Abstract

Francisella tularensis, sometimes called as a „stealth pathogen“, causes zoonotic disease tularemia. Uniqueness of this intracellular bacterium is due to its ability to infect, survive and replicate within host phagocytic cells and evade the host immune response. Because of its extreme infectivity, ability to cause disease via inhalation route, and absence of a vaccine licensed for human use, *F. tularensis* is classified as a potent biothreat agent. The escape from phagosome plays a key role in the virulence of the bacterium. Type VI secretion system and *F. tularensis* pathogenicity island proteins are involved in this process; however, the exact molecular virulence mechanisms of *F. tularensis* are not fully characterized yet. The aim of this work was to characterize host-pathogen protein-protein interactions, which direct the infection process to *F. tularensis* benefits.

The minimal experimental approach was selected for identification of protein-protein interaction between the host and the pathogen. The selected secreted proteins from FPI of *F. tularensis* subspecies *novicida* were fused with an epitope anchor FLAG tag and expressed in HEK 293T cell line. Interaction partners were identified by affinity purification followed by nanoLC-MS/MS analysis.

The data indicate that the bacterial protein IglJ interacts with BAG family molecular chaperone regulator 2 and mitochondrial apoptosis-inducing factor 1. The interaction between IglJ and AIF may have impact upon the intrinsic pathway of apoptosis in host cell. CLIP-associating protein 1, ATP-citrate synthase, Ran GTPase-activating protein 1 and Exocyst complex component 2 were identified as interacting partners for VgrG. VgrG protein may affect through the interaction with ATP citrate synthase acetylation of proteins or may reduce the levels of NOS and ROS in the host cell. Some components of the exocyst complex are involved in autophagy or in phagosome maturation. Therefore, the interaction of VgrG protein of *F. tularensis* with this pathway may contribute to the ability of bacteria to survive in phagosomes or in the cytosól of host cell.

Key words: *F. tularensis*, effector protein, VgrG protein, IglJ protein, protein-protein interaction, host-pathogen interaction, AP-MS, SILAC