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Role of Toll-like receptor 5 in the development of post-myocardial infarction inflammation

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Background: Inflammatory processes play a key role in the pathophysiology of myocardial infarction (MI). Genetic deletion of toll-like recpetors (TLRs), especially TLR2 and TLR4 have shown protective role in murine models of MI. The role of other TLRs remains unknown. We have previously shown that cardiomyocytes express TLR5 and that the ligand of TLR5, flagellin, activates the NF-kappaB and MAPK pathways in cardiomyocytes. We also have shown that injection of flagellin induces acute systolic dysfunction in vivo in mice.
Aim: Determine the role of TLR5 in the development of post-MI inflammation.
Methods: A murine model of myocardial infarction was done by a 30 minutes ligation of the left anterior descending coronary artery followed by 2 hours of reperfusion. Infarct size was measured by standard Evans blue/TTC staining. Plasma creatine kinase (CK) was quantified as a read out of myocardial necrosis. Tissue and plasma cytokines (MIP-2, MCP-1, IL-6) were quantified by ELISA. To determine the extent of tissue lipid peroxidation we used malondialdehyde and 4-hydroxynonenal-HIS adduct assays. Tissue protein oxidation was tested by protein carbonyl ELISA kit. Phosphorylation of MAPK was analyzed by western blot.
Results: Genetic suppression of TLR5 induced a significant increase of myocardial infarct size and plasma CK, of biochemical markers of myocardial oxidative stress, and cytokine levels in the heart and the plasma after MI. These effects were associated with a marked enhancement of p38 phosphorylation in the heart from TLR5 KO mice.
Conclusion: TLR5 protects from acute myocardial injury and reduces local and systemic inflammation during myocardial infarction. The mechanisms may involve reduced p38 signaling, decreased oxidative stress and attenuated cytokine expression.
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