Acute brain injury triggers MyD88-dependent, TLR2/4-independent inflammatory responses.

Endogenous molecules released from disrupted cells and extracellular matrix degradation products activate Toll-like receptors (TLRs) and, thus, might contribute to immune activation after tissue injury. Here, we show that aseptic, cold-induced cortical injury triggered an acute immune response that involves increased production of multiple cytokines/chemokines accompanied by neutrophil recruitment to the lesion site. We observed selective reductions in injury-induced cytokine/chemokine expression as well as in neutrophil accumulation in mice lacking the common TLR signaling adaptor MyD88 compared with wild-type mice. Notably, attenuation of the immune response was paralleled by a reduction in lesion size. Neutrophil depletion of wild-type mice and transplantation of MyD88-deficient bone marrow into lethally irradiated wild-type recipients had no substantial impact on injury-induced expression of cytokines/chemokines and on lesion development. In contrast to MyD88 deficiency, double deficiency of TLR2 and TLR4 -- despite the two receptors being activated by specific endogenous molecules associated to danger and signal through MyD88 -- altered neither immune response nor extent of tissue lesion size on injury. Our data indicate modulation of the neuroinflammatory response and lesion development after aseptic cortical injury through...
MyD88-dependent but TLR2/4-independent signaling by central nervous system resident nonmyeloid cells.