Anisakis simplex, one of the most prevalent parasitic nematodes (Nematoda) of marine organisms is characterized by a complex life cycle. Humans can be accidental hosts for this parasitic species, and nematodes may cause either debilitating diseases or may initiate immune hypersensitivity states. The consumption of raw or undercooked fish containing larvae may pose a serious health risk because the parasites are able to penetrate mucous membranes of the gastrointestinal tract and cause damage to the gastric and intestinal walls as well as induce allergic reactions. The pathological changes caused by nematodes of the *Anisakis* genus are known as anisakiasis. The incidence of the disease continues to increase, and 20,000 new cases were reported to 2010. According to the quantitative risk assessment model, the prevalence of anisakiasis in Europe will increase from 500 to ~8000 cases per year. Therefore, *A. simplex* was acknowledged as biohazardous organism. Parasitic nematodes may cause severe abdominal pain, nausea and vomiting. The presence of *Anisakis* larvae in the intestinal wall induces a Th2-type immune response characterized by an increased host production of eosinophils and elevated secretion of cytokines, the symptoms similar to those of Crohn's disease. Interestingly, the exposure to *Anisakis* larvae was reported as a potential risk factor for gastric or colon adenocarcinoma. Anisakis larvae and their secretions interfere with host immune responses. The finding that nematodes can release exosomes – extracellular vesicles, which are able to enter host cells – was the breakthrough discovery in parasite research. Recently, exosomes were found to operate as signal molecules in parasite-host interactions leading to host pathology. It was also demonstrated that exosomes contain miRNAs, non-coding RNAs involved in post-transcriptional down- or -upregulation of gene expression. Recent studies suggested that exosomes-associated miRNAs are instrumental for the parasite-host interactions. In addition to miRNAs, exosomes contain proteins, which also may play a role in numerous aspects of parasite-host communication. Although studies of the parasite-host interactions led to the identification of potential targets for diagnosis and therapy of nematodiases, further studies are required to search for new and more specific targets to more effectively treat these diseases. In this context, evidence that exosomes can act as signal molecules in parasite-host interactions may pave the way to novel strategies for nematode infection control. The better description of exosome functions in nematodes have the potential both to transform our understanding of parasite adaptation to the host and to develop possible therapies for immune-mediated diseases.

In a preliminary study, we have demonstrated that exosomes are secreted by *A. simplex*. It was also confirmed that these vesicles contain RNA and proteins. Furthermore, it was shown that host intestine cells respond to *A. simplex* exosomes with significant changes in cytokine secretion. The results of our preliminary studies and literature data prompted us to formulate the following **research hypotheses: *i)* exosomes secreted by *A. simplex* L3 larvae transfer miRNAs and specific proteins to the host intestine cells to modulate their immunological response; *ii)* host cells respond to *A. simplex* L3 larvae with changes in their transcriptomes and proteomes as well as with the changes in miRNA and protein expression profile of their exosomes.** The following general research objective has been formulated to verify the above hypotheses: *To recognize the exosome-based mechanism of A. simplex larvae-host cell communication.* To meet this goal *A. simplex* L3 larvae and human intestine cell line - Caco-2 will be used as a research model. Transcriptomic and proteomic approach (Small RNA-seq, RNA-seq, LC-MS/MS) will be applied to examine the content of exosomes produced by the larvae and host cells cultured separately and in co-culture. Therefore, the proposed study aimed to examine exosomes secreted by *A. simplex* L3 larvae and characterize their miRNAs and proteins to evaluate the potential role of parasite exosomes in the host response to the infection. The host defense mechanisms will also be investigated by analysis of the transcriptomic and proteomic profiles of both the host cells (mRNA, proteins) and exosomes (miRNA, proteins) secreted by these cells. Characterization of the exosome and host cell content and evaluation of the potential role of exosomes in the modulation of the host immunological response to parasite will help to understand mechanisms of the initial establishment of the parasite within the host organism and its subsequent survival. Furthermore, the analysis of differentially expressed genes and proteins in host intestine cells affected by the parasite will provide valuable information pertaining with immunological mechanisms which determine the survival of nematodes in their accidental hosts i.e., humans.

The examination of the parasite-induced changes in transcriptomic and proteomic profiles of host (human) intestine cells as well as the examination of the content of exosomes produced by larvae and host cells cultured alone or together constitute a new approach in parasite nematodes research. Such a more complex approach will enable for the first time to investigate at the same time larval exosomes and the host cells. The novelty of the current project is also associated with the fact that the content of the exosomes and cells will be submitted to both transcriptomic and proteomic analysis. The secretion of exosomes by parasitic nematodes and their host response has not yet been profoundly studied. The obtained results should provide better understanding of molecular processes underlying the development of *A. simplex* infection in humans. This knowledge, in turn, will allow for finding effective treatments to cure the disease. It is also possible that the results of the present project will help to develop future studies leading to *A. simplex* eradication.