Reviewer's report

Title: Unraveling the chromosome 17 patterns of FISH in interphase nuclei: an in-depth analysis of the HER2 amplicon and chromosome 17 centromere by karyotyping, FISH and M-FISH in breast cancer cells

Version: 3
Date: 28 August 2014
Reviewer: Matteo Brunelli

Reviewer's report:

The Authors evaluated chr17 rearrangements in metaphases of 9 breast cancer cell lines and a primary culture from a triple negative breast carcinoma by using G-banding, FISH and M-FISH. They found high frequency of complex chr17 abnormalities, such as losses, gains and break-riarrangements.

The study is of interest and innovative.

Minor:

#the characterization of triple negative breast carcinoma has been performed on a single case, thus the conclusion of the key cytogenetic features of chr17 in this subtypes of breast cancer must be chary. Insert a statement in which the Authors explain the heterogeneity of triple negative breast carcinoma and conclude that these features have to be confirmed on further cases.

#monosomy of chromosome 17 has been reported in a subset ranging from 1% to 30% of breast carcinomas. Do the Authors interpret any cases be characterized by monosomy of chromosome 17 after the analytical phase showing losses of more loci? Did any techniques used in the study reveal any interpretation of monosomy of chr17? If not, please insert few rows in the Discussion making a statement on monosomy of chromosome 17.

#the study has been well conducted, however my view is that the conclusion proposed from the study is not the most appropriate: 1) the several pattern of abnormalities revealed from the study pose the attention to the design of new clinical trials in which the subtypes of chromosomal complexity of chr17 may explain, at least in part, resistance to targeted therapies or scheme of chemotherapies. Again, the complexity of abnormalities may help correlation with clinical end-points, such as prognosis when focusing on DFS or OS; 2) the ASCO/CAP 2013 guidelines well described the difference between the analytical and interpretative phases and they updated the rules to interpret at best the differences of counting the locus specific probes versus the centromeric ones, visible during the analytical phase. I believe the conclusion is not avoid counting chr17, is to improve guidelines of interpretation. Differently, if we use only the single Her-2/neu probe we could lose many information that might be of interest at clinical level. Therefore, my suggestion is to modify the conclusion in the Abstract and at the bottom of the manuscript. The complex abnormalities of chr17 merit further investigation at clinical level, being potentially in correlation
with responsiveness or resistance to targeted or personalized scheme of therapies. I agree with the Authors, in addition to the aforementioned statements the cytogenetic complexity of chr17 must be taken in account when consensus guidelines are encountered.

#when dealing with external and internal quality control assessments on molecular Her-2/neu testing, main focus is posed on the problematic located at the pre-analytical phase. Your findings again reflex the fact that some discordances in between immunoistochemical and cytogenetic analysis may be due (in part) to biological reasons rather than pre-analytical problematics. Insert a statement in the Discussion focusing on this problematic.

#Tables. Insert a column or an small insert into the images, showing Her-2 testing as performed by blinded dual color Her-2/CEP17 probes and as performed by blinded single Her-2 probe, showing if discordances are observed per each of the 10 cases.

#do the Authors have chances to perform immunophenotypical analysis on 10 breast carcinomas?.

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