Reviewer's report

Title: Somatic mutation analysis of MYH11 in breast and prostate cancer

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Reviewer: Malek Faham

Reviewer's report:

The paper “Somatic mutation analysis of MYH11 in breast and prostate cancer” has a clear and simple objective- investigating whether MYH11 mutates in breast and prostate cancers.

The paper is clearly written and the manuscript is easy to read. On the positive side is that the authors studied a reasonably large sample size (155 breast and 71 prostate). The authors investigate only 8 of the 42 exons of the gene (with one of these exons being only marginally covered in breast cancer samples).

If the important finding is the lack of mutations of this gene in these samples, it seems to me that further work needs to be done to ensure that this is not due to technical problems.

1) Most importantly, one reason why somatic mutation may be missed is if the samples are contaminated by normal tissue. This will lead to the presence of less than heterozygous mutations that can be missed by sequencing. Therefore it is important to get an idea about the level of contamination in these samples. One way to do that, is to look for loss of heterozygosity (LOH) in regions in the genome known to frequently undergoes LOH in these cancer types. If the sample is not contaminated at all, regions of LOH should be detected (heterozygous in the normal tissue but homozygous in the tumor). The presence of contamination will keep both alleles present but causes one of the alleles to be lower than the other one. Quantitative analysis of the reduction can help in the estimate of the degree of contamination.

On the minor side:

1) The authors that most of the exons are covered in 80-100% of samples. What are the criteria used to determine something is covered or not? Is it some phred score- that needs to be clarified. Can the authors comment on the potential false negative rate?

2) The authors refer to c.5798delC as a somatic mutation. Since its absence in the normal sample could not be verified, it should be described as a potential or candidate somatic mutation.

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