Reviewer's report

Title: Increased serum Sclerostin down-regulates Wingless protein-3a signaling and is linked with lesser structural damage in ankylosing spondylitis patients with high disease activity

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Reviewer: Evan Romas

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Sclerostin is a very interesting factor in relation to bone. The investigators measured serum sclerostin using a commercial ELISA and correlated the levels to AS disease activity and other soluble factors. While the assay data have to be accepted at face value and some limitations are noted, the study suffers from additional limitations which the authors should recognise; ie: the concept and relevance of serum sclerostin as a systemic factor on bone is controversial, the validity of the specific ELISA for 'antigenic' versus 'bioactive' sclerostin is unknown and BASDAI and other indicators of disease activity are measured only at single time points and therefore may not reflect the actual underlying disease 'status' of the patients.

major revisions

1. The title of the manuscript is misleading because no true biological down regulation is demonstrated, merely correlations.
2. The authors use SOST and sclerostin interchangeably in a manner which may confuse a non expert. SOST is the gene and sclerostin is the gene product
3. para 1 in the discussion concludes that “this confirms lack of connection between inflammatory markers and inhibitors of bone formation in AS”. This conclusion is not supported by the data
4. the authors state, in the penultimate paragraph of the discussion, that “this confirms formerly reported inhibitory effect of SOST on Wnt 3a. However their data, while consistent with these other reports, cannot confirm them because of the descriptive nature of their study.
5. serum sclerostin levels do vary remarkably with age, pubertal growth, gender and menopausal status, as well as the type of assay used. The absence of these key demographic data along with uncertainty of the true underlying disease activity or severity makes the data difficult to interpret.

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.