Abstract:
Mycoplasma arthritidis mitogen (MAM) is a superantigen (SAg) from M. arthritidis, an agent of murine toxic shock syndrome and arthritis. We previously demonstrated that C3H/HeJ and C3H/HeSnJ mice that differ in expression of TLR4 differed in immune reactivity to MAM. We show here that MAM directly interacts with TLR2 and TLR4 by using monoclonal antibodies to TLR2 and TLR4 which inhibit cytokine responses of THP-1 cells to MAM. Also, using macrophages from C3H substrains and TLR2-deficient mice, we confirmed that both TLR2 and TLR4 are used by MAM. Levels of IL-6 in supernatants of MAM-challenged macrophages were higher in mice which expressed only TLR2, lesser with both TLR2 and TLR4, and absent in mice lacking both TLR2 and TLR4. In addition, expression of TLR2 and TLR4 was moderately upregulated in wild-type cells but cells lacking TLR4 showed a fivefold increase in TLR2 expression. Further, blockade of TLR4 on macrophages of C3H/HeN mice with antibody greatly increased expression of TLR2 and release of IL-12p40 in response to MAM. These results indicate that the SAg, MAM, interacts with both TLR2 and TLR4 and that TLR4 signalling might downregulate the MAM/TLR2 inflammatory response.