Tumor Necrosis Factor-Related Apoptosis Inducing Ligand (TRAIL) is a cytokine of TNF family, which participates in the non-exclusive regulation of survival and proliferation of mainly hematopoietic cells. Shortly after its discovery it also brought significant attention as specific and potent inducer of apoptosis of cancer cells of various origins, and since then it has been investigated as a potential novel anti-tumor therapeutics. Recently, cancer stem cells (CSCs) were suggested to be a distinct subset of tumor cells that could be responsible at least in some tumors for their sustainment, recurrence and drug resistance. These cells in the "hierarchic" model of tumorigenesis thus represent an important and attractive target for efficient tumor therapy.

In this study we use several colorectal adenocarcinoma cell lines as an experimental model for the analysis of CSC-prone cultivation conditions on TRAIL-induced apoptosis of these cells. For enrichment of eventual cancer stem cells we cultivated cell lines in a serum-free medium, originally developed for cultivation of neural stem cells, and assessed the expression of putative CSC markers CD133 and ABCG2 by flow cytometry (FACS). Simultaneously, we tested the expression of TRAIL receptors and susceptibility to TRAIL-induced apoptosis in these cells. We observed correlation between appearance of stem cell-like signs (spheroid formation, expression of CD133) and increased resistance of these cells to TRAIL-induced apoptosis. Profiling of surface proteins revealed that compromised apoptosis was not inherent in expression of death receptors, since these were mostly upregulated after serum-free cultivation.

Recently it has been reported, that fibroblasts isolated from tumor stroma could induce de-differenitated, stem cells-like phenotype in normal human keratinocytes and thus these stromal cells represented an attractive tool for the analysis of their effect on TRAIL-induced apoptosis of co-cultivated tumor e.g. colon cancer cells. In our initial attempt we analyzed effect of both normal skin and tumor stroma-derived (basal cell carcinoma, spinal cell carcinoma and benign fibrous histiocytoma ) fibroblasts on TRAIL-induced apoptotic signaling in selected colorectal adenocarcinoma cell lines. We observed no unequivocal effect of either stromal or normal fibroblasts on TRAIL-induced apoptotic signaling in two co-cultivated colon cancer cell lines HCT 116 and DLD-1. We cannot however exclude possible cancer cell-type specific influence of stromal cells on TRAIL-induced apoptosis and thus further analysis using different cancer cell lines is required.