Reviewer's report

Title: ErbB3 mRNA leukocyte levels as a biomarker for Major Depressive Disorder

Version: 2 Date: 3 May 2012

Reviewer: Shusuke Numata

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Major Compulsory Revisions

The authors demonstrated reduced mRNA of ERBB3 genes in leukocytes of MDD patients without medications, suggesting ERBB3 might be considered as a potential biomarker for MDD. This paper is interesting.

I wrote several comments.

1. It is better to showed only the data of 26 patients with MDD. There are no reasons to analyze their samples with MDD separately (17 and 26 patients) and their sample size is not large to separate.

For examples, mRNA expression levels of ERBB3 and FGFR1 genes in leukocytes from 26 patients with MDD and 19 control subjects were measured using a quantitative real-time PCR method. Expression levels from 17 patients were followed up after 12 weeks - treatments.

In methods

2. It is better to show one table for samples` information in methods (at Subjects), not in Results.

In results

3. They used three housekeeping genes. However, they showed only one data and it is unclear which ones they showed in results. They should show all data done by other two housekeeping genes using a supplemental table.

4. Is it really possible to calculate deltaERBB3? Their mRNA levels are relative expression, not absolute expression.

5. P13 L7. They should change $0=0.004$ to $p=0.004$.

6. In figure 2, they should write comments of numbers (controls and patients) analyzed and mean values of mRNA expression.

7. Were mRNA levels of ERBB3 at T12 also significantly decreased compared with that of controls?

8. They should show animal data in detail although they wrote data not shown.

In discussion
9. They concluded that ERBB3 could be considered a biomarker of depressive status in discussion. However, mRNA levels of ERBB3 were not changed before and after treatment (both decreased) and average MADRS scores after treatment looked low (6.53±4.58). So some patients who were not depressive status at T12 might show decreased ERBB3 levels. These suggest that ERBB3 may be a trait marker for MDD, not a biomarker of depressive status.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**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