TLR2 Knockout attenuates adverse cardiac remodeling in mice subjected to chronic pressure overload

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Aims: The inflammatory Toll-like receptor (TLR) pathway is associated with maladaptive cardiac remodeling in ischemic injury, but involvement upon chronic pressure overload (PO) is not yet fully understood. In this study, we investigated the effect of TLR2 knockout (KO) on cardiac remodeling during chronic PO in mice subjected to transverse aortic constriction (TAC) surgery.

Methods and Results: 35 male mice (age 10-12 weeks; wildtype (WT) or TLR2 KO) underwent sham or TAC surgery. Echocardiography and electrocardiography were recorded 2, 6 and 12 weeks after surgery. At 12 weeks, hearts were extracted for molecular and histological analysis. Interestingly, TAC in TLR2 KO mice (n=14) was associated with less hypertrophy, attenuated characteristics of contractility, and lower levels of inflammatory cytokines compared to WT TAC animals (n=11), which presented with reduced left ventricular ejection fraction (<35%), greatly enlarged hearts (heart weight/tibia length ratio 16.6±0.7mg/mm), abnormal contraction characteristics, increased fibrosis and inflammation compared to Sham animals (n=10). Furthermore, in WT TAC animals, high levels of TLR4 and TLR2 correlated with highest degree of hypertrophy and increased levels of the inflammatory cytokine interleukin 6 (IL-6).

Conclusion: These data show the association of adverse cardiac remodeling with high levels of TLR2 and TLR4, as well as attenuation of adverse remodeling in TLR2 KO mice. This suggests that the TLR pathway may represent an important modifiable target in cardiac remodeling under chronic pressure overload.