Reviewer's report

Title: A genetic polymorphism of the osteoprotegerin gene is associated with an increased risk of advanced prostate cancer

Version: 2 Date: 27 June 2008

Reviewer: Jovanny Zabaleta

Reviewer's report:

In this paper the authors study the frequencies of two SNPs in the OPG gene and their association with prostate cancer (PC) and PC progression. The authors found that one SNP (950T/C) is associated with PC advanced disease. In this reviewed version of the paper the authors did answer all the questions raised by me and by Dr. Yen Chin Chen, the other reviewer. I see that Dr. Chin Chen and I raised several similar questions, especially those about the linkage disequilibrium between the two SNPs described in the paper, and the possibility that they are in LD with some other surrounding SNPs that may help explain the association with advanced prostate cancer.

Some minor suggestions I have about this new version:

-Page 2, lane 2: change “…(OPG) polymorphisms as a genetic modifier in the…” for “…(OPG) polymorphisms as genetic modifiers in the…”.
-Page 2, lane 3: change “…and its disease progression…” for “… and disease progression…”
-Page 2, lane 6 and 7: change “…frequencies between the PCa patients and the controls…” for “…frequencies between PCa patients and controls…”
-Page 4, lane 8: change “…a genetic polymorphism of the insulin-like growth factor I (IGF1) is a strong…” for “…a polymorphism in the insulin-like growth factor I (IGF1) gene is a strong…”
-Page 5, lane 10: change “…The polymorphisms of OPG in this region may contribute…” for “…Polymorphisms in this region of the OPG gene may contribute…”
-Page 11, lane 6: change “…No SNP has been reported, which is in strong…” for “There are not reports showing any linkage disequilibrium between the polymorphism at 950 T/C with any other surrounding SNP…”
-Page 14, lanes 6, 8, and 14: what are the authors pointing out in Table 1B with “(Table 1B, 2)”
-Page 14, lane 1: change “…950 T/C polymorphism, the age, initial…” for “…950 T/C polymorphism, age, initial…”
-Page 14, lane 10: for consistency change “…variant C allele of 950 TC in the OPG…” for “…variant C allele of 950 T/C in the OPG…”
-Page 15, lane 10: change “…serum level and the 149 T/C and…” for “…serum
level and the 149 T/C and…”

-Page 17, lane 15: change the word mutation (s) for SNP(s) because mutation implies a quite different genetic situation.

Please use the same justification of the text through all the manuscript.

In general I think that this is greatly improved version of the paper and after doing these minor corrections I suggest its publication.

Jovanny Zabaleta, MS, Ph.D

**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 I have no competing interests