**Multi-modal meta-analysis of 1494 hepatocellular carcinoma samples reveals significant impact of consensus driver genes on phenotypes**

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## **Supplementary File S1**

## **Associations between miR expression and consensus driver gene mutation/CNV**

We extended the linear modeling approach described earlier to examine the association between consensus driver genes and miR expression. As a result, we found 167 miRs significantly associated with the consensus drivers. Among them, 127 miRs are associated with driver gene CNV-level changes, 90 miRs are associated with the driver mutations, and 50 miRs are associated with both of them. The bipartite graphs of associations between miRs and driver gene mutations and CNVs, respectively (**Figures S5A and S5B)**. Overall, *CTNNB1* and *TP53* are most influential drivers, as expected, associated with 78 and 60 miRs respectively. From the mutation perspective, *CTNNB1* is dominantly associated with the most number (61) of miRs (**Figure S5A**), whereas from the driver gene CNV perspective, *TP53* is associated with the most number (51) of miRs (**Figure S5B**). From the miR-centric view, two miRs were associated with maximum number (3) of genes: *mir-374b* (*CTNNB1*, *RB1* and *RPS6KA3*) and *mir-548b* (*ALB*, *RB1*, *ARID1A*). The former has been shown to have a role in inhibition of liver cancer (1). On the other hand, *hsa-mir-181c* is associated with the most number (3) of genes (*CTNNB1*, *AXIN1* and *RB1*) at the mutation level. This miR is reported to reduce *SMAD7* expression at gene and protein level in neuroblastoma cells (2).

Since the miRs discovered above are based on linear models, they may directly or indirectly target the consensus drivers. To help narrow down the miRs that may directly target these drivers, we searched miRDB resource (3), in which miR and targets are predicted by correlational analysis of thousands of miRNA-target interactions from CLIP-Seq experiments. As results, we obtained 28 mature miRs (corresponding to our list of precursor miRs) that are predicted to target one or more consensus driver genes. *CTNNB1* is the predicted direct target of 8 miRs: *hsa-miR-214-3p*, *hsa-miR-330-3p*, *hsa-miR-4668-3p*, *hsa-miR-5586-3p, hsa-miR-150-5p*, *hsa-miR-885-5p*, *hsa-miR-3591-p* and *hsa-miR-6715b-5p*. Out of these, *hsa-miR-214* and *hsa-miR-885-5p* have been reported to be targeting *CTNNB1* based pathway(4,5). *hsa-miR-149-3p* is predicted to target *TP53* in our analysis, and interestingly latter has been shown to directly upregulate miR-149\* in melanoma cells (6). *ARID1A* is the potential target of *hsa-miR-181b-3p*, *hsa-miR-1976*, *hsa-miR-92a-2-5p* and *hsa-miR-511-5p*. Future experimental studies are warranted to decipher if these miRs are indeed associated with driver genes at primary target level, or secondary, tertiary levels.

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