

Discovering the role of ADAM17 pathway in dog and cat pathophysiology

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Objectives: ADAM17, from the disintegrin and metalloproteinase (ADAM) family, also called tumor necrosis factor converting enzyme (TACE), is a pleiotropic protease involved in numerous diseases. ADAM17 pathway has been extensively studied in mouse models and in human diseases, but very poorly in dog and never in cat pathophysiology. Therefore, this project intends to unveil the roles of ADAM17 pathway in impactful canine and feline inflammatory disorders, cancers and in obesity for the purpose of finding novel prognostic factors and/or therapeutic targets.

Material and Methods: A characterization of the gene and/or protein expression level of ADAM17 pathway members will be performed in samples (serum and specific tissues) from canine and feline patients with selected inflammatory diseases, cancers and obesity versus correspondent healthy controls from the Veterinary Hospital of Faculty of Veterinary Medicine of Lusófona University. A correlation analysis with clinically relevant parameters and the disease stage will be performed. The study will be complemented with *in vitro* cellular models of the same diseases, where the expression level of ADAM17 pathway members and ADAM17 substrates level of release will be compared between diseased and steady state conditions. In these cellular models the effects of chemically blocking ADAM17 pathway will be also assessed.

Results: We expect to demonstrate and characterize, for the first time, the involvement of ADAM17 pathway in highly prevalent and/or socio-economical important canine and feline inflammatory diseases, cancers, and in obesity. Moreover, we intend to identify which ADAM17 pathway members may be more relevant to target and expect to show the mechanisms mediated by ADAM17 pathway in the studied conditions.

Conclusion: This work may help on the development of novel prognostic and therapeutic strategies for important canine and feline diseases, and therefore may improve the dog's and cat's health and welfare and owner's well-being, having a positive impact on society.

Keywords: ADAM17/TACE, Dogs and cats, Inflammatory diseases, Cancer, Obesity.