Reviewer's report

Title: Tumor Necrosis Factor-alpha Attenuates Starvation-Induced Apoptosis through Upregulation of Ferritin Heavy Chain in Hepatocellular Carcinoma Cells

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Reviewer: Yun-Bo Shi

Reviewer's report:

This is an interesting paper reporting studies on the mechanism by which TNFa inhibits starvation-induced apoptosis. The authors carried out parallel studies in two different cancer cell lines with similar findings. They showed that the effect of TNFa could be inhibited by an inhibitor of autophagy and involved the TNFa-induced FHC. Consistent with a role of FHC in this process, they showed that FHC knockdown reversed the effect of TNFa on ROS and that a ROS scavenger suppressed TNFa inhibition of caspase activation. The conclusions are supported by the data presented and the findings are of significance toward the understanding of TNFa effect on cell death and autophagy.

Minor Essential Revisions:

1. The data showed that TNFa at 100 or 1000 ng/ml, not only failed to block reduction in live cells by starvation but actually enhanced it. Some discussion on why this happened should be provided even though the doses might be pharmacological.

2. The authors used NF-kB reporter gene in the studies. A more detailed description should be provided in the text and figure legend. A reference should also be provided.

3. Fig. 3 legend: the nuclei were stained “blue” not “red” as indicated in the legend. Also, it seems that the antibody against p65 was used for immunofluorescent and that the green nuclear signal was an indication of the activation. If so, they should be stated in the legend and/or text clearly. In the text, the authors indicated “…NF-kB p65 binding activity were evaluated by immunofluorescence…”, however, there was no such evaluation. The data merely analyzed the localization of the protein, with the nuclear accumulation suggestive of activated form.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

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