Reviewer's report

Title: WRN polymorphisms affect expression levels of plasminogen activator inhibitor type 1 in cultured fibroblasts

Version: 2 Date: 23 November 2007

Reviewer: Josune Orbe

Reviewer's report:

General
This article describes the association of the WRN polymorphisms with plasminogen activator inhibitor type-1 (PAI-1) in cultured fibroblasts. The authors show fibroblasts carrying the 1367CC/1074FF genotype produce more PAI-1 in culture. Healthy individuals with polymorphic variants (C and F alleles of WRN) have higher circulating PAI-1 levels. Finally, the authors suggest that WRN may negatively regulate PAI-1 expression, based on silencing and induction experiments.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The article has been rewritten and all the references to tables and figures have been removed from the Discussion section. Meanwhile, the results are not properly discussed in this section and is too speculative.

In the first paragraph of the Discussion section the association of Werner syndrome and elder subjects proposed by the authors is not clear.

In the second paragraph previous references explaining that the studied polymorphisms are functional and how they affect the activity of the protein must be added. The last sentence of this paragraph must be removed because this study does not describe the "mechanistic link"; this study shows an "association" between PAI-1 and WRN polymorphism.

The last paragraph is too speculative and must be shortened. Authors can just suggest that further work analyzing intracellular signaling and promoter regions implicated in the observed effect could be of interest.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Previous minor comments have been properly corrected.

Other comments:

Page 8: The assay used for PAI-1 measurement in plasma samples must be moved into the Material section.
Pages 9 and 12, the last sentences of the corresponding first paragraphs must be removed from the Results section.
Page 13 line 11: plasminogen must be replaced by fibrinogen.
All the authors in reference 20 are underlied.
There are some typing errors in the manuscript

Discretionary Revisions (which the author can choose to ignore)

What next?: Accept after minor essential revisions

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'