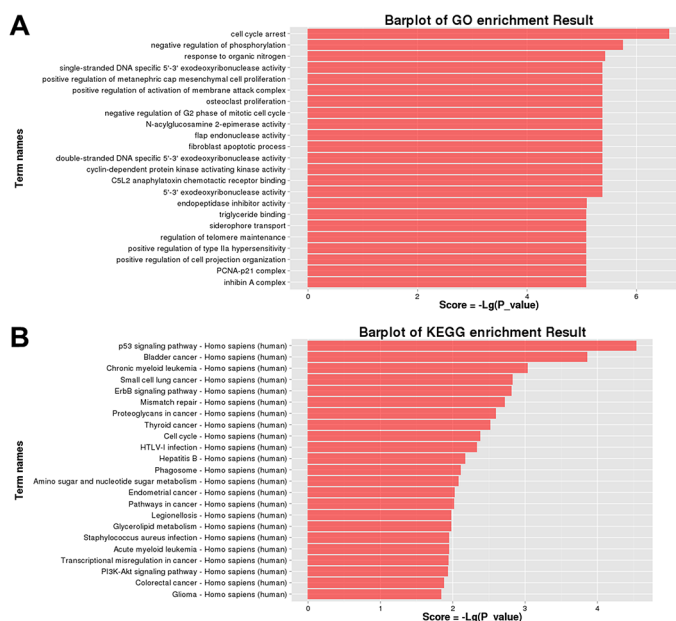


# Folic acid supplementation acts as a chemopreventive factor in tumorigenesis of hepatocellular carcinoma by inducing H3K9Me2-dependent transcriptional repression of LCN2

## SUPPLEMENTARY MATERIALS



**Supplementary Figure 1: Gene ontology (GO) and pathway analysis (KEGG) on data of RNA-sequencing assay. (A)** GO analysis was applied to analyze the function of the differentially expressed genes according to the key functional classification of genes in the NCBI. **(B)** Important pathways containing the differentially expressed genes were also performed by the Kyoto Encyclopedia of genes and Genomes (KEGG).

Supplementary Table 1: Primers and oligonucleotide sequences enrolled in this study

Description	Name	Sequence
Primers for quantitative real-time PCR	CD133-human-real-F	5' ACGGAAGTCAGCTCCCATCA 3'
	CD133-human-real-R	5' GGCTCTCCAGATCGGTTCTG 3'
	OCT4-human-real-F	5' TTGAGGCTCTGCAGCTTAG 3'
	OCT4-human-real-R	5' GCCGGTTACAGAACCACAC 3'
	CK19-human-real-F	5' CCCGCGACTACAGCCACTACTAC 3'
	CK19-human-real-R	5' GTCGGCCTCCACGCTCATG 3'
	AFP-human-real-F	5' AGCTTGGTGGTGGATGAAAC 3'
	AFP-human-real-R	5' CCCTCTTCAGCAAAGCAGAC 3'
	CEBPA-human-real-F	5' CAAGAACAGCAACGAGTACCG 3'
	CEBPA-human-real-R	5' AGGCGGTCATTGTCACTGGT 3'
	ALB-human-real-F	5' CTGAGCAAAGGCAATCAACA 3'
	ALB-human-real-R	5' CACAGTCTGCTGAGGTTGGA 3'
	CK18-human-real-F	5' GAGCTGCTCCATCTGTAGGG 3'
	CK18-human-real-R	5' CACAGTCTGCTGAGGTTGGA 3'
	E-cadherin-human-real-F	5' GCCCATCAGGCCTCCGTTT 3'
	E-cadherin-human-real-R	5' ACCTTGCCTTCTTTGCTTTTGTGGA 3'
	Snail-human-real-F	5' TGCCTCTGCGGAACCTG 3'
	Snail-human-real-R	5' GGAATCTTGGTGCTTGTGGA 3'
	CK8-human-real-F	5' TCATAGACAAGGTACGGTTC 3'
	CK8-human-real-R	5' GCCTAAGGTTGTTGATGTAGC 3'
	<i>Slug-human-real-F</i>	5' CCTGGTTGCTTCAAGGACAC 3'
	<i>Slug-human-real-R</i>	5' TCCATGCTCTTGACGCTCTC 3'
	<i>CDC20-human-real-F</i>	5' CGCCAGAGGGTTATCAGAACAGA 3'
	<i>CDC20-human-real-R</i>	5' TTCCAGAACTCCAATCCACAAGG 3'
	<i>TNFRSF10D-human-real-F</i>	5' GAGATGTGCCGGACGTGTAG 3'
	<i>TNFRSF10D-human-real-R</i>	5' CTATGATGATAAGGTAGTGATAGGGAG 3'
	<i>MYC-human-real-F</i>	5' GGGGCTTTATCTAACTCGCTGTA 3'
	<i>MYC-human-real-R</i>	5' TATGGGCAAAGTTTCGTGGAT 3'
	<i>TP53INP1-human-real-F</i>	5' CACGGGCACAGAAAGTGAAG 3'
	<i>TP53INP1-human-real-R</i>	5' GGTGGCAATCCCTGGTAAGA 3'
	<i>ZMAT3-human-real-F</i>	5' TCAGCAGGTCCTTACTTCAA 3'
	<i>ZMAT3-human-real-R</i>	5' CTATACATATCCCAGATTCTCCA 3'
<i>CDKN1A-human-real-F</i>	5' TCCTGTGGGCGGATTAG 3'	
<i>CDKN1A-human-real-R</i>	5' GTCAGTGTCTTGTACCCATGTG 3'	
<i>LCN2-human-real-F</i>	5' TGAGCACCAACTACAACCAGCAT 3'	
<i>LCN2-human-real-R</i>	5' CGATTGGGACAGGGAAGACG 3'	
<i>LCN2-mouse-real-F</i>	5' CCAGTTCGCCATGGTATTTTTTC 3'	
<i>LCN2-mouse-real-R</i>	5' CACACTCACCACCCATTCAGTT 3'	

(Continued)

Description	Name	Sequence
	<i>GDF15-human-real-F</i>	5' TTGCGGAAACGCTACGAG 3'
	<i>GDF15-human-real-R</i>	5' GGGACAGCCGGAACAGAG 3'
	<i>RTEL1-human-real-F</i>	5' ACGGACATCCCAAAGATTATTACGC 3'
	<i>RTEL1-human-real-R</i>	5' GTTGTGTAGAAATGACAGGAGCGACTT 3'
	<i>SESNI-human-real-F</i>	5' TCCAACATTTTCGTGTCCAGG 3'
	<i>SESNI-human-real-R</i>	5' TAGTTCCAAATTGCCCGTCT 3'
	<i>CCNG1-human-real-F</i>	5' TAGTCTAACTCAGTTCTTTGGCTTTG 3'
	<i>CCNG1-human-real-R</i>	5' ATGGGACATTCTTTCTCTTC 3'
	<i>FPGS-human-real-F</i>	5' CCCCAGGTTTCGAGTCTTGCTC 3'
	<i>FPGS-human-real-R</i>	5' TGAAGTTCTGTTGGTCTGCGTTGC 3'
	<i>CDC45-human-real-F</i>	5' AGAAAGGAAGGCTGGAACTAAG 3'
	<i>CDC45-human-real-R</i>	5' CACGTCCGAGGCCACGAAGA 3'
	<i>GAMT-human-real-F</i>	5' CCCACCCTGCCTGACGGTCACTTT 3'
	<i>GAMT-human-real-R</i>	5' GGGCACCTGCGTCTCCTCAAACAT 3'
	<i>DHFR-human-real-F</i>	5' TTCGCTAAACTGCATCGTCTG 3'
	<i>DHFR-human-real-R</i>	5' GGTCTTCTTACCCATAATCACCAG 3'
	<i>RRM2-human-real-F</i>	5' AACTTGGTGGAGCGATTTAG 3'
	<i>RRM2-human-real-R</i>	5' CATAGGTAGCCTCTTTGTCCC 3'
	<i>P53-mouse-real-F</i>	5' AGCTTT GAGGTTCTGTGTTT 3'
	<i>P53-mouse-real-F</i>	5' GGAACATCTCGAAGCGTTTA 3'
	<i>GAPDH-human-real-F</i>	5' CTCTCTGCTCCTCCTGTTCG 3'
	<i>GAPDH-human-real-R</i>	5' ACGACCAAATCCGTTGACTC 3'
	<i>β-Actin-human-real-F</i>	5' TGTGTTGGCGTACAGGTCTTTG 3'
	<i>β-Actin-human-real-R</i>	5' GGGAAATCGTGCCTGACATTAAG 3'
	<i>β-Actin-mouse-real-F</i>	5' GCACCACACCTTCTACAATGAG 3'
	<i>β-Actin-mouse-real-R</i>	5' ACAGCCTGGATGGCTACGT 3'
	<i>U6-human-real-F</i>	5' CGCTTCACGAATTTGCGTGTCAT 3'
	<i>U6-human-real-R</i>	5' GCTTCGGCAGCACATATACTAAAAT 3'
Primers for clone of LCN2	<i>LCN2-clone-F</i>	5' GGGGTACCCATGCCCTAGGTCTCCTGTGGCT 3'
	<i>LCN2-clone-R</i>	5' CGGAATTCCGTCAGCCGTCGATACACTGGTTCG 3'
Primers for BSP	<i>Methy-LCN2-F</i>	5' AAGTGTGGAGTTATAGGYGAGAG 3'
	<i>Methy-LCN2-R</i>	5' ACCTTAAAAAATATCCTCTACCAAAC 3'
	<i>Produce 1-F</i>	5' CTCCAGATGGCAAACATACGCAAG 3'
Primer for identification of HBx positive mice	<i>Produce 1-R</i>	5' CAGGATCCAGTTGGCAGCACAG 3'
	<i>Produce 2-F</i>	5' CAAACTGATGACCATACGTGAAGAC 3'
	<i>Produce 2-R</i>	5' CCAAGGTCTTACATAAGAGGACTC 3'
	<i>LCN2-sense</i>	5' CCACCAUCUAUGAGCUGAATT 3'
siRNA of LCN2	<i>LCN2-anti-sense</i>	5' UUCAGCUCAUAGAUGGUGGTT 3'
	<i>NC-sense</i>	5' UUCUCCGAACGUGUCACGUTT 3'
	<i>NC-anti-sense</i>	5' ACGUGACACGUUCGGAGAATT 3'