Loss of Rubicon increases autophagic flux and protects against lipopolysaccharide-induced cardiac injury

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Autophagy is required to maintain cardiac myocyte homeostasis. Cardiac autophagy is up-regulated in response to a variety of factors and enhanced autophagy in the heart can be either adaptive or maladaptive depending upon the context. Previous in vitro studies has shown that rubicon, a component of PI3KC3 complex, suppresses autophagosome/endosome maturation by sequestering UVRAG, which prevents Rab7 activation. We have recently demonstrated that UVRAG deficiency causes impairment of autophagic flux in the heart, leading to age-related cardiomyopathy and cardiac dysfunction accompanied by enhanced inflammation. In this study, we hypothesize that loss of rubicon increased autophagic flux in the heart and protected against sepsis-induced cardiac injury. Rubicon knockout mice were generated by insertion of PiggyBac construct into intron 1 of rubicon gene and loss of rubicon in various tissues were demonstrated by reverse transcription polymerase chain reaction (RT-PCR) and western blot. Rubicon deficiency increased autophagic flux without altering transcript expression of autophagy-related genes in the heart. At baseline, cardiac morphology and function were preserved in rubicon-deficient mice. To determine the effect of rubicon deficiency on inflammatory heart disease, we treated rubicon-deficient mice and corresponding wild type (WT) controls with lipopolysaccharide (LPS). Rubicon deficiency prolonged survival of LPS-treated mice. Quantitative RT-PCR revealed that LPS-induced expression of inflammatory cytokines was attenuated in rubicon-deficient hearts. Autophagy was further enhanced in the heart from rubicon-deficient mice compared with WT controls in response to LPS. In conclusion, Rubicon deficiency enhances cardiac autophagy and attenuates sepsis-induced cardiac injury.

Biography

Hongxin Zhu is an Associate Professor in Bio-X Institutes, Shanghai Jiao Tong University. He has completed his Ph.D. degree at the age of 29 from Fudan University and postdoctoral studies in UT Southwestern Medical Center at Dallas. He has been serving as an editorial board member of International Journal of Clinical Therapeutics and Diagnosis, and Journal of Biochemical and Pharmacological Research. He is a guest editor for the Journal of Medical Imaging and Health Informatics.

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