Response to Reviewer 1 Comments

Unfortunately, this work is superficial, rough, and out of scope. Major issues:

Point 1. In the review, there is almost nothing related to epigenome. All discussion are not focusing and superficial.

Responses: Thank you for your comments. We have revised the title to emphasize our main focus: "The way to malignant transformation: can epigenetic alterations be used to diagnose early-stage head and neck cancer?" We have also removed one figure and contents that are not directly related to epigenetic alterations. In addition, we reorganized the contents in subsection 7 and introduced new paragraphs on how to incorporate new technologies for constructing epigenetic landscapes denoting malignantly transformed OPMDs in Future Directions (subsection 8).

Point 2: The review is distractive and less updating. It is of few scientific value.

Response 2: In the revised manuscript, we have provided a comprehensive illustration of how modern technologies can be employed to decipher epigenetically-driven molecular events in archived specimens of OPMD. These events can serve as benchmarks of key steps involved in the malignant transformation process, as well as their potential as noninvasive diagnostic biomarkers for early-stage tumors in clinical settings. We have also ensured that all references have been updated accordingly to reflect the latest research in the field.