Reviewer's report

Title: Treatment outcome of chronic low back pain and radiographic lumbar disc degeneration are associated with inflammatory and matrix degrading gene variants: a prospective genetic association study.

Version: 1 Date: 24 October 2012

Reviewer: Minna Mannikko

Reviewer's report:

The paper describes an association study with previously identified candidate genes on lumbar disc disease. The results give further support for these genes/gene variants having a role in the development of lumbar disc degeneration. The novel findings in this study are that the results are also suggesting these variants having an influence on pain and disability. The article is well written and describes clearly the used methods and results. The previous work that has provided basis for this study are clearly acknowledged and the findings are discussed thoroughly in the light of earlier studies.

Major Compulsory Revisions

The significance of the findings should be discussed more, since only p-values are provided (OR? CI?) and no corrections have been made for multiple testing. Although the authors do bring this out in the methods (“We considered our study to be an explorative genetic association study, and therefore the p-values were not formally corrected for multiple testing”), in interpreting the results, the possibility of a chance finding should be considered. Correcting p-values has reduced the number of false positive findings and improved the possibilities for replication. Nevertheless, here the authors were able to replicate some earlier findings, but also detected association that they found difficult to explain.

The authors speculate on that different variants in IL18RAP would have an effect on different aspects in the DD phenotype (severity of the degeneration, improvement in outcome). This may well be, but are there any functional data on these variants to support this or is the current data only suggesting the involvement of this gene/gene product in general?

Minor Essential Revisions

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Discretionary Revisions

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"Minor issues not for publication"

• In the abstract (results) remove italics from “and” that is between IL18R and IL1A.
• In Statistical analysis, 2nd paragraph, 4th line from the bottom: carriers.
• In Statistical analysis, 3rd paragraph, 3rd line: Reference for R is missing.
• In table 3, IL18RAP-column, rs is missing in front of the number (rs917997).
• In the discussion, 3rd paragraph, first line, add rs to rs1420100.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.