Relapse of blood cancer is still the main cause of death in patients treated with hematopoietic stem cell transplantation. In order to improve the outcomes of these transplants and to offer patients a chance of a successful cure of their disease, new strategies to prevent and treat relapse are urgently needed. Making use of novel and cutting-edge technologies including CRISPR-based genetic editing, immunopeptidomics, T-cell receptor sequencing and transcriptomics, this project will pursue the generation of new biological tools for the targeting and elimination of leukemic cells by harnessing the anti-tumor capacity of the adaptive immune system. Alloreactive immune responses will be mined for relevant peptides and T-cell receptors, and new ways for intelligent modulation of antigen presentation by HLA molecules in leukemic cells will be explored. We expect our results to contribute to expanding the arsenal of anti-leukemia cellular and immunotherapy, providing new insights of translational potential for the benefit of blood cancer patients.