Reviewer’s report

Title: Type X collagen levels in serum are elevated in human Osteoarthritis and associated with markers of cartilage degradation and systemic inflammation

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Reviewer: Robert Terkeltaub

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The paper is of interest and the new antibody with immunoassay appears to discriminate OA of various grades, and better so than C2M or CRP, which I think the best data to focus on interpreting this study. Instead, there are problems here, since it is not clear if the immunoassay is picking up changes in subchondral bone chondrocytes and osteophytes rather than articular chondrocytes. The correlation studies are not convincing for CRP or C2M, since neither appears to discriminate OA or OA of advancing degrees here, which is not adequately discussed by the authors of this commercially based work for a potential reimbursed lab test.

The references are not complete, since the key work on HIF-2alpha and chondrocyte hypertrophy linked to inflammation, and on key role of hypertrophy in OA progression, by H Kawaguchi, and others, are not cited.

Also, the Methods Section is especially long and tedious, and should be cut by 40%.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

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

Declaration of competing interests:

No conflicts