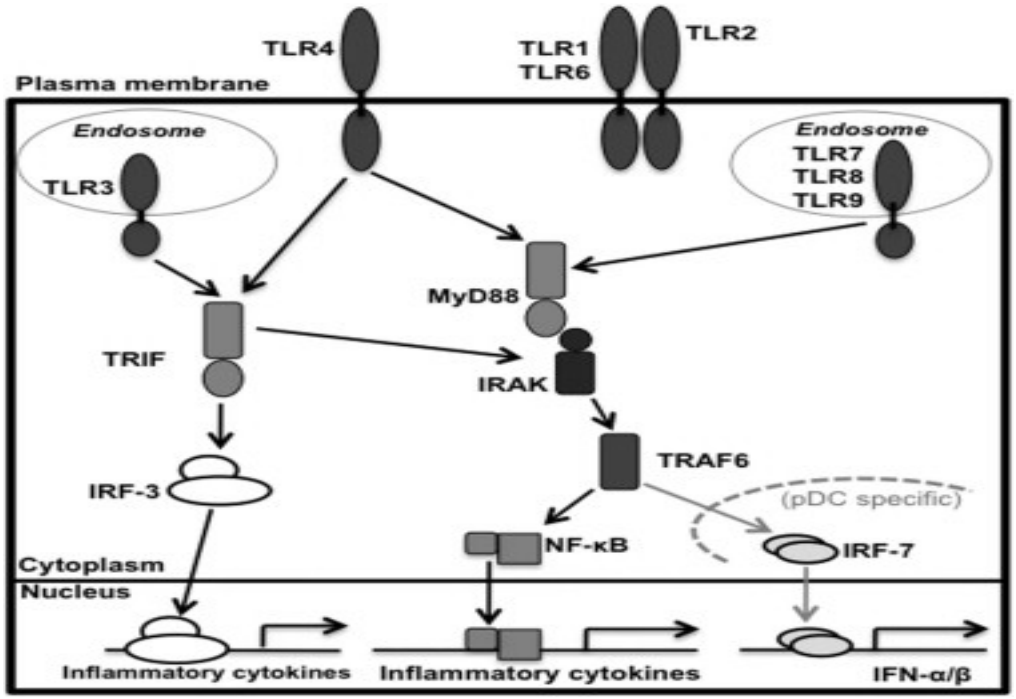
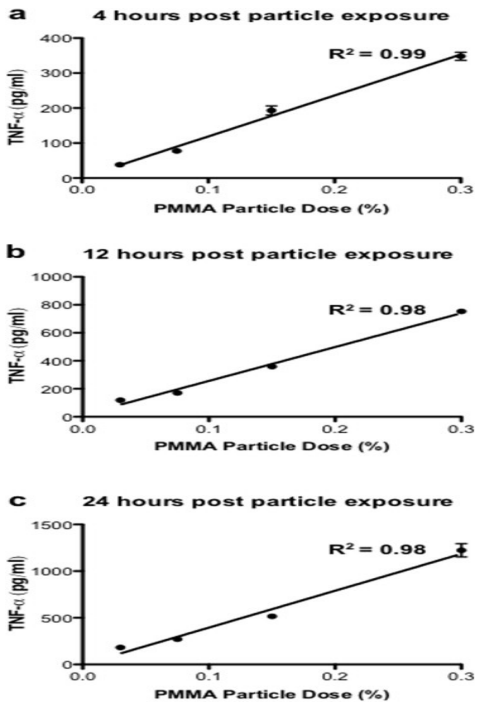


Supplementary Figure 1. Overview of the TLR signaling pathway. All of the TLR signaling receptors, except TLR3, utilize the MyD88-dependent signaling pathway which induces inflammatory cytokine production. TLR4 signals through both MyD88-dependent and TRIF-dependent pathways. In MyD88-dependent pathways, IRAK1 and IRAK4 are phosphorylated and dissociate from the complex to activate TRAF6, which activates numerous downstream signaling components leading to the nuclear translocation of NF-κB and induction of inflammatory cytokine gene transcription. The TRIF-dependent pathway can result in either the nuclear translocation of IRF-3 and transcription of Type 1 IFN-inducible genes or in a delayed NF-κB response. Plasmacytoid dendritic cells (pDC) express TLRs 7–9 in the endosomal compartment and utilize a unique pathway culminating in the nuclear translocation of IRF-7 and induction of IFN-α transcription.



Supplementary Figure 2. Correlation between PMMA particle concentration and TNF-α production. The murine macrophage cell line RAW 264.7 was incubated with PMMA particles at a concentration of 0.03, 0.075, 0.15 and 0.30% v/v for (a) 4, (b) 12, and (c) 24 h (n = 3). At all time points assayed correlation analysis demonstrated a robust correlation between PMMA particle dose and TNF-α production.