Structural and functional studies of key proteins involved in the interaction between ticks, mammals, and pathogens, with a focus on the OspC protein from *Borrelia*

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Lyme disease, caused by spirochetes of the genus *Borrelia*, is a zoonotic disease affecting the entire northern hemisphere of the Earth, posing a significant challenge to health services. Despite ongoing research on the causative agents of Lyme disease since the 1980s, the lack of an effective vaccine and the high number of cases maintain constant interest in this disease in scientific community. The spirochetes of the genus *Borrelia* are distinguished by their ability to produce numerous surface lipoproteins, which play a key role at various stages of their life cycle. In particular, the surface protein OspC (*Outer Surface Protein C)* plays an important role in the initial phases of infection, enabling effective adaptation of the spirochete in the mammalian body. Studies have shown that OspC interacts with mammalian bloodstream proteins and tick saliva proteins to promote effective infection and pathogen survival.

The aim of this study was an in-depth analysis of the OspC proteins from various *Borrelia* species. The research focused on identifying differences between these proteins and analyzing interactions with selected derived ligands from both ticks and humans. The *in vitro* interactions of OspC with human fibrinogen and Iric proteins, homologues of Salp15 (*Salivary Gland Protein 15*), present in tick saliva were analyzed using MST technology, which enabled a precise assessment of these interactions.

The obtained research results revealed new interactions between OspC and fibrinogen, and the values of K_d binding constants at the nanomolar level indicated their strong affinity. Based on SAXS data, a spatial model of the OspC-fibrinogen complex was proposed. Interactions of OspC with Iric proteins were also confirmed and a binding site for the Iric protein by OspC was proposed. The developed protocols for the production of OspC and Iric proteins made it possible to obtain high-quality protein preparations, also used for structural studies. Although crystallization screening tests did not result in the production of an OspC-Iric protein complex, the OspC structure from *Borrelia garinii* added a new *Borrelia* species to the database. The optimizations carried out during the presented research may contribute to further attempts to crystallize the above complex.

These results provide valuable information on the diversity of OspC proteins, their structure and interactions with various ligands, which is crucial for understanding the mechanisms of Lyme disease pathogenesis. These discoveries may contribute to the development of effective preventive and therapeutic methods, constituting an important contribution to the dynamically developing research on Lyme disease and its pathogens, and also highlight the need to continue further research in this area.