Reviewer’s report

Title: Circulating levels of Insulin-like Growth Factor-I (IGF-I) correlate with disease status in leprosy

Version: 1 Date: 24 August 2011

Reviewer: David Scollard

Reviewer’s report:

The authors have determined levels of IGF-1 and its major binding protein, IGBP-3, in leprosy patients and healthy controls, and correlated these with different types of leprosy and leprosy reactions. The report addresses important and little-studied aspects of endocrine-immune interactions in leprosy. The investigators are very well qualified and experienced in studies of leprosy. The question is well defined, the methods are appropriate, and the data are sound.

Major compulsory revisions:

1. The results section of the abstract is confusing, e.g. lines 49-54, and should be revised for clarity.
2. There are some concerns re patient selection:
   a. Are healthy staff appropriate controls?
   b. The male-female ratio for HC is not comparable to that for the patients
   c. Were specimens for HC taken at the same time as those for the patients (years ago) or were they more recent? I.e., is there a bias for old vs new specimens?
   d. What is known about diabetes or other endocrinopathies (e.g. thyroid) among patients? Were patients with diabetes excluded?
   e. Nutritional status affects endocrine function – what is known about malnutrition or obesity among patients?
3. Line 134 – T1R is not an acute inflammatory syndrome
4. The findings during and post-treatment are very interesting, but the authors should avoid over-interpreting these because the numbers are small and many other factors have potentially changed – age, nutritional status, other illnesses, etc.
5. Overall, the discussion is too long and often too speculative. The sample size is not great enough to reach too many conclusions, although the findings are interesting and provocative.
6. Line 275-6 – the findings may be over-interpreted here. They suggest that ML infection may have modulated IGF-1 but do not ‘clearly indicate’ this, due to the small sample size and retrospective nature of the study.

Discretionary revisions:
7. It would be useful to have some sentence in the abstract that indicates why IGF-1 was chosen instead of a myriad of other endocrine markers.

8. Some references are rather dated (e.g., 2, 4, 5, 19, 22, 23, 24) and for most of these there are more recent papers on the subject.

9. Fig 2E (TNF declined during ENL in one patient – did this patient have any different pattern for IGF-1?

10. Results, Line 226 ff and Fig 2: The suggestion that IGF-1 levels at baseline might be predictive of future reaction is interesting but is certainly not proven by these preliminary findings in a retrospective study. Can the time variable be explored here? i.e., were increases in baseline RLL greater when the initial blood sample was taken closer to the time of subsequent reaction? Or is the sample not large enough to evaluate this?

11. In the paragraph beginning on line 302, immunosuppression is invoked as an explanation. If so, then might some reduction if “LL suppression” also be associated with ENL?

12. The paragraph starting at line 332 might be omitted or greatly condensed, since it discusses medical conditions quite unlike infection.

13. Is there some literature on IGF-1 levels in tuberculosis that might be enlightening?

**Level of interest:** An article of outstanding merit and interest in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare I have no competing interests.