A continuing rise of multidrug-resistant (MDR) microbes has become one of the biggest threats to the public healthcare of our time. The number of healthcare-associated infections (HAI) is steadily increasing and is estimated to amount to 4.5 million yearly cases in Europe. A group of pathogens referred to as the 'ESKAPE' pathogens, have been found responsible for the majority of HAI. Ability of these bacteria to form biofilms, aggregates of bacteria embedded within a self-produced matrix of extracellular substances, further complicates the treatment because biofilm-encased bacteria can be 10 to 1,000 times more resistant to antibiotics than planktonic counterparts. The MDR bacteria are also believed to contribute largely to recalcitrance and recurrence of biofilm-associated infections and the development of non-growing, dormant antibiotics-resistant persisters. Indisputably, novel, non-antibiotic approaches are in an urgent need for battling these MDR bacteria in a timely fashion, which is pivotal not only for the health of the infected patients but also for restricting the MDR bacterial spread and slowing down resistance development.

In seeking such strategies, we have been studied Antimicrobial Photodynamic Inactivation (aPDI) as a therapeutic option in the treatment of infectious diseases for last fifteen years and recognized this approach as one of the most promising non-antibiotic microbicidal technology. aPDI exhibit a multi-target and broad spectrum of antimicrobial activity, which would be more likely to prevent resistance development, in contrast to the single molecule-action mode of most antibiotics. It is based on a combination of a photosensitizer (PS), light and oxygen to remove highly metabolically active cells. These cells may be microorganisms such as fungi, viruses or bacteria. The main element in aPDI is excited photosensitizer, which action can lead to the formation of singlet oxygen and radicals. These reactive species are responsible for damage to biological molecules, thus promoting cell death, which is the desired effect of aPDI. **However, this strategy, despite its broad application, has also evoked several unresolved challenges, and among them the most significant is that the mechanisms of the bacterial response to aPDI are poorly understood. Thus, within the current project we aim to identify the genetic basis and pathways implicated in the aPDI-induced stress response providing a system analysis concerning short- and long-term transcriptomic responses of *Escherichia coli* to phototreatments.**

Research project methodology: The realisation of the project involves: **i)** exposure of *E. coli* to 5 most commonly studied aPDI approaches (i.e., aPDI employing PSs representing various classes of chemical compounds like porphyrins, phenothiazines, xanthenes, and antimicrobial blue light (aBL) that can excite intracellular photosensitizing compounds generated within bacteria with no induction and ALA-induced), **ii)** comparison of the transcriptional responses between a short-term (30 min) and a long-term exposure (8 to 12 h) to photo-induced stress, **iii)** establishment of the common gene and pathway clusters that are implicated in general and PS-specific stress responses, **iv)** validation of our findings due to the susceptibility assays with knockout mutants to provide clear targets for downstream investigation of the implicated mechanisms of action, and **v)** determination of the optimal protocol for light-based approaches based on computer modelling. In our opinion presenting the successful evaluation of underlying mechanisms is indispensable for the dissemination of its effective clinical use and extending current knowledge concerning aPDI treatment.