

DESCRIPTION FOR THE GENERAL PUBLIC

Inducible DNA damage response plays fundamental role in cell viability of and health of whole organism. This response is activated in nucleus and its role in stimulation of repair and tolerance of damages in nuclear DNA is well documented. Our recent study indicated that this response significantly affects also the stability of mitochondrial genome. The objective of this proposal is the identification of proteins and mechanisms engaged in this important for mitochondrial functions but unrecognized until now process. We plan the investigations designed to clarify the role of mitochondrial replicative DNA polymerase Mip1 and specialized translesion polymerases in the mitochondrial response. In this study we will analyze, in the stress conditions, hypomorphic *mip1* alleles, encoding the forms of investigated enzyme carrying mutations in polymerizing activity, generated on the basis of POLG variants found in mitochondrial disease patients. Additionally, we plan to identify mitochondrial and mitochondria associated proteins, which are phosphorylated by Mec1/Tel1 (ATR/ATM) kinases governing the DNA damage response. This identification will help to define the mitochondrial pathways activated by the response initiated in nucleus. The role of some of these processes in the control of mitochondrial DNA stability will be analyzed. Altogether, proposed study will help to decipher a network of indirect and direct interactions affecting mitochondria, and especially mitochondrial DNA, in response to the conserved signal transducing pathway of DNA damage response.