

## BCS Conference 2017 (Basic Science)

**Abstract Title:** THE EFFECT OF INTERLEUKIN 1B ON VASCULAR ANGIOPOIETIN 1 SIGNALLING

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**Keywords**

Angiopoietin 1, Tie2, Interleukin 1 $\beta$

**Abstract Body**

**Introduction:** Angiopoietin 1 (Ang1) is a growth factor that plays a crucial role in maintaining normal vascular function. The main role of Ang1 is to maintain vessels in quiescent, inhibit vascular inflammation and maintain endothelial survival. Ang1 exerts its protective effect by activating Tie2 receptors, which are predominantly expressed on endothelial cells. The ratio between Tie2 and its co-receptor, Tie1, is a regulatory factor in Ang1 signalling with high levels of Tie1 capable of reducing Ang1-induced Tie2 activation. The activity of Ang1 is aided by Tie2 phosphorylation followed by activation of cascade of downstream signalling pathways including Phosphatidylinositol 3-kinase (PI3Kinase)/AKT and Erk1/2. Interleukin 1 Beta (IL1 $\beta$ ) is a proinflammatory cytokine that acts on microvasculature and large vessels and has been implicated in a range of vascular pathologies including vascular inflammation and atherosclerosis. Various pathophysiological mediators including VEGF and TNF alpha have shown to affect the levels of Tie receptor expression and subsequently influencing Ang1 signalling in endothelial cells; however the involvement of Interleukin 1  $\beta$  on this pathway has not been reported.

**Aim:** To examine the impact IL1 $\beta$  has on Tie2:Tie1 expression ratio and Angiopoietin1 signalling in endothelial cells.

**Method:** Primary Human umbilical vein endothelial cells (HUVEC) were stimulated with 25ng/ml of IL1 $\beta$  at different time periods in the presence or absence of 300 ng/ml of human recombinant Ang1. Cell lysates from the treated cells were then subjected to immunoprecipitation and Western blotting to analyze Tie receptor levels and signaling molecules associated with Ang1 cellular transduction including Phospho-Tie2 (pTie2), and phospho-AKT (pAKT). The levels of target proteins were compared between reactions by quantifying mean intensity of bands. Data is presented as means and SEM of three independent experiments. Statistical significance represented with  $p < 0.05$  using Student's t test.

**Results:** The expression of Tie2 and Tie1 protein in endothelial cells treated with IL $\beta$  was significantly altered with different Tie2:Tie1 ratio patterns observed at 1h and 24h. These changes to the Tie2:Tie1 expression patterns also altered the ability of Ang1 to induce Tie2 phosphorylation and downstream signaling molecules including pAKT.

**Conclusion:** This study demonstrates for the first time that IL1 $\beta$  is capable of altering Tie2:Tie1 ratio that subsequently leads to the regulation of Ang1 signalling. These findings provide further insight on how the Angiopoietin1 signalling pathway adapts to the acute and chronic effect of IL1 $\beta$  and how this signalling pathway is important in limiting pro-inflammatory responses of the vasculature.

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<b>Names</b>	<b>Presenting Author</b>	<b>Conflict of Interest</b>
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Dr Harprit Singh	No	No conflict of interest