DNA replication is a process of copying genetic material. This process requires a coordinated action of many catalytic and non-catalytic proteins assembled at the replication fork into a complex called replisome. The first step in the DNA replication process is its initiation. It involves the recruitment of specific proteins to the appropriate place on the double-stranded DNA called the replication origin. The CMG complex (**C**dc45 protein- **M**cm2-7 proteins – **G**INS complex) acts as active DNA helicase, which is responsible for the unwinding of double-stranded DNA. First, Polymerase α (Pol α) binds to the unwound DNA and synthesizes RNA / DNA primers on both leading and lagging DNA strands. These primers are then extended by polymerase ε (Pol ε) and polymerase δ (Pol δ), that catalyze the attachment of subsequent complementary nucleotides and thus synthesize new DNA strands. Polymerase ε synthesizes the leading strand, whereas polymerase δ is responsible for the synthesis of the lagging strand. Additionally, a mutator polymerase ζ (Pol ζ) may participate efficiently in the replication of undamaged DNA.

Maintaining high fidelity of DNA replication is essential to ensure faithful transmission of genetic information during cell division, as well as the transfer of genetic material from parents to their offspring. It is known that such an important element, which is the genetic material, should be copied with the greatest precision, because any error (in this case a mutation) can lead to synthesis of incorrect protein or even absence of protein synthesis, which in turn can lead to loss of cell function or its death. Improper rewriting of genetic information to a new DNA template may result in development of cancers or genetic diseases.

The main guardians which maintain fidelity of the replicated genomic material are DNA polymerases, whose role in the DNA replication process has been analyzed in detail for many years. Research conducted at the Laboratory of Mutagenesis and DNA Repair showed that other components of the replisome are also essential for maintaining fidelity of DNA replication, and thus for maintaining genome stability. One of these elements is the CMG complex, acting as the major active helicase. It is known that the helicase activity is mainly associated with Mcm 2-7 proteins, while GINS complex and Cdc45 protein seems to serve as a platform for the proper functional co-ordination of individual proteins in the replisome. However, the precise function of Cdc45 protein remains poorly understood. **The main scientific goal of this project is to investigate *in vivo* the role of the non-catalytic protein Cdc45 (a component of the CMG helicase complex) in the faithful maintenance of chromosomal DNA replication, and identify the biological consequences of mutations in the *CDC45* gene.**

The process of DNA replication is highly conserved in all organisms and it justifies the use of baker's yeast (*Saccharomyces cerevisiae*), which are an excellent model organism, in our research. In this project we will use mutants in the *CDC45* gene, which is essential for survival of each cell. The level of spontaneous mutagenesis in yeast cells carrying the *cdc45* alleles and the impact of mutations in the *CDC45* on cell cycle progression will be examined. The mutants in the *CDC45*gene are an excellent tool for *in vivo* studies of the mechanism of the polymerases recruitment to the leading and lagging strands and of the consequences of changes in contribution of individual polymerases to the DNA replication. The analysis of interactions between mutant forms of the Cdc45 protein with other proteins of the CMG helicase complex or with subunits of polymerase ε which replicate the leading DNA strand, will identify interactions that are crucial in maintaining the fidelity of DNA replication process.