Analysis of Molecular and Microenvironment Landscape and Its Role in Drug Resistance in Waldenström macroglobulinemia (WM)

The objective of our project was to integrate the analysis of tumor microenvironment (TME) features with clinical, cytogenetic, and molecular data in MGUS, asymptomatic (aWM), and symptomatic WM (sWM) patients. It was postulated that WM samples may exhibit distinctive TME characteristics with regard to their composition, phenotype, organization, and interaction, which could drive disease evolution and resistance to therapy. On-slide imaging mass cytometry (IMC, Hyperion, 35-marker panel) was employed to investigate the characteristics of the TME in bone marrow (BM) samples. The preliminary data from different stages of the disease (MGUS, n=5; aWM, n=11; sWM, n=48) indicated inter-sample heterogeneity in the density, architecture, and composition of the TME, including cell populations such as T lymphocytes, NK cells, macrophages, and endothelial cells. The distribution of the 21 clusters identified through unsupervised analysis revealed significantly disparate proportions of clusters between MGUS, aWM, and sWM. A supervised analysis revealed that the proportion of CD11b+ cells was significantly lower in sWM compared to the other groups, while the proportion of Tregs, CD8+ T-cells, and endothelial cells was found to be higher in sWM/aWM patients compared to MGUS. Correlations with the main cytogenetic/molecular data and outcomes will be presented at the IWWM12 meeting.