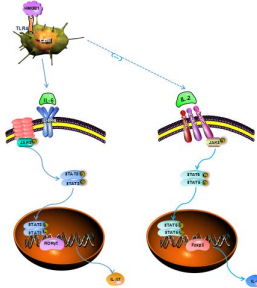
HMGB1
TLR4
T cell
IL-6
IL-6R
gp130
JAK1/2
STAT3
STAT3
STAT3
STAT3
RORγt
IL-17A
STAT3
STAT3
Foxp3
IL-10

Fig.S2. HMGB1 mediated Treg and Th17 cell differentiation and function. Within atherosclerotic lesions, HMGB1 can be actively secreted or passively released by VSMCs and macrophages exposed to some stimuli. After binding to TLR4 on macrophages or other cells, HMGB1 may stimulate the release of inflammatory cytokines, such as IL-6, resulting in downstream STAT3 activation, and suppress IL-2-mediated STAT5 activation. Treg and Th17 cell function, as well as IL-10 and IL-17A production, can be influenced by Foxp3 and RORγt expression in response to HMGB1-mediated signalling.