



ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA
DIPARTIMENTO DI SCIENZE MEDICHE VETERINARIE

Title

Mitochondrial dysfunction and lung inflammation as a cause of mitochondria-derived vesicles biogenesis and release in cystic fibrosis.

Project description

In addition to traditional endocrine and paracrine communication, the cells converse via extracellular vesicles (EVs) under physio-pathological conditions. EVs cargo includes plasma membrane and endosomal proteins, but EVs also contain material from other cellular compartments, including mitochondria. Recent evidence suggests that mitochondria-derived vesicles (MDVs) may be transferred and that mitochondrial content may alter the metabolic and inflammatory response of recipient cells. MDVs levels and cargo may be altered when mitochondrial dysfunction occurs, indicating that MDVs biogenesis and release are conditioned by the onset of several pathological conditions where mitochondrial physiology is compromised, such as in cystic fibrosis (CF). This could have important implications for their pathological progression and treatment.

Proposal plan

The mitochondrial permeability transition pore (mPTP) has been linked to multiple human pathologies that are characterized by mitochondrial dysfunction, including CF. The project aims to evaluate the pharmacological and/or genetic modulations of the mPTP phenomenon to understand the MDVs biogenesis and release in healthy and CF airway cell models. To understand the molecular mechanism of MDVs effect and formation connecting the mitochondrial homeostasis will be considered the biochemical features of MDVs and evaluate their bioenergetic structure and mitochondrial parameters. To provide new findings on the correlation between mitochondrial status and immunomodulatory effects in the airway-phagocyte crosstalk in CF lung pathology, recipient immune cells obtained from donor and CF patients will be analyzed and validated for *i)* the impact of MDVs as immune modulators, *ii)* their effect on the mitochondria-related process, and *iii)* the activities of recipient immune cells.