Reviewer's report

Title: Serum Protein Gamma-Glutamyl Hydrolase, Ig Gamma-3 Chain C Region, and Haptoglobin are Associated with the Syndromes of Pulmonary Tuberculosis in Traditional Chinese Medicine

Version: 1 Date: 3 February 2015

Reviewer: Karen M. Dobos

Reviewer's report:

Summary review for “Serum Protein Gamma-Glutamyl Hydrolase, Ig Gamma-3 Chain C Region, and Haptoglobin are Associated with the Syndromes of Pulmonary Tuberculosis in Traditional Chinese Medicine”; Jiang et al

The manuscript describes a proteomic mass spectrometry approach to identify biomarkers associated with different TCM syndromes that are observed in tuberculosis patients. The work is interesting, but lacks rigor in data description, handling, and analysis for iTRAQ procedures, as well as general mass spectrometry based identification of serum proteins. The manuscript also over interprets the results, with a lack of regard that these serum proteins have been identified from a number of proteomics studies and may represent general inflammatory or chronic disease processes.

Specific to the review for this journal, the following questions are addressed:

1. Is the question posed by the authors well defined? Yes, the question is well defined and TCM and subsequent syndromes are well described.

2. Are the methods appropriate and well described? The methods are adequate. However, the sample size and technical replicates are way too small to be useful in this type of study. In addition, detail is lacking to assist the reviewer in determining if the proteomics mass spectrometry analysis conformed to the Minimum information about a Proteomics Experiment (MiAPE), and also lacked detail as to how peptide quantitative differences within a protein compared, how this was handled statistically, and how this intra-data set behaved (deviation, etc). Without this type of analysis one cannot accurately interpret iTRAQ data sets.

3. Are the data sound? This question cannot be accurately addressed based on the lack of information provided (see response to question #2). Regardless, the sample # and technical replicates, and grouping information suggests that the data may not be complete.

4. Do the figures appear to be genuine, i.e. without evidence of manipulation? Yes.

5. Does the manuscript adhere to the relevant standards for reporting and data
deposition? No (see response to question #2).

6. Are the discussion and conclusions well balanced and adequately supported by the data? No—the authors over-interpret the significance of their findings. For example, the authors conclude that “GGH is associated with Mycobacterium proliferation” in their patient samples (and in general?) without any clear physiological and/or biochemical evidence to support such conjecture. In addition, the authors state that there is a bona fide relationship between DTH and the presence of “degenerative lesions” of Mycobacterium; with no evidence (and no mention of the millions of DTH positive persons in the world with no evidence of lung lesions—with some studies identifying these persons as having LTBI). Another example is the statement correlating hypoxia as infection limiting—this is totally taken out of context, has not been shown, and hypoxia, in any in vivo event, has been associated with the granuloma environment and potentially organisms and an environment that contributes to drug tolerance.

7. Are limitations of the work clearly stated? No.

8. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Not outside of TCM (see response to question #6).

9. Do the title and abstract accurately convey what has been found? Yes, but that data is questionable.

10. Is the writing acceptable? Yes.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests