Reviewer's report

Title: Effects of ATRA Combined with Citrus and Ginger-Derived Compounds in Human SCC Xenografts

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Reviewer: Voichita Bar Ad

Reviewer's report:

I read with great interest the article “Effects of ATRA Combined with Citrus and Ginger-Derived Compounds in Human SCC Xenografts” by Kleiner-Hancock et al.

The study was well-designed and the manuscript well-written.

The inhibitory effects of the dietary compounds ACA and AUR and ATRA and their combinations against human skin squamous cell cancer growth in a xenograft model were analyzed.

ATRA was very effective at doses of 30 ppm in the diet inhibiting the tumor volume in this human SCC xenograft model by 93%, but did have modest inhibitory effects when used at lower doses. The treatment with AUR 1000 ppm alone in the diet did not reduce the tumor volume significantly, either. However, when lower doses of ATRA were used in combination with AUR, this combination strongly suppressed the skin tumor growth by 84%, suggesting a synergistic effect. In the light of potential side effects of retinoids, this synergistic effect may have important clinical implications. I suggest the author to emphasize this important aspect in the abstract and final conclusions.

The researcher group hypothesized that simultaneous suppression of Stat3 and NF-κB activation pathways by using ATRA and dietary compounds ACA may be more effective than either agent alone at suppressing skin SCC growth. ACA 500 ppm alone in the diet modestly suppressed the tumor volume. The combination of ATRA 5 ppm and ACA was associated with an inhibitory effect maintained to the end of the study. The study suggested that chemoprotective effects of ATRA against human skin cancer cell growth in this xenograft model seem to be extended when combined with ACA. Further studies are required to verify the efficacy and safety of these dietary compounds combined with ATRA against human skin SCC growth.

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

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the
Statistics.

Declaration of competing interests:

I declare that I have no competing interests.