Abstract (EN)

Ticks are ectoparasites found worldwide that feed on the blood of their hosts and transmit several important pathogens to humans and domestic animals. Tick saliva contains bioactive molecules that are injected into the host tissue to aid in successful blood feeding. Among these molecules, proteinaceous protease inhibitors are being extensively studied for their potential biomedical applications.

This work focuses on novel protease inhibitors from the saliva of the ticks *Ixodes ricinus*, vector of Lyme disease and tick-borne encephalitis, and *Ornithodorus moubata*, vector of relapsing fever and African swine fever. Research has focused on the biochemical and structural characterization of three members of the protease inhibitor families of cystatins, serpins, and tyropins, and has attempted to elucidate their biological function in tick-host interactions.

Cystatin OmC2 from *O. moubata* was identified as a broad-spectrum inhibitor of host cysteine cathepsins with both endopeptidase and exopeptidase activity. Crystal structure determination allowed description of the relationship between the structure of OmC2 and its inhibitory specificity. The ability of OmC2 to modulate the host immune response was demonstrated in bioassays and a suppressive effect on *O. moubata* in vaccination experiments. The serpin IRS-2 from *I. ricinus* is a potent inhibitor of two host immune cell serine proteases, chymase and cathepsin G. As a result, IRS-2 inhibits the processes of platelet aggregation and acute inflammation in which these proteases are involved. The functional specificity of the IRS-2 reactive center was analyzed by crystal structure analysis. The tyropin IrThy from *I. ricinus* has a narrow inhibitory specificity limited to only three host cysteine cathepsins with endopeptidase activity that are involved in immune responses. The unique inhibitory specificity was explained by the solved NMR structure, and the specificity was found to be further modulated by glycosaminoglycans from host tissues.

The thesis provides new insights into the mechanism of molecular interactions between ticks and hosts, as well as bioactive proteins that could serve as antigens for the development of anti-tick vaccines and drugs with unique pharmacological effects.