Reviewer’s report

Title: Alterations of Leptin in the Course of Inflammation and Severe Sepsis

Version: 1  Date: 11 March 2012

Reviewer: Peter Mancuso

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Major compulsory Revisions:
1. While TNF-a is used to stimulate adipocytes in vitro, the inclusion criteria for the sepsis patients included patients with a proven infection. Therefore, the in vitro data would be strengthened if measurements of leptin were performed using LPS (a more relevant proinflammatory stimulus for infection induced sepsis) stimulated of adipocytes in vitro.
2. The introduction should describe the clinical purpose of DAA and background on its ability to regulate inflammation.
3. In the Methods section, 1st paragraph, line 16, the dose of TNF-a added to the cell cultures was 1 pg/ml. However, in the results and figure legends, a 1 ng/ml dose is indicated. Did the authors use 1 pg/ml or 1 ng/ml?
4. The inclusion of patients with renal failure with all of the others may be a problem. Leptin levels rise dramatically with renal failure due to impaired excretion of this adipokine. Were the levels of leptin in the few patients with renal failure elevated compared with the rest of the sepsis patients?
5. In figures 4 and 5, the authors mention the reduction of leptin following stimulation with TNF-a. Is the dose (1 ng/ml?) cytotoxic? Are these cells dying in response to TNF-a and this may explain the reduced leptin production. This is an important issue since leptin levels appear to be elevated in the sepsis patients compared with the controls.
6. If the authors believe that TNF-a is a relevant stimulus for leptin production in adipocytes, what were the levels of TNF-a in the septic patients?
7. The authors should state that there were no differences between the control and TNF-a + DAA in the in vitro cultures at 6 and 24h post-TNF-a challenge in figures 4 and 5.
8. What do the asterisks indicate in Figure 4?
9. Since BMI is highly correlated with leptin, this information should be included in this manuscript.

Minor issues
1. Results section, 6th paragraph, “…compared to those who deceased..: Di the authors mean to write “who were deceased?”.

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

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

I declare that I have no competing interests.