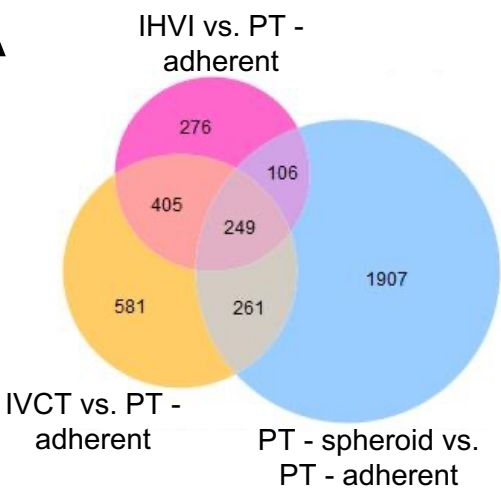


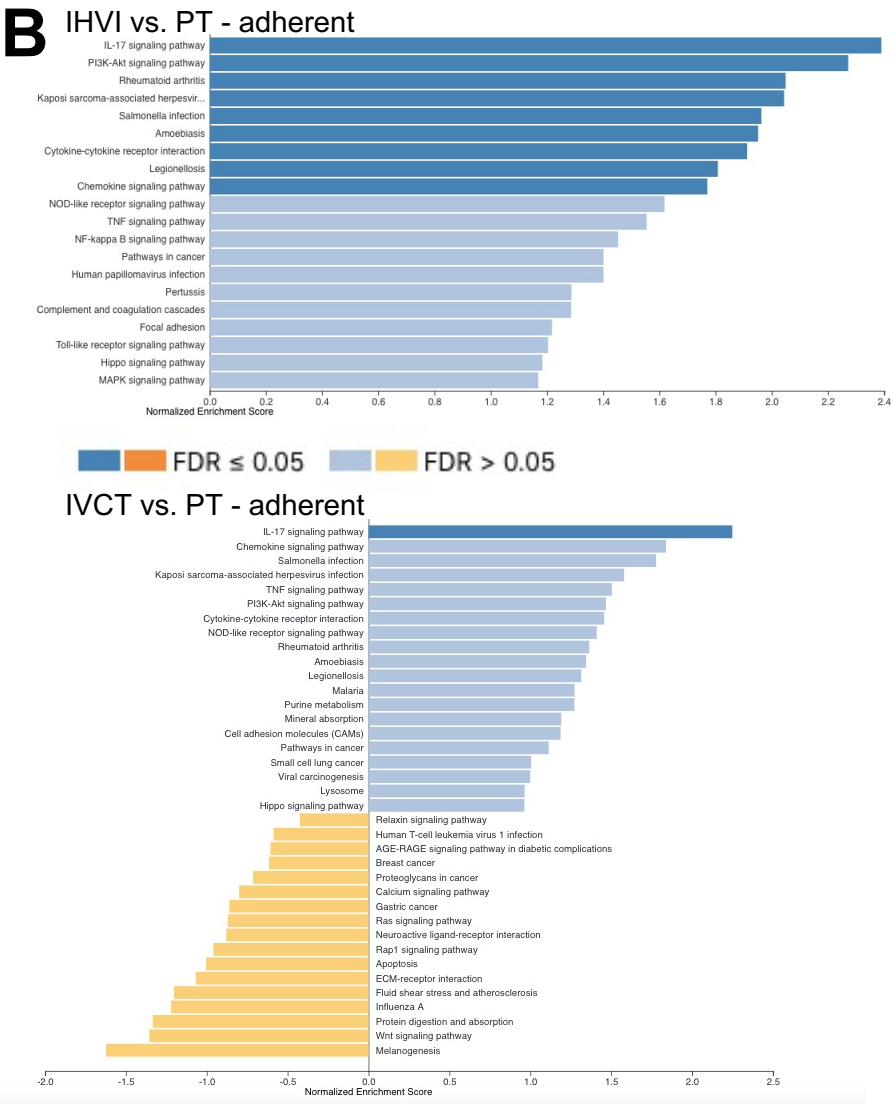
A

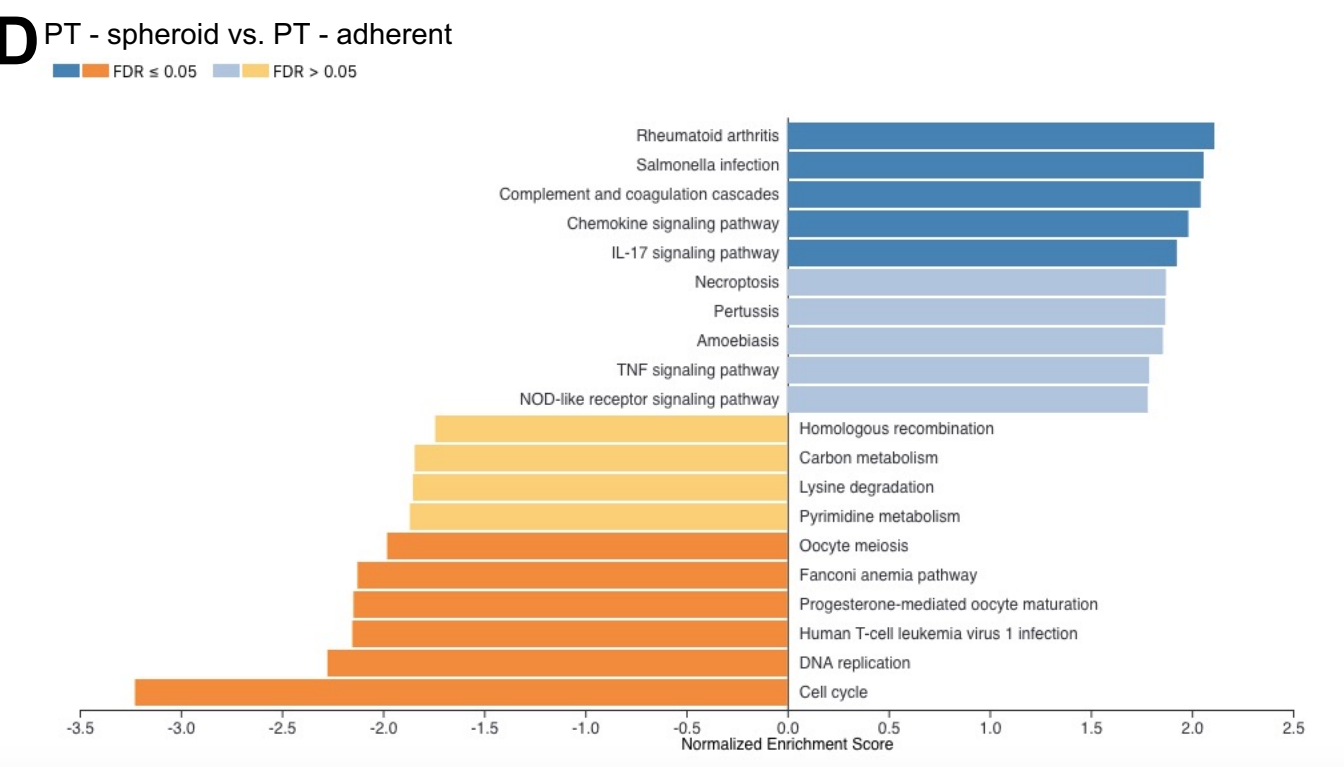


C

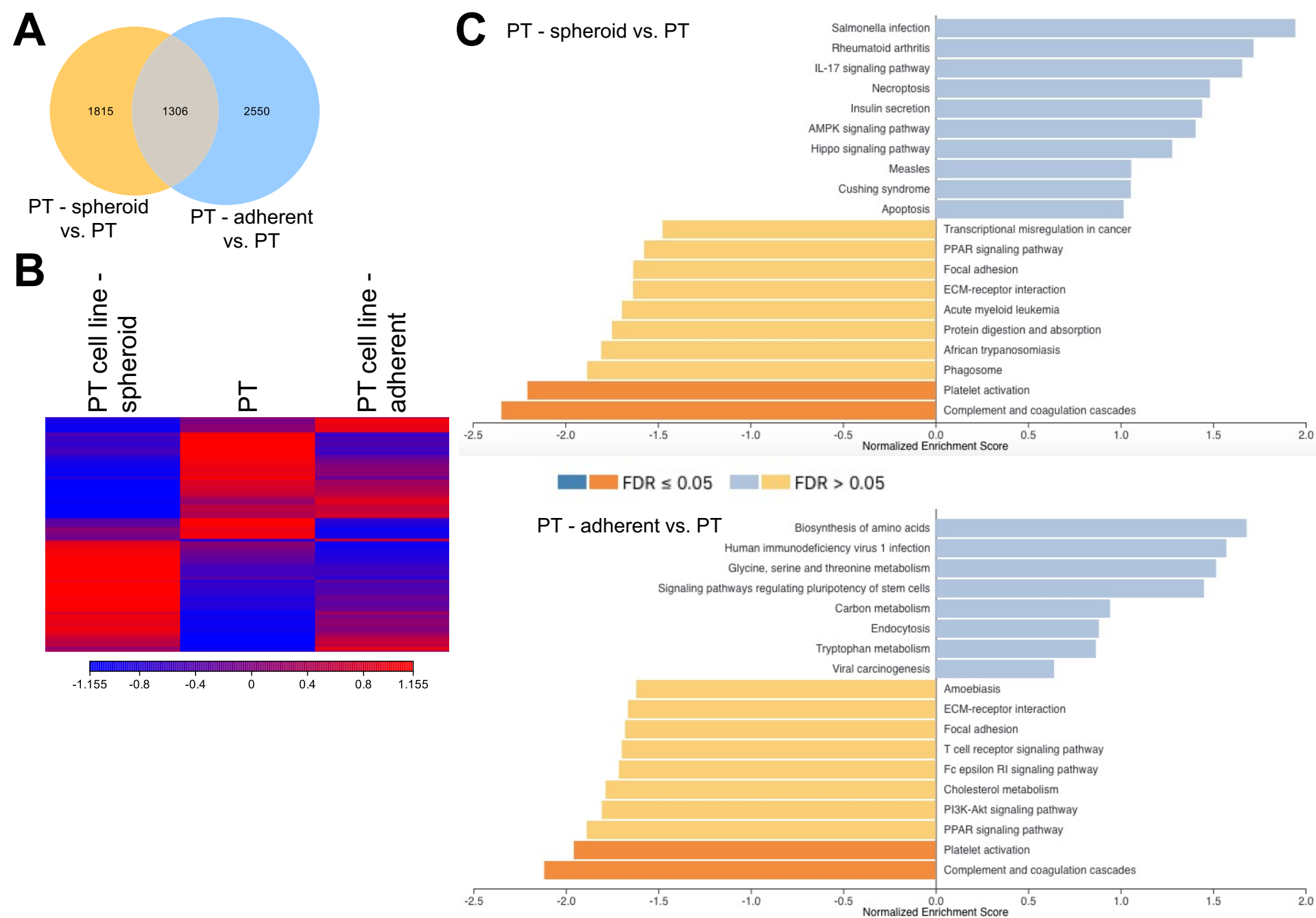
Pathways upregulated in common in vascular invasion cell line samples
IL-17 signaling pathway
PI3K-Akt signaling pathway
Rheumatoid arthritis
Salmonella infection
Amoebiasis
Cytokine-cytokine receptor interaction
Legionellosis
Chemokine signaling pathway
Kaposi-sarcoma associated herpesvirus infection
NOD-like receptor signaling pathway
TNF signaling pathway
Pathways in cancer
Hippo signaling pathway

B





**Fig. S1. GSEA analysis of transcriptomic profiling of cell line samples.** (A) Venn diagram of significantly changed genes with a p-value of < 0.05 and log2 fold change > 1.5 or < -1.5 among the cell line samples. (B) Bar graphs of KEGG pathways significantly upregulated and downregulated between the primary tumor cell line (adherent) and IHVI cell line samples (top) and between the primary tumor cell line (adherent) and IVCT cell line samples (bottom). (C) List of KEGG pathways upregulated in common among the vascular invasion cell line samples. (D) Bar graph of KEGG pathways significantly upregulated and downregulated in between the primary tumor cell lines grown in adherent and spheroid conditions.



**Fig. S2. GSEA analysis of transcriptomic profiling of primary tumor cell line samples.** (A) Venn diagram of significantly changed genes with a p-value of < 0.05 and log2 fold change > 1.5 or < -1.5 among the primary tumor tissue sample and primary tumor cell line (adherent, spheroid) samples. (B) Hierarchical clustering heat map of differentially expressed genes with p-value < 0.05 from primary tumor tissue and tumor cell line samples. (C) Bar graphs of KEGG pathways significantly upregulated and downregulated between the primary tumor tissue and primary tumor cell line (spheroid) samples (top) and between the primary tumor tissue and primary tumor cell line (adherent) samples (bottom).

Table S1. Genetic alterations identified in the HepT1 parental cell line.

Gene	Pos(hg19)	RefSeq RNA	CDS	Protein
<i>CTNNB1</i>	chr3:41265705	NM_001904.3	c.13+133_242-87del	p.Ala5_Ala80del
<i>EP300</i>	chr22:41525910	NM_001429.3	c.1186delT	p.Ser396LeufsTer35
<i>NF2</i>	chr22:29999992	NM_000268.3	c.6_15del	p.Gly3LeufsTer4
<i>NFE2L2</i>	chr2:178098956	NM_006164.4	c.89T>C	p.Leu30Pro
<i>TERT</i>	chr5:1295250	NM_198253.2	c.1-146C>T	
<i>TP53</i>	chr17:7577534	NM_000546.5	c.747G>T	p.Arg249Ser
<i>PTEN</i> loss				

Table S2. Primers used in PCR and Sanger sequencing.

Gene	Size of PCR Product (bp)*	Primer Sequence
<i>CTNNB1</i>	1187 (wild-type) 533 (exon 3 del)	FW: 5'-AGCGTGGACAATGGCTACTCAA-3'
		REV: 5'-ACCTGGTCCTCGTCATTTAGCAGT-3'
<i>EP300</i>	289	FW: 5'-GGGCTGTTAGGAAGATGAAATAAGT-3'
		REV: 5'-CAGCATTTTTTGAGGGGGGAGAC-3'
<i>NF2</i>	304	FW: 5'-CTGTGCAGCAACTCCAGGG-3'
		REV: 5'-ACTGTCACCGCAGCAGTC-3'
<i>NFE2L2</i>	458	FW: 5'-CCCACCATCAACAGTGGCATA-3'
		REV: 5'-GGCAAAGCTGGA ACTCAAATCCAG-3'
<i>TERT</i> promoter	271	FW: 5'-AGTGGATTCGCGGGGCACAGA-3'
		REV: 5'-CAGCGCTGCCTGAAACTC-3'
<i>TP53</i>	269	FW: 5'-AGAAATCGGTAAGAGGTGGGC-3'
		REV: 5'-GCTCTGACTGTACCACCATCC3'

\*Except for NFE2L2, size of PCR product includes addition of M13F and M13R sequence tags utilized to streamline Sanger sequencing procedures. M13F tag: 5'-TGTAACGACGGCCAGT-3' and M13R tag: 5'-CAGGAAACAGCTATGACC-3.'