

Oral presentation

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MMP-7 inhibits CTL – tumor cell interaction

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MMP-7, the smallest member of the MMP-family, is a zinc-dependent metalloproteinase and is overexpressed in colon cancer and many other human cancers. Along with its prometastatic function, a fundamental role for MMP-7 has also been established in early tumor development, but the mechanism by which MMP-7 contributes to this, is still unknown.

Tumor specific cytotoxic T cells (CTLs) play a critical role in the control of tumor growth. They can induce apoptosis by CD95 as well as perforin/granzyme mediated pathways. Loss of CD95 may contribute to apoptosis resistance and immune escape of tumor cells leading to successful tumor outgrowth.

In our project we analyzed MMP-7 for its influence on CD95 mediated apoptosis and the cytolytic effector functions of CTLs. Furthermore we investigated the influence of MMP-7 cleavage activity on the adhesion and deadhesion of peptide specific CTL's to tumor targets.

In a cleavage assay with recombinant CD95 protein, we could show that MMP-7, cleaved approximately 2–3 kDa from the extracellular N-terminal end of CD95. In coculture experiments with ⁵¹Cr-labeled HepG2-cells, we found a significant decrease of cytotoxic action of peptide specific CTLs in the presence of MMP-7. In addition MMP-7 leads to a higher adhesion of CTLs and inhibits their deadhesion from HepG2 cells. Considering that CTL's are serial killers, alteration in adhesion/deadhesion functions can be detrimental for tumor specific CTL killing.

Our results show, that MMP-7 can contribute to the apoptosis resistance of tumor cells by different mechanisms. These activities may explain the contribution of MMP-7 to early tumor growth.