Reviewer's report

Title: The Immunosuppressant FTY720 (Fingolimod) enhances Glycosaminoglycan Depletion in Articular Cartilage.

Version: 1 Date: 17 June 2011

Reviewer: Stefan Toegel

Reviewer's report:

I have reviewed the manuscript „The Immunosuppressant FTY720 (Fingolimod) enhances Glycosaminoglycan Depletion in Articular Cartilage“, submitted to BMC Musculoskeletal Disorders as research article. This work describes the in vitro effect of FTY720 on bovine chondrocytes using GAG, WB and qPCR assays as well as histological examinations.

In general, the manuscript addresses an interesting topic and shows some new descriptive data which may be of importance for those with closely related research interests. The study has some limitations which, however, are partly discussed in the manuscript.

The following issues should be addressed before publication can be taken into account:

Major Compulsory Revisions

*) The Methods section needs revision regarding the description of experiments and statistical aspects. Please address the following issues:

+) How were the cartilage explants prepared (size, amount/weight for each assay,...)?

+) How many animals were included in the study (n=?)

+) Viability assay: Information on technical replicates and time periods for incubations are missing. How many times were the experiments repeated? The results of the viability assay are not given or discussed in the manuscript.

+) Information on cell culture conditions (including treatment, incubation periods,...) preceding RT-qPCR assays must be given in the methods section. It remains unclear (also from the figure legend) how many technical replicates were used within each experiment. Were the 3 individual experiments conducted with cells from different animals? Did the authors validate the use of GAPDH as reference gene for the experimental setup of the study? For guidelines on the documentation of RT-qPCR methods and results see: http://www.ncbi.nlm.nih.gov/pubmed/20858237

+) Again, cell culture details (including replicates) for WB assays are unclear.

+) GAG release: Again: n=?, replicates, how many individuals? Furthermore, description on IL1ß and TNFa treatments is missing.

+) Histological examination: Again: n=?, replicates, how many individuals?
*) Statistics: Consider ANOVA (plus post-hoc) test as the appropriate statistical test for comparing the means of three or more unmatched groups.

*) The authors should discuss their findings with respect to recent studies on the impact of FTY720 in animal models:

Minor Essential Revisions

*) From my understanding, Angyal et al in their study (reference 14) do not conclude that FTY720 enhances damage severity as stated by the authors in their discussion (page 10, first paragraph). Could the authors justify this point?

*) The standard deviation of one bar (TNFa treated, 1μM FTY720-P treated) is missing.

*) An interesting point of the study is the “dichotomous” effect of FTY720 in bovine chondrocytes, which might warrant a more detailed discussion.

Discretionary Revisions
No discretionary revisions.

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

Quality of written English: Acceptable

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.