Abstract: P5390

Adipolin/C1q/Tnf-related protein 12 attenuates adverse cardiac remodeling in a mouse model of myocardial infarction

Authors:
T Takikawa¹, K Ohashi¹, L Fang¹, H Kawanishi¹, N Otaka¹, H Ogawa¹, T Murohara¹, N Ouchi¹, Nagoya University Graduate School of Medicine, Department of Cardiology - Nagoya - Japan,

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Background: Ischemic heart disease is one of leading causes of death worldwide. Obesity is closely linked to the development of cardiovascular diseases including ischemic heart disease. Adipose tissue produces various secretory bioactive proteins called as adipokines, and dysregulation of adipokine production contributes to the pathogenesis of obesity-related complications. Previously we identified adipolin, also referred to as C1q/Tnf-related protein12, as an insulin-sensitizing adipokine that is down-regulated in obesity. Here, we investigated the effects of adipolin on cardiac remodeling in a mouse model of myocardial infarction (MI).

Method: Male adipolin-knockout (APL-KO) and wild-type (WT) mice were subjected to the permanent ligation of the left anterior descending coronary artery to create MI. Echocardiographic and histological analyses were performed to evaluate cardiac function and myocardial remodeling at 4 weeks after MI. Apoptosis was detected by terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay. Cardiomyocyte cross sectional area was evaluated by Wheat Germ Agglutinin staining. Perivascular fibrosis was assessed by Masson’s trichrome staining. Neonatal rat ventricular myocytes were used as cultured cardiac myocytes for in vitro study.

Results: APL-KO mice exhibited increased ratios of the heart weight/body weight and lung weight/body weight after MI compared with WT mice. APL-KO mice showed increased left ventricular diastolic diameter and decreased fractional shortening after MI compared with WT mice. APL-KO mice had increases in myocardial apoptosis, cardiomyocyte hypertrophy and perivascular fibrosis at the remote zone of infarct hearts as compared with WT mice. Treatment of cultured cardiomyocytes with adipolin protein reduced apoptosis in response to 24 hours of hypoxia. Treatment with adipolin protein also increased the phosphorylation of Akt in cardiomyocytes. Inhibition of PI3 kinase/Akt signaling by LY294002 reversed the anti-apoptotic effects of adipolin in cultured cardiomyocytes. Conclusion: Our data indicate that adipolin prevents pathological myocardial remodeling after chronic ischemia, at least in part, by suppressing myocardial apoptosis through an Akt-dependent mechanism.