Reviewer's report

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

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Reviewer: Andreas Nechansky

Reviewer’s report:

The data lack novelty and do not contribute significantly to the current knowledge. In detail, it is known that non-fucosylated mAbs show improved ADCC activity as compared to their fucosylated counterparts and that target antigen binding is not affected. Also, it has been published two groups (Preithner et al., Nechansky et al.) that non-fucosylated mAbs are not inhibited by endogenous IgG present in serum. Ferrara et al demonstrated that the increase in ADCC is due to their increased affinity to FcgammaRIII (Ferrara et al). Also, the finding that addition of fucosylated to non-fucosylated mAb decreases ADCC can be deducted from the existing data. The existing FcγRIII polymorphism on donor effector cells (Shields et al) and its relation to ADCC is not discussed at all.

The testing of serum of 12 donors regarding their IgG1 content makes sense although the slight differences in donor IgG concentration can not really be discussed because they might reflect the error of the method. In analogy, the determination of the percentage of non-fucosylated mAbs in endogenous (normally fucosylated) IgG is interesting but when looking on Figure 5 and comparing individuals 3 and 6, the percentage of non-fucosylated Fc oligosaccharide (Fig. 5c) does not correlate with cytotoxicity (Fig. 5d).

The method description is limited and without retrieving additional information from the referenced paper it is probably not possibly to replicate the work. The data are generally well presented although (i) the quality of Fig.4 has to be improved and (ii) the error bars in Fig. 5 are missing.

The writing is acceptable although checking Grammar and Style will most likely improve the quality of the manuscript.

What next?: Reject because too small an advance to publish

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

Collaborating with greenovation, a company that produces non-fucosylated mAbs in moos.
Publications relating to the topic of this paper.