

The main goal of the project is to establish on molecular level how information can be passed from one region of the protein to the other without any external mediators. Rad50/Mre11 protein complex is responsible for repairing the DNA double-strand break, which occurs naturally in cell division or can be caused by harmful factors such as ionizing radiation *e.g.* gamma radiation. Rad50 is a protein with heterogeneous structure. It has a long coil-coiled region which resembles a rope made from two strings and in one end there is a globular (spherical) domain which binds Mre11 protein and on the other zinc hook domain responsible for zinc binding which connects to the zinc hook from another Rad50 protein forming a homodimer. This connection forms an eye of a needle through which DNA is tethered. We previously established that the two protein connection through hook domain has an effect on globular domain. That would mean that the coiled-coil region function similarly to a gear lever, shifting between several structural states of the protein. We suspect that changes in the protein structure are caused not only by zinc binding but also for example by DNA or ATP binding. We will focus our efforts on the protein from yeast, which is closely related to the human one, because it is much easier to create mutants of this organism. In order to achieve our goal and solve the scientific problem we will use several different analytical methods such as fluorescence measurements or mass spectrometry. Our laboratory produces unique fluorescent molecules that can be attached specifically to selected place in protein, which is a great advantage in proposed research. Completion of the objective requires also introduction of several mutations to the protein. Each time we will have to be ensured that our modifications did not affect the functionality of the proteins. Therefore this study will require multiple rounds of optimization of protein production and analytical methods, but we hope that we will establish the molecular machinery behind structural changes of the Rad50 protein due to binding to different cellular components and chemicals. This will be an important piece in understanding the puzzle of DNA repair.