Reviewer's report

**Title:** Two mechanisms of the enhanced antibody-dependent cellular cytotoxicity (ADCC) efficacy of non-fucosylated therapeutic antibodies in human blood

**Version:** 1  **Date:** 30 January 2008

**Reviewer:** Francisco Hernandez-Ilizaliturri

**Reviewer's report:**

As investigators strive to improve the biological activity of monoclonal antibodies against cancer (including lymphoma), their contribution is of high importance and timely.

The structure of the manuscript is good and the experiments are well planned with adequate controls. There are some concerns that in somehow diminish the significance of their contribution and that need to be addressed by the authors.

First and very important to address; the contribution presented is not original, 50% of the experiments presented in this manuscript had been actually published by the same group at the Journal Clinical Cancer Research (Reference 25 of the current manuscript) Clin Can Res 2006; 12:2879. This manuscript is actually a follow up seeking to investigate why the non-fucosylated antibodies are able to induce better ADCC.

The authors demonstrate that the most likely reason for the improved ADCC with non-fucosylated anti-CD20 is the biding to NK cells as demonstrated by in vitro studies. The flow cytometry studies are of good quality and suppor the authors conclusions. The ADCC assays in which plasma is added to the effector cells, B-cells and anti-CD20 antibodies can potentially oscure the actual ADCC as plasma contain complement proteins that can induce CMC. A better way to present the data would be to actually perform standard ADCC assays.

Finally, in vivo studies using lymphomas xenograft models could further enhance the authors report, especially as half of the data presented has been already published. Previous investigators had demonstrated that effector cells are extremely important for rituximab anti-tumor activity and therefore lymphoma SCID models can be useful to further demonstrated that the anti-tumor activity of newer non-fucosylated anti-CD20 is primarily via NK cell ADCC.

Statistical analysis of the data is necessary to demonstrate the significance of the findings observed.

**What next?:** Accept after minor essential revisions

**Level of interest:** An article of importance in its field
Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

'I declare that I have no competing interests'