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INTERLEUKIN-6-MEDIATED UPREGULATION OF BRAIN NATRIURETIC PEPTIDE EXPRESSION VIA THE JAK2/STAT3 SIGNALLING PATHWAY IN NEONATAL RAT CARDIOMYOCYTES

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¹Wen-Jing Xia, ²Yi-Yi Huang, ¹Jian-Gui He. ¹Department of Cardiology, First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; ²Department of Emergency, First Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Objectives We have shown that interleukin-6 (IL-6) upregulates brain natriuretic peptide (BNP) expression in rat cardiomyocytes under ischaemic conditions, partly via the transforming growth factor β 1 (TGF- β 1)/SMAD2 signal pathway. Studies have shown that the IL-6/Janus kinase 2 (JAK2)/signal transducer and activator of transcription 3 (STAT3) signalling pathway plays a significant role in myocardial ischaemic injury. We have questioned whether JAK2 and STAT3 proteins also participate in IL-6-mediated regulation of BNP in neonatal rat cardiomyocytes.

Methods Direct drug intervention with IL-6 showed that IL-6 independently activates the JAK2/STAT3 pathway in neonatal rat cardiomyocytes.

Results Moreover, increased phosphorylation of the STAT3 protein was first detectable after 5 min of IL-6 stimulation; phosphorylation was highest at 15 min and returned to basal level within 1 h. A specific inhibitor was then chosen to investigate the role of the JAK2/STAT3 pathway. Pretreatment with 10 mM AG490, a specific inhibitor for JAK2 protein, could suppress the increase in BNP levels induced by the administration of 10 ng/ml of IL-6, and maximal inhibition is achieved at a 50 mM concentration of AG490. Furthermore, combinational inhibition with neutralising antibody, which blocks the TGF- β 1/SMAD2 pathway, and AG490 failed to completely suppress the increase in BNP levels.

Conclusions Thus, apart from the TGF- β 1/SMAD2 signalling pathway, the JAK2/STAT3 pathway is also important in the IL-6-mediated regulation of BNP in neonatal cardiomyocytes; other signalling pathways may also be involved in this process.