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The innate-like T cells are required to modulate acute inflammatory response (P1050)

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Macrophages infiltration and activation in myocardium is a pivotal immunopathological lead to hypertensive cardiac micro-injury, but underlying mechanisms remain elusive. We have found that CD8 KO or CD8+ T cells depletion by antibody significantly reduce cardiac pro-fibrotic inflammatory responses induced by angiotensin II (Ang II) infusion, whereas CD8 KO mice reconstituted with CD8+ T cells became sensitive. More importantly, CD8+ T cells are required for macrophage infiltration in myocardium and subsequent activation to express pro-inflammatory cytokines and chemokines, including MCP-1. Furthermore, transwell experiments showed that macrophage activation requires direct contact with activated CD8+ T cells, but with TCR dispensable. TCR-independent activation of macrophage is further confirmed in vivo, where OT-I transgenic mice show a similar cardiac pro-inflammatory response to Ang II as wt mice. Finally, IFNγ seems required for influx and activation of CD8+ T cells in myocardium in response to Ang II, that subsequently activate macrophages in the onset of cardiac inflammation. Thus, TCR-independent innate nature of CD8+ T cells is both necessary and sufficient for macrophage-induced hypertensive cardiac fibrosis. In conclusion, TCR-independent activation of macrophages by CD8+ T cells casts yet a novel innate function of T cells that is required to activate inflammatory response of macrophages to danger signals.