

Stroke: Opposing roles of STAT1 and STAT3 in the Ischemic Myocardium Mechanisms and Pathways of Cardioprotection

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Abstract

Cardiovascular pathologies are an enormous burden in human health and despite the vast amount of research; the molecular mechanisms and pathways that control the underlying pathologies are still not fully appreciated. The Janus kinase (JAK)-signal transducers and activators of transcription (STAT) pathway has recently been shown to be an integral part of the response of the myocardium to various cardiac insults, including myocardial infarction, oxidative damage, myocarditis, hypertrophy and remodeling, in addition to having a prominent role in cardioprotective therapies such as ischaemic preconditioning. A substantial literature has focused on the roles of STAT1 and STAT3 in ischemic heart disease, where, at least in the acute phase, they appear to have a yin-yang relationship. STAT1 contributes to the loss of irreplaceable cardiac myocytes both by increasing apoptosis and by reducing cardioprotective autophagy. In contrast, STAT3 is cardioprotective, since STAT3-deficient mice have larger infarcts following ischemic injury, and a number of cardioprotective agents have been shown to act, at least partly, through STAT3 activation. Thus, targeting the JAK-STAT activities in the diseased heart may lead to potential benefits in manipulating this pathway in cardiovascular therapy.