Reviewer's report

Title: Association between mutation of the NF2 gene and monosomy 22 in menopausal women with sporadic meningiomas.

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Reviewer: Maurizio Genuardi

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The finding of an association between monosomy 22/NF2 mutations and postmenopausal age is of potential interest. The authors should consider the following suggestions.

-Abstract, Results: “…involved five different exons and they all leaded to a truncated …” # “…involved five different exons and they all led to a truncated …”

-Introduction, p.3, 1st paragraph: “…has rapidly lead to the identification of the NF2 gene coded…” # “…has rapidly led to the identification of the NF2 gene located…”

-Methods, p. 5-6: “DNA from the 20 meningioma samples as well as PB DNA from two of these patients (M13 and M20 tumors) who had mutations which have been previously reported in neurofibromatosis type 2 patients [20, 31], was amplified by conventional PCR for further assessment of the presence of the NF2 mutations identified in the corresponding tumor sample from the same patient.” # “DNA from the 20 meningioma samples was amplified by conventional PCR; in addition, PB DNA from two of these patients (M13 and M20 tumors) who had mutations previously reported in neurofibromatosis type 2 patients [20, 31] was analyzed for further assessment of the presence of the NF2 mutations identified in the corresponding tumor sample from the same patient.”

Also, why were constitutional DNA samples investigated only in these 2 cases?

-Results, p. 7: Mutation description is too detailed in the text, there is no need to explain each single mutation, Fig. 1 is sufficient to this purpose.

“The remaining deletion identified involved three consecutive bp (“CTT”) at exon 3 (c.357_359del), also leading to a truncated p.Phe119del protein”: this is a single aminoacid in frame deletion, not a truncating mutation.

-Results, p. 8, 2nd paragraph: “Consequently, NF2-mutated meningiomas accounted for most (6/9; 67%), including cases with isolated monosomy 22 (4/6; 67%) or monosomy 22 and other chromosomal alterations (2/3, 67%); …” # “Consequently, NF2-mutated meningiomas accounted for most cases associated with monosomy 22 (6/9; 67%), including cases with isolated monosomy 22 (4/6; 67%)”
or with monosomy 22 combined with other chromosomal alterations (2/3, 67%);… 

-Discussion, p. 11: “monosomy 22 is typically found at higher frequencies than NF2 mutations”: the frequency of NF2 mutations could be higher depending on the detection methods used (the authors later mention the possibility of epigenetic changes, but more frequent than these are gene rearrangements identifiable by MLPA or other techniques; mutations in promoter and other non coding regions are also possible)

-Discussion: The authors mention the possible involvement of a second gene on chromosome 22: SMARCB1 should mentioned in this regard.

-Discussion, p. 11, last paragraph: the inclusion of the transitional histotype among the features of NF2 mutated meningiomas with monosomy 22 is questionable, since the difference with the other meningiomas was not significant.

-Discussion, p. 12, 1st paragraph: “…each NF2-mutated meningioma case, they all leaded to a truncated…” # “…each NF2-mutated meningioma case, they all led to a truncated…”

In addition, as mentioned above, one mutation is a small in frame deletion, so this sentence has to be modified.

-Finally, the authors could discuss the LOH results in table 2 and the significance of lack of LOH in 2 cases with complete or partial monosomy 22.

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

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.