As we all know there is nothing pleasant about having a cold, neither for our nose nor our look. When it happens our organism pulls the heaviest guns to fight with it. There are two major lines of defense. The first one is the innate immune system, which is the faster, but the less selective way. The other one, adaptive immune system, found only within Vertebrata (lucky us!), is more specific to particular pathogen and longer-lasting. There are few types of cells participating in adaptive immunity and one of these is a T cell. It matures in the thymus and differentiate into T helper cells (also known as CD4), which assist other white blood cells in immunologic processes or cytotoxic T cells (CD8), which specialize in destroying infected cells. Both of these cells possess a T-cell receptor, the special protein, which enables getting a signal from the outside to the inside of the cell. So you can imagine how important are the processes involving that receptor molecule. The CDζ coreceptor is also needed in the process of binding the extracellular messenger molecule (p-MHC) to the T-cell receptor. In order to bind it to the T-cell receptor there is one more protein needed: the CD4 coreceptor. It also interacts with extracellular p-MHC domain, which stabilize the whole complex. On the other hand its cytoplasmic tail interacts with another protein: Lck. It is necessary for further signaling. CD4-Lck interaction is critical for the T-cell activation process and getting us out from the infection! Imagine that such an important process happens through just one ion, zinc ion [Zn^{2+}]. There is no doubt, that research on CD4-Zn^{2+}-Lck interaction is crucial and worth investigating.

Within this project I will establish the effect of palmitoylation of the CD4 and Lck on the formation of the Zn^{2+}-mediated CD4-Zn^{2+}-Lck heterodimer complex. Palmitoylation is a process of attaching very long fatty acid molecules to the same sites as Zn^{2+} binds (sulfhydryl groups from cysteine residues). It is known, that molecules with such a long, hydrophobic parts (water insoluble) attach to the membrane (which inner part is insoluble as well) and to each other. Such effect is documented within activation of T-cells along with increase of cytoplasmic Zn^{2+} concentration. Moreover, Zn^{2+} ions could bind to enzymes catalyzing palmitoylation process (palmitoyltranserases) and, in consequence, affect their catalytic activity. Considering main goals of this project, answering the following questions: how many Zn^{2+} ions are bonded by palmitoyltransferses?, how strong is this binding?, which cysteine residues participate in it?, if palmitoylation affects Zn^{2+} binding by CD4 and Lck? is really worth the effort. In the final step of this project I will build the artificial membrane model and attach protein domains to it in order to mimic cellular behavior of CD4, Lck, palmitoyltransferase and Zn^{2+} ions network.

Zn^{2+} ion, besides its small sizes (there is just one atom involved), is extremely important for proper cell functioning. It is estimated that Zn^{2+}-binding proteins account for approximately 10% of the human proteome. Although zinc ion interactions on proximal T-cell activation events are documented, the exact mechanisms have not been understood yet. Bearing in mind that availability of Zn^{2+} ions is strictly regulated by complex protein machinery, even minor fluxes lead to the formation or dissociation of zinc complexes interfering with cell homeostasis. Determination of Zn^{2+} to proteins affinities (strength of the binding), especially in the environment mimicking on-membrane one, is crucial to understand and predict zinc proteome behavior. Although the complexity of the mechanisms regulating this system is high, there are strong indications that it is worth the effort to gain new insight into these processes.