Reviewer's report

Title: Expression of BNIP3 in invasive breast cancer: correlations with the hypoxic response and clinicopathological features

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Reviewer: Matthias Bache

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The authors investigated the impact of BNIP3, a hypoxia related member of the Bcl-2 family, by in situ hybridization and immunohistochemistry in 40 patients with breast cancer. A significant correlation between BNIP3 mRNA and protein expression was found but no relation with immunohistochemical staining of hypoxia related genes. Furthermore, tumors without BNIP3 expression had more metastases and proliferation activity. The study is interesting in the field of detection of BNIP3 expression in breast cancer patients. However, there are some comments, which should be considered to improve this study.

Major Compulsory Revisions:

1. In the introduction the relation between BNIP3 and VHL should be explained.
2. What are the controls for detection of Hif1a, Ca9 and Glut1 expression?
3. Dependent on the graduation in the methods chapter; in table 1 and 2 expression of Hif1a, Ca9 and Glut1 should be separated in positive and negative.
4. A figure for the immunohistochemical staining of Hif1a, Glut1, Ca9 should be added.
5. In the discussion it was described a correlation between Hif1a and Ca9 or Glut1, respectively. However p-values are missing.

Minor Essential Revisions:

6. P-values should be given uniformly with 3 decimal places
7. Abbreviations should be given in table 2.
8. In figures 3 and 4 the magnifications should be added.

Discretionary Revisions:

9. Does the expression of Hif1a, Glut1 or Ca9 have an impact on clinical parameters?
10. The actual literature about the role of BNIP3 in hypoxia should be added.
**Level of interest:** An article of importance 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 have no competing interests’.