Abstract

Sustaining the integrity of DNA throughout the lifetime is critical for every living organism. Therefore organisms evolved numerous ways to detect and repair different types of DNA damage caused by various endogenous and exogenous factors resulting in replication stress. Defects in these repair mechanisms can lead to severe human diseases such as neurological disorders, familial cancers or developmental syndromes. In presented master thesis, we investigated the function of a yeast protein named Wss1, a metalloprotease that participates in a recently discovered DNA repair pathway that proteolytically removes DNA-protein crosslinks. Wss1 shows strong negative interaction with another DNA repair protease, Ddi1, in which case was discovered, that double-deleted yeast strain lacking WSS1 and DDI1 is hypersensitive to hydroxyurea. Hydroxurea is a ribonucleotide reductase inhibitor that, in the end, arrests cells in the S-phase of cell-cycle. Based on previous studies, we performed rescue experiments with various deletions and single-site mutants of Wss1p to assess the involvement of particular yeast Wss1p domains in the replication stress response to hudroxyurea.