

**P023** The MyD88-independent pathway is not mobilized in human neutrophils stimulated via TLR4

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Lipopolysaccharide (LPS) activates both MyD88-dependent and -independent signalling via TLR4, but the extent to which each cascade is operative in different cell types remains unclear. This prompted us to revisit the intriguing issue of CXCL10 production, which we previously showed to be inducible in neutrophils stimulated with LPS and IFN $\gamma$ , but not with either stimulus – contrary to other myeloid cells. We now report that in neutrophils the MyD88-independent pathway is not activated by LPS. Indeed, microarray and real-time PCR experiments showed that neither IFN $\beta$  nor IFN $\beta$ -dependent genes (including CXCL10) are inducible in LPS-treated neutrophils, in contrast to monocytes. Further investigation into the inability of LPS to promote IFN $\beta$  expression in neutrophils revealed that transcription factors regulating the IFN $\beta$  enhanceosome, such as IRF-3 and AP-1, are not activated in LPS-treated neutrophils. Moreover, we show that the upstream (TANK)-binding kinase-1 is not activated by LPS in neutrophils. These results identify a disconnected activation of the two signalling pathways downstream of TLR4 in key cellular components of the inflammatory and immune responses, and help to better understand the primordial role of neutrophils in host defence against non-viral infections.