Reviewer's report

Title: Serum Biomarkers for Neurofibromatosis Type 1 and early detection of malignant peripheral nerve sheath tumors

Version: 1 Date: 10 October 2012

Reviewer: Matthias Bache

Reviewer's report:

Title: Serum Biomarkers for Neurofibromatosis Type 1 and early detection of malignant peripheral nerve sheath tumors

Based on a literature review the authors chose 56 tumor markers and cytokines in order to analyze their protein levels in serum samples from NF1 patients with different degree of disease using array technology. Compared with healthy controls 6 proteins (EGFR, IFN, IL-6, TNF, IGFBP1 and RANTES) have significantly different protein levels. Two of them (IGFBP1 and RANTES) showed the highest protein levels in NF1 patients with MPNST. This is an interesting report. However, there are some comments that should be included in the manuscript.

Major Compulsory Revisions:
The pre-screening of 30 proteins in 60 patient samples selected five proteins. How were the five proteins identified?

An additional screening of this five identified proteins and further 26 proteins were carried out at least with all 104 patients. A total of 6 proteins were identified. However is not clear whether all five markers from the pre-screening were also identified in the final screening.

The verification of the identified proteins using ELISA was not documented in the results. Which 11 samples were re-evaluated? Could you give a correlation between the protein array data and ELISA or CBA? The data should document in supplement.

Minor Essential Revisions:
Which test was used for a reassessment of the EGFR data?

The average age of the healthy controls is 10 to 15 years higher than in NF1 patients. Are the levels of the identified proteins also regardless of age of healthy control subjects?

Is there a significant correlation between IGFBP1 and internal tumor burden? I miss the p-value.
In Figure 4: Unit of the x-axis is wrong. The correct term is “1-specificity”.

In additional file 1 the data of control group is missing.

In additional file 2 the authors should indicate which of the 115 proteins they have analyzed.

Discretionary Revisions:
The authors should discuss the fact of the higher EGFR serum levels in healthy controls.

When assessing the work, please consider the following seven points:
1. Is the question posed by the authors new and well defined? yes
2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work? see my recommendations
3. Are the data sound and well controlled? see my recommendations
4. Does the manuscript adhere to the relevant standards for reporting and data deposition? see my recommendations
5. Are the discussion and conclusions well balanced and adequately supported by the data? yes
6. Do the title and abstract accurately convey what has been found? yes
7. Is the writing acceptable? yes

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests