

Transcriptional control of hematopoietic stem cell function during aging

Team Kastner-Chan (IGBMC, Strasbourg, France)

Hematopoiesis is the process by which hematopoietic stem cells (HSCs) give rise to a variety of immune and blood cell types. HSCs are unique, as they sit at the apex of a complex developmental program that must be active during the entire life of the animal, and adapt to variations in the organism physiology, notably during infection and aging. Our team is interested in understanding the function of a key group of transcription factors, the Ikaros family. Two of these factors, Ikaros and Helios, are highly expressed in HSCs. Published data for Ikaros, and our unpublished data for Helios, indicate that they control several aspects of HSC function, such as self-renewal or commitment to the lymphoid or myeloid lineages. Both factors are also regulated during aging. Several key questions remain: What are their key targets? Do they have specific or overlapping functions? Do they regulate the aging of the hematopoietic system? How do they influence transcriptional and epigenetic events in HSCs? The student will address these questions by studying the HSCs from single and double mutant mice for Ikaros and Helios. The student will use a broad range of techniques, ranging from manipulation of animals (HSC transplantations) to analysis and purification of cell populations by flow cytometry, ex-vivo cell cultures, genomic analyses (single cell RNA-seq, ChIP-seq and ATAC-seq) and bioinformatics.