Swim and adhere – regulation of *Salmonella's* virulence factors expression and its impact on infection

Salmonella, a Gram-negative bacteria, belonging to the *Enterobacteriaceae* family, is one of the most common causes of food-borne diseases. *Salmonella* infections are considered a serious epidemiological issue worldwide, affecting public health and generating huge economic losses. The most common source of infection is the consumption of food of animal origin, hence the diseases caused by *Salmonella* are referred to as zoonosis.

The pathogenesis of *Salmonella* infection is a multistage process of interactions between bacteria and host, focused on reaching, attaching, and invading the host cells. Those processes are driven by specific structures created by *Salmonella*-virulence factors. Among them, two types – flagella and adhesins, responsible for motility and adhesion respectively, determine the potential success of the infection. Flagella help bacteria to reach the infection site, whereas adhesins allow for bacterial survival in the hostile environment of the animal intestine, and avoid mechanical removal by the host organism. As a consequence, both structures are responsible for the first stages of bacteria invasion and allow further invasion of *Salmonella*.

Flagella are composed of three basic elements: the basal body, hook, and filament. The filament is made of two different proteins, FliC and FljB, that are coordinately regulated in the so-called phase variation mechanism. Among *Salmonella*'s adhesive structures, type 1 fimbriae (T1F) are one of the most extensively studied. T1F are relatively long, rod-shaped structures with FimH protein present at the tip, which is directly responsible for binding to host cells.

Despite numerous studies focused on the role and regulation of the initial stages of *Salmonella's* virulence factors, there is no sufficient data on how flagellins and T1F are regulated - when and for how long expressed during *Salmonella* infection. The role and significance of T1F-flagella cross-talk remain relatively unknown.

Our preliminary studies shed a light on this interaction. We revealed that T1F expression is dependent on growth conditions and correlates with adhesion level to intestinal epithelial cells. What is more, elements involved in T1F production directly affect the level of flagella proteins at selected time points.

Taking it all into consideration, we decided to propose a research project investigating the cross-talk between the adhesive and motility structures of *Salmonella* during the first and crucial stages of the pathogen infection. We are planning to make the new experimental models which allow us for the first time real-time tracking of *Salmonella*'s virulence factor expression through the course of infection. We will manipulate the expression levels of flagella and fimbriae and investigate their impact on the infection process using various cellular models.

We expect, that the realization of this grant proposal will improve our current understanding of *Salmonella* pathogenesis, which can further lead to the improvement of current methods of salmonellosis prevention and treatment. This is especially relevant because taking into account *Salmonella's* survival ability in variable conditions and adaption to new niches, together with the growing antibiotic resistance of microbes all over the world, salmonellosis prevention and treatment become more and more difficult. The results of this project might be used as a starting point for the development of prevention or alternative treatment therapy for bacterial infections.