The misuse and overuse of antibiotics contributes to the development of multi-drug-resistant bacteria, the so-called "superbugs." Bacteria are acquiring resistance faster than new antibiotics are discovered, and it is predicted that if this continues, the number of people dying annually from bacterial infections will increase tenfold (to about 10 million) by 2050. Multidrug-resistant bacteria are one of the greatest global threats, and the lack of effective forms of treatment is a great challenge for modern medicine. For this reason, the development of new, effective drugs and therapeutic solutions are extremely needed. One such therapeutic option may be cold plasma and visible light-based approaches: antimicrobial photodynamic inactivation (aPDI), antimicrobial blue light (aBL) and antimicrobial sonophotodynamic inactivation (SPDI), which are attracting increasing research attention. In the natural environment, bacteria are exposed to various types of stress. The primary challenge for bacteria living in an aerobic environment is oxidative stress caused by the accumulation of reactive oxygen species (ROS) in the cell. Various environmental pollutants and stress factors exert selective pressure on microorganisms, as a result of which bacteria mutate, evolve and adapt to unfavorable environmental conditions. For this reason, it is necessary to identify the factors contributing to the emergence of antibiotic resistance in environmental reservoirs and to conduct research on the phenomenon of adaptation to various factors and therapeutic approaches. For example, many studies indicate the development of co-selection, a phenomenon where one factor, e.g. an antibiotic, can select for resistance to other antibiotics, disinfectants and heavy metals. Mechanisms underlying co-selection include phenomena such as tolerance, cross-resistance, co-resistance and pleiotropic resistance. When new antimicrobial treatments are developed, it is important to assess the risk of adaptation development (tolerance and/or resistance). aBL, aPDI, SPDI and cold plasma are considered low-risk therapeutic approaches for the development of resistance by microorganisms, due to the formation of ROS that affect multiple targets in the bacterial cell (as opposed to antibiotics that act on a single, specific target in the cell). However, as a result of the mutagenic properties of ROS and the heterogeneous environment of the infection site, it is very likely that surviving bacterial cells will mutate to form more tolerant phenotypes. There is also a risk that as a result of repeated exposure of bacterial cells to the cyclic oxidative stress conditions, bacteria may adapt to a different therapeutic solution as a result of co-selection. The main objective of this project is to assess the risk of developing co-selection under various stress conditions [i.e. aBL, aPDI, SPDI, cold plasma, UV radiation, hypochlorous acid (HOCl), hydrogen peroxide (H_2O_2) and antibiotics]. *Escherichia coli* will be the main object of research. Adaptive laboratory evolution (ALE) is an important scientific approach contributing to the understanding of the adaptation mechanisms of microorganisms to various environments, including stress conditions. This approach provides significant insights into evolutionary microbiology under controlled and defined conditions, helping to understand the genetic basis of increased microbial resistance. Tolerance is a phenomenon that drives the evolution of resistance, therefore an appropriate therapeutic approach limiting the development of tolerance should be the key to preventing the development of resistance. For this reason, it is very important to assess the risk of developing tolerance and resistance of microorganisms to new and alternative antimicrobial treatments, as well as to assess the risk of co-selection, e.g. to antibiotics and/or other antimicrobial agents. As part of this project, we expect to assess the risk of developing adaptation (tolerance and/or resistance) to stress conditions generated by antibiotics and alternative therapeutic solutions, as well as assess the risk of developing co-selection for these factors. The results of the project may indicate possible limitations of the tested therapeutic solutions, which can be overcome after applying a responsible treatment policy. In addition, the obtained results may contribute to expanding knowledge on co-selection under various stress conditions, and thus to the development of appropriate therapeutic protocols.