Classical Hodgkin lymphoma (cHL) is a cancer of lymphatic system, occurring predominantly in young adults. Its microscopic picture is unusual – tumor cells constitute only 5-10% of the tumor mass and are outnumbered by surrounding reactive, infiltrating cells. Tumor cells of Hodglkin lymphoma (Reed-Sternberg cells, R-S) communicate bidirectionally with the microenvironment. Importantly, the stromal cells support them and stimulate their divisions. A specific type of infiltrating cells - macrophages – have recently received special attention, since increased number of cHL- associated macrophages were linked to inferior prognosis. However, the functional status of macrophages and their relationships with R-S cells in the cHL microenvironment remain undefined.

Standard chemotherapy induces durable remission in most cHL cases (75-80%), but fails long-term disease control in nearly one quarter of patients. The interim evaluation of treatment response currently represents the strongest predictor of treatment failure. Nevertheless, these predictions are incorrect in about 30% of patients. Our group has recently demonstrated that analysis of markers reflecting microenvironment's involvement – including number of infiltrating macrophages – substantially improves the predictions based on early treatment response.

Since the cellular composition and clinical characteristics of cHL is critically dependent on cell-intrinsic genetic abnormalities and cooperation with the microenvironment - **we hypothesize that more thorough characterization of the genetic background of R-S cells and mechanisms of communication with microenvironment would more precisely explain the biology of cHL relapse.** Thus, we plan to investigate the genetic abnormalities in isolated R-S- cells from patients with known early treatment response and available clinical follow up. Since macrophages are key players in the R-S cell microenvironment, influencing clinical behavior of the disease - we will also analyze the functional status of cHL- infiltrating macrophages. Understanding the R-S cell genetics and molecular patterns of communication between these cells and macrophages will elucidate the biological background of cHL treatment failues. In addition – these results will potentially identify mechanisms amenable to a selective pharmacologic intervention.