

SPECIFIC COMMENTS TO AUTHORS

This work combines all publicly available high-throughput data from patient HCC tumors, including all miRNA, methylation, genomic, transcriptomic and proteomic profiling data present in the literature. It is a very interesting and novel work, because through the analysis of these different types of data it determines the key deregulated genes and pathways in HCC. The methodology is described in detail and the analysis is well-conducted, covering 85 studies and 3,355 HCC patient sample profiles. The authors found that EGFR, β 1-integrin and Axon guidance are common and overlapping pathways in HCC. They also confirmed the prognostic value of the 9 deregulated genes associated with the 3 common deregulated pathways using KMplotter from TCGA. Five genes were reported as upregulated: CDK5, COL2A1, LAMC1, RPS6KA3 and ITGB1; whereas four other genes: FGA, FGG, EPHB1 and EGFR were found downregulated. Besides, they identified estradiol as a therapeutic agent that appropriately targets those altered HCC genes. This manuscript could be published after addressing some concerns: - Why did the authors not include data obtained from HCC experimental animal models in the integrative analysis? It would have been interesting to compare this with the analysis from HCC patient tissues. - Discussion would be improved if authors discuss other articles describing this type of integrative analysis of big 'omics' data from other tumor types, for instance, breast cancer, ovarian cancer.