Corrigendum. In the 'note added in proof' it was erroneously stated that NO does not affect *in vitro* proliferation. It should have read that aminoguanidine did not have a direct toxic effect on *in vitro* proliferation of *B. bovis*. In fact, other groups have found that NO was inhibitory to *B. bovis* in culture[6].

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Parasite Candidate Vaccines: A Warning from Polymorphic *Leishmania* Populations

In a recent paper in *Parasitology Today*[1], Gupta and Anderson highlighted how host immune responses shape pathogen population structure. Two of their predictive models caught our attention. First, in case of strong conserved or polymorphic protective antigenic determinants (immunogens), population structure should evolve towards a single-strain or discrete-strain structure, respectively. Second, when comparing the nucleotide sequence of polymorphic antigen genes (under immune selective pressure) and housekeeping genes (supposed to vary neutrally), the absence of overlapping of both structures might be indicative of the protective nature of the polymorphic antigens.

Our current work involves exploring these models among natural populations of *Leishmania infantum*. Isolates, mostly of human origin and previously characterized by multilocus enzyme electrophoresis (neutral markers), were obtained from Tunisia, Algeria, France and Spain. Their gp63 genes (the major immunogens in *Leishmania* and candidate vaccines)[2] were amplified and cleaved by PCR–RFLP (restriction fragment length polymorphism)[3], and the obtained polymorphic patterns were processed by a clustering algorithm. The results (Fig. 1) illustrate clearly the polymorphism of gp63 genes, the structuring of *L. infantum* strains according to the geographical origin, and most of all the absence of overlapping with the zymodeme structure. This suggests the existence of a different selective pressure on genes encoding gp63 and isoenzymes. According to the models of Gupta and Anderson[1], this might be indicative of the polymorphic nature of gp63 immunogens. This prediction is supported by two previous reports. First, gp63 contains variant antigenic domains: amino-acid sequence variability (at both inter- and intra-specific levels) was shown to be higher in the surface of the molecule and was correlated with structural flexibility[4]. Second, recognition of gp63 by canine sera showed to be heterogeneous, reactivity being preferentially observed against most divergent regions of the glycoprotein[5].

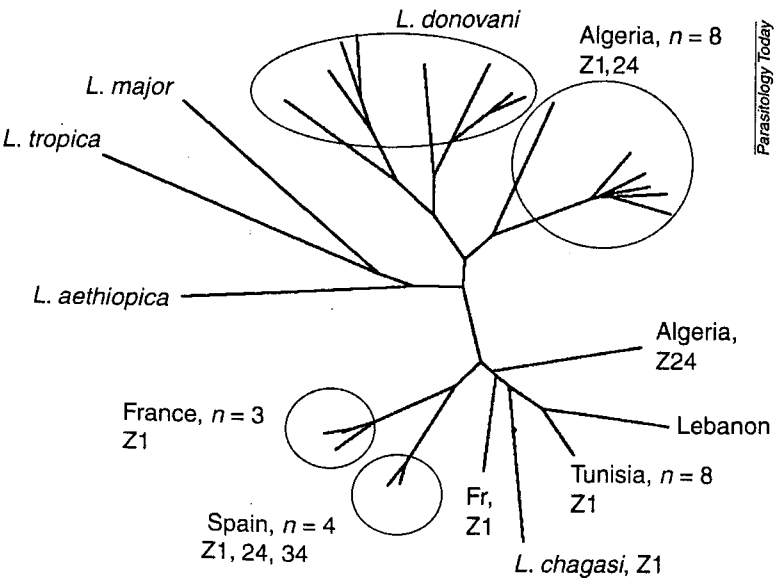

Fig. 1. gp63 Gene polymorphism among natural populations of *Leishmania infantum* (Jaccard distance and Fitch–Margoliash). Other *Leishmania* species are included as outgroups; *n*, number of stocks in a given branch (if >1); Z, zymodeme number according to Montpellier classification.

In conclusion, the convergence between the different gp63 results illustrates and supports the models of Gupta and Anderson[1]. It should stimulate further research on the potential immune-genetic bases of selection among host populations (humans and dogs, in the case of visceral leishmaniasis). In addition, the risk that major protective antigenic domains of gp63 might be polymorphic is a concrete warning for the design of vaccines against *Leishmania* and the assessment of vaccine trials. The warning might also be valid for other parasite candidate vaccines.

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