ABSTRACTS

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Canine mammary tumors: the metastatic potential can be assessed by expression analysis of connective tissue modulators

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OBJECTIVES AND METHODS: Mammary tumours are the most important neoplasm in the female dog¹. Invasiveness and neovascularisation, which are the main processes in tumour progression, need a cleavage of extracellular matrix to allow migration of cells, so called tissue remodelling. This connective tissue remodelling is a prerequisite for invasiveness and angiogenesis, which are crucial processes in the progression of canine mammary tumours (CMT). In the present study, the impact of the peptide hormone relaxin (RLX) and its receptors on matrix-metalloproteinase (MMP) expression, genesis of metastases and survival was analysed using the qRT-PCR and immunohistochemistry of CMT samples from 59 bitches from TNM stages I to III².

RESULTS: Local RLX mRNA expression and RLX plasma levels had no prognostic value, but the mRNA expressions of RLX, RXFP1 and MMP-2 expression were positively correlated. The main RLX expression was seen in myoepithelial cells, whereas the strongest RXFP1 signals came from epithelial cells which are known to express MMP-2 and MMP-9³. However, high mRNA levels of the RLX receptor RXFP1 were an independent marker of metastatic potential, with a more than fifteen-fold risk increase, and a predictor for shorter survival.

CONCLUSION: The correlation of the expression intensities of the three factors, RLX, RXFP1 and MMP-2, involved in connective tissue remodelling indicates a common pathogenetic linkage and an autonomous stimulation of metastasis via RLX and RXFP1. The co-localisation of the expression sites of RXP1 and MMPs in the epithelial cells propose that these cells can react to a RLX stimulus with an increased synthesis of MMP, which is a key feature of malignant invasion and dissemination. Thus, RXFP1 is proposed as a new early marker of metastatic potential in CMT and a possible therapeutic target (RXFP1-antagonist). In general, the analysis of early metastatic markers through qRT-PCR can become a helpful tool for routine diagnosis of CMT, if certain basic requirements for sampling and assay design are considered.