Reviewer's report

Title: Influence of Statins locally applied from orthopedic implants on osseous integration

Version: 1 Date: 3 August 2012

Reviewer: Michelle Ghert

Reviewer's report:

This is a very interesting, well executed and fairly well written study evaluating the effect of Simvastain on bone-implant integration using biomechanical assays and histomorphometry in a rat model. I believe it is well worth publishing this paper. However, several aspects of the methodology and results should be clarified prior to publication. In addition, the paper should be copyedited by an English editor.

Specific points to be addressed are listed below. All are considered MAJOR COMPULSORY REVISIONS:

Abstract:
Page 2, line 38: In what cell systems does Simvastatin increase BMP-2 expression?
Page 2, line 44: Methods should include a heading
Page 3, lines 61-64: The conclusion that Simvastatin does not improve osseous integration is not strong enough: it actually appears to negatively affect osseous integration. The conclusions should be modified as such.

Background:
Page 4, line 71: the word 'aspired' is not correct. Please choose another expression.
Page 4, line 76-78: what cell systems have shown increased BMP-2 expression with Simvastatin?
Page 4, line 87: Please briefly, in one sentence, summarize the results of these studies (the results are later well described in the Discussion section, but a summary would be helpful here).

Methods:
Page 13, lines 269-273: The total number of animals is provided. However, the authors should provide the number of animals used in each arm of the experiment (how many under each condition and how many of those were evaluated by biomechanical tests and histomorphometry?).
Page 14, lines 288-290: What is the definition of radiographic or macroscopic signs of infection? Please clarify.
Page 16, line 331: The authors should be lauded for using randomization and blinding in the animal experiments
Results:
Page 6, lines 104-109: Again, what were the specific numbers in each group examined?
Page 6, line 109: What was the histological appearance/features of the tissue from the limbs that appeared to be infected? (acute/chronic inflammation, etc).

Discussion:
In general, the Discussion covers the pertinent issues extremely well.
Page 7, line 37: Again, ‘do not suggest improved’ is an understatement and the authors should concede that Simvastatin, based on the data in this study, appears to impede osseous integration.
Page 9, lines 194-195: The authors bring up a very interesting point regarding the timeline of the experiment. Why did they choose 56 days when previous studies have stopped much earlier? What are the elution characteristics of Simvastatin in polymer coating?
In fact, the authors may have uncovered the very interesting fact that perhaps longer-term statins may have deleterious effects on osseous integration, whereas earlier effects are anabolic.
Page 10, lines 216-217: Please clarify what is meant by ‘show a more health oriented behaviour’.
Page 11, line 241: ‘disencouraging’ should be changed to ‘discouraging’

Conclusions:
Page 12, lines 249-250: This should be a stronger conclusion against Simvastatin based on the data presented.
Page 12, lines 250-252: This statement should be excluded from the conclusion as it is not the focus of the study.

Figures:
Page 25, lines 514-516: What is the rationale for using this specific site of interest? Previous publications? Please include rationale here and in the Methods section.
Page 25, line 531: Please provide p-values for the ‘*’s in the figure legends (provided in text of manuscript but not legends).
Figure 4: What does the number ‘14’ refer to?
Figure 5: What does the number ‘23’ refer to?
Figure 7: What do the numbers ’10, 28 and 23’ refer to?

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:**

I declare that I have no competing interests'