Reviewer's report

Title: 5-allyl-7-gen-difluoromethoxychrysin enhances TRAIL-induced apoptosis in human lung carcinoma A549 cells

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Reviewer: Yongkui Jing

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In this manuscript authors reported that the derivative of Chrysin augmented TRAIL-induced apoptosis through upregulation of DR5. The data showing that AFMC enhanced TRAIL-induced apoptosis are interesting and convincing. However, studies of supporting DR5’s role in this combination treatment are too preliminary and need to be improved.

1. In Figure 2C, the actual FACS data should be shown.

2. It is not known how authors pick DR5 as the primary target of AFMC action (Fig. 3), other potential targets influenced or not influenced by AFMC treatment should be shown and discussed.

3. To support that silencing DR5 would block AFMC plus TRAIL-induced apoptosis, the actual FACS data should show (Fig. 4). Western blot analyses of showing cleavage of PARP and caspase-8 should be performed. To support the specificity of DR5 siRNA, the levels of DR4 should be measured.

4. Although authors claimed that AFMC did not increase the levels of DR5 and did not enhance TRAIL-induced apoptosis in WI-8 cells, WI-8 cells express certain content of DR5. It seems that DR5 upregulation-independent pathway is involved in the action of AFMC to enhance TRAIL-induced apoptosis in A549 cells. The levels of DR4 and DR5 as well as the signaling of death receptor-mediated apoptosis should be compared in both cell lines.

5. More cancer cell lines should be used to test the induction of DR5 by AFMC and enhancement of AFMC on TRAIL-induced apoptosis.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.