

June 4, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 10421-revised.doc).

**Title:** Pea3 Expression Promotes the Invasive and Metastatic Potential of Colorectal Carcinoma

**Author:** Aruz Mesci, Samira Taeb, Xiaoyong Huang, Rishi Jairath, Darshan Sivaloganathan, Stanley K. Liu

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 10421

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 We believe that the language of our manuscript has reached Grade A and would be willing to sign a guarantee.

3 Revision has been made according to the suggestions of the reviewer

(1) The title has been revised to "Pea3 expression promotes the invasive and metastatic potential of colorectal carcinoma" as recommended.

(2) We utilized female nude mice for our xenograft experiments, since our group and many others note reproducible tumor formation using this system. Additionally, since colorectal carcinoma cells are not estrogen or androgen dependent for cell growth, we did not consider it necessary to use both male and female nude mice. However, we agree that future studies could utilize both male and female nude mice, and this has been reflected in the discussion. "We employed female mice for our studies, and although to our knowledge, colorectal carcinoma cells are not estrogen or androgen-dependent for their growth, future studies could utilize both male and female mice to rule out any gender-specific differences for Pea3 in CRC tumorigenesis and metastasis."

(3) Euthanasia was performed by cervical dislocation. This has been added to the materials and methods.

(4) We have since performed flank tumor xenograft growth experiments with LS.shPea3 and LS.shCtrl cells. We have added the following statement to our results: "Interestingly, LS.shPea3 tumours grew faster than their shCtrl counterparts (Figure 3D, LS.shPea3  $4.62 \pm 1.37$  fold vs LS.shCtrl  $2.80 \pm 0.69$  fold,  $p < 0.05$ )." Collectively, our in vitro and in vivo results indicate that the loss of Pea3 expression is not associated with a proliferative disadvantage. The materials and methods, figure 3D and figure legend has been updated.

\*Changes to the manuscript have been noted by yellow highlighting

4 Core Tip and Comments sections have been added.

5 Figures and Tables are now provided as PPT format as requested.

6 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

A handwritten signature in black ink, reading "Stanley K Liu". The signature is fluid and cursive, with the first name "Stanley" and last name "Liu" clearly distinguishable.

Stanley K Liu, Ph.D., M.D., F.R.C.P.C.

Assistant Professor,

Depts. of Radiation Oncology and Medical Biophysics,

University of Toronto

2075 Bayview Avenue, T2-142, Toronto, Ontario, M4N 3M5

ph: (416) 480-4998

fax: (416) 480-6002

STANLEY.LIU@SUNNYBROOK.CA