

## **Description for the general public**

Domesticated dogs (*Canis lupus familiaris*) are excellent models of human complex diseases for several reasons, including their easy accessibility and prominent status in diverse cultures. They are considered to be a “family member”. In western countries the amount of money spent annually on dog health care, is second only to humans in the level of health care received. That, combined with the availability of the complete genome sequence, the shared environment of owners and dogs, can be exploited for epidemiological studies of diseases common to dogs and humans. Next to humans, domesticated dogs have the most phenotypic diversity and known naturally-occurring diseases of all land mammals. For example, the average weight of Chihuahuas and English Mastiffs differs by 65-fold. Dogs share over ~650 Mb of ancestral sequence in common with humans that is absent in mice, and canine DNA and protein sequence is more similar to human than mouse is. Thus, many aspects of human biology are presumably more relevant in dogs than in mice. Approximately 400 inherited diseases similar to those of humans are characterized in dogs, including complex disorders such as cancers, heart disease, and neurological disorders. Indeed, more than 40 naturally occurring canine diseases have mutations in a homologous human gene associated with a similar disease. Additionally, depending on breed size, dogs have a five to eight-fold accelerated aging process compared to humans. Aged dogs like beagles develop losses in executive function, learning and memory. In parallel, dogs naturally accumulate several types of neuropathology consistent with human brain aging and Alzheimer’s disease. Moreover, dogs are kept as companion animals well into their old age. The most recently available data shows that ~45% of companion dogs were >6 years old, the human equivalent of ~60-95. In addition, human kind has a strong desire to cure diseases of the dog. Thus, dog models hold great promise for accelerating the understanding of genetic and environmental contributions to human disease, particularly those that are chronic or associated with aging.

Diabetes mellitus is common disease in dogs. The most common form of diabetes in dogs resembles type 1 diabetes in humans. Studies suggest that genetics, an immune-mediated component, and environmental factors are involved in the development of diabetes in dogs. A variant of gestational diabetes also occurs in dogs. Diabetes mellitus can be produced readily in dogs by any of several chemical or surgical methods, and in recent years genetically diabetic dogs have also become available for study. These models are suitable for investigating a wide variety of questions relevant to human diabetes mellitus. Especially noteworthy is the occurrence in diabetic dogs of a number of ocular and other complications typical of human diabetes mellitus.

Tear film is a thin liquid layer covering the eye, being responsible for its protection, lubrication and nutrition. All components of the tear film in diabetes are altered resulting in abnormal tear film breakup time (BUT), fluorescein staining, Schirmer I testing and Rose Bengal or Lissamine Green staining. The severity of the tear film dysfunction correlates with the severity of the diabetic retinopathy, with proliferative diabetic changes associated with a more diminished tear film function. In addition conjunctival impression cytology demonstrates a higher grade of conjunctival squamous metaplasia as well as a lower goblet cell density in the diabetic patients. These changes have been related to the status of metabolic control and stage of diabetic retinopathy.

In this project we try to deepen our knowledge of tear film protein composition – called proteome, in diabetic dogs, with aim of identifying proteins that would be specific for the disease – so called biomarkers. They could be later on used for both diagnostic or treatment of dog patients, as well as further research concerning human diabetes in animal model. It should be underlined, that similar research has been already successfully conducted in human patients, providing valuable data for both clinical and research appliances. For their comparison with dog model, analogic study is required.