Reviewer's report

Title: Zinc/Copper Imbalance Reflects Immune Dysfunction in Human Leishmaniasis: an ex vivo and in vitro study

Version: 1 Date: 23 September 2004

Reviewer: Joanna Kubar

Reviewer's report:

General
This work reports on Zn decrease and Cu increase, significant in plasma of patients affected by different clinical forms of leishmaniasis in North and Northeast of Brazil. It prolongs and extents earlier observations on Zn and Cu concentration alterations in patients with the Old World localized cutaneous leishmaniasis. The study is well conducted and is of interest for potential therapeutic applications (especially if a confirmation of Zn deficiency in VL patients could be also shown in endemic/epidemic areas of the Old World). Discussion would deserve to be improved.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Abstract
To avoid conferring any erroneous impression that Leishmania are eliminated entirely, I would start the first sentence by "Process of elimination …" instead of "Elimination …". I would also add in this sentence "a dominant Th2 response…", instead of "a Th2 response…", since a right balance (distinct for man and mouse) between Th1 and Th2 responses is required to control the parasite in different forms of the disease.

Discussion section:
There is a misprint in the 2nd sentence; through instead of trough.

Discussion section:
The third sentence appears tautologous. Please modify.
One entire paragraph is erroneously duplicated (LCL patients… possibly fatal visceral form.). The sentence "We observed a reciprocal … in untreated LCL patients, …" is not clear. In its present formulation it appears untrue.
In healthy controls from rural areas, both Cu and Zn levels are increased as compared to the urban controls. In patients, Zn concentrations are decreased and Cu concentrations are increased. Are distinct mechanism(s) involved in regulation of homeostasis of these elements? The authors state (speculate) that plasma Cu increase might be due to environmental factors (or genetic factors), and this increase might be an agent of alteration of the immune response. How do they explain the absence of Cu increase in ML patients, living in the same area than the LCL patients? Or should the control group for ML patients be separated from that for LCL patients?
Hypotheses about possible mechanism(s) or factors responsible for Zn decrease in patients would be welcome.

Reference 1: Please, quote a more recent reference with epidemiological data.
What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

None