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CORRESPONDENCE

Reply to 'Comment on 'MicroRNA-199b-5p attenuates TGF-β1-induced epithelial-mesenchymal transition in hepatocellular carcinoma''

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We read with considerable interest the comments made by Cristóbal et al.[1], in which they highlighted that SET deregulation could be playing a key role in the miR-199b/N-Cadherin interplay. We appreciate their thoughtful insights on the miR-199b-induced effects and their thoughts on the role of SET in cancer.

First, our study demonstrated that N-cadherin expression was markedly elevated in HCC. We investigated the epigenetic mechanisms of N-cadherin expression using computational and experimental approaches and we screened out miR-199b-5p, which directly targets N-cadherin in HCC. As Cristóbal et al. pointed out, miR-199b has been found to target SET, which plays a key role in miR-199b induced effects[2, 3]. Bioinformatic analysis and experiments have indicated that one miRNA may repress more than 100 mRNAs. Similarly, one mRNA may be targeted or regulated by quite a number of miRNAs[4, 5]. As previously reported, N-cadherin mRNA can be regulated using miR-145 and miR-124 in lung cancer[6, 7]. It has also been shown that miR-199b directly targets hypoxia-inducible factor 1α (HIF-1α) and SIRT1 in prostate and colon cancer, respectively[8, 9]. Therefore, miR-199b can exert its functionality by regulating a considerable number of targeted genes; however, its effects can only be partially reversed by a single gene.

Second, during our study, miR-199b was found to be involved in TGF-β-induced epithelial mesenchymal transition (EMT) in HCC. SET, as Cristóbal et al. pointed out, has been shown to play a role in EMT in pancreatic cancer through N-Cadherin regulation[10]. Similarly, HIF-1α and SIRT1, as target genes of miR-199b, have been found to trigger EMT by regulating N-Cadherin in cancer cells[11–14]. It is implied that miR-199b could regulate multiple pathways to affect TGF-β-induced EMT in HCC. The precise mechanism underlying TGF-β induced EMT remain unclear. Additional experimental studies are needed to explore and demonstrate which type of regulation is dominant.

Finally, we discovered that miR-199b suppresses both migration and invasion, and reduces TGF-β-induced Akt phosphorylation in HCC. A positive regulatory loop between N-cadherin and Akt signalling has been found as well. We are grateful to Cristóbal et al. for their insights on the possible molecular mechanisms involved in TGF-β-induced Akt phosphorylation. The interaction between miR-199b/N-Cadherin and Akt signaling needs to be further investigated to unveil the mechanisms of TGF-β-mediated EMT in HCC cells.

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ADDITIONAL INFORMATION

Competing interests: The authors declare no competing interests.

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