Author's response to reviews

Title: Phenethyl isothiocyanate upregulates death receptors 4 and 5 and inhibits proliferation in human cancer stem-like cells

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

We greatly appreciate your questions/concerns in email dated 7/10/2014. We have detailed our response below. Please also note that text modifications in response to your comments are tracked and highlighted in the revised manuscript (both tracked and un-tracked versions are uploaded).

We will look forward to hear from you,
Sincerely,

Moul Dey
July 16, 2014

Response to Editor
1. Please further clarify in Figure 3B, whether PEITC and Trail combination induced apoptosis is statistically significant (P<0.05) compared to PEIT or Trail alone. Since in Figure 3C, the combination did not show statistically significant and in Figure 3A, only combination with PEITC 15 mM (but not with 10 mM), it should be important to verify these results to justify the use of title "PEITC sensitizes TRAIL-induced apoptosis" as mentioned by Reviewer # 1.

Response: In Figure 3B PEITC and TRAIL combination induced apoptosis is NOT statistically significant (P<0.05) compared to PEITC or TRAIL alone but statistically significant (P<0.001) when compared with vehicle control.

We noticed the trend of PEITC sensitizing TRAIL-induced apoptosis is not highly striking in cancer stem cells. Cancer stem cells have the nature to repel drugs and resist to apoptosis. With this consideration, we discussed cautiously the potential synergistic effect of PEITC to TRAIL-induced apoptosis. In figure 3A, 15μM PEITC and TRAIL showed significant higher level of cPARP compared to either Trail or PEITC alone. In figure 3B, only TRAIL, or only PEITC still induced cell apoptosis, but synergistic treatment of PEITC and TRAIL resulted in a greater but statistically insignificant induction of apoptosis. Further, TRAIL sensitization by PEITC was observed in context of receptor (DR4, DR5) up regulation in Figure 4. Combining our own observations with the known information from science literature that TRAIL is the ligand for DR4 and DR5 receptors, we believe TRAIL sensitization by PEITC is very likely.

Nevertheless, given the concern of reviewer1 and the Editor we would like to propose following changes to the article title:

Current Title: Phenethyl isothiocyanate upregulates death receptors 4 and 5, sensitizes TRAIL-induced apoptosis, and inhibits proliferation in human cancer stem-like cells

Proposed title subject to approval of the editor: Phenethyl isothiocyanate upregulates death receptors 4 and 5 and inhibits proliferation in human cancer stem-like cells

2. Also Figure 4 was submitted twice (one as Figure 6) in the revised manuscript.

Response: We have deleted the extra Figure 4 file.