

## **Mitochondrial DNA alterations in malignant tumours of spleen in dogs - assessment of their role and diagnostic value**

Currently, the occurrence of various types of tumours in dogs, which are the leading cause of death in these animals, is increasingly observed. The development of carcinoma is resulted by many reasons, among which genetic and environmental factors are important. At present, the diagnosis of cancerous diseases in dogs is based mainly on the histopathological evaluation. In contrast to genetic tests which are performed rarely. Only with regard to frequently reported tumours, single reports referring to changes in the nuclear genome (nDNA) are reported. However, it should be noted that the vast majority of cells, apart from nDNA, also have genetic material in the form of the mitochondrial DNA (mtDNA). Mitochondria play a very important role in the cell, including predominant responsibility of the production of energy in the form of ATP (~ 90%), the regulation of calcium levels and apoptosis. Therefore, mtDNA disturbances adversely effect on cell homeostasis, leading to disturbances in many cellular processes. The instability of cells combined with a disturbance in the apoptotic process leads to the accumulation of abnormal cells without their control, which is an important cause of the cancer formation.

The observed increase in scientific reports in the field of oncogenomics indicates the presence of changes in the form of mutations, polymorphisms and heteroplasmy in mtDNA in various cancers (including breast, prostate, liver, lung, bladder) in humans. However, research on mitochondrial oncogenomics in dogs is currently very limited.

Among rare tumours, both in dogs and in humans, there are malignant tumours of the spleen, which are characterised by a severe course and a high mortality rate among patients. At present, little is known about the causes of this disease, apart from a few recent reports of nDNA changes. Therefore, research of the molecular changes occurring in mtDNA in these cancers may be the missing link that allows for a better understanding of the aetiology of the disease.

Planned research includes the analysis of biological material including a malignant tumour of the spleen, healthy tissue and blood from each sick dog. The advantage of the proposed research work is the analysis based on the re-sequencing of entire mitochondrial genomes, not just its fragments, which will allow to conduct a detailed analysis of the genetic material. This workflow allows the comparison of changes in the mitochondrial genome in several tissues in the same individual, indicating changes associated with the disease.

At the moment, the increased development of oncogenomics of domestic dog shows that there is a need to continue work that would allow to recognise the molecular causes of the disease. As a consequence, the obtained results may be used in the diagnosis of tumours, which would significantly improve the time of diagnosis and thus, the survival of animals.