Reviewer's report

Title: Btbd7 contributes to reduced E-cadherin expression and predicts poor prognosis in non-small cell lung cancer

Summary: The authors demonstrated that Btbd7, of which expression is significantly high in NSCLC and also linked to the poor prognosis of lung cancer patients, contributes metastasis and may be closely associated to the phenotype of epithelial mesenchyme transition.

First of all, it is unclear how the authors investigate Btbd7 in NSCLC, although the authors address the possible role of Btbd7 in epithelial dynamics (or remodeling) in the background. Without lack of lead to study Btbd7 in this aspect, the value of their finding cannot be fully supported.

More introduction of Btbd7 is required in the background.
It is less clear what BTB/POZ domains are and why they are important.
Why the protein level of Btbd7 is firstly examined in the lung cancer and why Btbd7 is assumed to play role in NSCLC metastasis.

If Btbd7 is closely associated to the level of N and E-cadherin, the level of N-cadherin and E-cadherin, shown in Figure 4 can be determined by Immunoblotting from the cancer tissues as similar as that of Figure 2A. The authors may have at least 12 cancer tissues (Fig. 2A), which show higher Btbd7 expression in 6 cancer tissues (T1, T2, T6, T7, T10, and T11). N or E-cadherin expression should be examined in this set of cancer tissue to address more convincing correlation.

Results in Figure 3 are less important to be present as a separate figure.
IHC data shown in figure 4 as a representative figure should be compared in the same set of sample with appropriate controls.

According to the data in Figure 6, H1299 cells, which show higher Btbd7 expression should express higher N-cadherin than the other cancer cell lines as well as higher invasive properties. Such positive correlation of Btbd7 to invasive and EMT properties in cancer cell line model would be able to convince their notion.
Among lung cancer cell line model, a number of NSCLC cell lines (such as H1650) showed the distinct mesenchymal properties, such correlation should be examined in those cancer cell line model (see PMID 22272264)

Migration experiment shown in Figure 7 should not be interpreted as a ‘invasive properties’.

Based on figure 7 (left panels), cells are still proliferating. To determine migration capacity solely, the cell growth should be arrested as growth retardation by knockdown of a gene of interest may also contribute the migration capacity. Due to the lack of sufficient description of the experiments in the method section and figure legend, any conclusion in this experiment is less valid.

DAPI staining was not positive to all cells in figure 8B.

Taken together, despite convincing pathoclinical data of Btbd7 in lung cancer, the less convincing data in in vitro cell model and lack of appropriate control in the experiment, the current version of manuscript appears not to satisfy the level of publication to BMC cancer.

Level of interest: An article of limited interest

Quality of written English: Not suitable for publication unless extensively edited

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