All living cells have to duplicate their genetic material before division to transmit their genes to the progeny. This process, called DNA replication must be coordinated with the cell cycle progression. This means that after the phase of cell preparation to DNA replication (phase G1), DNA synthesis starts and proceeds (during S phase) and after it is completed (phase G2), the cell divides in the M phase. The progression through the cell cycle is unidirectional – once entered into a new cycle, the cell is committed to division. Perturbations in cell cycle progression regulations are often associated with diseases caused by genome instability and loss of cell cycle control, namely cancers.

DNA replication is performed by a multiprotein complex called the replisome. This complex includes a halicase which unwinds the DNA double helix and DNA polymerases which use the two DNA strands to synthesize complementary DNA strands. In eukaryotic cells, the helicase is a multi-subunit complex and its activity is stimulated by interactions of many essential elements of the replisome. The CMG helicase complex is composed of protein Cdc45, the six-subunits Mcm2-7 ring, the four-subunits GINS (Psf1-3, Sld5). The CMG complex associates with DNA polymerase epsilon (Pol ε) to form the CMGE helicase-polymerase complex.

Coordinated action of the CMG and Pol ε supports leading-strand synthesis, and it was shown that Pol ε plays a separate role in replication and as essential component for CMG formation in cells. Pol ε also stimulates the DNA unwinding function of the CMG helicase. Mutations in the genes encoding proteins that constitute the helicase-polymerase complex have been shown to increase the frequency of mutagenesis what results from various perturbations in DNA synthesis. These perturbations result from impaired reciprocal interactions between proteins of CMGE, what affects the whole complex assembly. Recent data suggest that proteins from this complex are also involved in the control of the cell cycle, including the transcription of genes whose products are necessary for both DNA replication and the regulation of cell cycle progression.

Therefore, we are planning to investigate in more details the role of CMGE helicase-polymerase complex in proper regulation of cell cycle progression and the control of DNA synthesis using the eukaryotic model organism - yeast *Saccharomyces cerevisiae*. We will use modern molecular biology techniques to monitor the timing of DNA replication start, the progression of DNA synthesis in cells with mutation in CMGE helicase-polymerase-encoding genes. We will also analyze the DNA replication at single-molecule level in these strains. Finally, using next-generation sequencing of all transcripts, we will identify in the mutated strains possible modifications of the transcriptional program that governs the synthesis of proteins necessary for DNA replication and the cell cycle control.

Our research will contribute to a better understanding of mechanisms involved in the regulation of cell cycle progression and DNA replication.