



THE ROLE OF SPERM MITOCHONDRIA IN THE ADAPTATION TO ENVIRONMENTAL STRESS

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Pollutants represent the most important threats to the health of all living species and the WHO estimates that around a quarter of human diseases are due to prolonged exposure to environmental pollutants obviously together to the Lifestyle as reported in the European Code against Cancer. The mechanisms of human health damage by environmental agents are largely unknown, although the imbalance of reactive oxygen species (ROS) and associated oxidative stress may be the common denominator through which pollutants alter the biomolecular cellular structures (proteins, lipids, DNA strand). In fact, the imbalance of antioxidant defenses and detoxification processes provides a logical explanation for the onset of oxidative stress diseases in humans increasing the organism's greater susceptibility to toxicity, including pollutants. The mitochondrion plays a central role in the balance of the intracellular redox state being the main site of energy and ROS production. Moreover, within mitochondria a wide range of central processes occurs for many cellular functions (i.e., signaling pathways of calcium and programmed cell death). Notably, mitochondria may activate adaptive responses to different stresses to provide the energy needed to support homeostasis. Therefore, a number of diseases result from mitochondrial alterations. Mitochondrion has recently also been better considered as an elective target of various pollutants, in fact, mitochondrial DNA (mtDNA) is more sensitive than the nuclear DNA, and various *in vivo* and *in vitro* studies indicate how exposure to pollutants induces: alteration of the respiratory mitochondrial function, reduction of mtDNA copy number (mtDNA-CN), alteration of mtDNA methylation of D-loop region, which regulates both transcription and replication of mtDNA. Considering the impact of pollutants on health in the perspective of safeguarding public health and prevention, the use of early health biomarkers is very important. In this regard, the male reproductive system is particularly sensitive to pollutants, and recent studies of EcoFoodFertility research project (www.ecofoodfertility.it) proposed it as a "Sentinel System Organ" and human semen as an early and sensitive environmental and health marker. In particular, spermatozoa are highly oxidative cells with high sensitivity to the pro-oxidant effects of environmental pollutants, due to the limited volume of the cytoplasmic space, with less antioxidant defenses. The aim of this PhD project is to investigate the associations between mitochondrial respiration, mtDNA copy number, mtDNA methylation of D-loop region in response to environmental exposures using a combination of *in vitro* and human studies. As human biological samples will be considered blood and semen samples from healthy young males residing in areas with different environmental exposures recruited during the EcoFoodFertility research project, comparing any differences in behavior between sperm and leukocyte mitochondria.