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Mitochondrial division/mitophagy inhibitor (Mdivi) ameliorates pressure overload induced heart failure

Background: We have previously reported the role of anti-angiogenic factors in inducing the transition from compensatory cardiac hypertrophy to heart failure and the significance of MMP-9 and TIMP-3 in promoting this process during pressure overload hemodynamic stress. Several studies reported the evidence of cardiac autophagy, involving removal of cellular organelles like mitochondria (mitophagy), peroxisomes etc., in the pathogenesis of heart failure. However, little is known regarding the therapeutic role of mitochondrial division inhibitor (Mdivi) in the pressure overload induced heart failure. We hypothesize that treatment with mitochondrial division inhibitor (Mdivi) inhibits abnormal mitophagy in a pressure overload heart and thus ameliorates heart failure condition.

Materials and Methods: To verify this, ascending aortic banding was done in wild type mice to create pressure overload induced heart failure and then treated with Mdivi and compared with vehicle treated controls.

Results: Expression of MMP-2, vascular endothelial growth factor, CD31, was increased, while expression of anti angiogenic factors like endostatin and angiostatin along with MMP-9, TIMP-3 was reduced in Mdivi treated AB 8 weeks mice compared to vehicle treated controls. Expression of mitophagy markers like LC3 and p62 was decreased in Mdivi treated mice compared to controls. Cardiac functional status assessed by echocardiography showed improvement and there is also a decrease in the deposition of fibrosis in Mdivi treated mice compared to controls.

Conclusion: Above results suggest that Mdivi inhibits the abnormal cardiac mitophagy response during sustained pressure overload stress and propose the novel therapeutic role of Mdivi in ameliorating heart failure.

Biography

Suresh C Tyagi is a professor in the Department of Physiology and Biophysics in the School of Medicine at University of Louisville. His research is supported by the National Institutes of Health. He is the recipient of numerous awards and honors including a medal of merit from the International Society for Heart Research. Tyagi has published more than 156 peer-reviewed articles, invited papers, and reviews. He is currently principal investigator on four NIH grants totaling $6.2 million

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