

Abrogation of MMP9 ameliorates cardiac dysfunction in diabetes

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Elevated levels of matrix metalloproteinase-9 (MMP9) is associated with heart failure, and ablation of MMP9 improves contractility of cardiomyocytes and mitigates cardiac dysfunction. To test the hypothesis that abrogation of MMP9 ameliorates cardiac dysfunction in diabetes, we created a double knock out (DKO: Ins2^{+/-} /MMP9^{-/-}) mice by cross-breeding diabetic Ins2^{+/-} Akita with MMP9^{-/-}. The structural and functional remodeling in the heart was assessed by measuring the levels of fibrosis, contractility (\pm dL/dt) of cardiomyocytes and LV dysfunction (% FS) in the WT (sibling of Akita with low glucose level), Akita and DKO mice. The degree of fibrosis is increased, contractility of cardiomyocytes is impaired, and % FS is decreased in Akita but ameliorated in DKO hearts suggesting that inhibition of MMP9 ameliorates cardiac dysfunction in diabetes. Since miR-133 regulates fibrosis, we also measured the levels of miR-133 in WT, Akita and DKO hearts. Interestingly, miR-133 is attenuated in Akita but up regulated in DKO indicating that miR-133 is involved in improvement of cardiac function in DKO. In conclusion, abrogation of MMP9 mitigates cardiac dysfunction in diabetes, in part, by inducing miR-133.

Biography

Paras Kumar Mishra has completed his Ph.D. at the age of 30 years from Banaras Hindu University, India and postdoctoral studies from Emory University, Atlanta, and University of Louisville, Kentucky, USA. He is working as Assistant Professor at University of Louisville since 2010. He has published more than 50 papers in peer reviewed international journals and serving as editorial board member of several reputed journals. He is currently funded with American Heart Association grant.

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