Recently, we have witnessed remarkable advancements in the treatment of hematological malignancies such as leukemias and lymphomas. Implementation of genetic engineering techniques led to the development of novel agents contributing to better prognosis for patients including cure for those previously relegated to palliative care. The most notable breakthrough is the advent of chimeric antigen receptor (CAR)-T cell therapy. This groundbreaking approach involves modifying a patient's T lymphocytes (a subset of white blood cells) to express a customized receptor known as a chimeric antigen receptor (CAR). This receptor enables the engineered T cells to selectively target and eliminate cancer cells. Notably, CAR-T therapy is associated with impressive response rates, ranging up to 54% for large B-cell lymphoma (LBCL) and up to 93% for B-cell acute lymphoblastic leukemia (B-ALL). Furthermore, a substantial proportion of patients experiencing disease remission exhibit long-lasting responses. Nevertheless, despite its efficacy, CAR-T therapy faces challenges. A significant subset of patients fails to respond to treatment, and there are associated adverse events (AEs) such as cytokine release syndrome (CRS), neurotoxicity, and persistent hematologic abnormalities. Unraveling the underlying reasons for variable treatment responses and AE susceptibility remains a complex task.

The pathogenesis of these phenomena likely involves intricate interactions occurring both systemically throughout the body and locally within affected tissues. Within the human body, myriad proteins, and small molecules (metabolites) are in constant flux, participating in diverse physiological or pathological processes. The collective assembly of proteins and metabolites constitutes the proteome and metabolome, respectively, and studying them falls under the purview of proteomics and metabolomics. Host proteome and metabolome serve as a fingerprint allowing to describe the reactions occurring in the organism and determining which substances are produced in excess, and which ones are lacking. Understanding the intricate interplay of these molecular components provides insights into disease mechanisms and facilitates the development of targeted therapeutic strategies.

Presently, little is known about the global impact of host proteome and metabolome on CAR-T efficacy and accompanying adverse events. This knowledge gap impedes efforts to maximize the efficacy of CAR-T therapy. The objective of this study is to better understand the proteomic and metabolomic profiles (collectively referred to as "omic profiles”) underlying the clinical phenotype of adult patients receiving chimeric CAR-T cell therapy. By elucidating the molecular underpinnings of clinical phenomena observed during CAR-T therapy, we aim to enhance the understanding of treatment response and ultimately optimize patient care strategies.

In this study, we will enroll adult patients receiving CAR-T cell therapy for relapsed/refractory CD19-positive B-cell lymphomas and B-ALL. Following informed consent, blood serum samples will be collected at multiple time points – before initiation of therapy and throughout the treatment course. Subsequent omics analysis of these samples utilizing mass spectrometry techniques will generate comprehensive molecular datasets. Bioinformatics techniques will then be employed to analyze these data in conjunction with clinical parameters.

Anticipated outcomes include the identification of omic profiles associated with clinical outcomes in patients undergoing CAR-T therapy. These insights promise to deepen our understanding of the molecular determinants of adverse events and treatment response, paving the way for personalized approaches to CAR-T therapy and optimizing patient outcomes.