

EFFECTS OF PROSTAGLANDINS ON SOCS EXPRESSION IN T-47D BREAST CANCER CELLS

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There is increasing evidence to suggest that prostaglandins can upregulate suppressor-of-cytokine-signalling (SOCS) expression and so modify cellular responses to cytokines. Here we examined this possibility in two breast cancer cell lines. Initially we characterised prostaglandin receptor expression by reverse transcription-PCR, and found that T-47D cells express EP2, EP3 and EP4 receptors but not FP or EP1 receptors whereas MCF-7 cells expressed EP1 and EP4 receptors. A range of prostaglandin agonists were then used to elucidate whether prostaglandins affect SOCS expression and the receptor subtypes involved. SOCS 1-3 and CIS expression were measured by Real-Time PCR. In MCF-7 cells, PGE2 caused only minor increases in SOCS1 and SOCS3 expression. However in T-47D cells, PGE2 strongly induced SOCS3 expression with 2- and 5-fold increases in mRNA at 30 and 60 min respectively, returning to baseline at 120 min. SOCS1 was also upregulated at 30 and 60 min (3- and 5-fold respectively) and remained elevated (6-fold) at 120 min. In contrast, CIS and SOCS2 were not induced. Cloprostenol, Butaprost, Latanoprost and Sulprostone had no effect on SOCS expression, suggesting that the PGE2 response is mediated via the EP4 receptor. The induction of SOCS expression by PGE2 was not due to increased STAT3- or STAT5-tyrosine phosphorylation, and indeed we observed a decrease in STAT5 tyrosine phosphorylation 10 min and 1 h after PGE2, as determined by ip/western blotting. In summary, we propose that prostaglandin-induced SOCS1 and 3 expression in T-47Ds could constitute a means whereby cellular resistance to PRL is induced. *Supported by the ARC.*