Probable molecular mechanism of transmission of the spirochete *Borrelia burgdorferi* sensu lato - comparative studies of the transcriptome and proteome of *Ixodes ricinus* and *Dermacentor reticulatus* ticks

Ticks are blood-feeding ectoparasites of vertebrates that can transmit a variety of pathogens, including bacteria, viruses and fungi. Tick-borne pathogens are the cause of chronic and troublesome diseases that often lead to permanent health damage. In the most severe cases, they even lead to the death of infected humans and animals. The number of diagnosed cases of tick-borne diseases (TBD) is constantly increasing. This is partly due to the increasing geographical spread of the parasites and pathogens they transmit.

In Poland, the predominant species are *Ixodes ricinus* and *Dermacentor reticulatus*, with *I. ricinus* playing the main role in the transmission of pathogens. *I. ricinus* is known to transmit a variety of pathogens of importance to both human and veterinary medicine, including the *Borrelia burgdorferi* sensu lato (s.l.) complex, the causative agent of Lyme disease (LD). In contrast to *I. ricinus*, the transmission of the LD pathogen by *D. reticulatus* ticks has not been confirmed. *D. reticulatus* is a tick species whose geographic range is expanding in Europe, increasing the potential for the spread of microorganisms of great importance to the veterinary and medical fields. LD is the most common tick-borne zoonosis and is considered the most common tick-borne infectious disease in North America and temperate Eurasian countries. Between 2015 and 2019, 94,715 cases of LD were reported in Poland. The ecological conditions are favourable for the increase in LD cases. It is therefore predicted that this will be a persistent public health problem. Due to the high variability of antigen proteins, the development of an effective vaccine against *Borrelia* is associated with great effort. More studies need to be conducted to effectively combat TBD.

Ticks are not only passive vectors of pathogens. **The interactions between the tick, the pathogen and the host are complex.** To act as a vector for a horizontally persistent pathogen, a tick species must have the ability to ingest the pathogen during the larval or nymphal stage. The vector must be able to retain the pathogen through the moulting stages and transfer it to a host during feeding in the next nymphal stage or in the adult stage. Arthropods have evolved to coexist with various microorganisms that can be efficiently transmitted to humans and other vertebrates. **The midgut serves as the first site of interaction between ticks and pathogens and is probably the most important organ for pathogen survival and multiplication. On the other hand, the salivary glands are the most important site for the transmission of pathogens to the vertebrate host.** The pathogens manipulate the biological processes of the ticks to facilitate infection, while the ticks activate innate, non-specific immunity to limit infection and maintain their feeding and vector competence, ensuring the survival of both the ticks and the pathogens. **However, the specific molecular mechanisms that make certain tick species suitable vectors for certain pathogens are not yet fully understood.**

The aim of our study is to investigate the effects of the presence of *B. burgdorferi* s. l. on the infection-related organs (salivary glands and midgut) of *I. ricinus* and *D. reticulatus* ticks. To achieve this goal, a transcriptomic and proteomic approach using high-throughput methods (RNA sequencing and liquid chromatography coupled with tandem mass spectrometry) will be applied. **Investigating differences between the transcriptomic and proteomic profiles of the infection-related organs (salivary glands and midgut) of *I. ricinus* and *D. reticulatus* ticks in the presence of *B. burgdorferi* s.l. could provide data for a better understanding of tick-pathogen interactions**. The pathogens are ingested with the blood meal of infected hosts and must evade the tick's immune responses on their way through the tick's body. The immune system of ticks relies exclusively on innate immune responses. Differences in vector competence between tick species can be probably related to different mechanisms of innate immunity. The scientific goal of the project is closely related to recent trends in global research aimed at understanding tick-pathogen relationships.

The results of such analyses will provide additional data to explain the different vector competence of *I. ricinus* and *D. reticulatus* for *B. burgdorferi* s.l. The conduct of the proposed research is fully justified as LD is a serious public health problem. The use of currently available modern research methods (RNA-seq, LC-MS/MS) could provide a wide range of scientists and the public with further data on the possible molecular mechanisms occurring in ticks that can transmit *B. burgdorferi* s.l. and reveal specific genes and proteins responsible for vector competence.