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In silico identification of B-cell epitopes of *Leishmania infantum* recombinant histone shared with human sera stably living in area where *Leishmania* species does perpetuate

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Visceral leishmaniasis (VL) can initially be misdiagnosed because its presentation is similar to many autoimmune diseases such as systemic lupus erythematosus (SLE), autoimmune hepatitis and dermatomyositis. Furthermore, serum antibodies from VL patients have been shown to strongly react against proteins that are conserved between the causative agent, *L. infantum*, and humans themselves. Some of these proteins, like histone, have also been described as immunogenic in several auto-immune syndromes, and the detection of antibodies against them is considered to be indicative of immune system disorders. The potential overlap of autoimmune diseases and VL presents a situation of confounding diagnoses if cross-reactive tests are used. To explore this possibility, we screened sera from three Tunisian populations for the presence, and relative quantity, of antibodies against a panel of *L. infantum* antigens comprising crude extract or recombinant molecules, with special attention being given to evolutionarily conserved histones. Our data indicate that antibodies in many of the SLE at-risk individuals recognized crude soluble *Leishmania* antigen (SLA). This compromised the specificity of SLA-based ELISA, providing many results falsely indicating *L. infantum* infection. Examination of the crude *Florentina Berianu, Olga Pinkston and Benjamin Wang* histone (CLH) mixture, which is expected to contain nucleosomal *Leishmania* histones H2A, H2B and H4, as well as recombinant versions of these *Leishmania* histones, suggested these to be a source of the cross-reactivity. For the purposes of diagnosing VL, it is therefore important to note that the rK39 antigen was found to be more specific and not conflicting with autoimmune presentations. *In silico* prediction data validate and indicate that the human histones are immunologically cross-reactive with *Leishmania* histones.

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