Description for the general public

The cells of the immune system communicate with each other through various types of chemical signals, most often -proteins. These compounds can be secreted outside the cell and travel to various parts of the human body carrying a particular message. Cells can also utilize their surface to place on it the so-called "molecular flags" –particles informing neighboring cells about their condition. In most cases they say "I'm OK", but sometimes the cells present the red flag saying "I'm in trouble!". The signal is received by the another cell using a molecular "antenna" called the receptor, also localized on the cell surface. The information is then translated into molecular language to trigger desired reaction from the cellular housekeeping systems. For example, virus-infected cells may expose on their surface a molecular "flag" informing the cells containing on their surface an appropriate receptor e.g. T-lymphocytes, that there is a problem and that T-lymphocytes should start to multiply, take care of the situation and bring the organism back to normal.

There are situations, however, when the immune system gets overstimulated as if the molecular antennas receive constant signal from the flags. This is the case of autoimmune diseases. In other cases, like allogeneic transplants (from other person), the immune system cells are eradicating xenogeneic ("not-mine") cells from the system. This activity is not desired for the sake of the organ recipient. In such cases, the silencing of the communication between cells is beneficial. It can be achieved by a carefully designed molecules, called inhibitors, that can bind to either of the partners (the flag or the antenna) and modify their communication.

In this project we focus on the design and synthesis of a set of such inhibitors that can modulate the interactions between the LIGHT protein, located on activated cells of the immune system, and the HVEM protein, mainly located on the surface of T lymphocytes. When these proteins get too "talkative", the autoimmune diseases like systemic lupus, multiple sclerosis might develop or the transplant rejection may occur. We propose an approach based on small molecules like peptides which are a natural-born modulators of interactions between proteins. These peptides will interact with binding fragments of HVEM and LIGHT proteins, and thus block the formation of HVEM/LIGHT complex.

It is a modern approach in the design of many immunological therapies. The project can therefore contribute to the development of new immunosuppressive drugs that may be used in the treatment of autoimmune diseases and transplant rejection reactions