

P032 Role of prostacyclin IP receptors in the sensing of Gram negative bacteria

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Prostacyclin (PGI₂) is a cardioprotective hormone released from endothelial cells. PGI₂ acts on cell surface IP receptors linked to activation of adenylate cyclase and cAMP formation. PGI₂ and other prostaglandins have been implicated in the inflammation caused by infection as well as in the signalling pathways associated with pathogen sensing. In the current study, we have investigated the role of IP receptors in the sensing of Gram negative *E. coli* by blood vessels and isolated vascular smooth muscle cells (VSMCs). Rat VSMCs were stimulated with whole heat-killed *E. coli* (10⁸ CFU/ml). Cell activation was assessed by the release of NO (via NOSII induction) using the Griess reaction. In separate experiments, whole aorta was dissected from wild type (C57 Bl6) or IP^{-/-} mice, cut into rings (5mm) and incubated in culture overnight in the presence or absence of *E. coli* (10⁸ CFU/ml). Sensing of whole bacteria by vessels was assessed by the induction of vascular hyporeactivity to contractile agents, measured using standard bioassay protocols in Mulvanny's myograph. The IP receptor agonist, treprostinil sodium (10⁻⁸ to 10⁻⁶M) increased *E. coli* stimulated NO formation by VSMCs. By contrast to wild type mice, vessels from IP^{-/-} mice were unresponsive to *E. coli*. These data suggest that IP receptors are central in the sensing of *E. coli*, leading to NOSII induction, by vascular smooth muscle. These observations have important implications for our understanding of pathogens and vascular dysfunction.