

**P058** TLR3 triggering induces caspase-1 independent IL-1 $\beta$  maturation and secretion

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IL-1 $\beta$  is a master cytokine that mediates several immune responses and is synthesized as an inactive precursor that is processed into biologically active IL-1 $\beta$  in response to various pro-inflammatory stimuli. It is generally accepted that IL-1 $\beta$  processing is mediated by caspase-1, which is activated upon formation of an 'inflammasome' complex that senses pathogen or danger associated molecules. Although these molecules are also recognized by TLRs, the role of most if not all TLRs in IL-1 $\beta$  production is believed to be limited to the production of the inactive proIL-1 $\beta$  precursor. We show that stimulation of macrophages with the double-stranded RNA analog poly(I:C) induces the proteolytic maturation of proIL-1 $\beta$  into its active form. Macrophages deficient in TLR3 or the TLR3 adaptor protein TRIF were unable to process proIL-1 $\beta$  in response to poly(I:C). Surprisingly, TLR3-induced proIL-1 $\beta$  maturation was independent of caspase-1, as poly(I:C) induced proIL-1 $\beta$  maturation still occurs in caspase-1 deficient macrophages. Evidence for a novel TLR3/TRIF induced signaling pathway leading to proIL-1 $\beta$  maturation will be presented.