**Biochemical and structural studies of retroviral reverse transcriptases evolution**

Proteins are the building blocks of each organism. They are encoded in genes made of DNA. At the first stage of protein synthesis an enzyme called polymerase copies DNA sequence of a gene to RNA. The reverse process of DNA synthesis from RNA is called reverse transcription and is used by retroviruses such as HIV-1 which causes AIDS. During reverse transcription RNA viral genome is converted into double-stranded DNA, which is integrated into the host genome. The enzymes which catalyze the process of reverse transcription are called reverse transcriptases (RTs). They contain two elements: polymerase and RNase H. Polymerase is responsible for making the DNA strand based on the RNA. RNase H removes the viral RNA strand from RNA/DNA double helices, which are intermediates of the reverse transcription reaction.

Majority of eukaryotic (animal and plant) genetic information does not encode proteins but comprises of so called non-coding sequences. Retrotransposons are parts of the genome that are able to multiply themselves. They constitute one of the most widespread type of the non-coding sequences. Approximately 40% of the human genome is derived from them. They have their own genes encoding a reverse transcriptase and, like retroviruses, use reverse transcription process to create their own copies in the new positions in the genome. Mechanisms responsible for replication, mobility and particularly reverse transcription of retrotransposons are particularly interesting research topics. Retrotransposons are among the most potent forces shaping the architecture of eukaryotic genomes. Importantly, retroviruses evolved from retrotransposons. For the reverse transcriptase this process involved an acquisition of a new element – an additional RNase H domain.

Research in the proposed project focuses on RTs. These enzymes are very diverse in their structure and mechanism of action. Our understanding of these fascinating enzymes is still limited. The aim of the project is to understand how RTs of retroviruses evolved. To this end, we plan to determine the three dimensional structure of the RT from a viral subfamily for which RT structures are not available. We assume that the architecture and mechanism of action of this enzyme is different from those already known. Another objective of our research will be to study RTs from retrotransposons, which, just like retroviruses, acquired a new domain RNase H in their RTs. We want to understand the advantages, resulting from the acquisition of the new RNase H for the multiplication of retroviruses and retrotransposons. Our biochemical and structural studies will lead to much better understanding of the RTs.