WHY A VACCINE SHOULD WORK?

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The elements of cell mediated immunity, including cytokine production that provides protective immunity against *Leishmania* spp. in dogs is at least partially understood. For protection from progressive clinical CanL there must be high IFN-gamma production by CD4+ T cells, with detectable but low levels of IL-10 and IL-4 production to prevent inflammation-based pathology (1). This profile can be observed during natural asymptomatic canine infection. Establishing how to produce protective immunity through vaccination has been more elusive. The ability of a vaccine to maintain low parasite load is essential for limiting transmission from dogs to people as an *L. infantum* reservoir. The cumulative work of many groups has led to multiple lead vaccine/adjuvant combinations potentially capable of producing a cell-mediated immune response against infection by *Leishmania*. Subclinical infection is featured by the detection of parasite by the PCR method and/or the appearance of low antibody titers. In these dogs, a strong cellular immune response persists. The severity of late stage disease is correlated with high antibody levels and increasing parasite load. In dogs that become sick, the transition from a resistant to a susceptible state is related to multiple factors, particularly the result of prolonged infection. During this chronic infection an immunological imbalance arises in dogs progressing to clinical disease because dysfunction of the Th1 cellular response, termed T cell exhaustion, coupled with an increased humoral response (2). Protection from CanL strongly depends on the ability of the dog immune system to respond since control requires balanced levels of tissue-specific immunity to not cause immune-mediated tissue damage and subsequent disease. Four commercial products (Leishmune®; Leish-Tec®, CaniLeish® and Letifend®) have been licensed on the market for the control of Canine Leishmaniosis (CanL), the first two in Brazil, the others in Europe. Recently, Leishmune® was withdrawn from the market under decision of Brazilian Health Authorities. Different antigens have been employed, varying from single antigen (A2 ; Leish-tec®) to a mixture of secreted/excreted proteins (LiESP ; Canileish®) or “chimeric” protein (Q protein; Letiend®). Canileish® and Leish-Tec employ saponin-derived adjuvants, Letifend® is composed by antigen alone (3). The main controversy regarding CanL vaccines is that they do not block the establishment of infection. This could potentially keep a dog without clinical disease healthy but able to spread infection to humans and dogs.
