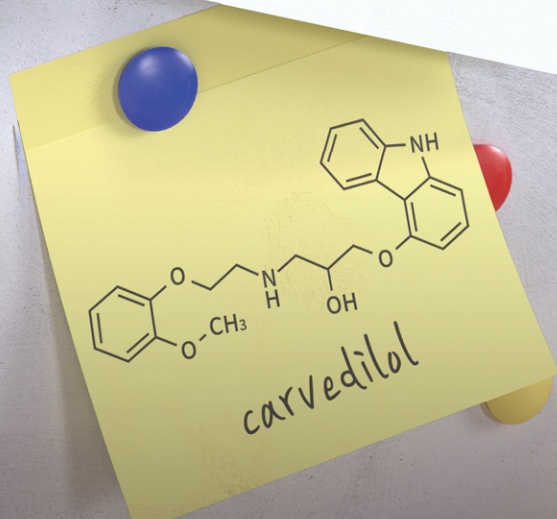
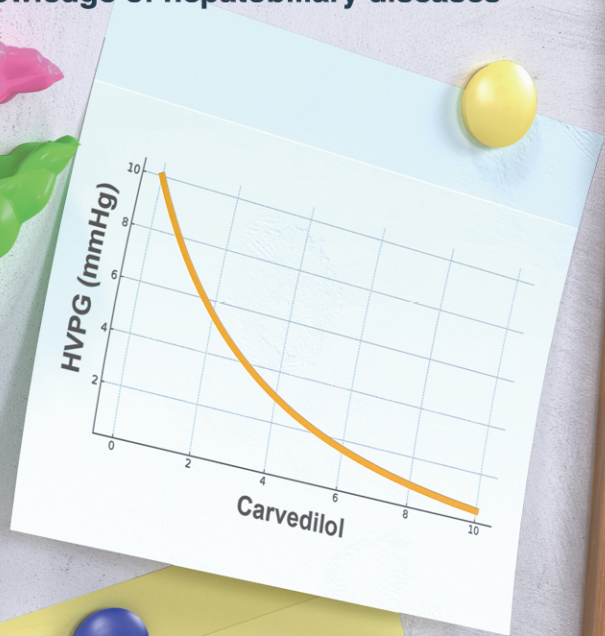


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## Reply to Correspondence

# Reply to correspondence on “UBE2S: A novel driver of HIF-1 $\alpha$ -induced metabolic reprogramming in hepatocellular carcinoma”

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**Keywords:**  $\beta$ -catenin; Hepatocellular carcinoma; HIF-1 $\alpha$ ; UBE2S

Dear Editor,

I would like to appreciate Renyu Zhang, Ding Wei, Zhi-nan Chen, Huijie Bian for their Correspondence<sup>1</sup> as a reply to my editorial entitled “UBE2S: A novel driver of HIF-1 $\alpha$ -induced metabolic reprogramming in hepatocellular carcinoma.”<sup>2</sup> I was deeply interested in reading the Correspondence as a cancer biologist specializing in liver cancer research. It is intriguing to demonstrate that UBE2S promotes HIF-1 $\alpha$ -driven glycolysis in hepatocellular carcinoma (HCC) cells by disrupting von Hippel-Lindau tumor suppressor (VHL) protein stability and enhancing  $\beta$ -catenin protein stability. Based on a previous study by Berndt et al.<sup>3</sup>, there is a possible interaction between the VHL and  $\beta$ -catenin. The observation of higher  $\beta$ -catenin levels in UBE2S overexpressing HCC cells could be attributed to reduced VHL-induced ubiquitylation via Jade-1. The results also suggested the inhibition of various pathways, such as HIF-1 $\alpha$ , glycolysis, and  $\beta$ -catenin, through the targeting of UBE2S. Based on the novel findings presented by Zhang et al.<sup>4</sup> showing the interplay of UBE2S/VHL/

$\beta$ -catenin/HIF-1 $\alpha$  in driving glycolysis in HCC, further investigations to examine the therapeutic efficacy of targeting this signaling pathway in PDTX and immunocompetent mouse HCC models are warranted. I would like to conclude this Reply by expressing my gratitude to the responses of Zhang and the colleagues for providing further mechanistic insight and therapeutic implications for the role of UBE2S in HCC.

### Authors' contribution

M.M.L drafted the manuscript. T.K.L reviewed and finalized the manuscript.

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### Conflicts of Interest

The authors have no conflicts to disclose.

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### Abbreviations:

HCC, hepatocellular carcinoma; VHL, von Hippel–Lindau tumor suppressor