What We have Learned about the Cardioprotective Effects of Adiponectin from the Adiponectin Knockout Mice

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Editorial

Adiponectin is a protein mainly secreted by adipocytes. Adiponectin couples regulation of insulin sensitivity with energy metabolism. Reduced adiponectin level and impaired adiponectin signaling are associated with various obesity-related disorders, including metabolic syndrome, diabetes, atherosclerosis, hypertension, and coronary artery disease [1]. Adiponectin knockout mice (APN-/-) demonstrate not only severe diet-induced insulin resistance, but also abnormal cardiovascular function. Therefore, the study of APN-/- elaborates our knowledge regarding adiponectin deficiency pertaining to obesity-related cardiovascular diseases.

Adiponectin deficiency is linked to impaired vasomotor function and cardiac function. In APN-/-, acetylcholine (ACh)-induced vasodilation in aortas was ameliorated, accompanied by increased superoxide and peroxynitrite production. Expression of endothelial NO synthase (eNOS) was conserved in APN-/- mice, but nitric oxide (NO) production and eNOS phosphorylation were significantly reduced [2]. APN-/- also revealed hypertension induced by salt diet [3]. APN-/- exhibited greater cardiac hypertrophy, pulmonary congestion, left ventricular (LV) interstitial fibrosis and LV systolic dysfunction following pressure overload induced by transverse aortic constriction [4].

Adiponectin plays a protective role against neointimal formation in response to injury [5]. APN-/- showed severe neointimal thickening and increased proliferation of vascular smooth muscle cells in mechanically injured arteries. Adenovirus-mediated supplement of adiponectin attenuated neointimal proliferation [6]. High-fat, high-sucrose feeding promoted the clearance of apoptotic cells by macrophages in both wild type mice and APN-/- [7]. Adiponectin deficiency leads to enhanced thrombus formation and platelet aggregation. There was no significant difference in platelet counts or coagulation parameters between wild type mice and APN-/-. However, APN-/- showed a reduced ability to clear early apoptotic cells that were injected into intraperitoneal cavities. Conversely, adiponectin administration promoted the clearance of apoptotic cells by macrophages in both APN-/- and wild type mice [8].

In summary, adiponectin deficiency is linked to impaired vasomotor/cardiac function, enhanced neointimal formation upon injury and exacerbated ischemic injury. Adiponectin also regulates function of VSMC, macrophages, and platelets. Results from APN-/- provide insights into the potential therapeutic benefits of adiponectin. In addition to its direct effects on cardiovascular system, adiponectin may also regulate the production/secretion of other downstream adipokines that represent an inflammatory phenotype in obesity and diabetes [19]. Therefore, increasing adiponectin level or enhancing adiponectin signaling may have a beneficial role in the treatment or prevention of obesity-related cardiovascular diseases.

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