Reviewer’s report

Title: LGR5 Overexpression Confers Poor Relapse-free Survival in Breast Cancer

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Reviewer: Mousumi Majumder

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Increase expression of LRG5 is associated with breast cancer specially stem cell induction has been established by other groups. In 2015, Yang L et al have shown the roles of LRG5 in breast cancer and established LGR5 overexpression was high in breast cancer and significantly associated with breast cancer recurrence and poor outcome. They have shown that HER-2 positive patients have high expression of LRG5.

The article by Ming-Feng Hou et al shown that LRG5 expression is high in non-triple-negative breast cancer (NTNB) and LRG5 expression is associated with poor patient survival in NTNB cancer samples. The immunohistochemistry data is very convincing and also supporting previous publications on LRG5. Authors has huge tissue to begin with and lot more can be done. While this article is important, clearly well designed, but it's lacking novelty.

Comments to improve:

TNBC is the most aggressive breast cancer but why LRG5 expression is not high in this group, explain?

Authors explained the importance of LRG5 in cancer stem cell. As LRG5 can regulate cancer stem cell via Wnt/beta catenin pathway; at least one marker of stem cell pathway along with LRG5 in both NTNB and TNB groups in serial sections need to be done. Co-staining would be best but it could be done in serial sections or may be if they can extract mRNA, multiple markers can be done from tissue extracted RNA/Protein. That could be new and novel findings.

Except in theory authors did not show any evidence of link between stem cell pathway and LRG5.

Figure 1: Can you make it two? Put breast cancer in one chart and rest of the cancers in other. In breast cancer plot, if you could separate out triple negative breast cancer and NTNB cancer data separated would be best representation.

Spell check require throughout. In many places authors has typo like "thant" instead of "that" beginning from abstract. Discussion needs to be more detail.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.
Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

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I am able to assess the statistics

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