Reviewer 3.
The authors demonstrated the oncogenic role of VGLL1 in gastric carcinogenesis. The found VGLL1 is positively regulated by PI3K/Akt/beta-catenin signaling. Through binding with TEAD transcription factor, VGLL1 activates the transcription of MMP9, thus to promote GC cell metastasis. The concluded VGLL1 serves as a prognostic biomarker and potential therapeutic target. In general, their findings are novel and the results are solidly generated. Major concerns are as follows:

The authors employed their own cohort for correlation analysis such as in Figure 1g. It is better to use other large-scale cohort for validation such as TCGA to get a solid conclusion.

► We appreciate your valuable comments. Therefore, we analyzed the correlation between VGLL1 and PIK3CA or PIK3CB in ACRG (n=300) and TCGA (n=375) cohorts. We can find correlation between VGLL1 and PIK3CA in the ACRG cohort. Unfortunately, there is no correlation between VGLL1 and PIK3CA in TCGA cohort.

Pearson correlations between VGLL1 and PIK3CA or PIK3CB in Asian Cancer Research Group (ACRG) cohort (n=300) (A, B) and TCGA cohort (n=375) (C, D) of gastric cancer patients
As the same, is any positive correlation observed between VGLL1 and MMP9 in primary samples?

► We appreciate your valuable comments. In the YSH (Yonsei University College of Medicine) cohort (n=556), VGLL1 and MMP9 showed a positive correlation (p<0.0001).

![Correlation coefficient](image)

**Pearson correlations between VGLL1 and MMP9 in gastric cancer patients (n=556).**

In Figure 2 and 3, the authors simply performed some functional tests, however several issues needed to be added. For example, it is better to confirm the VGLL1 expression level by Western blot or qRT-PCR in the xenografts to make sure the in vivo data are reliable.

► We appreciate your valuable comments. In the xenograft experiment of Figure 2, VGLL1 expression levels in tumor tissues were confirmed by RT-PCR (Supplementary Material Figure S1d,e). Now, we move this result to Figure 2d and e.

As VGLL1 regulates MMP9 expression through TEAD4. It is better to demonstrate if knocking out TEAD4 abolishes the regulatory effect. Any co-IP data supporting the direct interaction between VGLL1 and TEAD4?

► We appreciate your valuable comments. We showed that TEAD4 knockdown decreased the VGLL1-induced MMP9 promoter activity (Figure 5h). In addition, Interaction between VGLL1 and TEAD4 was observed by co-immunoprecipitation assays (Figure 5i).