The important role of Atg5 in the pathogenesis of tularemia

Ina Kelava[1], Mirna Mihelčić[1], Mateja Ožanič[1], Valentina Marečić[1], Maša Knežević[1], Marija Ćurlin[2], Sanja Štifter[1], Anders Sjöstedt[3] and Marina Šantić[1]

[1]University of Rijeka, Croatia
[2]University of Zagreb, Croatia
[3]Umeå University, Sweden

Statement of the Problem: *Francisella tularensis* is a gram-negative, facultative intracellular bacterium that causes tularemia in humans and animals. *Francisella* escapes the phagosome early after infection and reaches the macrophage cytosol where the bacteria replicate. After the replication, bacteria re-enter the double-membrane vacuole via autophagy. The role of autophagy in the replication of this cytosolic pathogen has not been fully elucidated. Previous studies showed that *Francisella* avoids degradation via autophagy mechanism *in vitro*. Also, Atg5-independent autophagy provides nutrients that support *Francisella* intracellular replication *in vitro*. Although the previous studies showed the role of autophagy in the *in vitro* models, the *in vivo* role is unknown. **Methodology & Theoretical Orientation**: We explored the role of Atg5- dependent autophagy on *Francisella* infection *in vivo*, by using mice deficient for Atg5 in the myeloid lineage. We determined intracellular replication of *F. tularensis* strain LVS in the lung, liver, and spleen of Atg5 deficient mice, as well as histopathological changes within the organs in comparison to the control group. Also, we determined the localization of bacteria within the autophagic vacuole during the infection. **Findings:** Intradermal infection Atg5-deficient mice resulted in significantly reduced bacterial burden and less severe histopathological changes in the lung, liver, and spleen tissues. **Conclusion & Significance:** We showed for the first time the *in vivo* role of Atg5-dependent autophagy in the pathogenesis of tularemia. We demonstrated that Atg5 supports *Francisella* intracellular growth and affects the pathology of the tissues *in vivo*.

Biography

Ina Kelava is a young scientist and third-year PhD Student at the Department of Microbiology and Parasitology at the University of Rijeka, Faculty of Medicine. Her PhD work is related to exploring the intracellular lifestyle of Francisella tularensis within different phagocytic and nonphagocytic cells, focusing on the mechanism of autophagy on F. tularensis. She performs in vitro experiments with cell cultures, as well as in vivo experiments on mice using laboratory technics as PCR, q RT-PCR, ELISA, immunohistochemistry, and flow cytometry analyses. She has already published 4 papers.