Reviewer’s report

Title: Decreased Hsp90 expression in the continuum of breast lobular lesions.

Version: 1 Date: 11 January 2010

Reviewer: Matthew H Herynk

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The manuscript entitled “Decreased Hsp90 expression in the continuum of breast lobular lesions” by Zagouri et al describes immunohistochemical evaluation of Hsp90 in lobular neoplasias and infiltrating lobular carcinomas. The authors find reduced Hsp90 in these lesions when compared with normal adjacent tissue. The work is intriguing and may have important clinical implications for the use of Hsp90 inhibitors in breast cancer.

Major Compulsory Revisions

1) The authors acknowledge the small sample size and its’ limitations in producing statistical significance. A larger cohort, confirmation through additional methods (as listed in the discussion), or a few in vitro mechanistic studies would allow the authors to make definitive conclusions thereby significantly enhancing the impact of this manuscript. (See related comment #2)

2) Previously, the same group has reported reduced Hsp90 in lobular neoplasias in 44 patient specimens (BMC Cancer 2008, 8:312). This current manuscript reports 65 patients with lobular neoplasia with similar staining percentages and intensities as previously reported. Are these 65 new patient samples or the same 44 plus an additional 21? Please describe in the text.
   a. If these are an additional 21 (for a 50% increase in sample size), this small increase in the sample size does not warrant publication.
   b. If this is 65 new cases (for a 150% increase in sample size), the authors should consider combining both cohorts (if the staining and quantitation methods allow) to increase the power of the study.

3) The LN data does not demonstrate statistical significance as analyzed and the three pictures demonstrate a broad range of staining. Analyses of the data comparing differential levels of staining within the group may provide additional insight.

4) The authors state “the area of maximum staining intensity was preselected…”. Please add the percentages of high, medium, and low expression. It has been reported that ductal carcinoma shows increased Hsp90 expression and herein lobular carcinomas show reduced Hsp90 expression, it may be pertinent to quantitate the lowest levels of expression rather than the highest levels as these will be the areas that deviate most from normal.

Minor Essential Revisions
5) Separate the patient characteristics by LN and ILC.
6) Please provide a dilution factor for the antibody used.
7) Are the numbers listed standard error or standard deviation?

Discretionary Revisions
8) Figures
   a. It would be easier to view the figures as grouped composites, i.e. normals (Figure 1), LN (Figure 2A-C), and ILC (figure 3A-C).
   b. As the quantitation of normals exhibits a similar standard deviation as the LNs, and the LN pictures demonstrate different levels of staining, please provide multiple representative images for comparison.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests