Author's response to reviews

Title: Growth Inhibition of Anaplastic Thyroid Cancer by Opioid Growth Factor (OGF)

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Author's response to reviews: see over
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BMC Cancer
Editorial Office

RE: 1911654074221379

Dear Editor:

On behalf of all authors, I am submitting the revised manuscript (with a revised title) entitled: "Growth Inhibition of Thyroid Follicular Cell-Derived Cancers by the Opioid Growth Factor (OGF) - Opioid Growth Factor Receptor (OGFr) Axis" for consideration in BMC Cancer. We have addressed all of the concerns of the reviewers. The major concern, which is the cause for the time delay in resubmission, was the need to locate more anaplastic thyroid cancer cell lines. As such we were able to obtain the FRO81-2 cell line. While putting the manuscript together with FRO81-2, we contacted Dr. Fagin (Memorial Sloan-Kettering), an expert involved with this cell line. When asked about the validity of this cell line, Dr. Fagin responded in an email: "I would not use FRO cells." As there are no other anaplastic thyroid cancer cell lines in the U.S. (getting them from Europe would be extraordinarily difficult), we elected to broaden our line of questioning by obtaining the WRO cell line - a follicular thyroid cancer cell line that has been confirmed in its origin. Thus, our manuscript does not deviate from its original intent, but is now broadened to focus on the OGF-OGFr axis in thyroid follicular cell-derived cancer - anaplastic and follicular.

All of the authors have participated in some way in this study, and have read and approved the enclosed document.

Details of the corrections are attached. Please thank the reviewers for their constructive suggestions.

We look forward to your editorial decision.

Sincerely,

Dr. Patricia J. McLaughlin
Professor
Reviewer: Jim Yeung. Reviewer’s comments are in italics.

#1. “…the data using KAT-4 and DRO cells in this paper need to be deleted, and the experiments need to be repeated….”
   Response: The data on contaminated cell lines have been removed. Because other anaplastic thyroid cancer cell lines are very difficult to obtain in the U.S., we asked if the OGF-OGFr axis is in another follicular derived cancer cell - WRO (see Fig. 6).

#2. A “me-too” story for anaplastic thyroid cancer…. “Is p53 involved?”
   Response: Unpublished gene array data document that p53 is not altered by OGF.

#3. “Tachyphylaxis?”
   Response: This is question is addressed by comparing growth curves between cells continuing to be exposed to OGF and those in which the original exposure to OGF is reversed by treatment with vehicle. Please note that the reversal experiment allows the cells to be "restored" to normal growth, whereas the OGF group continues to grow subnormally.

Minor essential revisions:

#1. “...rate measurements need to be repeated…”
   Response: Growth rate experiments were repeated and similar results obtained.

#2. “Figure 4A&B: It would be more convincing to show the protein level of OGFr ……”.
   Response: We have performed semi-quantitative densitometry of OGFr expression - along with a statistical presentation (see new Fig. 4)

Reviewer: Joshua Klopper. Reviewer’s comments are in italics.

“Unfortunately, two of the cell lines utilized from this study are likely not of thyroid origin……”
   Response: See response to #1 above.