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: Mayda Gursel

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This study by Sigurd M. Hald et al analyzed the impact of CXCR6 and CXCL16 expression on prognosis in non-small cell lung cancer (NSCLC). For this, expression of CXCR6 and CXCL16 were analyzed using 335 stage I-III A NSCLC patient tumor tissues. The study found that high stromal cell CXCL16 expression and combined high stromal and cancer cell CXCL16 expression are positive prognostic factors. Furthermore, knockdown of CXCL16 with a specific siRNA resulted in increased cell proliferation in NSCLC cell lines, supporting a role of CXCL16 as a positive prognostic marker. Although the impact of CXCL16 and CXCR6 expression on survival was previously investigated in different malignancies, this study would be of general interest to the field as it analyzed these parameters in non-small cell lung cancer for the first time. However, the manuscript must be revised carefully to include the following major points:

Results section needs to be edited so that all data summarized here is attributed to a specific figure or table. For example, the authors declare that “CXCL16 was expressed in both stromal and cancer cells, whereas CXCR6 was only expressed in cancer cells” but no Table was assigned for this observation.

Each Table should contain information about the abbreviations used. For example what is HR in Table 3?

The Figure legends are inadequate. This section should include brief information about the experiment carried out, the read-outs used and relevant calculation methods.

The authors declare that “Of the controls, 50% showed varying degrees of positivity for CXCR6 while 100% showed strong positivity for CXCL16”. It is not clear what is meant by “controls”. This should be explained.

Pertaining to the following observation: “There were no significant correlations between CXCR6 or CXCL16 and adaptive immunological (CD4, CD8, CD20), innate immunological (CD68, CD56, CD1A) or angiogenic (vascular endothelial growth factors and receptors, platelet derived growth 221 factors and receptors and fibroblast growth factor-2 and receptor-1) markers”. Where is this data? If this is an observation where no data is given, then the authors should say so by including the following: (data not shown).

The authors claim that “knockdown of CXCL16 with siRNA caused activation of proliferation compared to the negative scrambled control”. Was this statistically
significant? No P values were given. How many times was this experiment repeated?

**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.