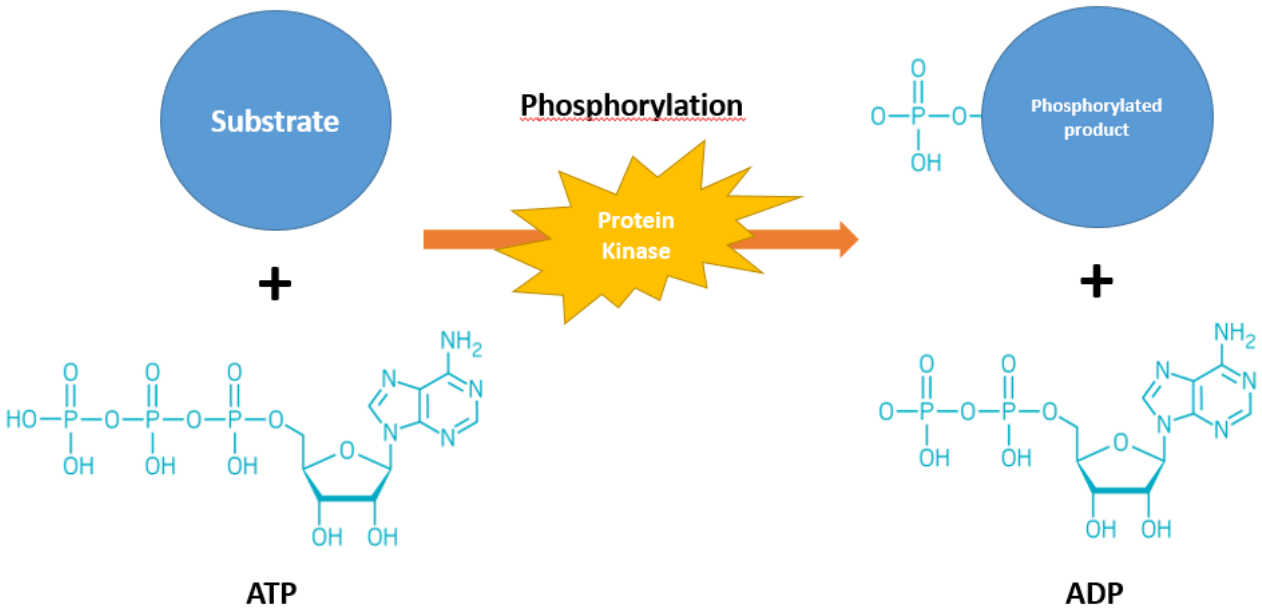
In all of living cells, there are many molecular processes that are possible due to the activity of enzymes. One of the basic enzymes involved in most cell processes - such as amino acid synthesis, cell signaling, regulation of other enzymes and proteins - are protein kinases (PKs). The PKs carry out a chemical reaction involving the transfer of the phosphate group from the high energy molecule (e.g. ATP) to the target molecule. In this way they modify it and change its activity, e.g. activate another PK. This process is called phosphorylation. Therefore, knowing all of the PKs of a given cell is crucial to understanding how it is functioning.

Novel PKs families are still being discovered, especially in bacteria, but in a non-standard way, with the use of expert knowledge, bioinformatic tools that can detect remote similarity to known protein families and meticulous manual analysis of the results (which gives additional quality control). The novel PKs differ from the known PKs in terms of the amino acid sequence, but they have some motifs important for PKs.

In the preliminary studies, I found many new families of bacterial PKs. Some of them are effector PKs (EPKs). EPKs belong to the effector proteins, thanks to which bacteria manipulate the cellular processes of host organisms, e.g. human.

One of the new PK families called HopBF1 that we found belongs to the pathogenic bacterium *Pseudomonas syringae* and causes the leaf tissue collapse of plants. More novel PK families found in the preliminary studies come from a dangerous human pathogen - antibiotic-resistant bacteria of the genus *Legionella*. These bacteria may cause fatal pneumonia in humans. Already several of these kinases are currently under experimental investigation by our collaborators. Among those kinases, there are also pseudokinases. These are kinases in which one or more functionally important amino acid residues are altered. As a result of such a change, kinase cannot fulfill its catalytic role. One of such effector pseudokinase SidJ was thoroughly examined by us and our collaborators and turned out to be a glutamylase - an enzyme that attaches glutamate molecule to its target protein. Its role is to block the important process by which the bacterium can survive inside human macrophages.

This shows that novel PKs and pseudokinases can be important and suprising. Human PKs are relatively well known, but this is not the case of bacteria associated with the human body (including pathogens). Therefore, the main goal of this project is to bioinformatically search for novel PK families and their distant relatives among the human microbiome proteins (the totality of microorganisms living in all body habitats, e.g. gut, skin, oral cavity). Microbiomes are known to be related to physical health, e.g. digestive system function. Moreover, microbiomes, as it turned out recently, have a direct impact not only on physical health, but also on the psyche. PKs can participate in these signaling mechanisms. The next goal is to examine novel and already known PK families, to catalogue them and to predict their role. This will be an important introduction to further experimental research, and in the long term to design alternatives to antibiotic therapy, e.g. in the form of blockers against EPKs of human pathogens.



Phosphorylation