundation for sensitive detection of post-transplant resistance phenotypes, which could enable early targeted intervention at time of incipient relapse, for example through specific immunomodulation, and may increase the chances of regaining effective graft-versus-leukemia mediated disease control.