



CYTED-RIMLEV

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Heterologous prime-boost vaccination with the *L. infantum* A2 antigen confers protection against the infectious challenge in macaques (*Macaca mulatta*).

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Studies in non-human primates have contributed to the progress in the field of vaccine development against leishmaniasis (Mem Inst Oswaldo Cruz 2008, 103:629-644). As with human trials, autoclaved *L. major* promastigotes administered with BCG fail to protect rhesus monkeys (*Macaca mulatta*) against infectious challenge despite eliciting antigen-specific recall proliferative responses (Mem Inst Oswaldo Cruz 2002, 97:1041-1048). In contrast, protection of macaques against experimental *L. major* infection was obtained by vaccination with a mixture of LmST11 and TSA proteins in IL-12 and alum (Infect Immun 2001, 69:4103-4108). We have recently introduced a viable *L. infantum*-macaque infection model (Trans R S Trop Med Hyg, 100:926, 2006), thus confirming their potential for pre-clinical evaluation of candidate vaccines. Here we compared the efficacy of three rA2-based vaccine regimens, in protecting macaques against infective challenge with *L. infantum*. When prime-boosted with a subunit protein-based vaccine [i.e., a mixture of rA2 protein, human recombinant interleukin 12 (rIL-12) and alum] (group 2) or combining naked rDNA-A2 priming with a live vectored [ie, a recombinant adenovirus vector expressing the A2 antigen, rAD5-A2] boost (group 6) macaques mounted only partial protection, but those primed with rAD5-A2 and boosted with rA2-plus-rIL-12/alum (group 4) exhibit pronounced control over challenged parasite burden (as indicated by real-time PCR-based quantification of *L. infantum* loads in liver samples from vaccinated and control macaques at week 18 PI) and disease progression (as characterized by the marked regression of immune granulomas following the infectious challenge). Moreover, the latter approach was found to be effective to induce strong A2-specific IgG antibody response in all vaccinated monkeys. Further analysis (using multi-parameter flow cytometry to assess antigen-specific recall T-cell responses after immunization) is in progress, and may result in a clear definition of what immune responses will be required for vaccine-induced protective immunity. The protective immunity induced by A2 in an animal model that is evolutionary close to humans qualifies this immunogen as a promising candidate DNA or subunit protein-based vaccine against human VL. The homology between

the *Macaca mulatta* immune system and that of humans has led to the believe that the efficacy of those antigens selected as being candidates for anti-*Leishmania* vaccine in this primate species may represent suitable vaccine candidates against human leishmaniasis.

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