Reviewer’s report

Title: Implication of metastasis suppressor gene, Kiss-1 and its receptor Kiss-1R in colorectal cancer

Version: 2 Date: 8 July 2014

Reviewer: Eiji Kikuchi

Reviewer’s report:

The authors evaluated the role of Kiss-1 and Kiss-1 receptor on clinical outcome using colon cancer patient tissues as well as investigated the mechanism by which Kiss-1 and Kiss-1 receptor could inhibit the metastatic or migration behavior using colon cancer cell lines. They concluded that mRNA expression of Kiss-1 receptor is associated with poor outcome in colon cancer and Kiss-1 has inhibitory effect against colon cancer cell lines by reducing MMP-9 expression through ERK pathway. Unfortunately the reviewer recommend more research to reach their conclusion. The detail comments are listed below.

Detailed comments:

Background

1 Page 4, line 74, the authors stated that, “In this study, we first examined the expression of Kiss-1 and Kiss-1R in human”. Please refer the paper published by Sánchez-Carbayo M group who intensively investigate the KiSS-1 peptide (Tumour Biol. 2013 Feb;34(1):471-9. doi: 10.1007/s13277-012-0572-3. Epub 2012 Nov 7.). Their group has already evaluated the association of the KiSS-1 protein expression with colon cancer patient’s clinical outcome using 352 tumor tissue samples.

Materials and Methods.

2 The reviewer strongly recommends that the authors need to describe more detail information of the methods in their study. Most of methods have referred to the section of Materials and Methods in other manuscripts and then the reader cannot understand the concentration of drug used, the optimized condition of the method in this study, etc.

Results and discussion

3 Page 8, line 169, the reviewer could not understand that, “The average copy numbers of Kiss-1 and Kiss-1R transcripts in Dukes B were then employed as the respective thresholds for the survival analysis.” Why could the authors decide such a way for the cut-off level of Kiss-1 and Kiss-1R? Other cut-off point of the values is needed to evaluate.

4 The authors need to perform multivariate analysis for survival in their study.

5 The authors demonstrated the immunochemical staining of tumor tissues in figure 1a. Then the authors need to evaluate more detail of the expression of
Kiss-1 and Kiss-1R protein expression in colon cancer tissues by IHC analysis with clinical outcome.

6 The author need to use the positive control such as placenta for the expression of Kiss-1 and Kiss-1R.

7 The authors state that, “in summary, it is suggested that Kiss-1 inhibits ERK activation and consequently reduces the enzymatic activity of MMP-9 caused by the degradation of NF-κB, which contributes to the suppression of tumor metastasis.” The reviewer strongly recommend to show the degradation of NF-κB in their original work.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

'I declare that I have no competing interests