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Myocardial atrophy regulated by the formation of TRPC3 protein complex

Motohiro Nishida[1], Tomohiro Tanaka[1], Kazuhiro Nishiyama[2], Akiyuki Nishimura[2]

[1]Div. Cardiocirc. Signal., NIPS & ExCELLS, Natl. Inst. Nat. Sci., [2]Dept. Translat. Pharm. Sci., Grad. Sch. Pharm. Sci., Kyushu Univ.

Myocardial atrophy, characterized by the decreases in size and contractility of cardiomyocytes, is caused by severe malnutrition and/or mechanical unloading. We have investigated the mechanism underlying induction of myocardial atrophy induced by anti-cancer drug treatment, and found that formation of protein complex between NADPH oxidase 2 (Nox2) and transient receptor potential canonical (TRPC) 3 contributed to ROS-mediated myocardial atrophy in mice. Here, we report that extracellular adenosine 5'-triphosphate (ATP) promotes nutrient deficiency-induced cardiomyocyte atrophy through TRPC3-Nox2 complex formation. Knockdown of either TRPC3 or Nox2 suppressed nutritional deficiency-induced ATP release, as well as ROS production and NRCM atrophy, suggesting that the formation of TRPC3-Nox2 protein complex amplifies ATP-induced myocardial atrophy. Taken together, we propose that TRPC3-Nox2 axis mediates nutritional deficiency-induced cardiomyocyte atrophy by promoting ATP release.