Research line (Laboratory of Genomics and Proteomics of Disease Vectors)

Protease inhibitors at the tick host interface

The relevance of tick salivary protease inhibitors for therapeutics development is increasingly highlighted as more and more proteins target host hemostasis, inflammation and immunity with a unique and highly-specific mechanism of action (1). We have characterized several tick salivary proteins that target vertebrate host immune reactions (2), the coagulation cascade (3), acute inflammation (4) and other host physiological pathways.

Our previous studies of *Ixodes ricinus* salivary glands and saliva allowed the isolation of proteins (i.e. serine and cysteine protease inhibitors) with unique and stringent target specificity as far as it concerns their action to the vertebrate host. By characterizing the pharmacological actions of tick salivary proteins, our overall goal is to improve our knowledge of basic molecular mechanisms at the tick-host interface, where pathogen transmission takes place, and to describe/characterize potential new therapeutic molecules derived from tick saliva. In addition, our transcriptomic and proteomic data will be used to 'mine' new antigens for anti-tick vaccine development and the development of diagnostic tests for exposure to ticks.

Non-coding RNAs in cell to cell communication at the tick-host interface

We have demonstrated that tick extracellular vesicles enable arthropod feeding and promote distinct outcomes of bacterial infection (5). We have previously demonstrated that tick microRNAs are found in tick salivary secretion, and they bear typical modifications which are characteristic of their exosomal origin (6). In the same work we have predicted that tick microRNAs target genes of the vertebrate host which are of medical relevance, for example the oncogene BRAF. We explore the detailed mechanism with which they affect vertebrate host gene expression (7), not only to improve our understanding of the molecular events that mediate pathogen transmission at the tick-host interface, but also towards drug development (for example the effect of tick microRNAs which target BRAF in preventing melanoma development).

While non-coding RNAs (ncRNAs) have been studied mostly in humans and animals that are used in medical research, there is very little research on ncRNAs in host-parasite interactions in arthropods (8). Many of the functions of ncRNAs in arthropods are unclear; our work hypothesis is that vector ncRNAs can be transported in salivary exosomes to the host. In the host cells they affect host homeostatic reactions by interacting with endogenous host mRNAs. Our data, paves the way for future mechanistic studies focusing on evaluating the biological functions of tick non-coding RNAs. By understanding the function of these tick ncRNAs at the tick-vertebrate host interface we will also support the development of novel gene expression modulators for treating different human diseases.

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