Reviewer's report

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

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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. Even though I think the data information presented is VERY INTERESTING, some questions should be addressed by the authors:

Minor:
-I suggest doing a general grammar checking to the manuscript, especially to the abstract section.
-Since these two SNPs (149T/C and 950T/C) are at the promoter region, I suggest denoting them as -149T/C and -950T/C to indicate that they are upstream of the transcription start site.
-The authors should state if the 950T/C SNP is in LD with some neighboring SNPs. This is an important point to understand the role of this SNP in the transcription of the OPG gene.
-The method for the OPG genotyping is a little repetitive. I suggest cutting it a little in order to make it easier to read.
-In the section dedicated to patient description, please do it consistently with the order in Table 1 (A through D).
-In Tables 1 and 2, in the footnote, the labels a, b, and c refer to what in the Tables?

Compulsory
-Why were the levels of OPG determined only in 66 patients with localized PC?
-In the genotyping of the OPG gene: the authors said that the 950T/C SNP is located at the promoter of OPG, but in this section they say it is 801 bp downstream of the 149T/C SNPs (also located in the promoter region). This means that the 950T/C would be located in the coding region of the gene. In other words, there is an inconsistence here that needs to be clarified.
-It looks that the common allele for both polymorphisms is the T allele. So, I wonder if the authors did the same analysis using the TT genotype as reference and if so, what results they obtained.
-It has been shown that PSA induces OPG production (Yonou H et al, Prostate
67(8):840, 2007), did the authors check the correlation of PSA and OPG?

**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