Reviewer's report

Title: The Src inhibitor dasatinib stimulates the differentiation of human bone marrow-derived mesenchymal stromal cells into osteoblasts

Version: 2 Date: 16 February 2010

Reviewer: Susannah M O'Sullivan

Reviewer's report:

General Comments:
The manuscript has been improved by the changes the authors have made. There have been significant attempts made to address the Reviewers’ comments. At present, it requires further revisions in order to be suitable for publication.

Specific Points:

Major Compulsory Revisions:
The manuscript is still too focused on the development and evaluation of the experimental system. It would be improved by a focus that is centred on the effects of Dasatinib.

In response to Reviewers’ comments regarding the methods used in quantitative PCR, the authors have changed the wording of the methods from ‘35 cycles of amplification’ to ‘optimal number of cycles’. Does this indicate that the previous wording was inaccurate or that the authors have repeated the experiments? It would be preferable for the authors to use the quantitative real time PCR data (and alter the methodology) given the doubt regarding the truly quantitative nature of the RT-PCR data.

The effects of Dasatinib on calcium deposition, ALP activity and gene expression vary with time (as might be expected) and are not significant at all time points. The authors Results section acknowledges this, but this variability should be more fully acknowledged and explained in the Discussion.

In order to address the question of whether the effect observed with Dasatinib can be attributed to Src inhibition, the authors have included experiments to show that the Src inhibitor, E804, has similar effects on ALP activity to Dasatinib. This goes some way towards answering this question, and the authors also cite other work that has shown a role for Src inhibition in modifying osteoblastic differentiation. Nonetheless, some discussion should be had regarding the potential for the observed effects to be due to PDGFR inhibition (or c-Kit inhibition) and I draw the authors’ attention to published work reporting significant inhibition of the PDGFR and c-Kit receptors by Dasatinib (Chen, Z et al. Molecular Pharmacology. 2006. Lombardo, J et al. J. Med Chem. 2004.), and an abstract reporting “Dasatinib Promotes Osteoprogenitor Differentiation and
Inhibition of Osteoclastogenesis” (Antonio Garcia-Gomez et al, ASH conference 2009).

**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