Every organism is composed of cells that are complex molecular machines. These machines are not infallible and due to external agents or internal error, they can start to function in an undesired manner. An example of such malfunction is the disruption of cell division mechanism that leads to its uncontrolled reproduction. To prevent such a multiplication, cells are equipped with a programmed cell death (PCD) mechanism. This system triggers the "self-destruction" of an affected cell in a way that does not pose a threat to neighboring cells. Unfortunately, sometimes the PCD failsafe mechanism may be also damaged, and in this case, the cell will keep on multiplying in an unrestrained manner – a condition that we know as cancer.

Previous studies indicated that neither cancer nor PCD processes are unique to humans. On the contrary, both are observed in a variety of multicellular organisms including starfish, freshwater polyp, and fungi. Moreover, it has been shown that the molecular circuits (i.e. group of proteins acting together) responsible for PCD are also present in bacteria characterized by a complex lifestyle, suggesting that the ancestors of the PCD systems appeared very early in the history of life. In this project, we will use computational tools to identify, characterize, and classify the individual components of PCD and PCD-like systems across thousands of the available sequenced genomes. These analyses will enable us to understand the differences in the composition of PCD systems originating from various organisms and to describe the evolutionary processes underlying this diversity.

The bioinformatics analysis will result in testable hypotheses which will be the starting point for laboratory studies. First, we will attempt to unravel the physiological role of the PCD-like systems in bacteria. To this end, we will culture selected bacterial species and check how do they respond, at the molecular level, to various conditions such as phage (viruses specific to bacteria) infection, population density, and stress. This analysis will be an important step towards understanding the role of bacterial counterparts of the "self-destruction" systems known from more complex organisms. The second branch of the experimental work will focus on studying the compatibility of PCD and PCD-like systems' components originating from different organisms. To this end, we will use genetic engineering methods to introduce selected components to yeast cells and examine the effects of their presence. As a result, we will understand why some components can act together and the others not, and thus we will validate the previous findings obtained with the aid of computational methods.

In summary, the project aims at obtaining a detailed picture of the evolution of systems involved in programmed cell death throughout the tree of life. This holistic description will guide two experimental works focused on the analysis of the systems' individual components and the whole systems. As the malfunctions in PCD processes are connected to cancer, such a broad yet experimentally validated view will open new paths in cancer research.