Vervet Monkeys Vaccinated with Killed Leishmania major Parasites and Interleukin-12 Develop a Type 1 Immune Response but Are Not Protected against Challenge Infection

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ABSTRACT

Leishmania major is a protozoan parasite that causes chronic cutaneous lesions that often leave disfiguring scars. Infections in mice have demonstrated that leishmanial vaccines that include interleukin-12 (IL-12) as an adjuvant are able to induce protective immunity. In this study, we assessed the safety, immunopotency, and adjuvant potential of two doses of IL-12 when used with a killed L. major vaccine in vervet monkeys. The induction of cell-mediated immunity following vaccination was determined by measuring delayed-type hypersensitivity, in vitro lymphocyte proliferation, and gamma interferon (IFN-γ) production. Protection was assessed by challenging the animals with L. major parasites and monitoring the course of infection. At low doses of IL-12 (10 μg), a small increase in the parameters of cell-mediated immunity was observed, relative to those in animals that received antigen without IL-12. However, none of these animals were protected against a challenge infection. At higher doses of IL-12 (30 μg), a substantial increase in Leishmania-specific immune responses was observed, and monkeys immunized with antigen and IL-12 exhibited an IFN-γ response that was as great as that in animals that had resolved a primary infection and were immune. Nevertheless, despite the presence of correlates of protection, the disease course was only slightly altered, and protection was low compared to that in self-cured monkeys. These data suggest that protection against leishmaniasis may require more than the activation of Leishmania-specific IFN-γ-producing T cells, which has important implications for designing a vaccine against leishmaniasis.