

Our research focuses on soil bacteria of the genus *Streptomyces*. These bacteria have an unparalleled talent for producing many biologically active substances. They produce most of the antibiotics that we use in medicine, industry and agriculture. Based on the analysis of their genes, we know that some species of these bacteria may theoretically be capable of producing up to 20-50 different active molecules. Unfortunately, under laboratory conditions, they usually produce only a few antibiotics. Those genes that remain inactive are called dormant genes. This is because *Streptomyces*, taken out of their natural environment, such as the soil, are not exposed to normal external stressors such as cold, heat, flooding and cutting off oxygen, ending with exposure to millions of other species of bacteria, fungi, plants and animals. All these organisms interact with each other by releasing various substances into the environment. It is these external factors that promote the production of antibiotics and other substances in order to gain an advantage by fighting off competitors for environmental resources.

In order to unlock the full biosynthetic potential of *Streptomyces*, we are researching the regulation of gene expression, i.e. the mechanisms of their activation from a dormant state. Through our research, we are contributing to the understanding of how *Streptomyces* perceive their environment at the molecular level. One of their sensory tools are so-called “histidine kinases” - proteins that are activated into action when a signal specific to them is detected. Most often, this signal is a dangerous external factor, for example the stress of lack of food, inadequate temperature for growth. Histidine kinases, upon detecting a threat, activate and transfer a phosphate group (-PO₄) from ATP to further proteins – “response regulators”, which can subsequently bind to DNA and switch on or switch off the activity of specific genes. Most often, histidine kinase and its partner are encoded on a DNA strand next to each other and, based on gene neighbouring, we know that these two proteins are most likely to interact with each other and regulate cell physiology. The subject of our research is an “orphan histidine kinase”, which does not have a “response regulator” protein encoded next to it on the DNA strand. We are focusing on finding this secret partner, or in other words the “interactome” of the histidine kinase CpkM in *Streptomyces coelicolor* A3(2). In addition, the aim of our research is to learn about the “regulon” of the CpkM kinase. The regulon is the set of all genes that are under the control of CpkM and its response regulator partner.

Research into histidine kinases and the characterisation of precise signal transduction pathways in bacterial cells is contributing to: 1) discovery of new antibiotics that can be used as the last line of defence in the fight against multidrug-resistant bacteria, which are continually increasing in number; 2) development of new anti-cancer therapies; 3) The sustainable and intelligent, targeted development of the production of active substances that are already used on a large scale. It is in the interest of companies and above all users of medicinal substances to develop genetically modified *Streptomyces* strains that overproduce selected substances. In this way, the price of medicines can be reduced.