Comments to the Authors,

This manuscript reported the MiR-34a-5p promotes multi-chemoresistance of osteosarcoma through the downregulation of the DLL1 gene. Although the mythology and the result were quite clear and very interesting, the study design was not strong enough to be qualified in Clinical Epigenetics. The essential suggestion and requirement were not solved in current version. What’s worse the reason for the expression change were not illustrated. Finally, the ‘direct’ regulation of the miR-34a-5p were not demonstrated whole manuscript were descripted as the direct regulation. In summary, the current version of the manuscript still need several major and important revision.

**Major Compulsory Revisions**

1, miRNA-seq section: How many biological or technical replication were applied in the study were totally unclear? Even the further analysis were needed, the current data could be also upload to GEO and set a private time such as 6 month or 1 year before the public share.

2, In the present manuscript, all the analysis were based on cell lines. The clinical relevance of the study should be focused. Clinical Epigenetics is a journal which is high focusing on Epigenetic research and application in clinical studies. The current study should be provided enough evidence in clinical application.

3, The mechanism of the aberrant expression of miR-34a-5p should be investigated in the current study.