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Heart Failure

EXPRESSION OF MITOCHONDRIAL MITOFILIN BUT NOT OF PORIN IS REDUCED IN LEFT VENTRICULAR MYOCARDIUM OF EXPLANTED FAILED HUMAN HEARTS AND IN HEARTS OF DOGS WITH EXPERIMENTALLY-INDUCED HEART FAILURE

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Background: The physiologic processes of mitochondrial (MITO) biogenesis, fission and fusion are abnormal in the failing heart and can result in MITO hyperplasia, reduced size and poor respiration. This study examined the regulation of two key MITO proteins; porin (PO), the outer membrane protein that forms the aqueous channel for metabolite flux between mitochondria and cytosol, and mitofilin (MF), a key player in maintaining MITO cristae morphology and is indispensible for normal MITO function.

Methods: SDS-extract was prepared from LV tissue of 6 explanted failed human hearts due to ischemic cardiomyopathy (ICM), 6 failed hearts due to idiopathic dilated cardiomyopathy (IDC), and 6 normal donor (DNR) hearts and from LV of 6 dogs with microembolization-induced heart failure (HF) and 6 normal (NL) dogs. Protein level was measured with Western blotting and band intensity quantified in densitometric units and normalized to the house keeping protein glyceraldehyde 3-phosphate dehydrogenase (GAPDH).

Results: Protein levels of PO did not change in LV of HF humans or dogs compared to normals. MF protein levels, however, were significantly reduced in ICM and IDC human hearts compared to DNR hearts and in HF dogs compared to NL dogs (Table).

Conclusions: Downregulation of the key MITO protein MF in LV myocardium of failing human and dog hearts provides support to the concept of energy deprivation in HF and emphasizes the need for developing therapeutics that target this key abnormality.

Protein Expression in LV Myocardium

	Dog		Human		
	NL	HF	DNR	ICM	DCM
PO/GAPDH	0.41 ± 0.02	0.38 ± 0.02	0.24 ± 0.02	0.25 ± 0.01	0.25 ± 0.01
MF/GAPDH	0.75 ± 0.01	0.29 ± 0.02*	0.26 ± 0.02	0.12 ± 0.01†	0.10 ± 0.01†
*=p<0.05 vs. NL; †= p<0.05 vs. DNR					