Macrophages Are Critical for Cross-Protective Immunity Conferred by Babesia microti against Babesia rodhaini Infection in Mice

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Abstract

AlthoughprimaryinfectionofmicewithBabesiamicrotihasbeenshowntoprotectmiceagainstsubsequentlethalinfection by Babesiarodhaini,themechanismbehindthecross-protection is unknown.To unravel lthis mechanism,we investigated the influence of primary infection of mice with n on lethal B.microtius ing different time course son the outcome of subsequent lethal B.rodhaini infection. Simultaneous infections of mice with these parasites resulted in rapid increases in parasitemia, with 100% mortality in BALB/cmice, as observed with control mice infected with B.rodhainial one. In contrast,mice with acute, resolving, and chronic-phase B.microti infections were completely protected against B.rodhaini, resulting in low parasitemia and nomortalities. Miceimmunized with dead B.microti were not protected from B.rodhaini infection, although high antibody responses were induced. Interestingly, the protected mice had significantly decreased levels of antibody response , cytokines (including gamma interferon[IFN-□],interleukin-2[IL-2],IL-8,IL-10,andIL- 12),and nitricoxide levels after infection with B.rodhaini.SCIDmiceandIFN-□-deficient mice with chronic B.microti infections demonstrated protective responses comparable to those of immunocompetent mice. Likewise ,invivoNK cell depletion did not significantly impair the protective responses. Conversely, macrophage depletion resulted in increased susceptibility to B.rodhaini infection associated with changes in the iranti body and cytokines profiles, indicating that macrophages contribute to the protection against this challenge infection. We conclude that future development of vaccines against Babesia should include a strategy that enhances the appropriate activation of macrophages.