## DESCRIPTION FOR THE GENERAL PUBLIC

Human cells have hundreds of mitochondria, each containing multiple DNA molecules, encoding core components of oxidative phosphorylation (OXPHOS). Although OXPHOS is a vital for providing cellular energy in the form of ATP, it also produces reactive oxygen species (ROS) which damage mitochondrial DNA (mtDNA). As a consequence, mutations in mtDNA lead to mitochondrial disorders with wide range of clinical symptoms and have been connected to cancer, premature aging, as well as, cardiovascular, skeletal muscular and neurological disorders.

Although great progress towards understanding mitochondrial DNA metabolism has been made, relatively little is known about the pathways in which mitochondria repairs DNA damage. It is believed that base excision repair (BER) pathway is the predominant DNA repair mechanism in mitochondria. While there are a number of DNA repair enzymes shared by the nucleus and mitochondria, only two are mitochondria-specific: Polγ and EXOG. During my postdoctoral work we solved crystal structures of human Polγ, the only polymerase in human mitochondria, thus responsible for both DNA replication and repair. We have recently solved atomic resolution structures of EXOG in the complex with DNA. Now, using the structural biology information, we plan to dissect the role of these two crucial enzymes as they cooperate to repair human mtDNA damage.