**A ROLE OF MYD88 IN THE ANTI-APOPTOTIC EFFECTS OF IL-10**

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Heart failure subsequent to myocardial infarction is associated with an increase in tumor necrosis factor-alpha (TNF-alpha) and a decrease in interleukin-10 (IL-10). In isolated cardiomyocytes, IL-10 has been shown to antagonize the pro-apoptotic effect of TNF-alpha. Although the anti-apoptotic action of IL-10 in cardiomyocytes is now generally accepted, its molecular basis is not yet well understood. We studied the role of Toll-like Receptor 4 (TLR4) and its downstream signals in the survival of adult cardiomyocytes in the presence of IL-10. In IL-10 stimulated cardiomyocytes, TLR4 expression followed the upregulation of myeloid differentiation primary gene 88 (MyD88). Its activation led to IRF3 dimerization and phosphorylation which augmented IL-1beta translational activity. Degradation of Ikk suggested that Ikkbeta is an activating kinase for IRF3-regulated NF-kappaB activation and its nuclear translocation. There was an activation of Bcl-xL which attenuated the proteolytic activity of Caspase3 and PARP cleavage. Inhibition of MyD88 modulated IL-10 induced expression of TLR4, IRF3-dependent IL-1beta production and NFkappaB p65 phosphorylation and translocation. There was a significant decrease in Bcl-xL expression leading to PARP cleavage. These data suggest that anti-apoptotic function of IL-10 through TLR4 activation, requires MyD88 activation for the cardiomyocyte survival signal. (Supported by CIHR.)