CATHEPSIN S ALTERATIONS INDUCE A TUMOR-PROMOTING IMMUNE MICROENVIRONMENT IN FOLLICULAR LYMPHOMA

Background By targeted DNA sequencing of 305 diagnostic follicular lymphoma (FL) biopsies, we identified somatic mutations of Cathepsin S (CTSS) in 8% of cases (24/305), mostly clustered at Y132 (19/24) converting Y to D (16/19). Another 13% of FL had CTSS amplifications (37/286), associated with higher CTSS expression (P=0.05). CTSS is a cysteine protease that is highly expressed in endolysosomes of antigen presenting cells and malignant B-cells. CTSS is involved in proteolytic cleavage over time. We then tested the impact of CTSS overexpression could phenocopy this high CD4+ T-cell tumor-promoting immune response, which could be amplified within the microenvironment and substantially impact the biological and clinical course of the disease. Thus, aberrant CTSS activity is a promising biomarker and therapeutic target in FL and potentially also other tumors.

REFERENCES