Reviewer's report

Title: CXCR4 expression on circulating pan-cytokeratin positive cells is associated with survival in patients with advanced non-small cell lung cancer

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Reviewer: Sidong Xiong

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Comment to Author:
This study described that the circulating pan-cytokeratin and CXCR4 positive cells were more prevalent in patients with NSCLC than normal subjects and the elevated co-expression of pan-cytokeratin and CXCR4 was significantly associated with poor survival in stage III and IV NSCLC.

Major Criticisms
1. The introductory material seems lacking of the information of cytokeratin and the significance and value of this traditional marker in diagnosis of non small-cell lung cancer.

2. According to Pan’s report (Mol Cancer 2006, 5:56), the expression of CXCR4 on circulating pan-cytokeratin+ cells in mRCC (renal cancer) patients was more than 1#10^6 cells/ml, why this expression in NSCLC patients in this study was low around 2500 cells/ml (Fig 3) ? If CA07 patient held very high levels of double positive circulating cells compared to other patients, is this level correlated with much more progressed disease stage or less survival?

3. Instead of discussing signaling pathways involved in the regulation of CXCR4 expression and the metastatic potential of tumors which was not studied in the current work, the discussion should refer to several other reported biomarkers for metastatic lung/other cancer cells such as adhesion molecules (Ep-CAM, CD44), metalloproteinases inducer (EMMPRIN), chemokine receptors (CCR6, CXCR4) and epithelial differentiation marker including p63, MOC-31, thyroid transcription factor-1 as well as their distinct diagnostic utility.

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

Quality of written English: Acceptable

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'