Chronic myeloid leukemia is a clonal hematopoietic stem cell disorder in which leukemic cells display a distinctive shortened chromosome, the Philadelphia chromosome, generated from a reciprocal t(9:22) translocation. This translocation results in the head-to-tail fusion of the breakpoint cluster region (BCR) gene on chromosome 22 with the ABL proto-oncogene on chromosome 9. The encoded chimeric Bcr-Abl oncoprotein exhibits constitutive tyrosine kinase activity leading to its autophosphorylation and activation of multiple signaling molecules. As a consequence, Bcr-Abl leads to increased proliferation, inhibition of apoptosis and altered adhesion of leukemic blasts to bone marrow (BM) microenvironment. This is characterized by different populations of accessory stromal and T cells along with other factors including extracellular matrix and vessels. Microvesicles shed by cancer cells, released in the tumor-microenvironment, can bind to target cells, transfer signals between different cells to mediate biological functions and may have a key role in disease progression.

Recently, attention is being focused on cell-cell communication that involves membrane fragments called exosomes. Exosomes are small vesicles of 40-100 nm diameter of endosomal origin which are secreted from different cell types including cancer cells. Several studies in the last years have showed that exosomes are messengers in intercellular communication and that tumor cells can use these vesicles to affect immune function. Several studies reported activatory and inhibitory effects of cancer-exosomes on lymphocytes; differences are probably dependent on the exosomes molecular composition. Mounting evidence is pointing to exosomes as major participants in immune evasion through the expression of a large array of bioactive molecules. We studied the effects of exosomes shed by Chronic Myelogenous Leukemia (CML) cell line, K562, on the function of γδ T lymphocytes to better understand the interaction between cancer exosomes and the immune system. γδ T cells act as first-line defenders in innate immune responses against infected and tumor cells. γδ T cells are activated with HMBPP and IL2. Exosomes affect also the IFN-γ release by γδ T cells, suggesting that exosomes from CML have an inhibitory effect on lymphocytes function. These initial findings on the role of CML exosomes on γδ T cell shed new light on the ability of cancer cells to hide from immune system through an exosomes-mediated mechanism.

Bibliografia:
6. Altincicek B. et al. Cutting Edge: Human γδ T Cells Are Activated by Intermediates of the 2-Cmethyl-D-erythritol 4-phosphate Pathway of Isoprenoid Biosynthesis. J. Immunol 2001