

Mammary tumors are the second most common canine cancer occurring mainly in females, accounting for 52% of all diagnosed cancers. These tumors are more than 80% malignant. One of the potential causes of cancer development, as well as tumor transformation in dogs, may be mutations found in mitochondrial DNA (mtDNA).

Mitochondria are vital organelles that form an intracellular dynamic network in the cytosol of eukaryotic cells. Disturbance of mitochondrial function can cause disruption in the protein folding environment and increased unfolded proteins and proteotoxicity.

Mitochondrial proteome comprises over 1500 proteins that are encoded by nuclear genes and translocated to the mitochondria to maintain mitochondrial function. However, only 13 polypeptides are encoded within mtDNA. Mutations in the mtDNA cause distinct metabolic and epigenomic changes at different heteroplasmy levels, potentially explaining transcriptional and phenotypic variability of mitochondrial disease.

Our knowledge of protein expression involved in the development and progression of canine tumors is limited, particularly in large-scale analysis. There are only rare reports on the role of mutations in mtDNA in dogs of one of the most common cancers - mammary gland tumors.

Issues such as re-sequencing of mtDNA genomes, assessment of methylation of mtDNA regions, as well as identification of proteins that are potential biomarkers of malignant transformation of mammary gland tumors in dogs have not yet been clarified, and therefore there are no reports on this subject in the literature.

There are some gaps in research aimed at understanding the pathway of cancer development in dogs, determined by the mitochondrial system of interaction and regulation of gene and protein expression that affect the ubiquitination profile of the transcriptome and proteome in cancer cells and its malignancy. Understanding the variability in regulatory proteins expression induced by a mutation of the mitochondrial gene may be the basis for inventing a new cancer treatment strategy. The implementation of new biomarkers in cancer diagnostics may have great potential for cancer characterization and treatment.

The combination of genomics and proteomic techniques in the proposed project can help in the determination of new prognostic and / or diagnostic markers. In addition, it will enable the recognition of biomarkers occurring in mammary gland tumors in dogs that can be used in the prospective screening of carcinogenic predisposition in dogs.