Reviewer's report

Title: Inhibition of Interleukin-1beta-Stimulated dedifferentiation of Chondrocytes via Controlled Release of CrmA from hyaluronic acid-Chitosan Microspheres

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Reviewer: João Mano

Reviewer's report:

The objective of this manuscript is quite clear, and the experimental design used seems adequate. The data contain interesting trends: basically GAG production increases with the presence of CrmA and this behaviour synergistically enhanced in the presence of HA. The differences are reported as being statistically significant, although not very expressive. I'm not totally sure if this differences are a consequence of the hypothesised mechanisms or if more simple reasons could explain it: for example we can have more or less production of GAGs and other proteins because the number of cells is distinct – the data should be normalised in this sense. In fact we see differences in cell viability that correlates very well with the changes in the chondrogenic markers. This should be carefully addressed by the authors.

Another aspect is related with the production of the particles: in the mixture of CH and HA the solid spherical objects are obtained by adding TPP; this molecule just cross-links the CH fraction. What happens to the non-crosslinked HA in the particles? The authors should show the possible release profile of this biopolymer.

Therefore I would advice that there are still major revisions to be addressed by the authors.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I have no conflict of interests with the authors.