Author's response to reviews

Title: Proneoplastic effects of PGE2 mediated by EP4 receptor in colorectal cancer

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Version: 2 Date: 29 April 2009

Author's response to reviews: see over
The Editor,
BMC Cancer,

Proneoplastic effects of PGE$_2$ mediated by EP4 receptor in colorectal cancer
MS: 1836327119253958
(Formerly titled: Induction of p21$^{WAF1/CIP1}$ via the EP4 receptor mediates the regulation of cell cycle progression by cyclooxygenase-2 in colorectal cancer)

Dear Dr Norton/Patel,

I am pleased, on behalf of the authors of the above manuscript, to submit a revised version of our manuscript for consideration for publication in BMC Cancer. We are grateful to have the opportunity to make several changes in response to the helpful comments of your reviewers.

The title of the manuscript has been amended to better reflect the totality of the findings in line with the suggestion of one of your Reviewers. We have revised several statements within the background section in order to emphasize that the rationale for searching for downstream targets is related to the adverse cardiovascular effects of current selective COX-2 inhibitors. We have not noted any additional effect of the combination of treatment with EP4A with and EGFR tyrosine kinase inhibitor in our model and have therefore not made any specific changes to Figure 4. We have expanded the initial portion of the discussion in order to recognize that the importance of the COX-2/PGE2/EP4/EGFR pathway has been recognized as significant in other tumour types. We have also amended our discussion to reflect that EGF signaling has also been implicated in the induction of COX-2 expression within tumours, suggesting a possible positive feedback loop between COX-2 and EGF signaling. We hope that these changes will be adequate in order to proceed with publication.

As we have previously stated, this manuscript has not previously been published elsewhere. As stated in the manuscript, none of the named authors have any financial conflict of interest to disclose. No professional writing assistance was used in the preparation of this manuscript.

I wish to offer, in advance, most sincere thanks for the time taken to consider our revised submission.

Yours faithfully,

Glen Doherty MB PhD MRCPI