Reviewer's report

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

Version: 1 Date: 15 August 2011

Reviewer: FRANCESCO GRASSI

Reviewer's report:

This is an interesting manuscript showing a potential damaging effect of the immunosuppressant drug FTY720-P (Fingolimod) on GAG depletion in cartilage under inflammatory conditions. In accordance with findings from a recent in vivo paper from Angyal A. et al., the authors show a significant increase in GAG depletion in cartilage explants only in the presence of inflammatory cytokines. These findings further highlight the important role of sphingosine-1-phosphate and its receptors, the likely target of FTY720-P, in the regulation of cartilage homeostasis.

However, a few concerns need to be addressed

Major compulsory revisions.

1. Statistical analysis needs some attention. Given the experimental design and the size of the sampling the use of Student T test for data analysis requires a more accurate justification. The authors should clarify what is the rationale for this choice over other tests (i.e. ANOVA analysis of data) and provide supporting information regarding their claim that data are normally distributed.

Minor essential revisions.

2. Methods, page 5: the method section for western blot analysis lacks several important details that should be provided in a revised version.

3. Methods, Results and Figure legends. Duration and range of concentrations of treatment with FTY720-P are incoherently stated (5 or 8 days of duration of treatment; 0.1-3 #M or 0.5-3#M concentration range). Please adjust accordingly.

4. The biological significance of iNOS downregulation by FTY720-P could be further discussed in the context of cartilage homeostasis. Did FTY720-P have any affect on unstimulated (basal) expression levels of iNOS?

5. In figure legend 1, the authors could restate tha the data refers to chondrocytes grown in monolayer

6. In figure legend 3, the label 'A' is missing in the text.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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