

Example of adequate research report

New insights into the pathogenesis and treatment of canine thyroid carcinoma

M Campos¹, J Doe²

¹Department of Medicine and Clinical Biology of Small Animals, Ghent University, Belgium.

²Department of Veterinary Medical Imaging, Utrecht University, The Netherlands.

The goals of this research were to investigate the presence of mutations and differences in relative expression of candidate genes, to explore new therapeutic targets and to investigate clinical, pathological and immunohistochemical prognostic markers in canine thyroid cancer.

Medical records were reviewed (1986-2013) and dogs diagnosed with histologically confirmed thyroid neoplasia were included.

Each tumor section (n=74) was reviewed and scored by a board-certified pathologist (histologic type, % necrosis, % hemorrhage, nuclear pleomorphism, mitotic index, evidence of vascular or capsular invasion) and immunohistochemistry was performed for calcitonin, Ki-67, E-cadherin, cox-2, VEGF, P-gp and p53. Differentiation between follicular cell tumors and medullary tumors was based on immunohistochemistry for calcitonin. RNA was isolated from snap-frozen left-over tumor samples (n=59) and healthy thyroids (n=10) and sequencing was performed for mutation hotspots of RAS (K, H and N), PIK3CA, RET and BRAF genes and for the complete coding region of PTEN. Quantitative RT-PCR was performed for VEGFR-1, VEGFR-2, EGFR, PIK3CA, PIK3CB, PTEN, PDPK1, Akt1, Akt2, cox-2 and calcitonin.

All tumors were carcinomas; 54 were follicular thyroid carcinomas (FTC) and 20 were medullary thyroid carcinomas (MTC). In 1 FTC and 1 MTC, 2 missense mutations (G12R and E63K respectively) were found in K-RAS.

Compared to healthy thyroid, FTC showed higher expression of VEGFR-1, VEGFR-2, EGFR, PIK3CA, Akt1, Akt2 and PDPK1; MTC showed higher expression of VEGFR-1, EGFR, PIK3CA, Akt2, PDPK1 and calcitonin.

80% of FTC and all MTC exhibited a very high percentage (76-100%) of neoplastic cells immunopositive for VEGF. 13% of FTC and 50% of MTC presented cox-2 expression. 7% of FTC and 70% of MTC presented P-gp expression. No tumor was immunopositive for p53.

46 dogs (30 FTC and 16 MTC; stage I-III) underwent thyroidectomy and were included in a survival analysis. Outcome was comparable between FTC and MTC. Inappetence ($P=0.007$), histologic vascular invasion ($P=0.027$) and surgical vascular invasion ($P=0.005$) were associated with shorter disease-free survival. Histologic vascular invasion ($P=0.009$), large tumor diameter ($P=0.004$) and high Ki-67 labeling index ($P=0.004$) were associated with shorter time to metastases.

Relative expression of candidate genes suggests PI3K/Akt pathway activation in FTC. VEGF is a potential therapeutic target in both FTC and MTC, while cox-2 and P-gp seem to be attractive molecular targets in canine MTC. Intensive monitoring and adjunctive therapy might be indicated when negative prognostic factors are identified.