the mean ± SD of three independent wells for each experimental treatment and were identical across three separate experiments.

Figure 11. Relationship between TLR2 and signaling pathways regulating IL-12 family member expression in microglia. Intact Gram-positive bacteria trigger TLR9 activation via CpG DNA, which stimulates IL-12 family member production. In the absence of TLR2, TLR9 activation remains unchecked, resulting in exaggerated cytokine release. Both PI3K and MAPK pathways influence IL-12 expression in response to intact bacteria.

Supplemental Figure 1. TLR2 loss leads to elevated IL-12 family cytokine production in macrophages upon exposure to intact *S. aureus*. Thioglycollate-elicited peritoneal macrophages from TLR2 WT and KO mice were seeded at 2 x 10^5 cells per well in 96-well plates and incubated overnight. After 24 h, cells were exposed to 10^7 cfu heat-inactivated *S. aureus* for 24 h, whereupon IL-12p40 (A), IL-12p70 (B), IL-27 (C) and CCL2 (D) production was quantitated by ELISA. Significant differences between TLR2 KO versus WT macrophages are indicated by asterisks (*, $p < 0.001$). Results are reported as the mean ± SD of three independent wells for each experimental treatment and were identical across three separate experiments.

Supplemental Figure 2. Exaggerated IL-12p40 production by TLR2 KO macrophages is conserved upon exposure to various streptococcal and staphylococcal species. Thioglycollate-elicited peritoneal macrophages from TLR2 WT and KO mice were seeded at 2 x 10^5 cells per well in 96-well plates and incubated overnight. After 24 h, cells were exposed to 2 x 10^5 cfu/well of live Gram-positive bacteria for 6 h, whereupon IL-12p40 production was quantitated by ELISA. Significant differences between TLR2 KO versus WT macrophages are

indicated by asterisks (*, $p < 0.05$). Results are reported as the mean $\pm$ SD of two independent wells for each experimental treatment and were identical across two separate experiments.

Supplemental Figure 3. Gram-negative bacteria do not augment IL-12p40 production in TLR2 KO macrophages. Thioglycollate-elicited peritoneal macrophages from TLR2 WT and KO mice were seeded at 2 x 10^5 cells per well in 96-well plates and incubated overnight. After 24 h, cells were exposed to 2 x 10^5 cfu/well of live Gram-negative bacteria for 6 h, whereupon IL-12p40 production was quantitated by ELISA. Results are reported as the mean $\pm$ SD of three independent wells for each experimental treatment and were identical across two separate experiments.

Supplemental Figure 4. TLR9 blockade prevents exaggerated IL-12p40 expression in TLR2 KO macrophages. Thioglycollate-elicited peritoneal macrophages from TLR2 WT and KO mice were seeded at 2 x 10^5 cells per well in 96-well plates and incubated overnight. After 24 h, cells were exposed to heat-inactivated *S. aureus* (10^7 cfu/well) $\pm$ the inhibitory CpG ODN 2088 for 24 h, whereupon IL-12p40 production was quantitated by ELISA. Significant differences between TLR2 KO versus WT microglia are indicated by asterisks (*, $p < 0.05$), whereas differences between TLR2 KO microglia treated with *S. aureus* only versus *S. aureus* + ODN 2088 are indicated by hatched signs (#, $p < 0.05$). Results are reported as the mean $\pm$ SD of three independent wells for each experimental treatment and were identical across two separate experiments.