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: 10 January 2008

Reviewer: Ronald Herberman

Reviewer's report:

This manuscript describes two mechanisms underlying the enhanced ADCC activity of non-fucosylated anti-CD20 monoclonal antibodies. This topic is timely given the revival of the interest in the application of antibody-based immunotherapy for the treatment of malignant diseases. The experiments are in general clearly described. Most, but not all of them are well controlled. The conclusions are in general supported by the experimental evidence presented. However, it is not clear how novel the information presented is. Specifically, the authors should clearly indicate how novel and different the information presented in this manuscript is from that they published in Clin. Cancer Res. 12:2879, 2006. Furthermore, the manuscript is lengthy and should be markedly shortened.

The pages of this manuscript should be numbered to facilitate the review process.

Specific Comments

Page 2, paragraph 3: It is not clear why the authors expect that non significant differences in the level of IgG1 and in the relative amount of non fucosylated Fc oligosaccharides should cause significant differences in the extent of inhibition of ADCC.

Page 4: The Introduction should be shortened.

Page 8: The Methods section should be shortened. Most of the methods described are standard. Therefore the description may be replaced by appropriate references.

Page 10, paragraph 1: The amount of anti-CD20 antibody used should be indicated.

Page 11, paragraph 1: The amount of non labeled anti-CD20 antibody used should be indicated. This comment applies to other parts of the manuscript.

Page 11, paragraph 2: More details should be provided about the inhibition experiments with anti-CD16 mAb.

Page 13, paragraph 1: Data should be shown to support the statement that the anti-CD20 variant does not differ from the parental antibody in its binding to CD20. Identity in the amino acid sequence of the variable region of the antibody
does not prove this point, because it does not exclude differences in conformation caused by the attachment of oligosaccharides.

Page 14, paragraph 2: Specificity controls should be added to figure 2 to show the specificity of the inhibitory effect of anti-CD16 mAb.

Page 17: The Discussion should be changed. As it stands, it is essentially a repetition of the description of the results presented.

Minor Comments

This manuscript contains many inaccuracies which need to be addressed. Only some of them are listed in this review.

Page 3, paragraph 1: What does fucosylated anti-CD20 in individuals mean?

Page 3, paragraph 2: What does antibody ingredients mean?

Page 5, paragraph 1: requires weekly should read requires weekly

Page 6: The summary of the results to be presented may be deleted in the interest of space.

Page 8, paragraph 2: instructions should read instructions

Page 12, paragraph 2: RPMI medium should read RPMI 1640 medium

Page 15, paragraph 1: than of should read than of

Page 17, paragraph 2: The sentence human B cells is too long and difficult to read. It should be changed.

Page 20, paragraph 1: What does yield a effect mean?

Page 23, References: Reference 6 should be reference 7
Reference 7 should be reference 8
Reference 8 should be reference 9
Reference 9 should be reference 6
Reference 11 should be reference 13
Reference 12 should be reference 11
Reference 13 should be reference 12
Reference 15 should be reference 17
Reference 16 should be reference 15
Reference 17 should be reference 16
Page 28, Figures: What does â##reaction as indicatedâ## mean?

**What next?:** Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

**Level of interest:** An article of importance in its field

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

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'