Hematopoietic stem cells decline in function as they age. Although multiple studies have aimed to identify genes that are differentially expressed between young and aged murine HSCs, very few HSC aging genes have been consistently reported. These variations in aging gene lists are likely due to the heterogeneous trajectories of HSC aging, and in addition to variation resulting from experimental noise. Nevertheless, in a large meta-analysis, using expression data from many independent studies, we have recently been able to identify several dozen transcripts that are consistently affected during HSC aging. Interestingly, many of these HSC 'aging genes' encode for cell membrane molecules, and include novel cell surface receptors. For a large number of these newly identified genes no function in hematopoiesis has been described.

In this project the PhD student will molecularly and functionally study most consistent HSC aging related genes. The methods that will be used range from stem cell purification using multicolor flow-cytometry, transplantation into myeloablated recipient mice, qPRC and RNA-Seq based gene expression studies, viral transductions of young and aged to increase or decrease expression of key aging genes, ChiP-seq or ATAC-Seq experiments to determine epigenetic changes, proteome studies to search for protein interaction partners, and bioinformatic approaches to understand and interpret global genome-wide molecular data.

Our overall aim is to understand how HSCs age, and use the knowledge obtained in these studies to identify methods and intervention strategies to improve the functioning of aged HSCs.