Reviewer's report

**Title:** ADAM33 gene silencing by promoter hypermethylation as a molecular marker in breast invasive lobular carcinoma

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**Reviewer:** William Coleman

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“ADAM33 gene silencing by promoter hypermethylation as a molecular marker in breast invasive lobular carcinoma”

G.G. Seniski, et al.

In this manuscript the authors have investigated DNA methylation-dependent silencing of ADAM33 in breast cancer cell lines and primary tumors using a variety of experimental approaches and methods. The results show that ADAM33 expression is (i) lost in 65% of breast cancer cell lines, (ii) is reactivated by 5-aza treatment, and (iii) corresponds with promoter methylation. While ADAM33 promoter methylation and gene silencing did not correlate with clinicopathologic features of the tumors examined, this methylation gene silencing was found to occur most often in lobular cancers. The authors suggest that ADAM33 methylation could be a useful marker to differentiate invasive lobular carcinoma from invasive ductular carcinoma.

This is a well written revised manuscript that describes an interesting study. The authors have employed excellent experimental design and methods, the figures and tables nicely present the data, and the conclusions of the authors follow the results obtained. The revised manuscript has been modified in response to reviewer comments and is improved over the original submission.

**Level of interest:** An article of outstanding merit and interest 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.