

POSTER PRESENTATION

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Constitutive expression and roles of interleukin-8 in canine hemangiosarcoma

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Background

Interleukin-8 (IL-8) is a pleotropic cytokine that promotes tumor cell proliferation and survival, inflammation, and angiogenesis; however, its role in the pathogenesis of canine hemangiosarcoma (HSA) is unknown.

Materials and methods

Six canine hemangiosarcoma (HSA) cell lines and 24 primary and metastatic HSA tumor tissues were used to investigate the biological functions of IL-8. Roles of IL-8 were examined by analyzing microarray data, qRT-PCR, ELISA, MTS cell proliferation assay, and sphere-forming assay.

Results

IL-8 mRNA expression was variable among the tissue samples and both IL-8 mRNA and protein were variable among the cell lines. In contrast, IL-8 receptor mRNA and protein showed minimal variance. "IL-8 high" and "IL-8 low" groups were defined from the HSA tumor samples based on gene expression profiles. The "IL-8 high" group was associated with a "reactive microenvironment," showing enrichment of coagulation, inflammation, and fibrosis networks. However, IL-8 added exogenously and IL-8 blockade using neutralizing antibodies had no effect on HSA cell proliferation, despite apparent response to these signals at the level of gene expression. Similarly, neither addition nor blockade of IL-8 protected cells from apoptosis. IL-8 mRNA was elevated in HSA cancer stem cells, but exogenous IL-8 attenuated self-renewal of these cells.

Conclusion

The results of this study suggest that IL-8 is a driver of tumor heterogeneity, steering cells away from self-renewal and towards partial differentiation. It also could act to recruit (or produce from the tumor) inflammatory and pro-angiogenic cells to the microenvironment. We are testing this hypothesis in a robust xenograft model. These experiments will establish if IL-8 plays a role in progression and metastasis of canine HSA, and allow us to define the therapeutic potential of IL-8 blockade.

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