macrophages from TLR2$^{-/-}$ mice showed a greatly exaggerated functional response (>6-fold) and produced much more tumour necrosis factor α (TNFα), interleukin 1β (IL-1β) and IL-6 upon FcγR triggering compared to WT cells.

To assess the functional consequence of enhanced FcγR response in TLR2$^{-/-}$ condition for arthritis, FcγR-driven serum-transfer arthritis was induced by intraperitoneal injection of serum from arthritic K/BxN mice. TLR2$^{-/-}$ mice showed an accelerated onset of arthritis and had a strikingly enhanced disease severity. Marked increase in inflammation was also obvious in the knee joints in addition to the paws. Furthermore, gene expression of several proinflammatory cytokines, including TNF, IL-1 and IL-6, and certain matrix metalloproteinases was enhanced in synovial tissue of TLR2$^{-/-}$ mice compared to WT.

PCR analysis revealed that basal expression of activating and inhibitory FcγRs in peritoneal macrophages, spleen and synovial tissue of arthritic mice was not affected by TLR2 deficiency. Furthermore, regulation of FcγR expression in macrophages upon stimulation with K/BxN serum and HAGGs was not affected. However, macrophages from arthritic TLR2$^{-/-}$ mice released significantly more TNF and IL-6 upon general phorbol myristate acetate/ionomycin stimulation, while having similar levels of IL-10 compared to WT cells. This indicates a potentiated M1 and similar M2 profile in macrophages from arthritic mice in the absence of TLR2. Importantly, FcγR triggering of macrophages isolated briefly after disease induction and before appearance of clinical differences using immune complexes resulted in markedly higher levels of TNF and IL-6, but not IL-10, in TLR2$^{-/-}$ condition. Unaltered response of TLR2$^{-/-}$ macrophages to IL-1 as control excluded a non-specific effect.

These findings indicate an important regulatory function of TLR2 in macrophage FcγR response with remarkable consequences for arthritis expression. A protective role of TLR2 in immune-complex driven arthritis beyond its previously described role in promoting regulatory T cell function may provide a relevant therapeutic intervention for the future treatment of RA.

## A84 TOLL-LIKE RECEPTOR 2 NEGATIVELY REGULATES FCγ RECEPTOR RESPONSE IN MACROPHAGES AND INHIBITS FCγR-MEDIATED ARTHRITIS

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10.1136/ard.2010.148973.2

Current evidence indicates that toll-like receptors (TLRs) and Fcγ receptors (FcγRs) are involved in the pathogenesis of arthritis and mutual regulatory functions for these innate immune receptors have been suggested as well. In the present study, the authors investigated the involvement of TLR2 in regulation of FcγR response and assessed the functional consequences for the development of arthritis.

Peritoneal macrophages from naïve wild-type (WT) and TLR2$^{-/-}$ mice were stimulated with heat-aggregated γ globulins (HAGGs) and immune complexes, and cytokine production was evaluated. Although no clear shift was noticed in the expression pattern of activating and inhibitory FcγRs,