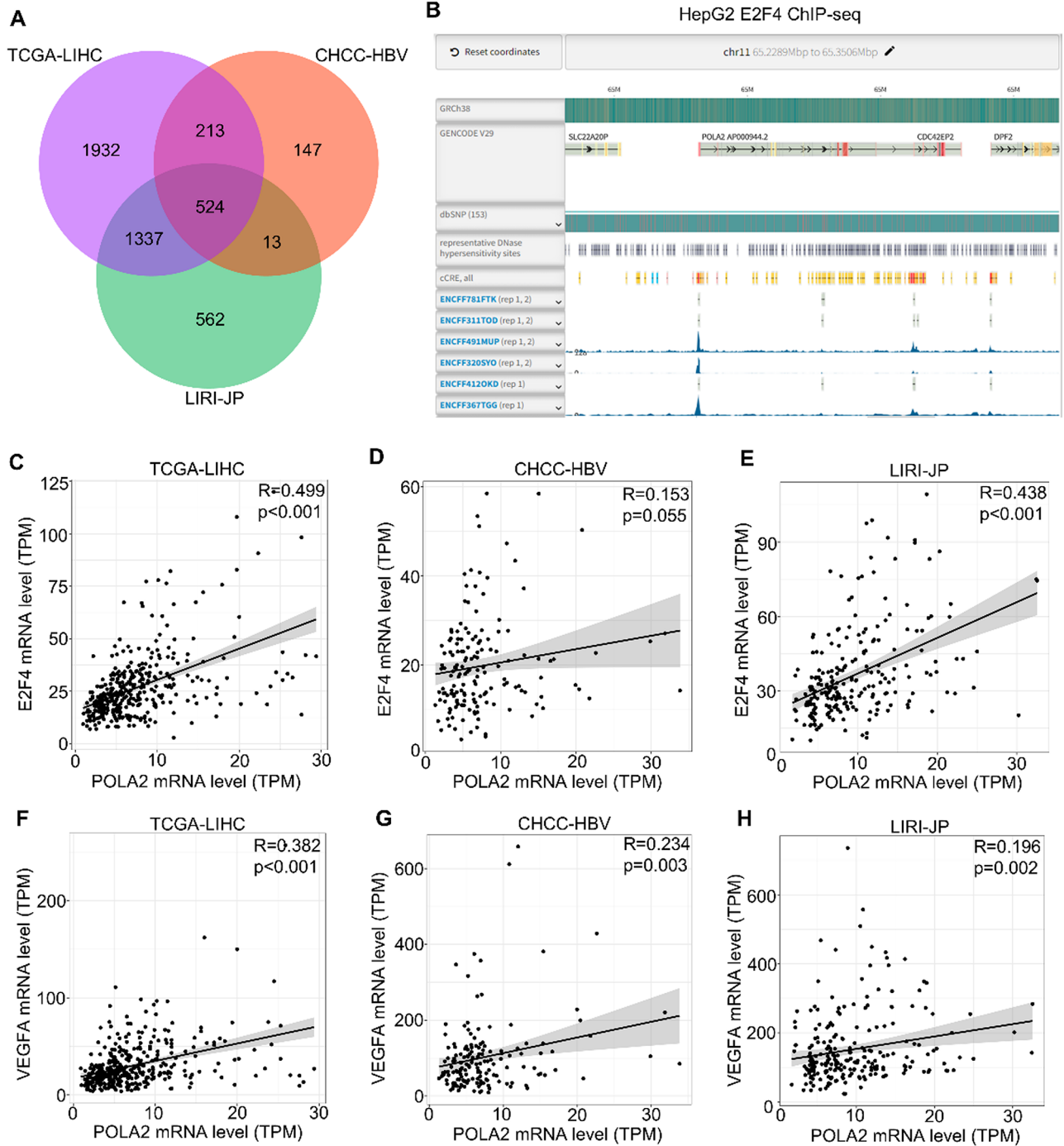


**Figure S1** The mRNA level of POLA2 in HCC. (A-F) Scatter plots, pair plots and diagnosis ROC curves to demonstrate POLA2 expression difference between tumor tissue and normal liver tissue in GSE77509 (A-C), GSE94660 (D-F) data sets. (G) Correlation between tumor size and POLA2 expression in CHCC-HBV data set. \*\*\*,  $P < 0.001$ . TPM, transcripts per million; N, normal; T, tumor; AUC, area under curve; CHCC-HBV, Chinese HCC patients with HBV infection; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; ROC, receiver operating characteristic.



**Figure S2** POLA2 is regulated by E2F transcription factor. (A) Venn diagram to show the overlap of genes co-expressed with POLA2 with Pearson correlation coefficients  $>0.4$  in TCGA-LIHC, CHCC-HBV, LIRI-JP data sets. (B) Screen shot of E2F4 ChIP-seq peaks near POLA2 transcription start site conducted in HepG2 cell line on ENCODE website. (C-E) Expression correlation between E2F4 and POLA2 in TCGA-LIHC (C), CHCC-HBV (D), LIRI-JP (E) data sets. (F-H) Expression correlation between VEGFA and POLA2 in TCGA-LIHC (F), CHCC-HBV (G), LIRI-JP (H) data sets. TCGA-LIHC, The Cancer Genome Atlas-Liver Hepatocellular Carcinoma; CHCC-HBV, Chinese HCC patients with HBV infection; HBV, hepatitis B virus; LIRI-JP, Liver Cancer-RIKEN, Japan; TPM, transcripts per million.

**Table S1** TCGA Cox regression results

Variables	Univariate			Multivariate		
	HR	95% CI	P	HR	95% CI	P
Age	1.15	0.78–1.7	0.481	NA	NA	NA
Gender	1.36	0.92–2	0.125	1.25	0.85–1.84	0.264
Grade	1.06	0.72–1.57	0.756	NA	NA	NA
POLA2	1.85	1.25–2.74	0.002	1.54	1.03–2.3	0.035
Stage	2.9	1.98–4.25	0	2.61	1.76–3.86	0

TCGA, The Cancer Genome Atlas; HR, hazard ratio; CI, confidence interval; NA, not applicable.

**Table S2** Intersection of GSEA\_GO\_BP results

GOBP_CELLULAR_AMINO_ACID_CATABOLIC_PROCESS
GOBP_ALPHA_AMINO_ACID_CATABOLIC_PROCESS
GOBP_MONOCARBOXYLIC_ACID_CATABOLIC_PROCESS
GOBP_FATTY_ACID_CATABOLIC_PROCESS
GOBP_ALPHA_AMINO_ACID_METABOLIC_PROCESS
GOBP_SISTER_CHROMATID_SEGREGATION
GOBP_NUCLEAR_CHROMOSOME_SEGREGATION
GOBP_CHROMOSOME_SEGREGATION
GOBP_ORGANELLE_FISSION
GOBP_SECONDARY_ALCOHOL_METABOLIC_PROCESS
GOBP_MEIOTIC_CELL_CYCLE
GOBP_XENOBIOTIC_CATABOLIC_PROCESS
GOBP_CELLULAR_RESPONSE_TO_XENOBIOTIC_STIMULUS
GOBP_XENOBIOTIC_METABOLIC_PROCESS
GOBP_DNA_TEMPLATED_DNA_REPLICATION
GOBP_MEIOTIC_CELL_CYCLE_PROCESS
GOBP_MITOTIC_NUCLEAR_DIVISION
GOBP_CELLULAR_RESPONSE_TO_ZINC_ION
GOBP_DETOXIFICATION_OF_COPPER_ION
GOBP_CELLULAR_RESPONSE_TO_COPPER_ION
GOBP_REGULATION_OF_MITOTIC_SISTER_CHROMATID_SEGREGATION
GOBP_REGULATION_OF_MITOTIC_NUCLEAR_DIVISION
GOBP_STRESS_RESPONSE_TO_METAL_ION
GOBP_PRIMARY_ALCOHOL_METABOLIC_PROCESS
GOBP_DNA_CONFORMATION_CHANGE
GOBP_DNA_REPLICATION
GOBP_RESPONSE_TO_ZINC_ION
GOBP_NEGATIVE_REGULATION_OF_NUCLEAR_DIVISION
GOBP_RESPONSE_TO_COPPER_ION
GOBP_REGULATION_OF_CHROMOSOME_SEGREGATION
GOBP_REGULATION_OF_CHROMOSOME_SEPARATION
GOBP_CHROMOSOME_SEPARATION
GOBP_TRIGLYCERIDE_METABOLIC_PROCESS
GOBP_MITOTIC_CELL_CYCLE_CHECKPOINT_SIGNALING
GOBP_CELL_CYCLE_CHECKPOINT_SIGNALING
GOBP_REGULATION_OF_MITOTIC_CELL_CYCLE_PHASE_TRANSITION
GOBP_MITOTIC_METAPHASE_PLATE_CONGRESSION
GOBP_MEIOSIS_I_CELL_CYCLE_PROCESS
GOBP_CELL_CYCLE_DNA_REPLICATION
GOBP_REGULATION_OF_NUCLEAR_DIVISION
GOBP_MICROTUBULE_CYTOSKELETON_ORGANIZATION_INVOLVED_IN_MITOSIS
GOBP_DNA_REPLICATION_INITIATION
GOBP_NEGATIVE_REGULATION_OF_CHROMOSOME_ORGANIZATION
GOBP_REGULATION_OF_MITOTIC_CELL_CYCLE
GOBP_OPSONIZATION
GOBP_BENZENE_CONTAINING_COMPOUND_METABOLIC_PROCESS
GOBP_POSITIVE_REGULATION_OF_CELL_CYCLE_PROCESS
GOBP_METAPHASE_ANAPHASE_TRANSITION_OF_CELL_CYCLE
GOBP_REGULATION_OF_CELL_CYCLE_PHASE_TRANSITION
GOBP_MITOTIC_CELL_CYCLE_PHASE_TRANSITION
GOBP_COMPLEMENT_ACTIVATION_LECTIN_PATHWAY
GOBP_CHROMOSOME_LOCALIZATION
GOBP_CELLULAR_RESPONSE_TO_CADMIUM_ION
GOBP_SPINDLE_ELONGATION
GOBP_REGULATION_OF_DNA_TEMPLATED_DNA_REPLICATION
GOBP_METAPHASE_PLATE_CONGRESSION
GOBP_MITOTIC_SPINDLE_ASSEMBLY
GOBP_POSITIVE_REGULATION_OF_CELL_CYCLE
GOBP_REGULATION_OF_CHROMOSOME_ORGANIZATION
GOBP_DNA_RECOMBINATION
GOBP_HOMOLOGOUS_CHROMOSOME_SEGREGATION
GOBP_NEGATIVE_REGULATION_OF_CELL_CYCLE_PROCESS
GOBP_TETRAPYRROLE_METABOLIC_PROCESS
GOBP_MEIOTIC_CHROMOSOME_SEGREGATION
GOBP_MITOTIC_SPINDLE_ORGANIZATION
GOBP_MALE_MEIOTIC_NUCLEAR_DIVISION
GOBP_CELLULAR_PROCESS_INVOLVED_IN_REPRODUCTION_IN_MULTICELLULAR_ORGANISM
GOBP_SPINDLE_MIDZONE_ASSEMBLY
GOBP_BRANCHED_CHAIN_AMINO_ACID_CATABOLIC_PROCESS
GOBP_REGULATION_OF_OPSONIZATION
GOBP_NEGATIVE_REGULATION_OF_MITOTIC_CELL_CYCLE_PHASE_TRANSITION
GOBP_ATTACHMENT_OF_SPINDLE_MICROTUBULES_TO_KINETOCHORE
GOBP_DOUBLE_STRAND_BREAK_REPAIR
GOBP_CELL_CYCLE_G2_M_PHASE_TRANSITION
GOBP_REGULATION_OF_DNA_REPLICATION
GOBP_KINETOCHORE_ASSEMBLY
GOBP_OMEGA_HYDROXYLASE_P450_PATHWAY
GOBP_NEGATIVE_REGULATION_OF_METAPHASE_ANAPHASE_TRANSITION_OF_CELL_CYCLE
GOBP_RECOMBINATIONAL_REPAIR
GOBP_MONOCARBOXYLIC_ACID_TRANSPORT
GOBP_FEMALE_MEIOTIC_NUCLEAR_DIVISION
GOBP_HOMOLOGOUS_RECOMBINATION
GOBP_SERINE_FAMILY_AMINO_ACID_METABOLIC_PROCESS
GOBP_NEGATIVE_REGULATION_OF_MITOTIC_CELL_CYCLE
GOBP_AMINO_ACID_BETAINE_METABOLIC_PROCESS
GOBP_CENTROMERE_COMPLEX_ASSEMBLY
GOBP_PROTEIN_LOCALIZATION_TO_CHROMOSOME_CENTROMERIC_REGION
GOBP_BILE_ACID_AND_BILE_SALT_TRANSPORT
GOBP_CELLULAR_AMINO_ACID_BIOSYNTHETIC_PROCESS
GOBP_EPOXYGENASE_P450_PATHWAY
GOBP_REGULATION_OF_CELL_CYCLE_G2_M_PHASE_TRANSITION
GOBP_UREA_METABOLIC_PROCESS
GOBP_NEGATIVE_REGULATION_OF_CELL_CYCLE
GOBP_REGULATION_OF_CELL_CYCLE_CHECKPOINT
GOBP_BILE_ACID_METABOLIC_PROCESS
GOBP_CHROMOSOME_CONDENSATION
GOBP_UREA_CYCLE
GOBP_CHROMOSOME_ORGANIZATION_INVOLVED_IN_MEIOTIC_CELL_CYCLE
GOBP_2_OXOGLUTARATE_METABOLIC_PROCESS
GOBP_KINETOCHORE_ORGANIZATION
GOBP_OXIDATIVE_DEMETHYLATION
GOBP_DNA_UNWINDING_INVOLVED_IN_DNA_REPLICATION
GOBP_REGULATION_OF_SYSTEMIC_ARTERIAL_BLOOD_PRESSURE_MEDIATED_BY_A_CHEMICAL_SIGNAL
GOBP_DNA_INTEGRITY_CHECKPOINT_SIGNALING
GOBP_REGULATION_OF_CYCLIN_DEPENDENT_PROTEIN_KINASE_ACTIVITY
GOBP_MITOTIC_DNA_INTEGRITY_CHECKPOINT_SIGNALING
GOBP_PROTEIN_LOCALIZATION_TO_CONDENSED_CHROMOSOME
GOBP_DNA_TEMPLATED_DNA_REPLICATION_MAINTENANCE_OF_FIDELITY
GOBP_ARGININE_METABOLIC_PROCESS
GOBP_POSITIVE_REGULATION_OF_CELL_CYCLE_G2_M_PHASE_TRANSITION
GOBP_POSITIVE_REGULATION_OF_CHROMOSOME_SEGREGATION
GOBP_POSITIVE_REGULATION_OF_CHROMOSOME_SEPARATION
GOBP_AROMATIC_AMINO_ACID_FAMILY_METABOLIC_PROCESS
GOBP_Glutamate_Metabolic_Process
GOBP_DNA_REPLICATION_CHECKPOINT_SIGNALING
GOBP_FEMALE_GAMETE_GENERATION
GOBP_ATTACHMENT_OF_MITOTIC_SPINDLE_MICROTUBULES_TO_KINETOCHORE
GOBP_PIRNA_METABOLIC_PROCESS
GOBP_HOMOLOGOUS_CHROMOSOME_PAIRING_AT_MEIOSIS
GOBP_REPLICATION_FORK_PROCESSING
GOBP_REGULATION_OF_DNA_DIRECTED_DNA_POLYMERASE_ACTIVITY
GOBP_DNA_STRAND_ELONGATION_INVOLVED_IN_DNA_REPLICATION
GOBP_MALE_MEIOSIS_I
GOBP_CELLULAR_RESPONSE_TO_GLUcAGON_STIMULUS
GOBP_REGULATION_OF_CELL_DIVISION
GOBP_MESODERM_DEVELOPMENT
GOBP_RESPONSE_TO_GLUcAGON
GOBP_CHROMATIN_REMODELING
GOBP_INTERSTRAND_CROSS_LINK_REPAIR
GOBP_POSITIVE_REGULATION_OF_DNA_METABOLIC_PROCESS
GOBP_PROTEIN_DNA_COMPLEX_SUBUNIT_ORGANIZATION

GSEA, gene set enrichment analysis; GO, Gene Ontology; BP, biological process.

**Table S3** Intersection of GSEA\_KEGG results

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KEGG\_FATTY\_ACID\_METABOLISM  
KEGG\_COMPLEMENT\_AND\_COAGULATION\_CASCADES  
KEGG\_PEROXISOME  
KEGG\_DRUG\_METABOLISM\_CYTOCHROME\_P450  
KEGG\_GLYCINE\_SERINE\_AND\_THREONINE\_METABOLISM  
KEGG\_RETINOL\_METABOLISM  
KEGG\_VALINE\_LEUCINE\_AND\_ISOLEUCINE\_DEGRADATION  
KEGG\_METABOLISM\_OF\_XENOBIOTICS\_BY\_CYTOCHROME\_P450  
KEGG\_STEROID\_HORMONE\_BIOSYNTHESIS  
KEGG\_TRYPTOPHAN\_METABOLISM  
KEGG\_ARGININE\_AND\_PROLINE\_METABOLISM  
KEGG\_PRIMARY\_BILE\_ACID\_BIOSYNTHESIS  
KEGG\_PROPANOATE\_METABOLISM  
KEGG\_CELL\_CYCLE  
KEGG\_LINOLEIC\_ACID\_METABOLISM  
KEGG\_CITRATE\_CYCLE\_TCA\_CYCLE  
KEGG\_DRUG\_METABOLISM\_OTHER\_ENZYMES  
KEGG\_TYROSINE\_METABOLISM  
KEGG\_LYSINE\_DEGRADATION  
KEGG\_DNA\_REPLICATION  
KEGG\_HISTIDINE\_METABOLISM  
KEGG\_BUTANOATE\_METABOLISM  
KEGG\_PRION\_DISEASES  
KEGG\_BETA\_ALANINE\_METABOLISM  
KEGG\_HOMOLOGOUS\_RECOMBINATION  
KEGG\_RENIN\_ANGIOTENSIN\_SYSTEM  
KEGG\_ALANINE\_ASPARTATE\_AND\_Glutamate\_METABOLISM  
KEGG\_MISMATCH\_REPAIR  
KEGG\_CYTOKINE\_CYTOKINE\_RECEPTOR\_INTERACTION

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GSEA, gene set enrichment analysis; KEGG, Kyoto Encyclopedia of Genes and Genomes.