Referee #1 (Remarks to the Author):   
  
This manuscript demonstrates that hypermethylation of ZNF132 promoter would be a novel biomarker in human esophageal squamous cell carcinoma (ESCC). The authors employed methylation target bisulfite sequencing (MTBS) to compare the methylation levels of cancer tissues to adjacent normal tissues in 91 ESCC patients, and found that the level is higher in cancertissues. After demonstrating that the methylation level of ZNF132 promoter affect its expression, the authors explored the function of ZNF132 on tumor growth, invasion and metastasis in vitro. They also used xenograft model to further verify the role of ZHF132 in inhibiting tumor growth. Lastly, they suggest that hypermethylation interfere with Sp1 in binding to the ZNF132 promoter by ChIP analysis.   
  
Questions:   
1. Is there any difference in the methylation level of ZNF132 in ESCC cell lines with different invasive and metastatic abilities?   
2. Fig4 suggests that overexpression of ZNF132 could inhibit tumor growth. how about using demethylation drugs in treating ESCC?   
  
  
  
Referee #2 (Remarks to the Author):   
  
In this manuscript, Jiang et al identified ZNF132 as a novel ESCC hypermethylation biomarker. They found that forced expression of ZNF132 in ESCC cells repressed cell growth, migration and invasion abilities in vitro, and xenograft tumor formation in vivo. They also found that hypermethylation of Sp1 biding site in ZNF132 promoter reduced Sp1 dependent transcription activation. Overall, this is an interesting piece of work which could be used as potential therapeutic targets in future. However, the manuscript should be improved by addressing the following concerns before publication in CDDis is recommended.   
  
  
Minor concerns:   
  
1. Forced expression of ZNF132 in each assays including transwell and xenograft mouse model should be validated by western blot instead of real-time PCR.   
  
2. It will be nice to examine the protein expression pattern of ZNF132 in clinical ESCC samples besides the real-time PCR examination.   
  
3. The scientific logic or references for analyzing Sp1 binding ability should be described in detail in P.13 after “As CpG was in silico predicted to be harbored in transcriptional activator Sp1-binding site at ZNF132 promoter……”   
  
4. How the promoter region of ZNF132 in ESCC is hypermethylated should be further discussed.