Reviewer's report

Title: Sphingosin-1-phosphate attenuates proteoglycan aggrecan expression via production of prostaglandin E2 from human articular chondrocytes

Version: Date: 2 December 2006

Reviewer: Yoe-Sik Bae

Reviewer's report:

General
The authors investigated the effect of S1P on PGE2 production and proteoglycan expression in human articular chondrocytes. They showed that human articular chondrocytes express functional S1P receptors. They also demonstrated that S1P attenuate aggrecan secretion and mRNA expression via COX. This paper is interesting because the authors suggest a putative role of S1P in cartilage degradation in arthritides. Overall the results of the manuscript are solid but several points should be appropriately clarified.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. The authors should specify or discuss which receptor (EDG5 or others) is involved in the S1P-attenuated aggrecan expression in the cells. The authors showed the expression of EDG5 in HAC in protein level. What is the rationale to focus on EDG5? What is the effect of pertussis toxin on the S1P-attenuated aggrecan expression? Since several previous reports showed that certain type of S1P receptors are associated with pertussis toxin-sensitive G-proteins, it will be informative to examine the effect of pertussis toxin on the S1P-attenuated aggrecan expression for the authors to discuss the role of each receptor. The author should consider using some S1P receptor antagonists to interpret which receptor is mainly involved in S1P-attenuated aggrecan expression.
2. It should be tested the effect of S1P on aggrecan expression and COX-2 expression with several concentrations of S1P.
3. Table 1 is missing from the manuscript.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1. The manuscript should be corrected by someone who is fluent in English, that are problems with sentence structure and many errors.
2. Page 2, from patients with rheumatoid
3. Page 4, endothelial
4. Page 6, Japan, (Tokyo, Japan)/(San Diego, CA, USA)/(Anti-COX-2/(St Louis, MO, USA)/(Japan, Tokyo)/(Cambridge, UK)
5. Page 7, SB203580 (10 microM)/PD98059 (50 microM)/SP600125 (10 microM)/LY294002 (50 microM)/(DAKO, City, USA)
6. Page 8, (Tel-Test, Inc., Friendswood, TX, USA)
7. Page 10, S1P increases PGE2 production/48 h
8. Page 11, Western blot/via p38 and ERK MAPKs
9. Page 12, S1P would affect
10.Page 14, The sphingolipid
11.Page 19, Western blot/
12.Page 20, SB203580 (10 microM)/PD98059 (50 microM)/SP600125 (10 microM)/LY294002 (50 microM)/Figure 4:

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

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

Quality of written English: Needs some language corrections before being published
Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests.