Reviewer’s report

Title: Prognostic impact of CXCL16 and CXCR6 in non-small cell lung cancer: combined high CXCL16 expression in tumor stroma and cancer cells yields improved survival

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Reviewer: Helmut Schaidler

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A comprehensive analysis on CXCL16 and CXCR6 expression in non-small cell lung cancer was performed. It is shown that high CXCL16 expression in tumor cells and cancer cells is associated with improved cancer specific overall survival, for reasons currently unknown. Silencing experiments of CXCL16 suggested that it might have some inhibitory effect on tumor growth.

Investigations into the clinical importance of chemokines is timely, the data are well presented and discussed. Some concerns have to be addressed.

Major concerns:

1. More information on the control samples have to be provided. Did the authors perform immunohistochemical analyses on non-neoplastic tissue specimens of non-cancer patients? Representative examples of control tissue slides should be shown for better appreciation of the expression in neoplastic tissue.

2. Staining of TMAs can be heavily biased towards selection of preferred areas. Was CXCL16 and CXCR6 expression on whole tumor tissue section performed in order to demonstrate how heterogeneously or homogenously both are expressed? If not it should be performed on selected cases.

3. The immunohistochemical data are central to the findings and should be presented in more detail. Information on the positive cells and the percentage of positivity should be added in the result section. Additionally, the tumor infiltrating immunological cells should be summarized in a table.

4. The in vitro silencing experiments are interesting. Based on our experience, I have some doubts concerning the xCELLigence system. The authors should repeat the experiments and demonstrate the reduced growth rate applying another more common in vitro assay like XTT-, MTT-, or MTS assay. Furthermore, it would be also interesting to demonstrate the effects of soluble CXCL16 on proliferation of lung cancer cells. Since CXCR6 was also silenced data on the effect of proliferation should be provided.

Minor concerns:

1. Some of the Figures can be merged: Figure 1 together with Figure 5, Figure 3 and 4 as Figure 2 A and B.

2. Significant differences in Figure 5 should be indicated.
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 declare that I have no competing interests