Both IL-12 and IL-18 contribute to small intestinal Th1-type immunopathology following oral infection with Toxoplasma gondii, but IL-12 is dominant over IL-18 in parasite control.

Oral infection of C57BL/6 mice with Toxoplasma gondii results in small intestinal Th1-type immunopathology mediated by local production of IFN-gamma, TNF-alpha, and NO. To analyze whether the proinflammatory cytokines IL-12 and IL-18 play a role in the induction of immunopathology, IL-12p35/p40(-/-) and IL-18(-/-) mice were orally infected with T. gondii. Wild-type mice developed massive necrosis in their small intestines and died 7-10 days post infection. Even though IL-12p35/40(-/-) mice did not develop the necrosis they all died between day 9 and 11 after infection. In contrast, 50% of IL-18(-/-) mice died during the acute phase of infection. Compared to wild-type mice, IL-12p35/p40(-/-) but not IL-18(-/-) mice showed significantly higher parasite numbers in their small intestines and significantly higher numbers of parasite-associated inflammatory foci in their livers. IFN-gamma production was similar in infected wild-type and IL-18(-/-) mice but significantly decreased in IL-12p35/p40(-/-) mice. Treatment of mice with anti-IL-12- or anti-IL-18 antibodies after infection prevented the development of intestinal necrosis. These results reveal that both IL-12 and IL-18 play an important role in the development of intestinal immunopathology.
immunopathology following oral infection with T. gondii. However, IL-12 is dominant over IL-18 in the host defense against parasite replication. Therefore, neutralization of IL-18 (rather than TNF-alpha, IL-12, and IFN-gamma) may be a safe strategy for the treatment of Th1-associated diseases.