Reviewer's report

Title: Tumor-suppressor activity of RRIG1 in breast cancer

Version: 2 Date: 9 November 2010

Reviewer: Balazs Györffy

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Zhang et al investigated RRIG1 in breast cancer and found reduced expression compared to normal tissues. The study is mainly cell-culture based with immunohistochemistry, western blot, RT-PCR and cell culture assays. Additionally, the gene has also been evaluated in a cohort of clinical patients.

Major revisions:

1. As RRIG1 is not in Pubmed Gene, the authors should add more description. Has the sequence for the primers been blasted?
2. There are error bars on the graphs, but the text does not describe whether any repetitions were made.
3. Is there a possible way to get correlation to survival? (see for example www.kmplot.com)
4. "It is unclear whether RRIG1 expression is controlled solely by RAR". Since RAR heterodimerizes with RXR to function, the answer for this question is quite obvious: the authors should add and discuss RXR-related literature.
5. Add more description about the of patients used (hormone receptor status, survival, HER2 status). ER and HER2 should also be evaluated for any possible correlation to RRIG1, as they also strongly influence the survival.

Minor revisions:

6. Check grammar! ("Next, we therefore used it immunohistochemically" "These cell lines were and grown in" etc)
7. The investigation of RhoA is insufficiently addressed. Why not another gene?

Discretionary revisions:

8. Previous results can be discussed in the discussion but do not belong in abstract.
10. Logical errors in sentences. (like: "It is unclear the underlying mechanism by which the restoration of RRIG1 expression was unable to suppress Stat3 phosphorylation, but knockdown of RRIG1 did so.")

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