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LETTER TO THE EDITOR

Bile acids for cachexia therapy

Reply to the letter by Shailendra Kapoor: Ursodeoxycholic acid and its emerging role in attenuation of tumor growth in gastrointestinal malignancies

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Dear Editor,

In a recent letter [1], Dr. Kapoor commented on our paper describing the effects of ursodeoxycholic acid (UDCA) in a model of severe cancer cachexia [2]. Dr. Kapoor is obviously correct in stating that there is emerging data showing that bile acids such as UDCA may be beneficial in gastrointestinal cancers by attenuating cancer progression. However, in our study, the aim was to characterize the effects of UDCA on cachexia development and progression in a cancer model, in which the effects of UDCA on tumor growth would be minimal to avoid biased results on cachexia development through a possible antineoplastic effect. Therefore, we chose to use the Yoshida hepatoma AH-130 rat model, in which rats develop severe cachexia very fast, but drug effects on proliferation—aside from chemotherapeutics—have been shown to be minimal, even when using growth factors like IGF-1 [3]. Indeed, UDCA had no effect on tumor proliferation in our model, but unfortunately its anti-cachexia effects were also limited. The latter was likely due to our study being underpowered, as a significant survival benefit was seen, when both UDCA groups were combined for the analysis [2]. In contrast to our in vivo results on tumor growth, an inhibition of proliferation by UDCA was reported in a paper using three human liver cancer cell lines [4]. These differences cannot be fully explained at the moment and to reduce these differences merely to the in vivo vs in vitro problematic may be too superficial. Therefore, we agree with Dr. Kapoor that more studies are necessary to characterize the effects of bile acids on cancer itself as well as on cancer-associated cachexia. Moreover, an addition of bile acids to established treatment regimes should be investigated and may further strengthen the argument to use bile acids outside of its primary use in cholelithiasis.

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