Leukocyte-expressed β2-adrenergic Receptors Are Essential For Survival Following Acute Myocardial Injury

Douglas Tilley, Temple Univ, Philadelphia, PA

Background: Immune cell-mediated inflammation is an essential process for mounting a repair response following myocardial infarction (MI). The sympathetic nervous system is known to regulate immune system function through β-adrenergic receptors (βAR), however their role in regulating immune cell responses to acute cardiac injury is unknown.
Methods and Results: Wild-type (WT) mice were irradiated followed by isoform-specific βARKO or WT bone-marrow transplantation (BMT) and after full reconstitution underwent myocardial infarction (MI) surgery. β2ARKO BMT mice displayed 100% mortality resulting from cardiac rupture within 12 days post-MI compared to ~20% mortality in WT BMT mice. β2ARKO BMT mice displayed severely reduced post-MI cardiac infiltration of leukocytes with reciprocally enhanced splenic retention of the same immune cell populations. Splenic retention of the leukocytes was associated with an increase in VCAM-1 expression, which was itself regulated via β-arrestin-dependent β2AR signaling. Further, VCAM-1 expression in both mouse and human macrophages was sensitive to β2AR activity, and spleens from human tissue donors treated with β-blocker showed enhanced VCAM1 expression. The impairments in splenic retention and cardiac infiltration of leukocytes following MI were restored to WT levels via lentiviral-mediated re-expression of β2AR in β2ARKO BM prior to transplantation, which also resulted in post-MI survival rates comparable to WT BMT mice.
Conclusions: Immune cell-expressed β2AR plays an essential role in regulating the early inflammatory repair response to acute myocardial injury by facilitating cardiac leukocyte infiltration.

Disclosure Block:
D. Tilley: None.