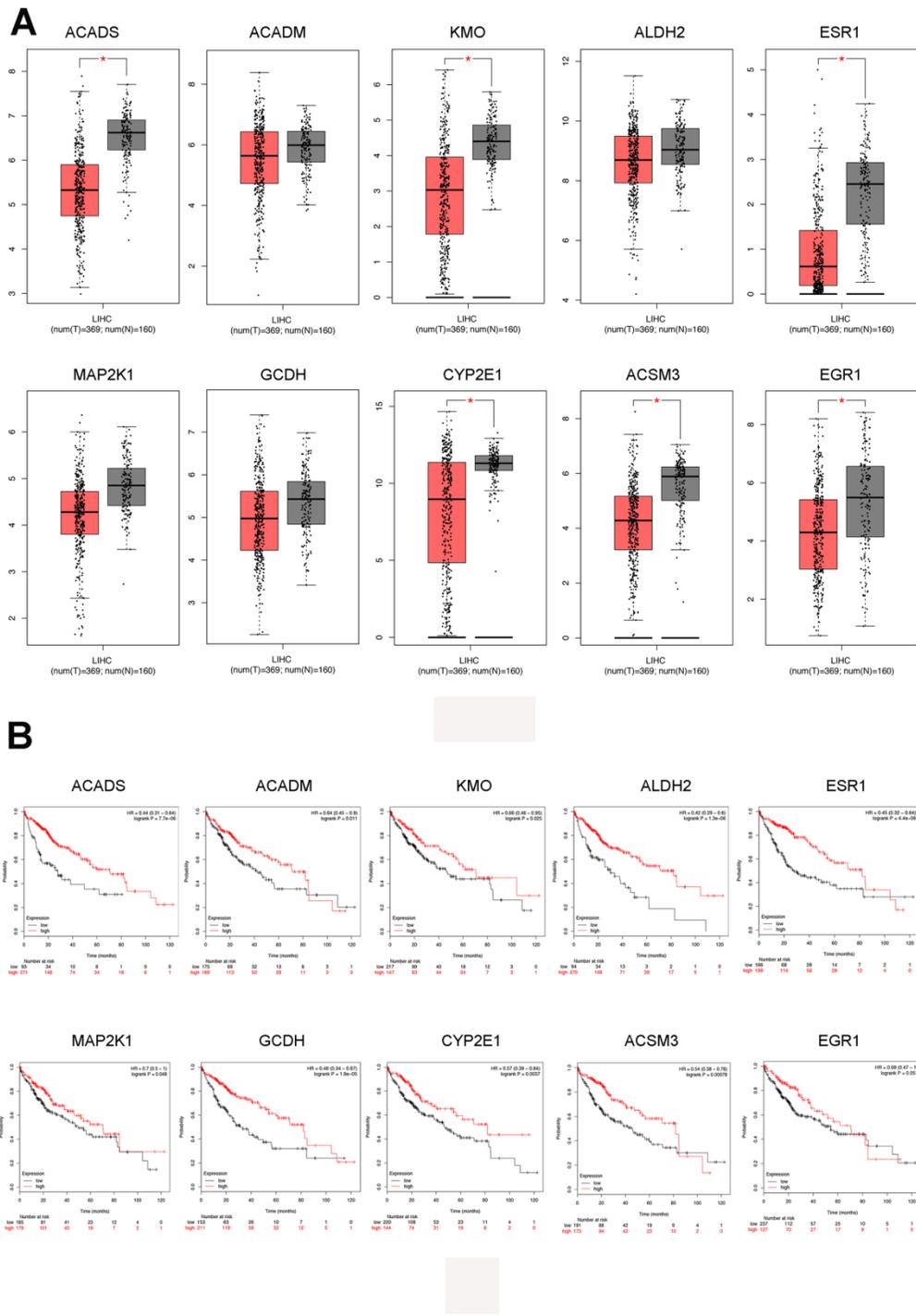
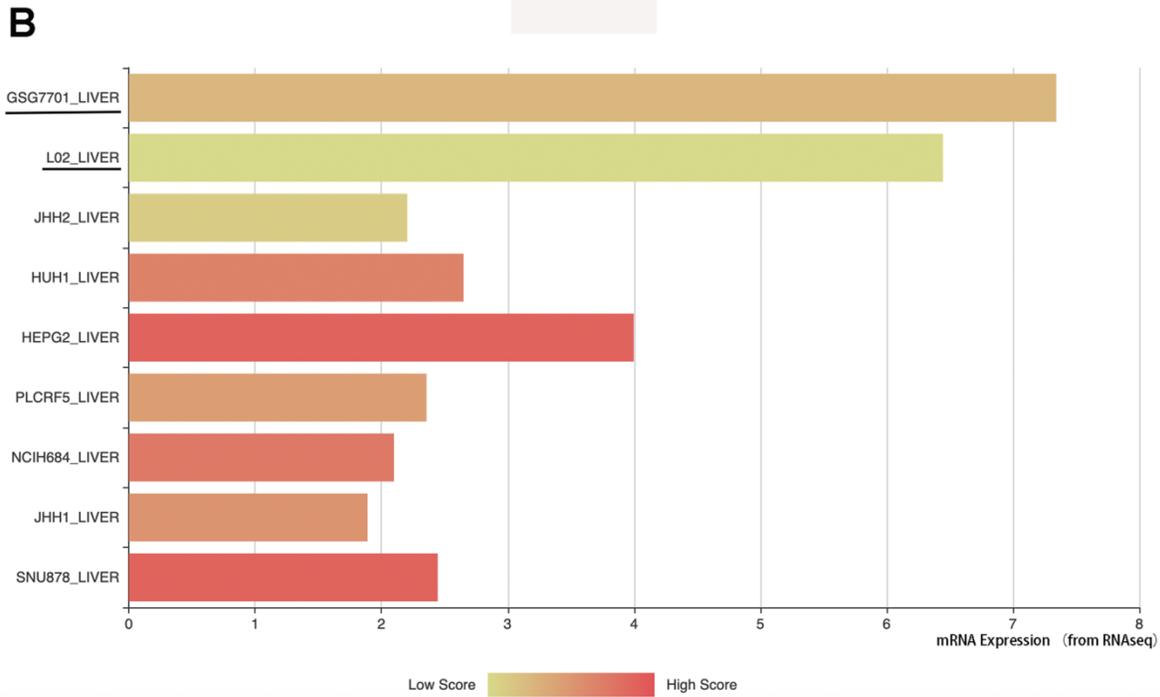
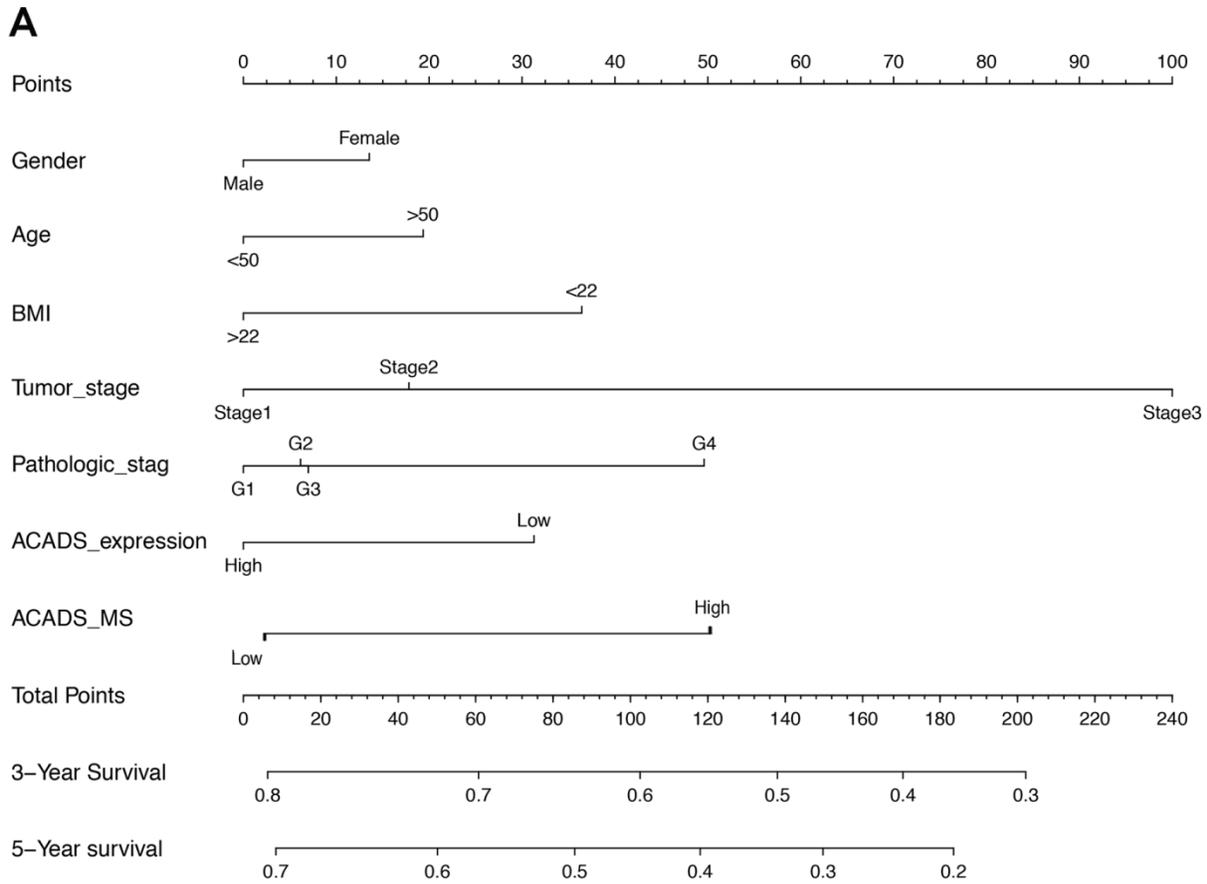


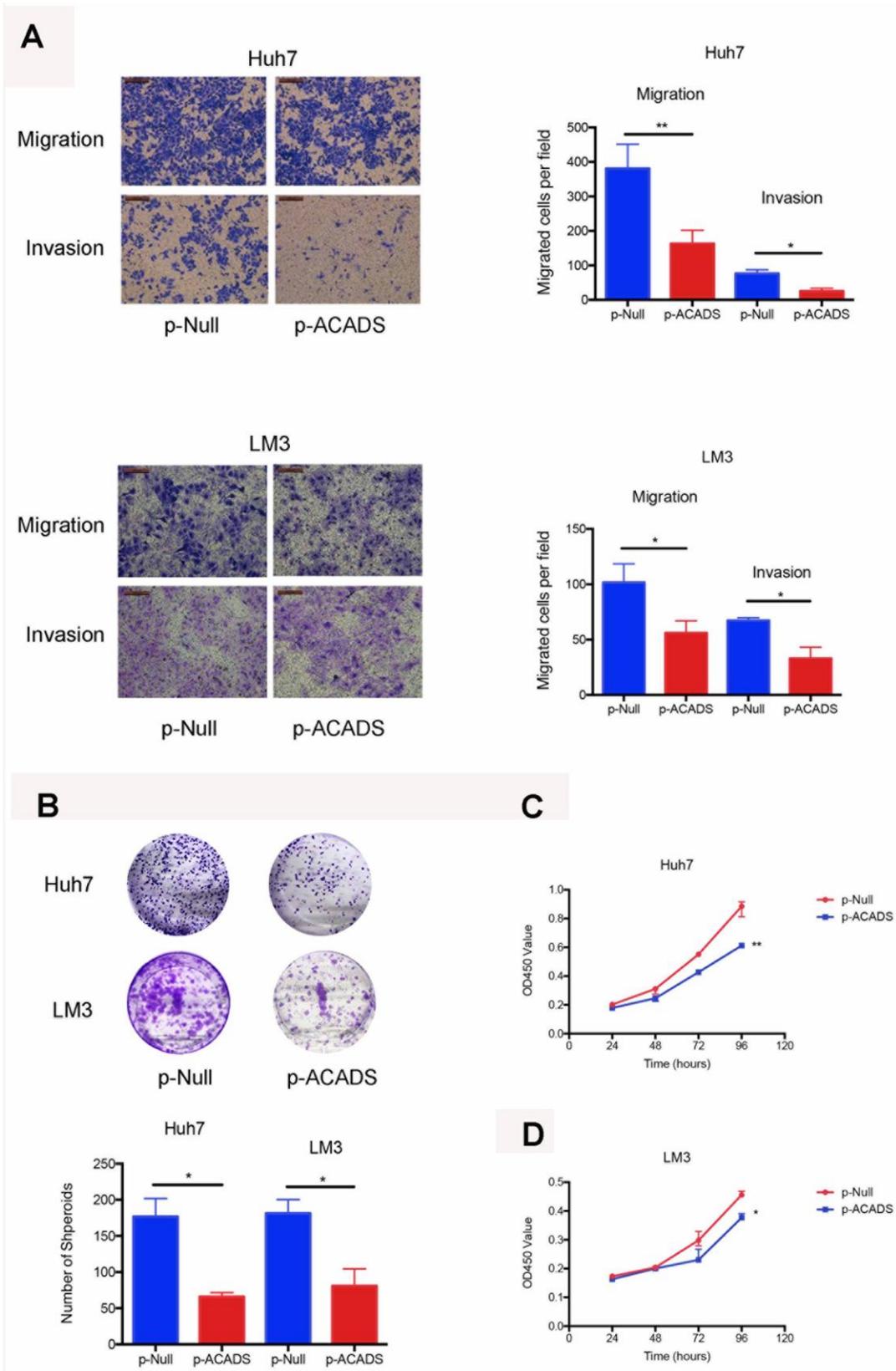
SUPPLEMENTARY FIGURES



**Supplementary Figure 1.** (A) These figures depict the gene expression profiles of the ten downregulated hub genes in normal tissues and HCC tissues and these were obtained with the assistance of the GEPIA database. (B) These figures depict the relationship between overall survival and gene expression in the ten hub downregulated hub genes in HCC tissues and their normal counterparts. (\*  $P < 0.05$ , \*\*  $P < 0.01$ ).



**Supplementary Figure 2.** (A) Using cell line webtool, we checked the ACADS expression in 2 normal liver cells and 7 HCC cell lines. (B) The survival-model established based on ACADS expression and methylation level in HCC patients.

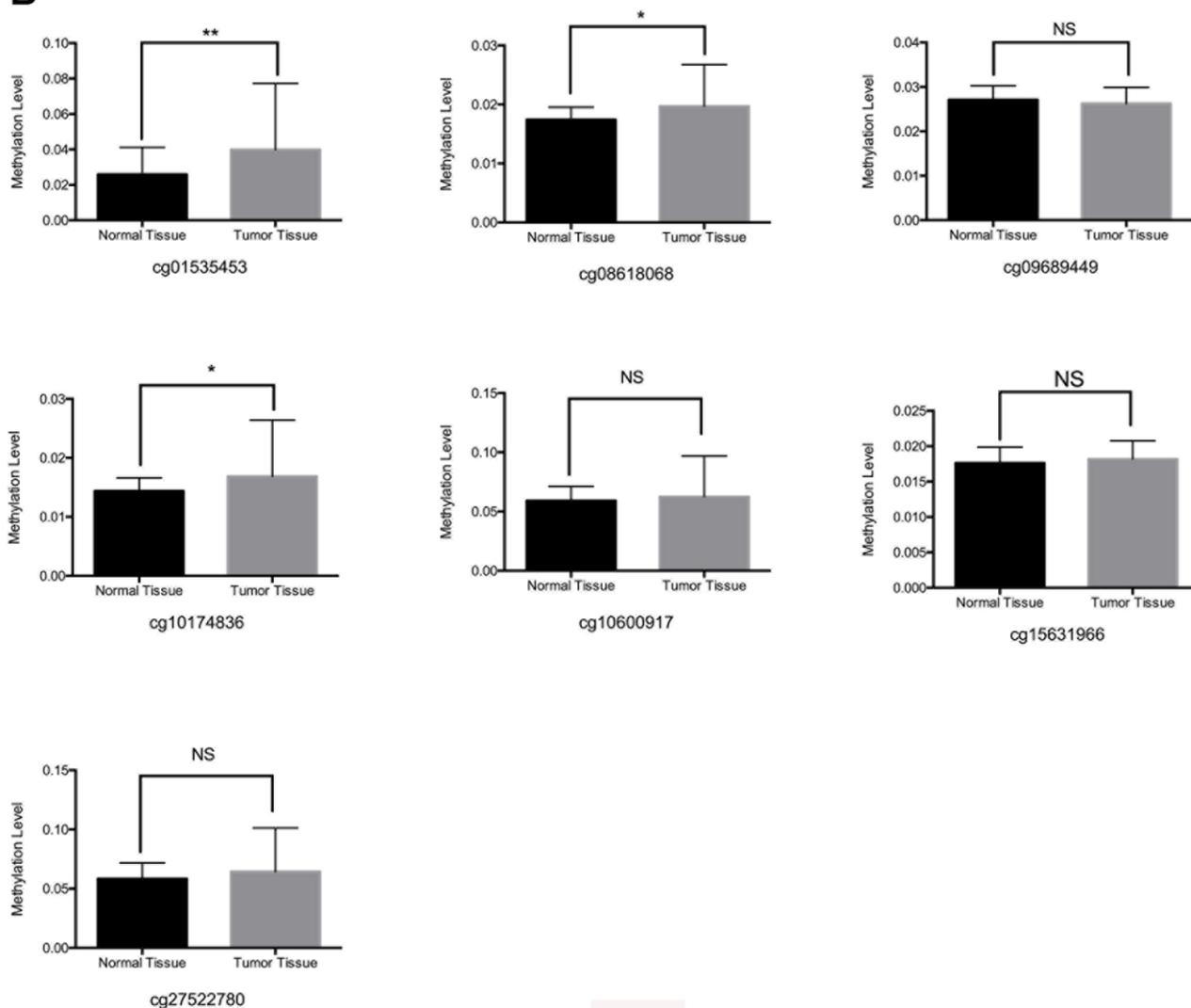


**Supplementary Figure 3.** (A) The overexpression of ACADS reduced both the migration and invasion potentials in Huh7 and HCCLM3 cells. Representative images are shown at the bottom. (B–D) CCK-8 assays and colony assays showed that the proliferation of HCC cells was reduced following the overexpression of ACADS. (\* $P < 0.05$ , \*\* $P < 0.01$ ).

# A

CpG Site	N1	N2	N3	N4	T1	T2	T3	T4	
cg01535453	0.01267634	0.01267634	0.01880426	0.01267634	0.04088781	0.02441884	0.0315173	0.04635761	$P=0.0051$
cg08618068	0.01478197	0.01465837	0.01430945	0.01427252	0.01902786	0.02251226	0.0202321	0.02522048	$P=0.0298$
cg09689449	0.0261375	0.02454539	0.02539693	0.02704205	0.02938368	0.03335231	0.03025093	0.02472145	NS
cg10174836	0.01505123	0.01400149	0.01444256	0.01291848	0.02152712	0.0239543	0.02152712	0.02152712	$P=0.0389$
cg10600917	0.0458522	0.05028736	0.04703915	0.05425579	0.06107908	0.05741343	0.05996209	0.04665435	NS
cg15631966	0.01808047	0.01636133	0.01728014	0.02364035	0.01402749	0.01569223	0.01678898	0.0203978	NS
cg27522780	0.04141936	0.0504287	0.03942948	0.07547326	0.06117267	0.05539256	0.08871268	0.05526977	NS

# B



**Supplementary Figure 4.** It can be noted that tumor tissues exhibited higher methylation levels as compared to the normal liver tissues at the sites cg01535453, cg08618068, and cg10174836 both in the samples sequencing data (A) from our center and TCGA database (B) – which are the target sites of the ACADS CpG islands.