Reviewer's report

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

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Reviewer: Rakesh K Srivastava

Reviewer's report:

I have reviewed the manuscript entitled “5-allyl-7-gen-difluoromethoxychrysin enhances TRAIL-induced apoptosis in human lung carcinoma A549 cells” by Xie et al. The authors have examined the interactive effects of 5-allyl-7-gen-difluoromethoxychrysin (AFMC) and TRAIL on DR5 expression, cell proliferation and apoptosis in A549 and WI-38 cells. AFMC sensitize human NSCLC A549 cells to TRAIL-mediated apoptosis. Combined treatment of A549 cells with AFMC and TRAIL significantly activated caspase-3, -8 and -9. The caspase-3 inhibitor zDEVD-fmk and the caspase-8 inhibitor zIETD-fmk blocked the apoptosis of A549 cells induced by co-treatment with AFMC and TRAIL. In addition, the treatment of A549 cells with AFMC significantly induced the expression of death receptor 5 (DR5). AFMC-mediated sensitization of A549 cells to TRAIL was efficiently reduced by administration of a blocking antibody or small interfering RNAs against DR5. In contrast, AFMC-mediated induction of DR5 expression was not observed in human embryo lung WI-38 cells, and AFMC did not sensitize WI-38 cells to TRAIL-induced apoptosis.

My comments are as follows.

1. By looking at the data of DR5 western blot, it appears that there is only one band. Generally, there are 2-3 isoforms of DR5 that can be recognized by the antibody. It is not clear why the authors have seen only one isoform.

2. The data on DR4, DcR1 and DcR2 should also be provided. Are there any effects of drugs on these receptors.

3. It has been shown that the DR proteins can be sequestered in the cytoplasm and thus can not be seen on the surface and also may nor enhance the effects of TRAIL. The expression of DR4, DR5, DcR1 and DcR2 should be measured by the flowcytometry technique. The experiments should also be performed to determine whether it is sequestered in the cytoplasm.


Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

'I declare that I have no competing interests'