Author's response to reviews

Title: Wnt Pathway Reprogramming During Human Embryonal Carcinoma Cell Differentiation and Potential for Therapeutic Targeting

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Version: 3 Date: 3 September 2009

Author's response to reviews: see over
Dear Dr. Norton,

Enclosed, please find the revised resubmission of our manuscript “Therapeutic Potential of Reprogramming the Wnt Signalling Pathway in Embryonal Carcinoma” (MS: 1123936251261352).

We thank the Reviewer for his favorable evaluation of our paper. We have made the requested changes in the text and added one additional figure.

In the subsequent pages we have detailed our response.

We thank you and the Reviewer for your time and consideration during this process.

Sincerely yours,

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Reviewer's report
Title: Wnt Pathway Reprogramming During Human Embryonal Carcinoma Cell Differentiation and Potential for Therapeutic Targeting
Version: 2 Date: 11 August 2009
Reviewer: Raymond Habas

Reviewer's report:
In this revised manuscript, Snow and colleagues has improved substantially with additional experiments and has addressed and resolved my major concerns. I therefore strongly recommend its publication in BMC Cancer.
This study together will deepen our understanding of the role of the Wnt signaling in reprogramming of this pathway during differentiation of human EC cells. I however have a few minor text changes or additions requested of the authors.

- On page 3, the authors should provide some references during their description of the Wnt pathway and its many branches.

Two additional references have been inserted to cover the different aspects of Wnt signaling.

- On page 12, please define CT scores for the reader.

This has been done. And is now on page 13.

- On page 14, I do not understand the sentence “this may be caused by a difference in the rate at which individual siRNA species silence their target genes”. Are there published studies that support this contention?

We are not aware of literature reports describing this. We were not clear why silencing onset would differ in this way. We have revised the sentence (now page 15) to include other possibilities to: “This may be caused by a difference in the stability or effectiveness of the individual siRNA species or possibly a difference in the rate at which they silence their gene targets. “

- On page 15, please show the phospho-JNK data either in the paper or as a supplemental figure.

The phospho-JNK data is now Additional file 5.

- On page 24, I am not sure what reference #46 has to do with Daam1 and Profilin1 in Wnt signaling?

Reference #46 (now #48) refers to a paper that reported that Profilin-1 levels were upregulated in embryonal carcinoma cells induced to differentiate along a neuronal lineage and our studies found that Daam1 is also upregulated as NT2/D1 cells are induced to differentiate. As both of these genes are involved in actin organization and non-canonical Wnt signaling we feel that the specific regulation of these genes may play a role in coordinating the cytoskeletal changes occurring during differentiation.