Author's response to reviews

Title: Leptin and Leptin Receptor Polymorphisms are Associated with Increased Risk and Poor Prognosis of Breast Carcinoma

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Responses to the reviewers’ comments

Reviewer 1:

- All changes suggested by the reviewer were made in the revised manuscript.
- A careful English editing was performed for the revised copy.
- Sentences in page 4 line 5, in page 14 line 14, in page 15 line 8 and the first sentence of the last paragraph in the discussion section are modified.
- Results from previous published reports on breast cancer patients of LEPR polymorphisms, serum leptin levels or in vitro demonstration of intracellular signalling pathways are included and discussed in the revised manuscript.
- More information about the functional significance of the LEPR Q223R polymorphism are provided in page 16 of the discussion section.
- In the revised manuscript, we have added more references for the in vivo studies undertaken in breast cancer (references number: 48, 52, 69 and 70).
- The $P$-value of Hardy-Weinberg testing is included in the results section of the revised manuscript but adjustments to other confounding variables (age at menarche, reproductive history, oral contraceptives, hormonal substitution therapy) can not be analysed because some of these data are not available.
- In page 12 of the results section we have explained why we have stratified patients in T1-T2 versus T3-T4 groups.
- For further studies, SNPs of the LEP and LEPR genes and a haplotype analysis will be carried out.
- The results found after adjustment for menopause status has been clarified in the discussion section of the revised manuscript.
- According to the reviewer comment, a descriptive paragraph of drugs used in chemotherapy treatment is added in the materials and methods section (patients treated by chemotherapy as a primary treatment) in the revised manuscript.
Reviewer 2:

- The two specific polymorphisms in *LEP* and *LEPR* genes are studied because they influence leptin production, thus being functional.
- Table 2 is in the results section of the manuscript.
- According to the reviewer suggestion, "223 Q/R" is replaced throughout the text of the revised manuscript by "Q223R".