MitoFORMSinHF - Mitochondrial cristae form, function, and organization dependent upon metabolic sources and implication in heart failure

Every year 15.9 million people worldwide suffer a myocardial infarction (MI) causing sudden death in some individuals and predisposing survivors to recurrent MI's and heart failure (HF), making ischemic heart disease the greatest contributor to human mortality. Research has uncovered molecular mechanisms that contribute to cellular demise during ischemic heart disease, however, to date there is no effective molecularly designed therapeutic. Recent studies implicate metabolism in ischemic cardiac injury pathogenesis. Optic Atrophy 1 (OPA1), a dynamin-related inner mitochondrial membrane (IMM) protein, orchestrates IMM fusion and maintains mitochondrial cristae form and structure. During MI disassembly of OPA1-containing oligomers ultimately induces apoptosis. Solute carrier family members (SLC25As) are thought to sense metabolic alterations and influence OPA1 oligomerization to regulate cristae function and shape, implicating metabolism in mitochondrial cristae formation. Whether metabolic sources or metabolic changes during IR injury contribute to disruption of OPA1 assembly, cristae maintenance, and apoptosis are yet to be elucidated. This is of great scientific interest because of the promising therapeutic potential to prevent pathogenic cristae remodeling and apoptosis during IR injury. I will work with state of the art imaging equipment within the Department of Biology at Padua University and receive expert training in mitochondrial biology under the supervision of Dr. Luca Scorrano in order to investigate if metabolic sources contribute to cristae maintenance and are implicated in ischemic cardiac injury. I will disseminate knowledge gained to American and European research societies focused on basic cardiovascular biology by attending conferences and the general public through the use of social media and scientific outreach. This proposals completion will launch my career as an independent investigator in Europe and forge international research connections.

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