Myeloid differentiation protein 1 protected myocardial function against high-fat stimulation induced pathological remodeling

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**Introduction**: Myeloid differentiation 1 (MD-1) is a secreted protein that regulates the immune response of B cell through interacting with radioprotective 105 (RP105). The disrupted immune response may contribute to the development of cardiac diseases, while the roles of MD-1 remain elusive. Our studies aimed to explore the functions and molecular mechanisms of MD-1 in obesity-induced cardiomyopathy.

**Methods**: H9C2 myocardial cells were treated with free fatty acid (FFA) containing palmitic acid and oleic acid to challenge high-fat stimulation and adenoviruses harboring human MD-1 coding sequences or shRNA for MD-1 overexpression or knockdown in vitro. MD-1 over-expression or knockdown transgenic mice were generated to assess the effects of MD1 on a high-fat diet (HD) induced cardiomyopathy in vivo.

**Result**: Our results showed that MD-1 was down-regulated in H9C2 cells exposed to FFA stimulation for 48 hours (figure 1). Both in vivo and in vitro, silencing of MD1 accelerated myocardial function injury induced by HD stimulation through increased cardiac hypertrophy and fibrosis (figure 2, 3, 4), while overexpression of MD1 alleviated the effects of HD by inhibiting the process of cardiac remodeling (figure 5, 6). Moreover, the MAPK and NF-κB pathways were overactivated in MD1 deficient mice and H9C2 cells after high-fat treatment. Inhibition of MAPK and NF-κB pathways played a cardioprotective role against the adverse effects of MD1 silencing on high-fat stimulation-induced pathological remodeling (figure 7, 8).

**Conclusion**: MD1 protected myocardial function against high-fat stimulation-induced cardiac pathological remodeling through negative regulation for MAPK/NF-κB signaling pathways, providing feasible strategies for obesity cardiomyopathy.