World Academy of Science, Engineering and Technology
International Journal of Animal and Veterinary Sciences
Vol:16, No:07, 2022

CSPG4 Molecular Target in Canine Melanoma, Osteosarcoma and Mammary Tumors for Novel Therapeutic Strategies

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Abstract : Canine and human melanoma, osteosarcoma (OSA), and mammary carcinomas are aggressive tumors with common characteristics making dogs a good model for comparative oncology. Novel therapeutic strategies against these tumors could be useful to both species. In humans, chondroitin sulphate proteoglycan 4 (CSPG4) is a marker involved in tumor progression and could be a candidate target for immunotherapy. The anti-CSPG4 DNA electrovaccination has shown to be an effective approach for canine malignant melanoma (CMM) [1]. An immunohistochemistry evaluation of CSPG4 expression in tumour tissue is generally performed prior to electrovaccination. To assess the possibility to perform a rapid molecular evaluation and in order to validate these spontaneous canine tumors as the model for human studies, we investigate the CSPG4 gene expression by RT qPCR in CMM, OSA, and canine mammary tumors (CMT). The total RNA was extracted from RNAlater stored tissue samples (CMM n=16; OSA n=13; CMT n=6; five paired normal tissues for CMM, five paired normal tissues for OSA and one paired normal tissue for CMT), retro-transcribed and then analyzed by duplex RT-qPCR using two different TaqMan assays for the target gene CSPG4 and the internal reference gene (RG) Ribosomal Protein S19 (RPS19). RPS19 was selected from a panel of 9 candidate RGs, according to NormFinder analysis following the protocol already described [2]. Relative expression was analyzed by CFX Maestro™ Software. Student t-test and ANOVA were performed (significance set at $P<0.05$). Results showed that gene expression of CSPG4 in OSA tissues is significantly increased by 3-4 folds when compared to controls. In CMT, gene expression of the target was increased from 1.5 to 19.9 folds. In melanoma, although an increasing trend was observed, no significant differences between the two groups were highlighted. Immunohistochemistry analysis of the two cancer types showed that the expression of CSPG4 within CMM is concentrated in isles of cells compared to OSA, where the distribution of positive cells is homogeneous. This evidence could explain the differences in gene expression results.CSPG4 immunohistochemistry evaluation in mammary carcinoma is in progress. The evidence of CSPG4 expression in a different type of canine tumors opens the way to the possibility of extending the CSPG4 immunotherapy marker in CMM, OSA, and CMT and may have an impact to translate this strategy modality to human oncology.

Keywords : canine melanoma, canine mammary carcinomas, canine osteosarcoma, CSPG4, gene expression, immunotherapy
Conference Title : ICVCO 2022 : International Conference on Veterinary and Comparative Oncology
Conference Location : Copenhagen, Denmark
Conference Dates : July 19-20, 2022