Reviewer's report

Title: Paraganglioma and pheochromocytoma upon maternal transmission of SDHD mutations

Version: 1 Date: 23 May 2014

Reviewer: Guiomar Perez de Nanclares

Reviewer's report:

Bayley and cols present three cases of SDHD-paraganglioma/pheochromocytoma putatively caused by maternally inherited alterations. Due to the rarity of this inheritance, this MS is quite interesting for reporting. However, there are some points that, in my opinion, can help to prove this inheritance.

Major Compulsory Revisions

Even if initially imprinting at SDHD was suggested (as indicated by the authors), more recent papers suggest that the deletion of the maternal 11p copy is enough for the development of the PGL/PHE as many other tumors. In fact, in a recent paper pat11pUPD has been suggested as the underlying mechanism for the tumorogenesis.

I think that if authors can confirm the absence of the maternal chromosome at 11p, they could confirm that the three tumors are due to SDHD mutations.

In fact, in other cancers as BRCA1-breast cancer, it has been demonstrated that when LOH is present both native or mutant alleles can remain in the tumor. I think this idea can be discussed.

Patient#2:

Microsatellite typing of 11p in tumor and germline DNA should be performed to discard/confirm the absence of maternal chromosome as the underlying causative mechanism of tumorogenesis.

Is there a real and proven need of only mutated allele to develop disease?

How do authors explain the absence of IHQ in this patient with normal allele present?

Patient#3

Microsatellite typing of 11p in tumor and germline DNA should be performed to discard/confirm the absence of maternal chromosome as the underlying causative mechanism of tumorogenesis

Minor Essential Revisions

1. Authors’ filiations should be listed in a orderly fashion
2. Background, first paragraph, last sentence. After ref#3, include a dot.

3. Background, third paragraph: "Germline mutations of the SDHD gene show a 'parent-of-origin' expression phenotype, with tumor development occurring only when mutations..." replace only by mostly (at least two cases of maternal inheritance have been reported"

4. Figure legends: figure numbering is quite confusing (a, ai, cii,...)

5. The electropherograms of microsatellite markers for LOH analysis could indicate both peak size and intensity

**Level of interest:** An article of importance in its field

**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