

## **SRC FAMILY KINASES MEDIATE INHIBITION OF INTERLEUKIN 6 SIGNALING BY FIBROBLAST GROWTH FACTOR-2 IN MOUSE AORTIC ENDOTHELIAL CELLS.**

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Interleukin 6 (IL6) is a key acute phase cytokine that causes a variety of effects in different cell types via activation of STAT3. Transcription of suppressor of cytokine signaling 3 (SOCS3) is mediated by STAT3 dimers that form upon phosphorylation of tyrosine (Y705). Here we monitored SOCS3 mRNA as an endogenous reporter of IL6 action in order to assess the ability of fibroblast growth factor-2 (FGF2) to modulate IL6 signaling in murine aortic endothelial cells (MAEC). MAEC were treated with IL6, FGF2 and the inhibitors of Src Family Kinases (SFKs), Su6656 or PP2. Cells were then extracted for measurement of specific proteins by western blotting or for measurement of SOCS3 mRNA by RTPCR. IL6 (10 ng/ml) increased SOCS3 mRNA 7-fold and 10 ng FGF2/ml reduced the induction by 40%. The inhibitory effect of FGF2 was blocked by Su6656 and PP2. IL6 caused phosphorylation of STAT3 at Y705. This was reduced by FGF2 treatment, and Su6656 and PP2 prevented the inhibition. The results suggest that SFKs are required for suppression by FGF2 of IL6-mediated STAT3 activation. The reduction of STAT3 phosphorylation may occur by a SFK-dependent activation of a STAT3 phosphatase or inhibition of a kinase.