Reviewer’s report

Title: Clinical array-based karyotyping of breast cancer with equivocal HER2 status resolves gene copy number and reveals chromosome 17 complexity

Version: 1  Date: 15 April 2010

Reviewer: anna Sapino

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In this study Gunn and colleagues analyse a series of 20 FFPE samples of invasive ductal carcinoma with “equivocal” HER2 status (by either IHC or FISH) by using a clinically validated genomic array containing 127 probes covering the HER2 amplicon, the pericentromeric regions, and both chromosome 17 arms, in the attempt to sort out whether or not they harboured HER2 amplification. Although the paper deals with a hot topic that has recently gained great interest following the publication of 2 papers (one authored by the same group) on chromosome 17 polysomy and on amplification of chromosome 17 centromere, the analysis performed in the study does not report very novel results (as it is a sort of expansion/ validation of previous findings on a selected cohort of cases); in addition, there are some issues that need to be addressed.

- Major comments:

1) The main concern regards the HER2 status of the cases. The authors state in the text that these were cases for which the HER2 status could not be clearly defined by both IHC and FISH, and this is actually a crucial point for the relevance of the paper itself, that would add something more to what has already been reported in the study published in Mod Pathol 2009. Although the claim made in the text, the table (table 1) in which cases are listed is confusing and makes understand there might be some missing data. Therefore the authors should provide a detailed description of the IHC score and of the FISH ratio for each individual case.

2) Authors state in the introduction that array-based karyotyping has been recently integrated into clinical laboratory: although several molecular techniques have been widely incorporated in the routine activity of clinical laboratory, this reviewer is a bit sceptic on the “integration status” of the array CGH in clinical laboratory routine practice: although it might represent a feasible technique in big centres where genetic laboratories, it is not a method pathologist are very familiar with at the time being. Therefore this reviewer believes the authors should temper this sentence and consider to discuss the issue posing the issue of array-CGH as a feasible technique in referral diagnostic centres, in collaboration between geneticists and pathologists.

- Minor comments:

1) Some typos can be found throughout the text and need the authors’ attention; a couple of examples are reported here below:
- “in situ” should be in Italic, as well as “HER2”, when author refer to the gene product and not to the protein.
- “unamplified” should be changed to “not amplified”

2) Table 1 reports information of OncotypeDx results only for cases EQ-18 and EQ-20: this is not acceptable, either provide the same information for all cases, or exclude these details form the paper.

**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:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests