BRIEF DESCRIPTION OF THE RESEARCH IN LAYMAN'S TERMS, AIMED AT THE GENERAL PUBLIC

Cancer is a complex disease caused by interactions of multiple factors, such as genetic predisposition, environmental and lifestyle influences, infectious agents and ageing. Due to the complexity of this pathology, cancer research includes basic research, strategies for prevention, development of early diagnostic tools, and translational approaches for treatment and cure. In basic cancer research “knowledge” is the key word because if you want to interfere with a biological system you must know how it works. For this reason, the main purpose of this project is to gain information about the mitochondrial form of a DNA repair protein.

Radiation therapy and chemotherapy are the mainstream options available for cancer treatment. Many chemotherapeutic drugs act by damaging DNA, leading to an accumulation of lesions that ultimately cause cell death. However, our cells have the ability to repair damages induced by chemotherapeutics drugs therefore vinifying their effects. Base excision repair (BER) is a cellular pathway able to repair the damage generated at nuclear and mitochondrial DNA. An essential protein for the correct functioning of this pathway is APE1. This protein is present both into the nucleus and the mitochondria, represents a key enzyme of the BER pathway and elevated expression levels have been reported in several carcinomas contributing to resistance to chemotherapy.

Current approaches to cancer treatment report more effective results when specific DNA repair inhibitors are used in combination with DNA damaging drugs. The foremost rationale of the combined therapy is that the repair of DNA is likely to sensitize cancer cells to chemotherapeutic agents. For this reason APE1’s inhibitors are currently in use in therapy as adjuvant to chemotherapeutic drugs. However, an alternative approach to inhibit APE1’s DNA repair function consists in blocking its mitochondrial translocation to alter the ability of the cell to repair DNA damage induced by chemotherapeutic agents.

Unfortunately, information about how APE1 protein reaches the mitochondria are still scanty and contradictory. With this project we intend to better characterize the molecular mechanisms responsible for the translocation into the mitochondrial matrix of the DNA repair protein APE1. This study will significantly contribute to fill the cultural gap about the mitochondrial nature of APE1 protein therefore opening the possibility for further translational approaches for cancer treatment that rely on APE1 protein as a target.