Public Abstract

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Title:FAST kinase domain-containing protein 1 in mitochondrial function, cell death and cardiovascular disease

Cell death occurs during myriad circumstances and varied physiological and pathological conditions. Identifying novel modulators of cell death pathways is crucial to understanding and controlling cell death. Therefore, we explored and identified Fas-activated serine/threonine phosphoprotein kinase domain-containing protein 1 (FASTKD1) as a novel modulator of cell death via its interaction with the known mitochondrial permeability transition (MPT) pore sensitizer, Cyclophilin D (CypD). In Aim 1, data indicate that FASTKD1 protects cells from oxidative stress-induced cell death. This protection is independent of the MPT pore, CypD and modulation of cellular antioxidant capacity. FASTKD1 is also shown to be a potent modulator of mitochondrial morphology. In Aim 2, we show that cardiac myocyte specific overexpression of FASTKD1 in vivo protects mice from myocardial infarction induced left ventricular free wall rupture. This protection is associated with modulation of inflammatory cell recruitment and extracellular matrix composition. Taken together, these data indicate that FASTKD1 presents a novel target for modulation of oxidative stress induced cell death and post-myocardial infarction healing.