Reviewer's report

Title: Immunodetection of nmt55/p54nrb Isoforms in Human Breast Cancer.

Authors:

Matthew Pavao (mpavao@bu.edu)
Yue-Hua Huang (yhhg@bu.edu)
Laurie J Hafer (laurie.hafer.2000@alum.bu.edu)
Robert B Moreland (robert.moreland@ln.ssw.abbott.com)
Abdulmaged M Traish (atraish@bu.edu)

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Reviewer: Dr R Sutherland

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Accept after revision, which I do not need to see

The authors have previously identified a 55kDa nuclear RNA binding protein (nmt55/p54nrb), the expression of which is decreased in ER-negative breast cancer. In the present study they evaluate mRNA and protein expression in a series of primary breast cancers. Northern blots and ribonuclease protection assays demonstrated that nmt/p54nrb mRNA is expressed independent of ER status and that the decrease in protein levels in ER-negative tumors was thus not mediated at the mRNA level. The development of domain specific polyclonal antibodies NMT-4 (amino terminus) and NMT-5 (mid region) together with the NMT-1 monoclonal antibody to the carboxy terminus facilitated an analysis of protein expression in ~40 breast cancers. ER-positive tumors had detectable expression; only ~60% of which were positive when the N-terminal antibody was employed. When this study was extended to immunohistochemical analysis a similar pattern of expression was observed i.e. several nmt/p54nrb positive tumors were not detected with the NMT-4 antibody supporting the presence of N-terminal truncated isoforms.

These data provide further insight into the expression of a protein with a potential role as a marker of breast cancer phenotype. In order to confirm these preliminary findings a more extensive study on a large cohort of patients with accompanying detailed clinicopathologic data including significant follow-up will be required. Until these data and further information on the function and regulation of this gene product are available the full implication of the current dataset remain unknown and thus several aspects of the Discussion are highly speculative e.g. relationships with known prognostic factors and its role in cell growth.

The manuscript could be improved by:
1. Providing more detail on the number and characteristics of the breast cancers understudy i.e. primary or metastatic, total number of tumours analysed by the different methodologies, clinicopathological parameters of the group and are they representative of the population from which they were collected

2. Shortening of the Discussion.

**Competing interests:**

None declared.