The discovery of the first antibiotic, penicillin, in the late 20's of the XX century, has revolutionized medicine and begun long-lasting antibiotic therapy, which has resulted in successful treatment of many dangerous infectious diseases. Currently, almost hundred years after the crucial A. Fleming's discovery, the newest antibiotics, improved during long-term research, are available. Nevertheless, their intensive exploitation, not only for treatment, but also for the prevention of livestock, where small amounts of antibiotics are used to achieve better body weight, lead bacteria to develop resistance to antibiotics used in their environment. It is caused by the natural resistance of some bacteria to particular therapeutics, via mutation, or through transmission of resistant genes from other bacteria.

Mycobacterium tuberculosis, causing forgotten tuberculosis (TB), is one of the bacteria, which develops antibiotic resistance. Unfortunately, quick adaptation of bacterium to its changing environment, results in increasing infection ratio and higher mortality worldwide. WHO estimates that one third of the world population is infected with TB and, only in 2014, 9.6 mln new cases of the disease were registered. What is more, mortality increases every year and it reached in 2014 1.5 mln deaths, whereas in 2012 mortality ratio reached around 0.9 mln. Additionally, TB becomes a serious problem for people suffering from immunosuppressive diseases, e.g. HIV positive patients. Currently, *M. tuberculosis* is the major cause of death among patients with AIDS, only in 2014 one third of HIV positive patients died because of the additional TB infection. Another bacterium, which shows antibiotic resistance is *Staphylococcus aureus,* often called MRSA (methicillin-resistant *S. aureus),* because of its resistance to methicillin. Although, in some people it is a common pathogen of nasal mucosa, showing no signs of disease, it can cause serious skin and soft tissue infection. Furthermore, due to its resistance to antibiotics, it can lead to life threatening sepsis. Approximately 80000 cases of infection are registered per year (2011), 12000 of which are fatal. It is possible that MRSA will be a growing problem among hospital related infections and also due to its treatment difficulties.

During the research we are not planning to create a new antibiotic against resistant bacteria strains. Our main aim is to study host pathogen interactions, as well as basic mechanisms of innate immunity response during bacterial infection. We would like to find a key factor, which will allow us to modulate innate immune system. It will be crucial step in the therapy of antibiotic resistant bacteria strains, which will lead to increase effectiveness of antibiotic treatment and patients' recovery. We propose galanin, a peptide produced by nerve cells, as a new modulator of innate immune system. Additionally, current research confirms that galanin has an impact on immune response during inflammation and bacterial infection.

In our project we would like, for the first time, to define the role of galanin during systemic bacterial infection, its influence on innate immunity response and possibility of using galanin as a new modulator of innate cells. To achieve these goals we would like to perform our research on larvae of *Danio rerio* fish (zebrafish, ZF). Zebrafish is becoming popular *in vivo* research model nowadays, which gives an opportunity to study various research subjects. Its system contains all cell types found in the other vertebrates, due to that, studies perform on zebrafish apply to higher vertebrates, including human. Furthermore, it is relatively easy to create a new fish line. During our research it is planned to use two special ZF lines, one with blocked galanin production and the other with its overproduction. Moreover, ZF embryos are susceptible to various bacteria, including *S. aureus* and mycobacteria. For TB research, *Mycobacterium marinum,* the natural fish strain of mycobacterium and close cousin of human *M. tuberculosis,* is commonly used. Fluorescent marked bacteria together with fluorescent innate immune cells, give opportunity to track precise interactions between immune cells and pathogens. What is more, transparency of skin of zebrafish larvae allows following *in vivo* bacterial burden in the organism. It gives also the possibility to use the newest laboratory techniques like flow cytometry, which estimates infection rate in ZF larvae, via its fluorescent lasers. Apart from study galanin role during the infection, we would like to describe galanin role in the function of on innate immune cells: macrophages and neutrophils, via quantitative real time DNA amplification technique.

Current problems during antimicrobial therapies require new endeavors, which will lead to improve present treatment methods. Furthermore, new medicines must minimalize bacteria ability to develop resistance against used treatments. The aims of this project it to reveal immunomodulatory role of galanin, as a potential factor, which will improve present antimicrobial therapies that are becoming significant problem in modern medicine.