

Mitochondrial division/mitophagy inhibitor (Mdivi-1) protects right ventricle from severe failure

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Myocardial infarction and chronic heart failure are common forms of cardiovascular disease and a leading cause of morbidity and mortality worldwide. Sustained pressure overload induces pathological cardiac dysfunction, linked to mitochondrial dysfunction (mitophagy) during right ventricle failure (RVF). We tested whether mitophagy division inhibitor (Mdivi-I) mitigates oxidative stress and leads to reverse pre-established advanced hypertrophy, fibrosis, and RV dysfunction. To verify this, C57 (less), FVB (intermediate), and C3H (most resistant to oxidative stress) strains of mice underwent pulmonary artery constriction (PAC) for 4 weeks with or without the Mdivi-I (50 mg/kg/day) treatment. After PAC mice developed increased cardiac mass, lowered ejection fraction, triggering oxidative stress, and mitochondrial dysfunction. Mdivi-I treatment reversed hypertrophy and fibrosis, lowered oxidative stress, and improved chamber and myocyte function, whereas untreated hearts worsened. To further support the claim of mitophagy occurrence during RVF, the levels of LC3A/B and P62 were measured. LC3A/B was increased in RV of PAC mice. Similarly, increased P62 protein level was also observed in RV of PAC mice. Treatment with Mdivi-I abolished this affect in PAC mice. RV pressure in PAC mice was increase up to 55 ± 3 mmHg, treatment with Mdivi-I decreased the pressure to 32 ± 4 mmHg. These results suggest that, Mdivi-I treatment reduces oxidative stress and ameliorates mitochondrial dysfunction that results in protection of RVF against mitophagy during PAH.

Biography

In 2004 Dr. Natia completed her MD at the age of 23 from Tbilisi State Medical University in Georgia. From 2005 till 2008, she worked as a junior physician in the cardiology department at the Tbilisi State Medical University hospital. Since 2008 she has been working as a postdoc at Dr. Tyagi's lab where she has successfully published more than 18 papers in reputed journals.

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