P074 Hck tyrosine kinase mediates TLR4 signalling in human macrophages

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Src family tyrosine kinases (SFK) are activated by LPS however their role in LPS signalling in human macrophages is unclear. Hck is a SFK member expressed exclusively in haematopoietic cells and previous studies using murine cell lines have shown a role for Hck in LPS-induced TNFα production. Here we show that in primary human monocyte-derived macrophages Hck is rapidly phosphorylated following LPS stimulation. We have manipulated Hck expression levels by using both adenoviral constructs to overexpress Hck and RNAi technology to knock it down. We then examined the protein and mRNA levels of TNFα in LPS-treated macrophages. Our data suggests that Hck has a positive regulatory role in the induction of TNFα. Interestingly, while its expression level did not affect the NF-κB pathway, Hck did influence the ability of AP-1 to bind DNA in LPS-stimulated cells. These data indicates that Hck is involved in early events following LPS stimulation of human macrophages.