

INTERLEUKIN (IL)-1 α IS AN INTRACRINE TRANSCRIPTIONAL REGULATOR OF IL-1 β IN MACROPHAGES: IMPLICATIONS FOR METABOLIC INFLAMMATION

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The diagram illustrates the TLR signaling pathway. It shows various TLRs (TLR1, 2, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13) on the cell surface and in endosomes. These receptors interact with ligands like LPS, Bacteria, LTA, PGN, BLP, Zymosan, and Flagellin. The signaling involves adaptors like MyD88, TRAM, TRIF, and TRAM, leading to the activation of transcription factors like NF-κB and IRF3/IRF7. This results in the production of cytokines like TNF, COX2, IL-18, and IFN-α, and the expression of costimulatory molecules like SLAM, CD80, and CD83.

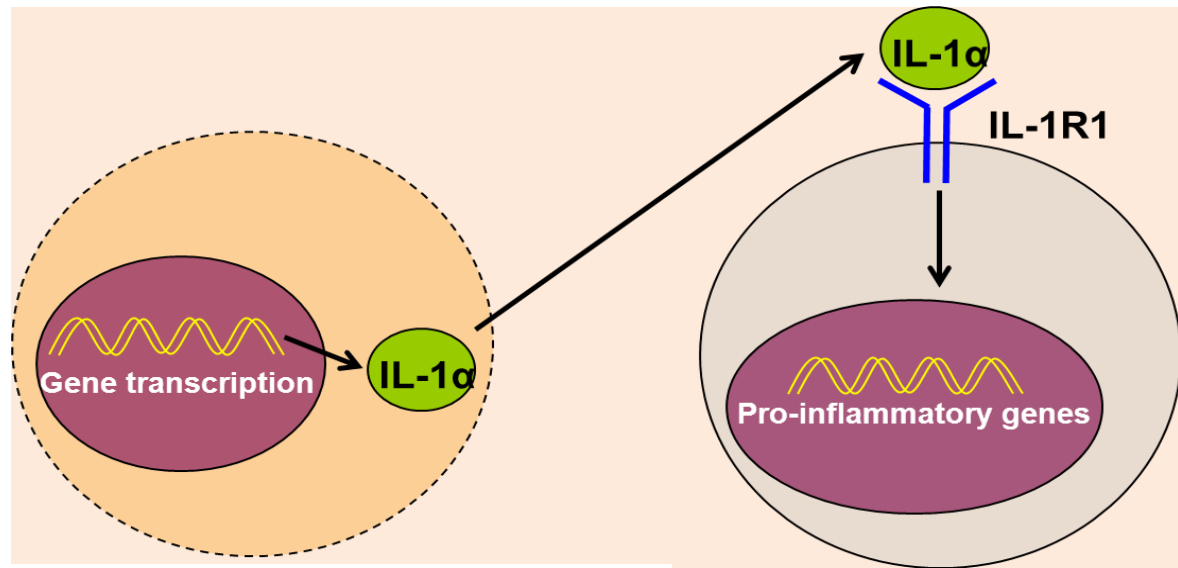


Cytokines

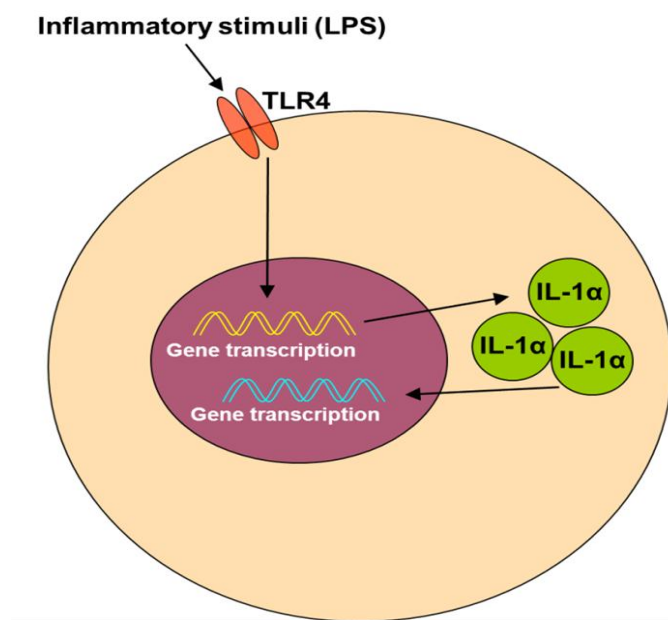
Cytokines

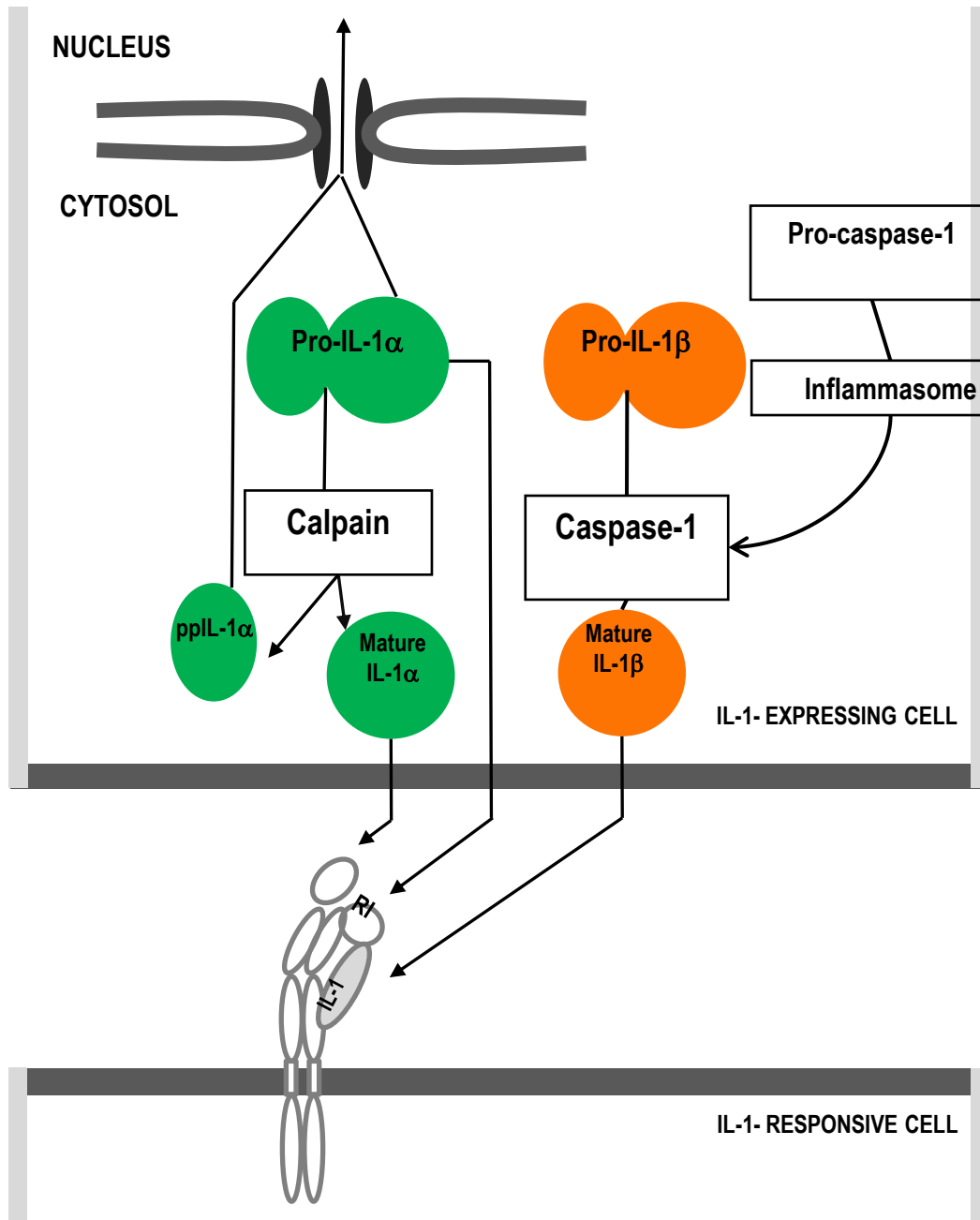
IL-1 α signaling

Extracellular effect



Nuclear effect

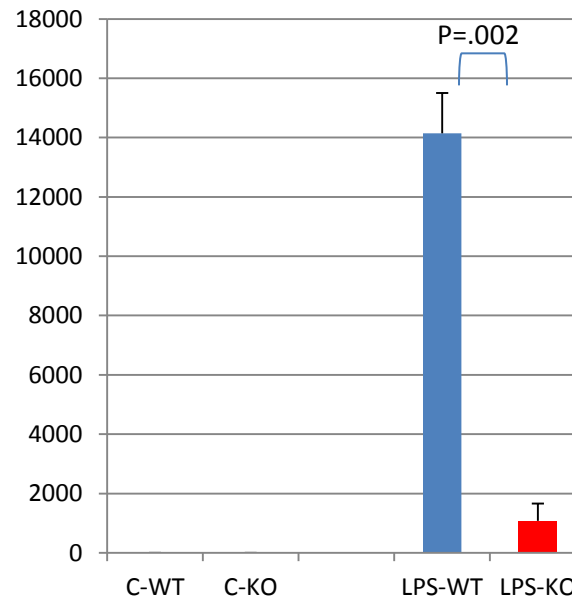




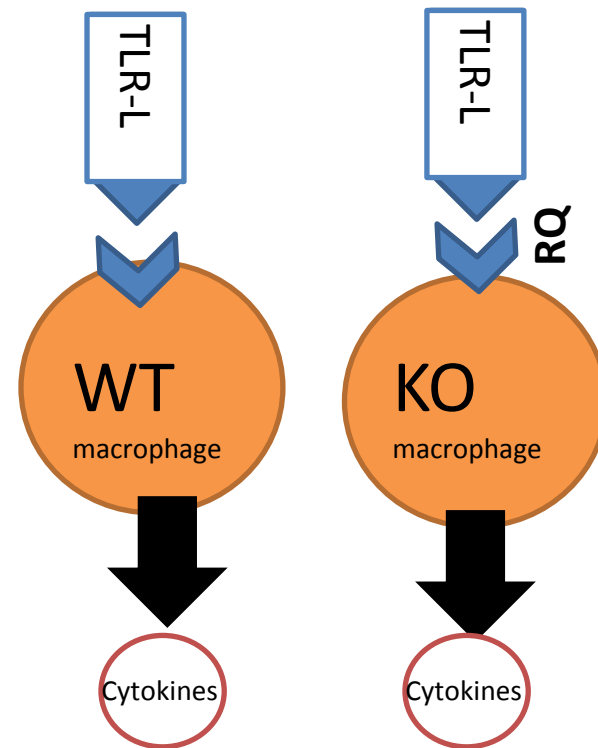
- IL-1 β is active only as a mature secreted molecule upon binding to IL-1 receptor.
- Transcriptional and post-translational regulation of IL-1 β activity

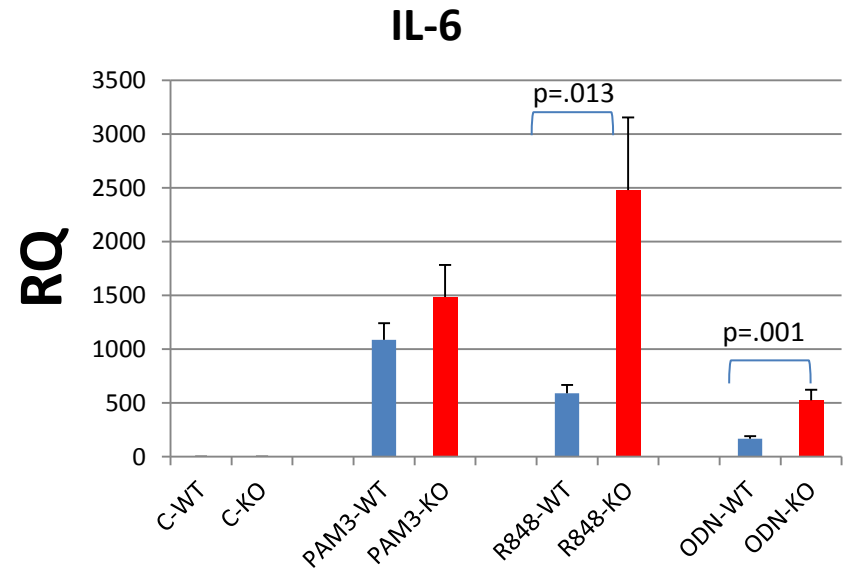
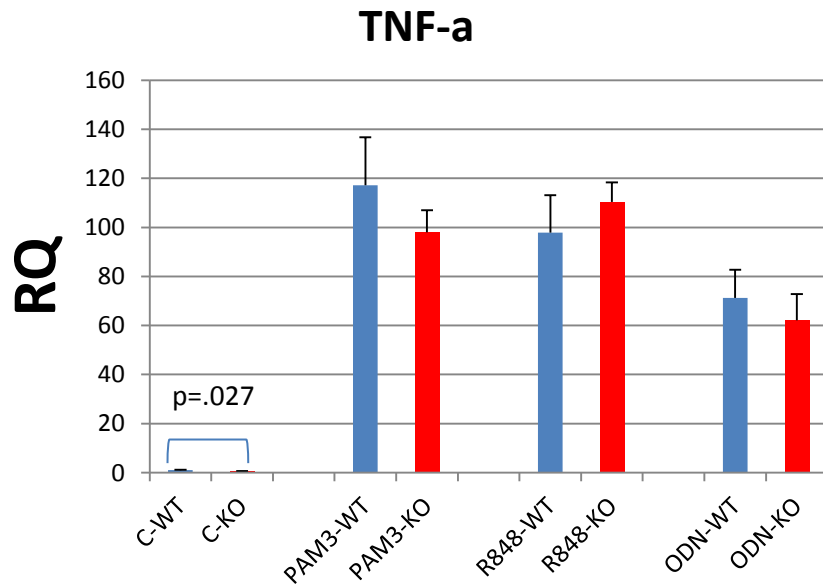
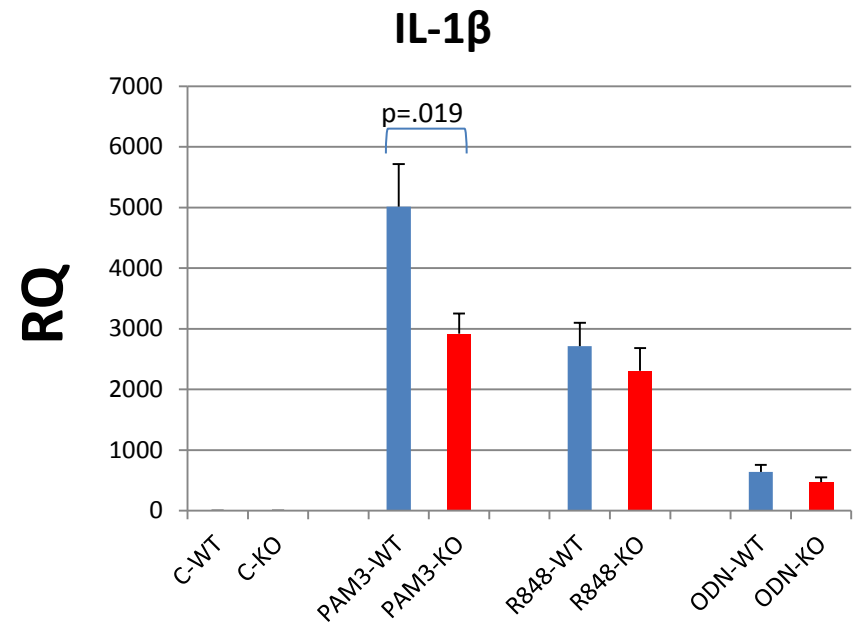
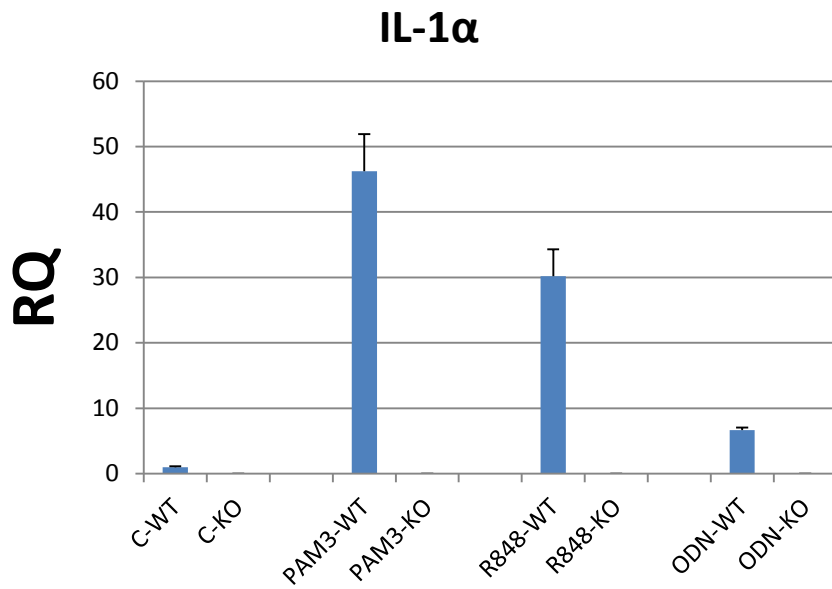
IL-1 α regulates the Transcription of IL-1 β in LPS (TLR4)
Stimulated Macrophages Independent of the IL-1R1

Does IL-1 α regulate the Transcription
of IL-1 β upon stimulation of other
TLRs in macrophages?



- **Methods:** IL-1 $\alpha^{+/+}$ and IL-1 $\alpha^{-/-}$ macrophages were stimulated with PAM3 (TLR2), R848 (TLR7), ODN (TLR9) and PGN (NOD2)
- mRNA levels of inflammatory cytokines including IL-1 β were examined with real-time PCR





LPS/PAM3 and R848/ODN: Cell surface receptor vs. endosome