Author's response to reviews

Title: Cross-species comparison of aCGH data from mouse and human BRCA1- and BRCA2-mutated breast cancers

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Amsterdam, February 11th, 2010

Dear Dr. Norton,

Please find attached our manuscript entitled ‘Comparative oncogenomics of BRCA1- and BRCA2-mutated human breast cancers and mouse mammary tumors’, by Holstege et al., which we would like to submit for publication in BMC Cancer. We expect this manuscript to be interesting for BMC Cancer for the following reasons:

1. This is the first unbiased cross-species comparison of array-CGH data of mouse and human breast tumors.

   We performed a cross-species analysis of array-CGH profiles of mouse and human BRCA1-, BRCA2-mutated and control breast tumors. We used two statistical methods to analyze and compare array-CGH data: one, KC-SMART, to identify genomic regions of significantly recurrent gain or loss within one tumor group, and the second, comparative-KC-SMART, to find between group differences. We then determined which of the regions detected by these methods co-occurred in mouse and human breast tumors.

2. Using KC-SMART, we find that MYC gain and RB/INTS6-associated loss co-occur in all groups of mouse and human breast tumors.

3. We find that the AURKA-associated gain co-occur in the mouse and human BRCA2-mutated breast tumors.

4. Using comparative-KC-SMART, we find that important gains and losses in human breast tumors, such as the 3q gain and the 5q loss in BRCA1-mutated human tumors do not occur in the syntenic regions in mouse BRCA1-mutated tumors. Vice versa, the gain on chromosome 10, characteristic for mouse BRCA2-mutated tumors, does not co-occur in the human BRCA2-mutated tumors.

5. We find that phenotypic qualities, such as tumor cell type, of mouse models very well recapitulate the human situation, but that selection of gains and losses in their oncogenomes show many differences.
These findings are important in the breast cancer field. As mouse models are used in preclinical studies, it is important to understand to what extent genotypic and phenotypic aspects of mammary tumors from mouse models are comparable with human breast cancers.

I am looking forward to hear from you.

Yours sincerely,

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