Reviewer's report

Title: Glucosamine increases hyaluronic acid production in human osteoarthritic synovium explants

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Reviewer: Assia Derfoul

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The current Manuscript by E.J. Uitterlinden et al, entitled: “Glucosamine increases hyaluronic acid production in human osteoarthritic synovium explants”, examines the hypothesis that glucosamine (GlcN) effects on pain reduction in knee osteoarthritic (OA) patients may result from an effect on hyaluronic acid (HA) synthesis. HA derives from glucoronic acid and N-acetyl-GlcN polymerization and HA viscosupplementation has been shown to reduce pain in patients with knee OA.

The question posed by the authors is well defined and the methods appropriate and well described. The data presented in this manuscript shows that treatment of human OA synovium explants with 5 mM glucosamine hydrochloride (GlcN-HCl) or glucose (Gluc) but not glucosamine acetate (GlcN-Ac) significantly enhanced HA levels in vitro. In addition, the authors show that a lower concentration of 0.5 mM GlcN but not Gluc were still able to upregulate HA levels. This upregulation does not seem to result from an increase in HA synthase (HAS) enzyme gene expression.

These findings are of interest however few points should be addressed prior to publication in “BMC”.

Major Compulsory Revisions:

1. The authors chose to use 0.5 and 5 mM GlcN-HCl to examine the effect of GlcN on HA production. These concentrations are 1000 to 10000 times higher than the concentration reached in the synovium following oral administration in humans corresponding to 3-22 µM (Persiani et al, OAC, 2007). However, the authors do not comment on their rationale for this choice. It would have been of interest to examine the effect of lower doses on HA production.

2. Since no effect of GlcN on HAS gene expression was observed, it would have been logical to measure HAS enzymatic activity or protein levels to substantiate a role of GlcN in the stimulation of HA synthesis.

Discretionary Revisions:

HA have been shown to affect the levels of specific OA-associated cytokines and enzymes in synoviocytes such as IL-8 and TNF-alpha. Evaluation of some of
these markers in the presence of GlcN treatment would strengthen the author’s data.

**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.