Human body is complex environment where microorganisms coexist with each other, often as polymicrobial biofilm communities. Living in a biofilm is beneficial for bacteria because it helps, for example, to protect themselves against human immune mechanisms or killing by antibiotics. An example of a chronic disease inherent in the presence of intracellular biofilm is persistent urinary tract infection. However, except benefits, living in a bacterial community creates a need to compete for space and nutrients with neighboring cells. Therefore, bacteria have evolved multiple systems to inhibit the growth of other microbes to survive harsh conditions. An important mechanism of such inter-bacterial battle includes the delivery of protein toxins to neighboring cells through contact-dependent growth inhibition (CDI) systems. Besides their role in competition, CDI toxins are used as a bet-hedging strategy that allows bacteria to survive stressful conditions such as antibiotics and nutrition starvation by increasing the fraction of dormant persister cells. Being in a persister state means 'to go to sleep and wait out antibiotic exposure and immunity factors' – the phenomenon that is called *antibiotic tolerance* (Figure 1). Interestingly, once the stress is depleted, persisters generate viable offspring which in consequence lead to the recurrence of the disease. *The entry of bacteria into growth arrest is readily explained through the activity of toxins targeting essential cellular processes. However, the mechanisms that allow persisters to resume growth are unclear.*

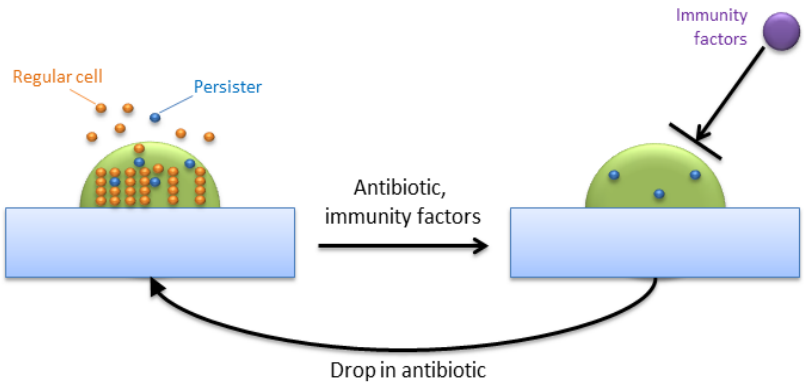


*Figure 1 Model of relapsing chronic infections. Antibiotics kill regular cells, and the immune system eliminates escaping persister cells. The matrix protects persister cells from the immune system, and when the concentration of the antibiotic drops, they repopulate the biofilm, causing a relapse.*

**In this project we will investigate how persister uropathogenic *Escherichia coli* cells resume growth by analyzing the process of detoxification.** To truly understand mechanisms underlying the exit of the dormant state, we will use single-cell techniques to analyze the role of carbon source, energy levels of persister cells and dynamics of changes in gene expression profile. The project starts from the more general *in vitro* studies and advances to the more specific imaging in bladder cell culture model.

A detailed examination of the growth resumption at the single-cell level will be an important step towards understanding the mechanisms that stimulates regrowth of persister cells. This will have potential application in devising approaches to awake persisters artificially, stimulate growth, re-sensitize them to antibiotics, and in consequence, help to manage and/or to eradicate chronic urinary tract infections. Therefore, the results of this project will be of interest of microbiological and biomedical societies.