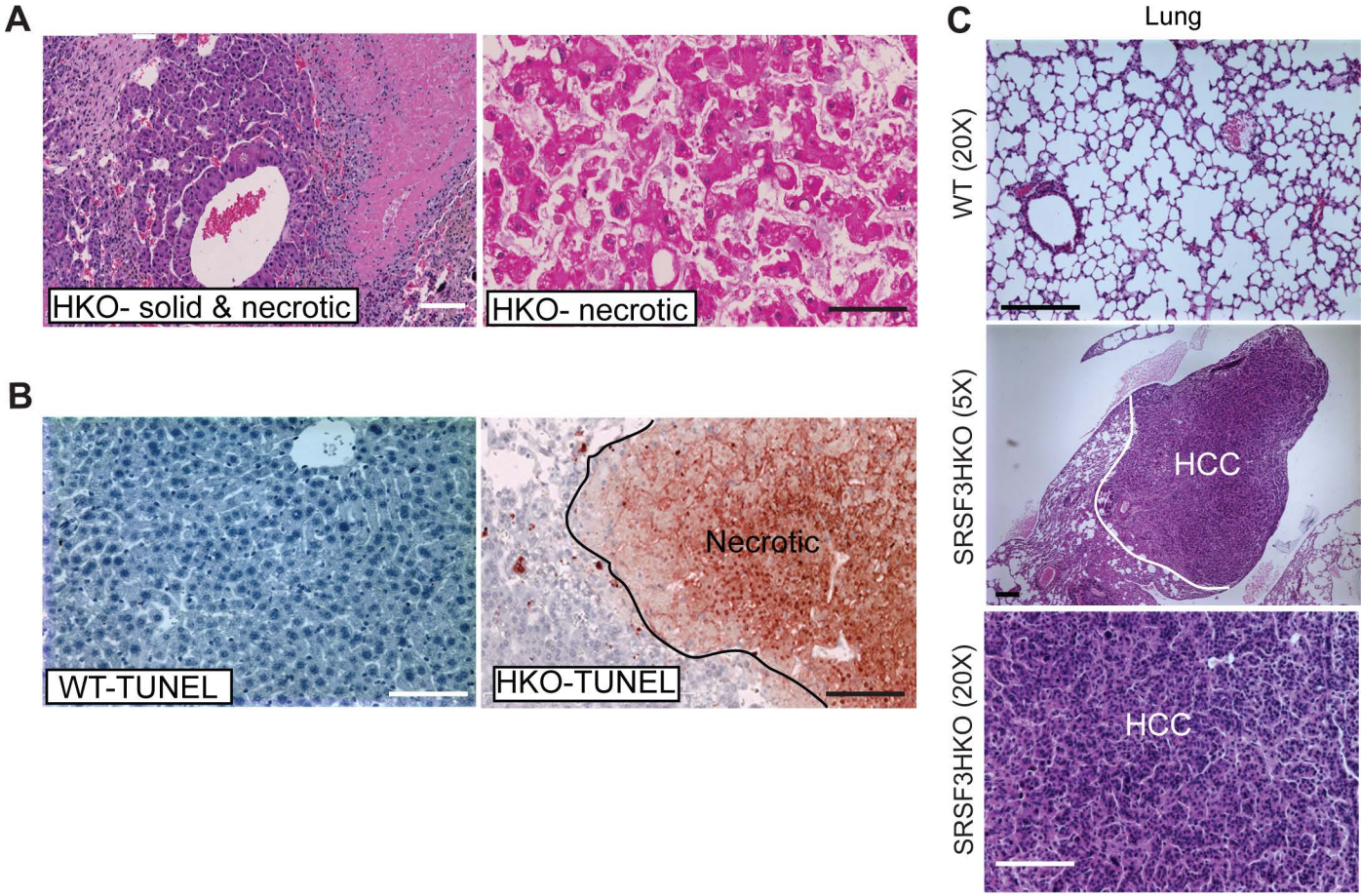

Figure S1. (A) Representative 20X images of liver sections from 24 month old SRSF3HKO mice stained with H&E. The SRSF3HKO section shows a dense cellular tumor with irregular nuclei and morphological pleomorphism and areas of necrosis. (B) TUNEL staining of necrotic tumor in SRSF3HKO liver. (C) Representative lung sections from WT and SRSF3HKO mice stained with H&E. Metastatic HCC in lung is marked by white line. For A, B, C, scale bar represents 100 μm.

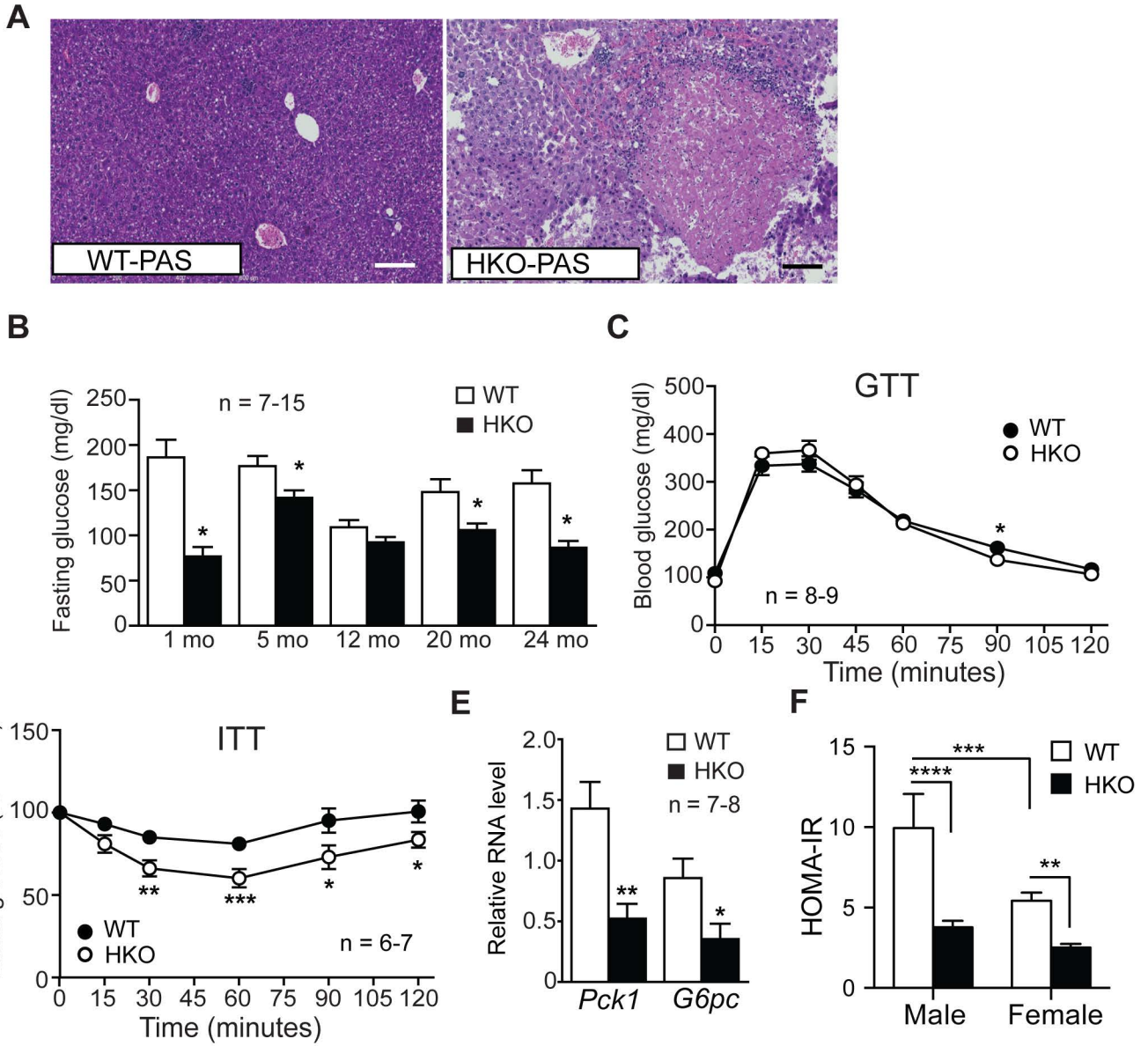

Figure S2. (A) Representative 10X images of liver sections from 24 month old WT and SRSF3-HKO mice stained for glycogen with PAS reagent. SRSF3-HKO livers have reduced glycogen in non-tumorous areas and glycogen is absent from tumors. Scale bar represents 100 μm. (B) Fasting blood glucose values with aging showing that SRSF3-HKO mice are hypoglycemic compared to WT. (C) Glucose tolerance tests on 12 month old mice showing comparable glucose tolerance in WT and SRSF3-HKO mice. (D) Insulin tolerance tests on 12 month old mice showing greater insulin sensitivity in SRSF3-HKO mice. (E) QPCR on liver RNA from 12 month old mice showing significantly reduced PEPCK (*Pck1)* and glucose-6-phosphatase (*G6pc)* expression in SRSF3-HKO livers. Results are shown as mean ± SEM. Asterisks indicate significance ($p<0.05$) vs. WT. N indicates the number of animals per group. (F) Calculated HOMA insulin resistance for WT and HKO, male and female mice. WT female mice are significantly more insulin sensitive that WT males. HKO mice are significantly more sensitive than WT for either sex. Asterisks show statistical significance (**$p<0.01$, ***$p<0.001$, ****$p<0.0001$) as indicated. HOMA-IR shows a signifiacnt sex ($p<0.01$) and genotype ($P<0.0001$) effect by 2-way ANOVA.

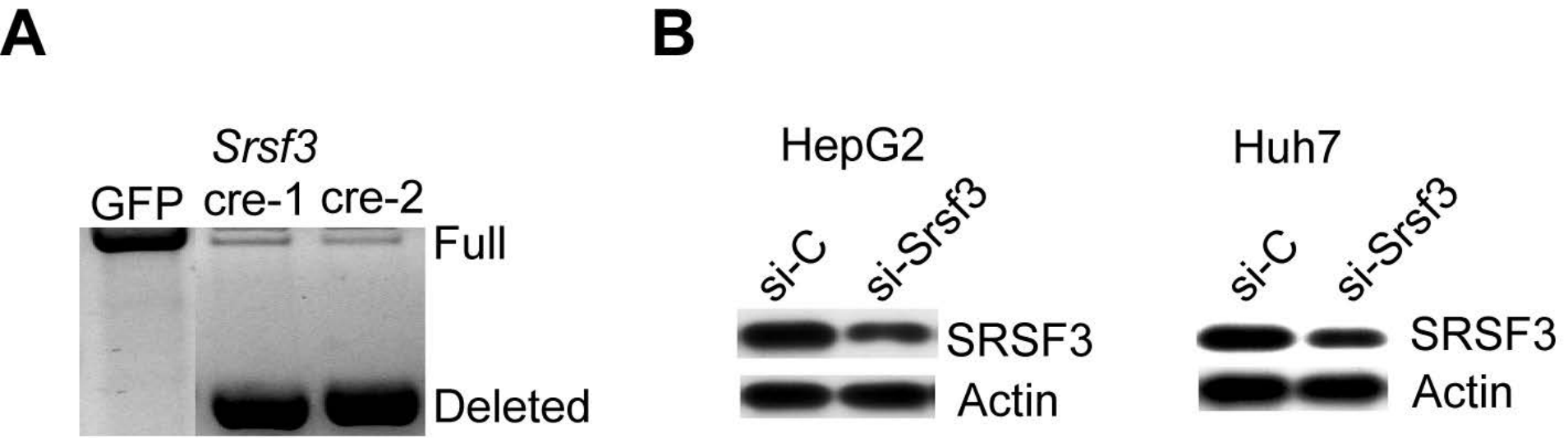

Figure S3. **A:** Acute deletion of SRSF3 by adenoviral delivery of cre. Representative gel for RT-PCR showing expression of deleted form of Srsf3 in Srsf3-floxed primary hepatocytes after adeno-cre infection. GFP-cre is used as negative control. **B:** Representative western blots showing decreased expression of SRSF3 in si-Srsf3 treated HepG2 and Huh7 cells compared to si-C control. The blots were stripped and blotted for actin as loading control.

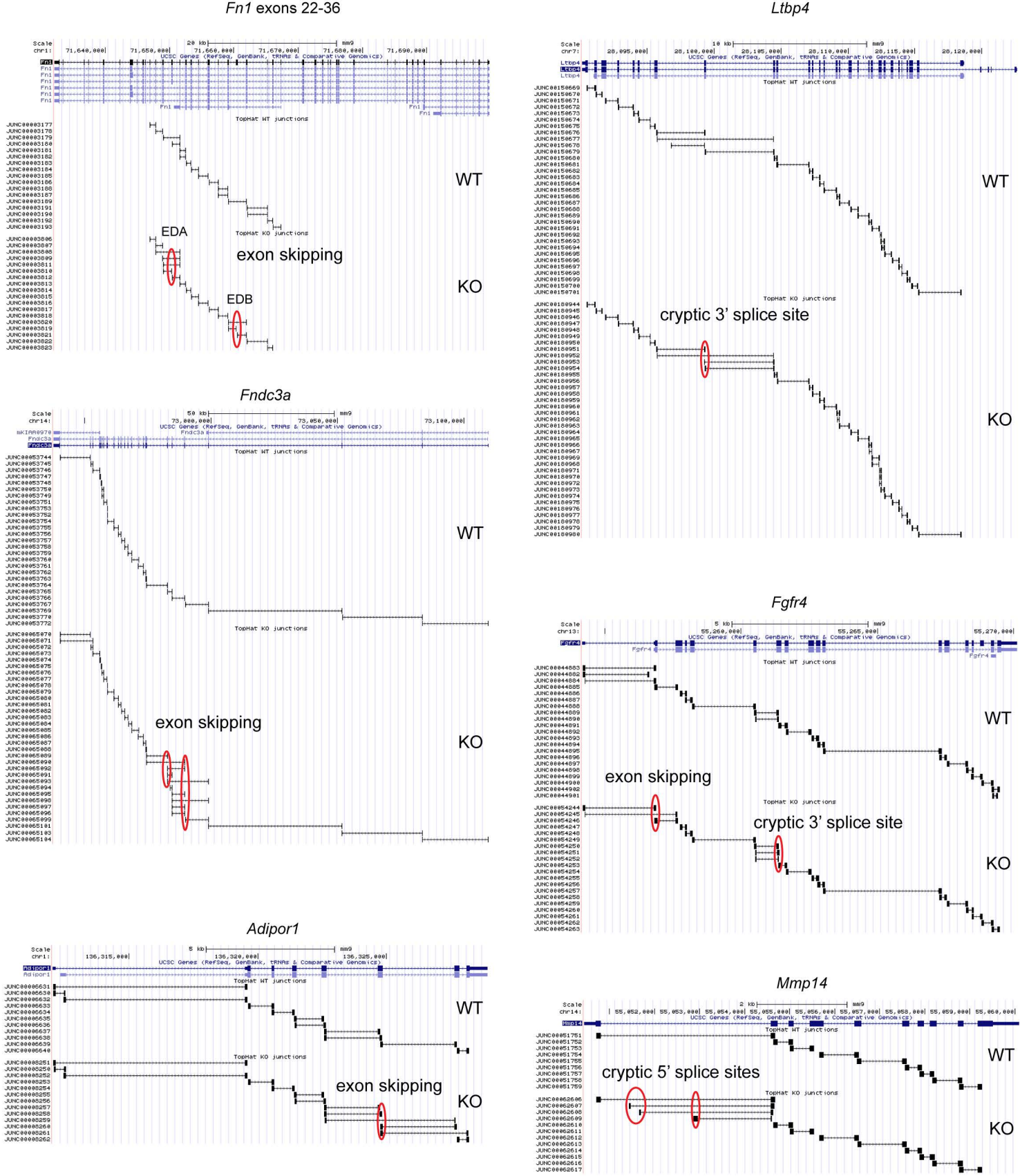

Figure S4. Altered exon-exon junction reads from RNAseq data aligned to genome using the UCSC genome browser. Altered exon usage is indicated in red. Reads from WT mice are given above reads from SRSF3HKO mice. Reads were aligned using Tophat.

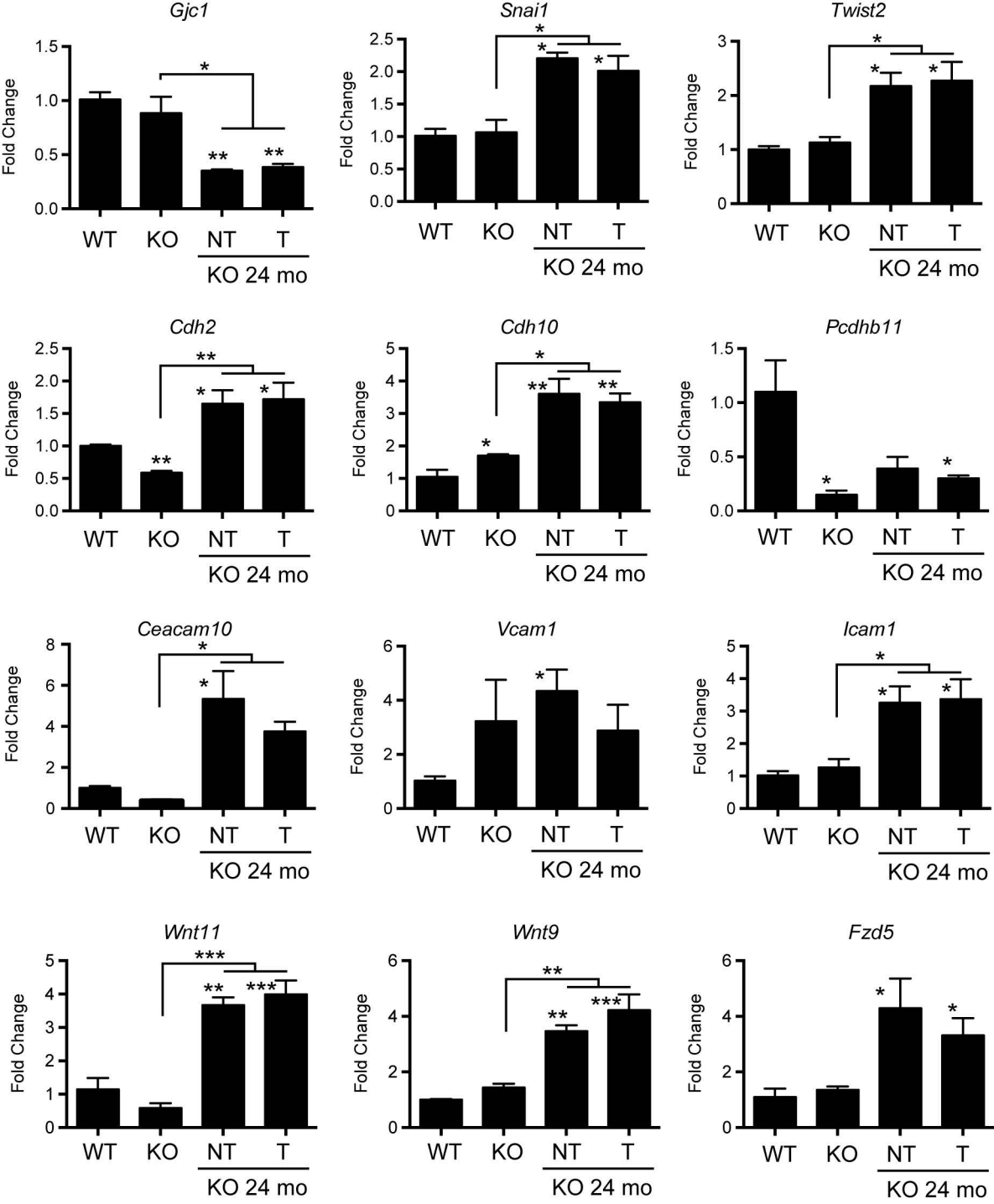

Figure S5. Alterations in EMT and Wnt signaling genes in SRSF3HKO mice. Gene expression was assessed in microarray data from wild-type mice (WT), SRSF3HKO mice at 1 month (KO), SRSF3HKO mice at 24 months (NT) and tumors from SRSF3HKO mice at 24 months (T). Asterisks indicate significance vs. WT or as indicated, *,**,*** p<0.05, 0.01, or 0.001.

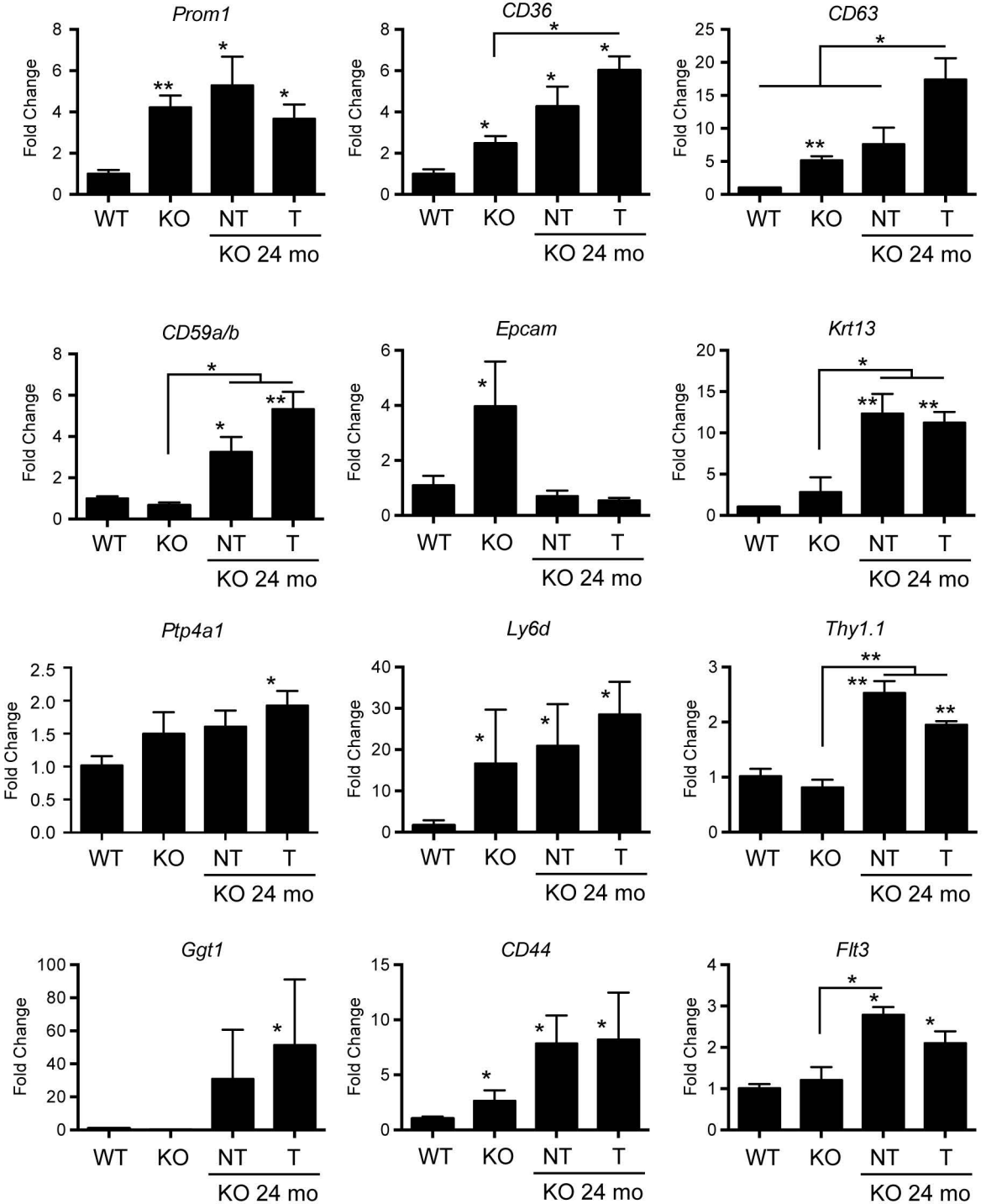

Figure S6. Alterations in progenitor and stem cell genes in SRSF3HKO mice. Gene expression was assessed in microarray data from wild-type mice (WT), SRSF3HKO mice at 1 month (KO), SRSF3HKO mice at 24 months (NT) and tumors from SRSF3HKO mice at 24 months (T). Asterisks indicate significance vs. WT or as indicated, *,** $p<0.05$, 0.01.

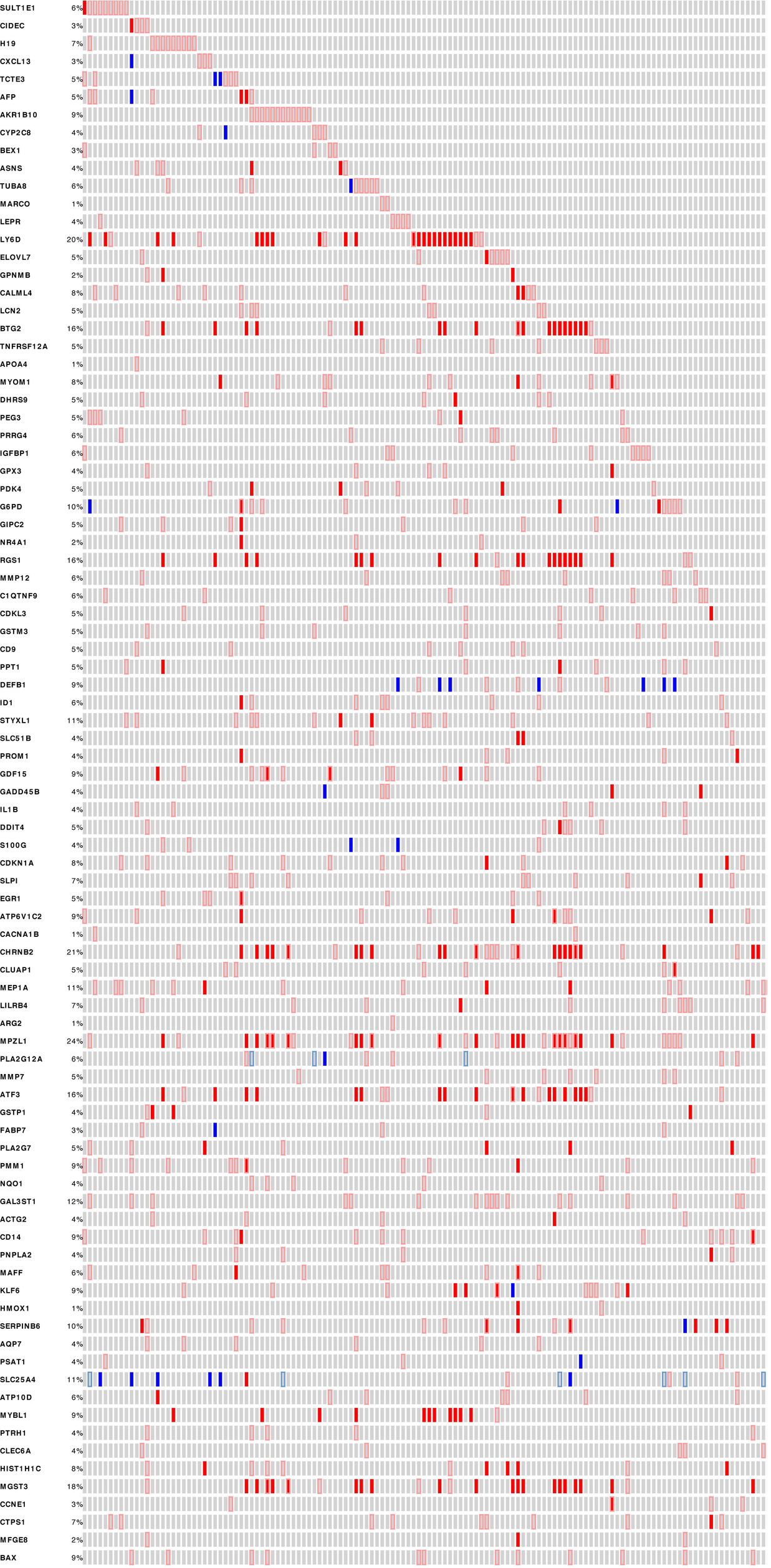

Figure S7. Alteration of the top 100 genes from the SRSF3HKO mice in the TCGA HCC database

Red indicates increased, blue indicates decreased, solid symbols represent amplification or deletion, hollow symbols represent expression changes.

Table S1: Tumor incidence in 24 month old mice

Age (month)	Genotype	# Mice Examined	# Mice w/ Tumor	Tumor Weight (g)	# Tumors per Mouse
Male Mice					
24	WT	14	1	1.2	1
24	HKO	8	8	1.59-4.16	1-10
Female Mice					
24	WT	22	0	0	0
24	HKO	15	15	1.71-3.81	1-10

Table S2: Changes of gene expression related to Fibrosis in SRSF3HKO mice at 1 mo

Locus	Description	SRSF3HKO/WT	p value
Mmp12	matrix metallopeptidase 12	8.013	1.36E-11
Cdkl3	cyclin-dependent kinase-like 3	7.207	2.87E-11
Cdkn1a	cyclin-dependent kinase inhibitor 1A (P21)	5.609	2.24E-10
Mmp7	matrix metallopeptidase 7	4.988	6.85E-10
Ctgf	connective tissue growth factor	3.814	1.31E-08
Pdgfra	platelet derived growth factor receptor, alpha polypeptide	3.582	2.85E-08
Krt23	keratin 23	3.425	5.05E-08
Ltbp4	latent transforming growth factor beta binding protein 4	0.488	1.62E-07
Mmp15	matrix metallopeptidase 15	0.446	5.15E-09
Fgfr3	fibroblast growth factor receptor 3	0.434	1.77E-09
Mmp19	matrix metallopeptidase 19	0.403	8.78E-11
Fgfr4	fibroblast growth factor receptor 4	0.332	2.37E-14
Fgf1	fibroblast growth factor 1	0.215	6.28E-22

Table S3: Hematology Analysis from 15-18 months old WT and SRSF3HKO mice; n=3

	WT	SRSF3HKO
WBC (K/μl)	2.5±0.47	1±0.1**
RBC (M/μl)	7.2±0.45	6.4±0.19
PLT (K/μl)	696±52	456±13**
Hb (g/dL)	10.4±0.67	9.9±0.38

Values are Mean±SE. Statistical significance was determined by Student's 2-tailed t test.

Table S5: GSEA enrichment of human HCC genesets in SRSF3HKO and WT mouse expression profiles

Geneset	Size	NES	FDR q-value
Enriched in SRSF3HKO			
CHIANG_LIVER_CANCER_SUBCLASS_UNANNOTATED_DN	141	-2.18	0.00
BOYAULT_LIVER_CANCER_SUBCLASS_G3_UP	139	-2.05	0.00
CAIRO_HEPATOBLASTOMA_CLASSES_UP	406	-1.91	0.00
LEE_LIVER_CANCER_SURVIVAL_DN	76	-1.70	0.02
HOSHIDA_LIVER_CANCER_SUBCLASS_S1	184	-1.55	0.07
IIZUKA_LIVER_CANCER_PROGRESSION_G1_G2_DN	17	-1.48	0.10
BOYAULT_LIVER_CANCER_SUBCLASS_G1_UP	82	-1.40	0.15
OKAMOTO_LIVER_CANCER_MULTICENTRIC_OCCURRENCE_UP	16	-1.37	0.16
HOSHIDA_LIVER_CANCER_LATE_RECURRENCE_UP	41	-1.36	0.15
YAMASHITA_LIVER_CANCER_WITH_EPCAM_UP	23	-1.31	0.17
HOSHIDA_LIVER_CANCER_SUBCLASS_S2	84	-1.31	0.16
Enriched in WT			
HSIAO_LIVER_SPECIFIC_GENES	175	2.50	0.00
CAIRO_LIVER_DEVELOPMENT_DN	189	2.37	0.00
BOYAULT_LIVER_CANCER_SUBCLASS_G123_DN	40	2.30	0.00
LEE_LIVER_CANCER_SURVIVAL_UP	94	2.29	0.00
BOYAULT_LIVER_CANCER_SUBCLASS_G3_DN	36	2.22	0.00
CHIANG_LIVER_CANCER_SUBCLASS_PROLIFERATION_DN	115	2.14	0.00
CHIANG_LIVER_CANCER_SUBCLASS_POLYSOMY7_UP	55	2.12	0.00
CAIRO_HEPATOBLASTOMA_DN	198	2.11	0.00
HOSHIDA_LIVER_CANCER_SUBCLASS_S3	193	1.98	0.00
CAIRO_HEPATOBLASTOMA_CLASSES_DN	145	1.95	0.00
HOSHIDA_LIVER_CANCER_SURVIVAL_DN	79	1.82	0.00
YAMASHITA_LIVER_CANCER_STEM_CELL_UP	41	1.78	0.01
CHIANG_LIVER_CANCER_SUBCLASS_CTNNB1_UP	132	1.75	0.01
ACEVEDO_LIVER_CANCER_DN	384	1.74	0.01
YAMASHITA_LIVER_CANCER_STEM_CELL_DN	49	1.74	0.01
WOO_LIVER_CANCER_RECURRENCE_DN	54	1.72	0.01
HOSHIDA_LIVER_CANCER_LATE_RECURRENCE_DN	53	1.56	0.03
ACEVEDO_LIVER_TUMOR_VS_NORMAL_ADJACENT_TISSUE_DN	192	1.53	0.04
CHIANG_LIVER_CANCER_SUBCLASS_CTNNB1_DN	127	1.42	0.07
ACEVEDO_NORMAL_TISSUE_ADJACENT_TO_LIVER_TUMOR_DN	243	1.35	0.11
YE_METASTATIC_LIVER_CANCER	19	1.31	0.14
IIZUKA_LIVER_CANCER_PROGRESSION_G2_G3_UP	20	1.30	0.14
CHIANG_LIVER_CANCER_SUBCLASS_INTERFERON_DN	38	1.27	0.16

Table S4: Genes altered in tumors compared to non-tumor liver in SRSF3HKO mice

			Fold Change				Raw Data				RMA Normalized Data				
Transcripts Cluster Id	genesymbol	p	Fold Change raw	SEM FC raw	Fold Change RMA	SEM FC RMA	mean Normal	SEM Normal	mean Tumor	SEM Tumor	mean Normal	SEM Normal	mean Tumor	SEM Tumor	genedescription
6972317	Igf2	1.46E--06	4.691	3.773	5.201	4.184	185.76	60.94	871.40	700.92	7.388	0.457	8.497	1.422	insulin-like growth factor 2
6989769	Calml4	8.10E--07	4.331	2.287	6.013	3.175	130.28	74.81	564.29	297.94	6.552	0.809	8.740	0.750	calmodulin-like 4
6883105	Wfdc2	4.974E--03	3.891	1.178	4.575	1.384	148.53	62.21	577.93	174.90	6.981	0.562	9.050	0.417	WAP four-disulfide core domain 2
6969698	Mogat2	7.004E--04	3.852	0.337	4.606	0.403	102.60	42.15	395.18	34.60	6.423	0.618	8.615	0.133	monoacylglycerol O-acyltransferase 2
6974582	Defb1	2.66E--06	3.630	1.190	13.077	4.288	525.44	476.07	1907.42	625.51	7.188	1.703	10.748	0.457	defensin beta 1
6901671	Emcn	4.42E--05	3.594	1.285	3.775	1.349	129.09	26.19	463.99	165.83	6.941	0.333	8.646	0.573	endomucin
6884348	Meig1	1.71E--08	3.548	1.325	4.088	1.527	50.01	19.80	177.42	66.28	5.440	0.523	7.190	0.691	meiosis expressed gene 1
6801914	Gpx2|Gpx2---ps1	4.883E--03	3.489	0.605	5.302	0.919	148.59	96.23	518.39	89.83	6.611	0.901	8.967	0.280	glutathione peroxidase 2 | glutathione peroxidase 2, pseudogene 1
6912517	Rragd	2.942E--03	3.438	0.752	4.022	0.879	90.57	37.68	311.36	68.08	6.275	0.550	8.218	0.300	Ras-related GTP binding D
6953443	Igf2bp3|2410003K1	6.091E--03	3.436	0.825	3.668	0.880	53.31	13.87	183.17	43.96	5.642	0.365	7.411	0.413	insulin-like growth factor 2 mRNA binding protein 3 | RIKEN cDNA 2410003K15 gene
6769255	Gadd45b	2.534E--03	3.434	0.968	3.537	0.997	143.59	25.68	493.05	138.98	7.123	0.242	8.804	0.476	growth arrest and DNA-damage-inducible 45 beta
6880033	Lpcat4	9.598E--04	3.344	0.493	4.734	0.698	341.19	192.15	1140.98	168.35	7.913	0.864	10.127	0.201	lysophosphatidylcholine acyltransferase 4
6768898	Vpreb3	2.26E--05	3.305	1.321	3.327	1.329	97.96	7.64	323.81	129.37	6.605	0.117	8.060	0.667	pre-B lymphocyte gene 3
6765716	Lrp11	2.15E--05	3.282	1.438	4.134	1.811	349.03	137.43	1145.66	501.78	8.114	0.763	9.804	0.769	low density lipoprotein receptor-related protein 11
6870971	BC021614	4.23E--05	3.162	0.896	3.441	0.976	310.94	95.28	983.05	278.73	8.158	0.406	9.820	0.423	
6996343	Ostb|Rasl12	5.98E--05	3.000	0.768	3.333	0.853	208.89	70.80	626.57	160.45	7.555	0.455	9.194	0.377	organic solute transporter beta | RAS-like, family 12
6850077	Slc44a4	1.37E--06	2.940	1.209	2.949	1.213	50.90	2.85	149.66	61.54	5.665	0.080	6.902	0.734	solute carrier family 44, member 4
6756541	Cd34|C030002c11ri	1.028E--03	2.893	0.996	2.897	0.998	125.83	4.99	363.96	125.32	6.973	0.058	8.327	0.518	CD34 antigen | hypothetical LOC320400
6916492	Cyp4a12a|Cyp4a12	7.40E--05	2.877	0.807	12.990	3.641	1205.12	1119.23	3467.65	971.94	8.060	1.902	11.651	0.391	cytochrome P450, family 4, subfamily a, polypeptide 12a | polypeptide 12B | polypeptide 29, polypeptide 30b
6825223	6330409N04Rik	7.571E--03	2.862	0.880	2.878	0.885	413.81	31.35	1184.27	364.12	8.685	0.106	10.077	0.434	RIKEN cDNA 6330409N04 gene
6880467	Disp2	7.333E--03	2.844	0.729	2.904	0.744	50.70	6.93	144.21	36.94	5.634	0.213	7.057	0.427	dispatched homolog 2 (Drosophila)
6869013	Slc1a1|4430402I18	7.41E--05	2.774	0.751	3.920	1.061	132.55	79.20	367.69	99.48	6.552	0.818	8.420	0.380	solute carrier family 1 (neuronal/epithelial high affinity glutamate transporter, system Xag), member 1
6916493	Cyp4a12b|Cyp4a12	8.62E--05	2.765	0.752	13.368	3.636	1243.49	1161.33	3438.25	935.15	8.007	1.964	11.647	0.374	cytochrome P450, family 4, subfamily a, polypeptide 12B | cytochrome P450, family 4, subfamily a, polypeptide 12a
6810333	Esm1	5.534E--05	2.743	0.600	2.865	0.627	142.41	27.22	390.66	85.47	7.091	0.313	8.529	0.356	endothelial cell-specific molecule 1
6756790	Mybl1	2.197E--03	2.584	0.529	2.677	0.548	76.45	14.99	197.51	40.46	6.205	0.265	7.562	0.307	myeloblastosis oncogene-like 1
6749530	4930444A19Rik	2.829E--03	2.541	0.255	2.673	0.269	402.72	90.50	1023.26	102.81	8.581	0.325	9.983	0.153	RIKEN cDNA 4930444A19 gene
6946406	Aqp1	8.548E--03	2.446	0.156	2.634	0.168	414.52	118.74	1013.90	64.68	8.588	0.381	9.980	0.090	aquaporin 1
6925829	Smpdl3b	8.788E--04	2.374	0.415	2.589	0.452	134.25	36.09	318.71	55.70	6.944	0.444	8.264	0.284	sphingomyelin phosphodiesterase, acid-like 3B
6885431	Tmem141	2.213E--04	2.368	0.454	2.395	0.459	846.39	88.89	2003.89	384.20	9.709	0.156	10.920	0.259	transmembrane protein 141
6769080	Cstb	1.705E--03	2.339	0.546	2.374	0.554	833.85	97.11	1950.12	455.35	9.682	0.180	10.855	0.323	cystatin B
6892325	Eif2s2|Gm9892	8.998E--03	2.306	0.422	2.434	0.446	307.89	73.52	710.01	130.05	8.189	0.329	9.424	0.263	eukaryotic translation initiation factor 2, subunit 2 (beta) | predicted gene 9892
6765218	Atf3	9.997E--05	2.204	0.287	2.224	0.289	129.10	12.17	284.60	37.00	7.000	0.134	8.126	0.200	activating transcription factor 3
6875720	Npdc1	5.636E--04	2.194	0.214	2.362	0.231	190.28	45.77	417.50	40.78	7.466	0.414	8.692	0.141	neural proliferation, differentiation and control gene 1
7016340	Ndufa1	3.751E--04	2.154	0.329	2.301	0.351	162.55	37.95	350.08	53.47	7.249	0.388	8.415	0.233	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 1
6881897	Naa20	2.072E--03	2.153	0.408	2.160	0.410	211.14	11.80	454.58	86.22	7.718	0.079	8.781	0.256	N(alpha)-acetyltransferase 20, NatB catalytic subunit
6941248	Rpl37	6.940E--04	2.130	0.227	2.195	0.234	207.70	35.52	442.48	47.10	7.656	0.250	8.774	0.149	ribosomal protein L37
6923411	Jun	9.796E--05	2.114	0.069	2.144	0.070	203.98	24.88	431.22	14.00	7.652	0.168	8.751	0.047	
6903185	Fabp4	5.142E--03	2.113	0.396	2.148	0.403	52.66	6.96	111.29	20.86	5.695	0.181	6.747	0.273	fatty acid binding protein 4, adipocyte
6850080	Neu1	1.978E--03	2.092	0.265	2.164	0.274	407.78	72.22	853.12	108.12	8.623	0.269	9.715	0.174	neuraminidase 1
6916147	Magoh	1.760E--06	2.090	0.398	2.181	0.416	72.70	13.74	151.95	28.96	6.122	0.311	7.186	0.310	mago-nashi homolog, proliferation-associated (Drosophila)
6754776	Brp44	5.136E--04	2.065	0.299	2.146	0.311	619.64	123.84	1279.54	185.47	9.220	0.280	10.287	0.228	brain protein 44
6901345	Rpl12	5.386E--04	2.057	0.177	2.065	0.178	429.88	26.36	884.27	76.28	8.742	0.091	9.778	0.121	ribosomal protein L12
6858868	Rbbp8	1.368E--04	2.044	0.357	2.065	0.361	158.83	16.45	324.66	56.74	7.297	0.144	8.297	0.260	retinoblastoma binding protein 8
6876227	Rpl12|Snora65	1.000E--03	2.035	0.181	2.048	0.182	2912.67	223.19	5927.30	528.14	11.499	0.115	12.522	0.127	ribosomal protein L12 | small nucleolar RNA, H/ACA box 65
6820574	Sugt1|Gm6649	1.276E--03	2.028	0.417	2.064	0.425	192.57	24.41	390.47	80.34	7.563	0.198	8.535	0.342	SGT1, suppressor of G2 allele of SKP1 (S. cerevisiae) | E74-like factor 1 pseudogene
6984473	Pllp	3.706E--03	2.017	0.269	2.127	0.283	167.65	40.40	338.17	45.02	7.312	0.324	8.373	0.207	plasma membrane proteolipid
6826116	9030625A04Rik	1.020E--04	2.008	0.291	2.017	0.292	289.14	19.75	580.56	84.13	8.169	0.096	9.150	0.212	RIKEN cDNA 9030625A04 gene
6852845	Rhoq|Pigf	1.726E--03	2.005	0.198	2.120	0.209	166.22	41.09	333.33	32.92	7.297	0.330	8.367	0.137	ras homolog gene family, member Q | phosphatidylinositol glycan anchor biosynthesis, class F
6880034	Nop10	5.996E--03	1.997	0.332	2.062	0.343	653.35	112.14	1304.48	217.04	9.305	0.264	10.308	0.246	NOP10 ribonucleoprotein homolog (yeast)
6865551	Ppic	3.474E--03	1.996	0.107	2.020	0.108	127.06	14.40	253.57	13.56	6.972	0.156	7.982	0.078	peptidylprolyl isomerase C
6818556	Psmc6	6.380E--03	1.993	0.392	2.029	0.399	492.29	66.23	981.10	193.05	8.918	0.192	9.878	0.301	proteasome (prosome, macropain) 26S subunit, ATPase, 6
6959848	Rpl17|Rpl17-ps3	4.950E--04	1.983	0.137	2.063	0.142	779.83	144.15	1546.17	106.67	9.550	0.298	10.588	0.098	ribosomal protein L17 | ribosomal protein L17, pseudogene 3
6949693	Rps27a	4.499E--05	1.981	0.175	2.034	0.179	74.45	12.43	147.51	13.00	6.181	0.228	7.193	0.134	ribosomal protein S27A
6959300	Blvrb	2.251E--03	1.974	0.236	2.121	0.254	1111.10	312.51	2192.94	262.53	10.014	0.375	11.078	0.171	biliverdin reductase B (flavin reductase (NADPH))
6984972	Tppp3	1.360E--03	1.973	0.385	1.974	0.385	80.53	2.32	158.87	30.97	6.330	0.041	7.254	0.291	tubulin polymerization-promoting protein family member 3
6854986	Rps18|Gm10260	9.084E--04	1.936	0.140	2.098	0.151	1285.89	382.74	2489.79	179.45	10.213	0.397	11.274	0.108	ribosomal protein S18 | predicted gene 10260
6831469	Ptp4a3	5.262E--05	1.933	0.145	1.940	0.145	195.44	12.08	377.73	28.31	7.605	0.089	8.553	0.107	protein tyrosine phosphatase 4a3
6889367	Eif3m	6.821E--04	1.933	0.333	1.971	0.339	375.98	50.25	726.63	125.14	8.526	0.207	9.466	0.233	eukaryotic translation initiation factor 3, subunit M
6836829	Dgat1	5.093E--04	1.928	0.198	2.036	0.209	716.57	163.88	1381.83	141.69	9.407	0.340	10.417	0.146	diacylglycerol O-acyltransferase 1
6857461	Cdc42ep3	4.134E--04	1.928	0.194	1.933	0.194	66.65	3.53	128.48	12.91	6.054	0.079	6.991	0.141	CDC42 effector protein (Rho GTPase binding) 3
6980871	Angpt2	3.475E--03	1.924	0.468	1.939	0.472	84.22	7.65	162.02	39.45	6.385	0.127	7.257	0.344	angiopoietin 2
7012698	Rpl17	7.827E--04	1.919	0.176	1.979	0.182	389.83	65.74	748.26	68.69	8.563	0.257	9.536	0.129	ribosomal protein L17
6876079	Mettl11a	7.243E--03	1.917	0.276	1.930	0.278	171.33	13.72	328.45	47.27	7.411	0.121	8.326	0.226	methyltransferase like 11A
6819662	Rnaseh2b	3.348E--03	1.911	0.353	1.912	0.353	87.43	1.45	167.12	30.84	6.450	0.024	7.329	0.294	ribonuclease H2, subunit B
6850552	Enpp5	4.742E--03	1.911	0.374	1.945	0.381	338.47	45.90	646.97	126.74	8.378	0.188	9.287	0.264	ectonucleotide pyrophosphatase/phosphodiesterase 5
6823696	Gnl3|Snord69	9.266E--03	1.906	0.381	1.921	0.384	326.87	29.68	622.89	124.63	8.341	0.129	9.230	0.269	guanine nucleotide binding protein-like 3 (nucleolar) | small nucleolar RNA, C/D box 69
6882630	1110008F13Rik|Sla	3.013E--04	1.905	0.251	1.919	0.253	2506.99	214.69	4774.86	628.73	11.281	0.124	12.195	0.195	RIKEN cDNA 1110008F13 gene | Src-like-adaptor 2
6861632	Sec11c	7.701E--03	1.904	0.318	1.942	0.324	157.24	22.10	299.39	49.98	7.269	0.201	8.189	0.227	SEC11 homolog C (S. cerevisiae)
7015454	Rbm3	2.139E--04	1.894	0.358	1.929	0.365	1052.23	135.85	1993.18	376.83	10.013	0.199	10.910	0.268	RNA binding motif protein 3
6988220	Esam	2.548E--03	1.893	0.299	1.934	0.306	210.07	31.40	397.67	62.83	7.684	0.207	8.602	0.216	endothelial cell-specific adhesion molecule
6775298	Ppap2c	1.241E--04	1.881	0.260	1.945	0.269	1465.63	259.07	2756.44	380.98	10.469	0.269	11.400	0.206	phosphatidic acid phosphatase type 2C
7015437	Glod5	1.269E--03	1.870	0.148	1.876	0.149	36.77	2.05	68.77	5.45	5.196	0.079	6.095	0.112	glyoxalase domain containing 5
6837373	Ndufa6	4.013E--04	1.870	0.354	1.924	0.364	363.13	57.04	679.07	128.58	8.463	0.251	9.359	0.258	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 6 (B14)

6848080	Pigp|Dppa5a	1.986E-03	1.868	0.346	1.869	0.346	231.77	5.73	433.00	80.09	7.856	0.035	8.711	0.258	phosphatidylinositol glycan anchor biosynthesis, class P | developmental pluripotency associated 5A
6858456	Cul2	2.773E-03	1.865	0.336	1.921	0.346	208.68	36.17	389.26	70.18	7.662	0.247	8.560	0.250	cullin 2
6792838	Sectm1b	9.288E-04	1.864	0.125	1.981	0.133	68.26	16.94	127.27	8.54	6.005	0.354	6.985	0.101	secreted and transmembrane 1B
6768125	Timm23	1.533E-03	1.849	0.336	1.861	0.339	1108.55	91.51	2049.26	372.71	10.105	0.120	10.957	0.246	translocase of inner mitochondrial membrane 23 homolog (yeast)
6862124	Rpl17|Snord58b|Rp	1.127E-04	1.847	0.209	1.878	0.212	1300.73	169.90	2403.03	271.33	10.321	0.185	11.213	0.157	ribosomal protein L17 | small nucleolar RNA, C/D box 58B | ribosomal protein L17, pseudogene 3 | predicted gene 10268
6880990	Adra2b	3.530E-03	1.847	0.160	1.930	0.167	163.60	32.04	302.16	26.18	7.291	0.312	8.229	0.123	adrenergic receptor, alpha 2b
6817900	Selk|LOC100134990	1.021E-03	1.822	0.113	1.827	0.114	434.90	23.65	792.31	49.36	8.760	0.081	9.624	0.089	selenoprotein K | selenoprotein K pseudogene | cDNA sequence BC052688
6850140	Nhp2l1	2.436E-03	1.812	0.351	1.828	0.355	282.12	26.36	511.12	99.17	8.127	0.138	8.948	0.261	NHP2 non-histone chromosome protein 2-like 1 (S. cerevisiae)
7021355	Rpl35|Gm10269	1.005E-02	1.810	0.324	1.818	0.326	278.31	18.25	503.77	90.30	8.115	0.092	8.930	0.260	ribosomal protein L35 | predicted gene 10269
6823002	2700060E02Rik	1.254E-04	1.803	0.311	1.815	0.313	370.01	30.10	667.16	115.00	8.522	0.115	9.342	0.234	RIKEN cDNA 2700060E02 gene
6823780	Timm23	1.822E-03	1.803	0.328	1.812	0.330	1550.59	106.10	2795.83	508.56	10.592	0.100	11.404	0.249	translocase of inner mitochondrial membrane 23 homolog (yeast)
6832200	Cyp2d9|Cyp2d11|C	4.58E-05	1.800	0.115	1.947	0.124	1614.74	471.96	2906.34	185.40	10.544	0.394	11.499	0.094	cytochrome P450, family 2, subfamily d, polypeptide 9 | polypeptide 11 | polypeptide 10
6773026	Rpl12|Gm16519	7.572E-04	1.799	0.152	1.817	0.153	5274.25	523.87	9489.70	801.38	12.351	0.142	13.202	0.122	ribosomal protein L12 | predicted gene, 16519
6913039	Reck	4.116E-04	1.795	0.241	1.806	0.243	117.69	8.76	211.29	28.42	6.871	0.110	7.699	0.184	reversion-inducing-cysteine-rich protein with kazal motifs
6832191	1500032L24Rik	4.028E-04	1.791	0.327	1.796	0.328	923.13	48.51	1653.19	302.30	9.846	0.077	10.646	0.248	RIKEN cDNA 1500032L24 gene
6934397	Bri3bp	5.201E-04	1.769	0.242	1.802	0.247	1323.51	184.58	2341.00	320.33	10.343	0.195	11.162	0.215	Bri3 binding protein
6917495	Atpif1	3.654E-03	1.768	0.110	1.768	0.110	530.42	5.24	937.81	58.48	9.051	0.014	9.867	0.093	ATPase inhibitory factor 1
6795689	Rpl17|Rpl17-ps3	1.936E-03	1.757	0.213	1.789	0.217	888.55	115.52	1561.54	188.98	9.769	0.196	10.589	0.167	ribosomal protein L17 | ribosomal protein L17, pseudogene 3
6884460	Cdc123	4.908E-05	1.736	0.258	1.738	0.258	389.07	11.93	675.48	100.27	8.603	0.044	9.370	0.205	cell division cycle 123 homolog (S. cerevisiae)
6953906	Nt5c3	6.462E-04	1.723	0.238	1.770	0.244	117.45	18.33	202.32	27.92	6.837	0.242	7.630	0.213	5'-nucleotidase, cytosolic III
6888937	Hsd17b12	1.012E-04	1.703	0.063	1.727	0.064	572.86	69.01	975.49	36.20	9.142	0.170	9.928	0.053	hydroxysteroid (17-beta) dehydrogenase 12
6996727	Uba52|Gm7866	4.080E-06	1.701	0.102	1.739	0.105	579.80	82.49	986.26	59.41	9.148	0.219	9.941	0.087	ubiquitin A-52 residue ribosomal protein fusion product 1 | predicted gene 7866
6755729	Cnih4	3.836E-03	1.698	0.148	1.771	0.154	358.93	69.03	609.29	53.03	8.427	0.306	9.240	0.124	cornichon homolog 4 (Drosophila)
6757331	Eif3m	2.294E-04	1.686	0.321	1.688	0.322	442.66	16.42	746.28	142.31	8.788	0.055	9.495	0.259	eukaryotic translation initiation factor 3, subunit M
6890193	Ccdc32	1.462E-03	1.685	0.273	1.691	0.274	243.02	15.06	409.39	66.35	7.919	0.090	8.635	0.255	coiled-coil domain containing 32
6924871	Atp6v0b	4.156E-04	1.684	0.188	1.730	0.193	800.14	129.93	1347.39	150.14	9.605	0.237	10.378	0.160	ATPase, H+ transporting, lysosomal V0 subunit B
6835634	Eif3h	1.453E-03	1.677	0.192	1.709	0.195	996.19	131.60	1670.42	191.03	9.933	0.202	10.688	0.159	eukaryotic translation initiation factor 3, subunit H
6817700	Arhgef3	3.753E-04	1.675	0.120	1.689	0.121	347.17	30.25	581.60	41.70	8.428	0.132	9.176	0.103	Rho guanine nucleotide exchange factor (GEF) 3
6834951	Cox6c	1.941E-04	1.671	0.179	1.686	0.181	3517.03	332.87	5877.18	629.26	11.767	0.136	12.504	0.154	cytochrome c oxidase, subunit VIc
6872661	Rpl9	1.285E-03	1.664	0.217	1.723	0.224	1065.89	203.77	1773.86	231.05	10.008	0.265	10.769	0.181	ribosomal protein L9
6749773	Nop58	6.884E-05	1.664	0.199	1.672	0.200	121.75	8.74	202.59	24.24	6.921	0.100	7.643	0.165	NOP58 ribonucleoprotein homolog (yeast)
6972710	Ttyh1	2.86E-05	1.664	0.654	1.725	0.678	165.41	32.72	275.24	108.11	7.318	0.268	7.901	0.525	tweety homolog 1 (Drosophila)
6860038	Paip2	9.649E-03	1.662	0.271	1.672	0.273	853.79	63.64	1419.29	231.77	9.730	0.107	10.431	0.242	polyadenylate-binding protein-interacting protein 2
6956748	Plxnd1	9.409E-04	1.660	0.225	1.709	0.232	292.78	51.65	486.16	65.97	8.152	0.241	8.900	0.187	plexin D1
6817984	Bap1	2.170E-03	1.660	0.173	1.667	0.174	337.31	22.11	559.95	58.39	8.392	0.092	9.113	0.152	Brca1 associated protein 1
6778719	Upp1	6.322E-03	1.653	0.132	1.653	0.132	66.35	0.80	109.65	8.79	6.052	0.017	6.768	0.113	uridine phosphorylase 1
6892364	Pigu	1.810E-04	1.651	0.103	1.668	0.104	671.40	68.54	1108.62	68.90	9.376	0.146	10.109	0.093	phosphatidylinositol glycan anchor biosynthesis, class U
6793677	Odc1	7.323E-05	1.643	0.029	1.652	0.029	367.81	27.66	604.31	10.61	8.515	0.105	9.239	0.025	ornithine decarboxylase, structural 1
6880040	2900064A13Rik	7.637E-03	1.641	0.291	1.644	0.291	1472.66	61.69	2416.82	428.25	10.522	0.062	11.196	0.247	RIKEN cDNA 2900064A13 gene
6823221	Comtd1|A430057M	6.171E-04	1.640	0.107	1.658	0.108	172.38	18.52	282.69	18.43	7.414	0.149	8.137	0.097	catechol-O-methyltransferase domain containing 1 | RIKEN cDNA A430057M04 gene
6834752	Cct5	2.553E-03	1.636	0.049	1.671	0.050	602.69	85.66	986.19	29.43	9.205	0.213	9.944	0.043	chaperonin containing Tcp1, subunit 5 (epsilon)
6984999	Cenpt	7.192E-05	1.627	0.063	1.645	0.064	126.02	13.64	204.98	7.99	6.962	0.150	7.677	0.055	centromere protein T
6820372	Nufip1	1.169E-03	1.626	0.262	1.641	0.264	248.88	24.74	404.57	65.10	7.945	0.142	8.624	0.226	nuclear fragile X mental retardation protein interacting protein 1
6888315	Clp1	7.869E-05	1.622	0.262	1.623	0.262	140.97	3.89	228.65	36.96	7.138	0.039	7.795	0.254	CLP1, cleavage and polyadenylation factor I subunit, homolog (S. cerevisiae)
6832259	Tspo	9.168E-03	1.597	0.081	1.623	0.083	624.93	80.26	998.30	50.82	9.265	0.180	9.960	0.073	translocator protein
6886229	Atp6v1g1	1.544E-04	1.597	0.198	1.620	0.201	296.55	35.72	473.47	58.68	8.191	0.175	8.865	0.181	ATPase, H+ transporting, lysosomal V1 subunit G1
6893173	Spata2	6.531E-03	1.587	0.169	1.588	0.169	157.66	3.76	250.28	26.65	7.300	0.035	7.950	0.163	spermatogenesis associated 2
6894283	Arfrp1	3.810E-04	1.572	0.164	1.585	0.165	146.56	13.16	230.40	24.02	7.183	0.131	7.831	0.160	ADP-ribosylation factor related protein 1
7016317	Nkrf	5.858E-03	1.564	0.127	1.577	0.128	161.07	14.69	251.97	20.50	7.320	0.127	7.968	0.118	NF-kappaB repressing factor
6892393	Eif6|BC029722	1.846E-03	1.559	0.121	1.598	0.124	1130.88	184.48	1763.17	137.23	10.108	0.222	10.775	0.116	eukaryotic translation initiation factor 6 | cDNA sequence BC029722
6878995	Mtch2	3.578E-03	1.551	0.179	1.583	0.183	1483.14	198.92	2300.93	265.45	10.506	0.209	11.148	0.173	mitochondrial carrier homolog 2 (C. elegans)
6858352	Tcp1	1.310E-05	1.548	0.123	1.560	0.123	682.14	57.93	1056.00	83.60	9.403	0.126	10.035	0.113	t-complex protein 1
6858936	Impact	1.139E-05	1.543	0.121	1.547	0.121	204.65	11.11	315.78	24.79	7.673	0.076	8.293	0.118	imprinted and ancient
6883098	Dbndd2	2.407E-03	1.532	0.122	1.554	0.124	81.51	10.21	124.86	9.97	6.328	0.172	6.954	0.120	dysbindin (dystrobrevin binding protein 1) domain containing 2
6946365	Plekha8	1.144E-03	1.523	0.169	1.524	0.169	151.62	4.06	230.90	25.63	7.243	0.039	7.832	0.171	pleckstrin homology domain containing, family A (phosphoinositide binding specific) member 8
6758361	Kdelc1|1700029F09	8.358E-04	1.523	0.075	1.563	0.077	69.57	11.75	105.93	5.20	6.082	0.229	6.724	0.069	KDEL (Lys-Asp-Glu-Leu) containing 1 | RIKEN cDNA 1700029F09 gene
6875662	Zmynd19	6.310E-03	1.521	0.182	1.544	0.184	155.13	19.78	235.92	28.18	7.255	0.175	7.863	0.164	zinc finger, MYND domain containing 19
6880623	Tmem62	7.085E-06	1.518	0.027	1.530	0.028	388.28	32.94	589.56	10.64	8.590	0.126	9.203	0.026	transmembrane protein 62
6884710	Rbm17	1.790E-06	1.513	0.055	1.522	0.056	372.33	28.51	563.21	20.54	8.531	0.115	9.136	0.054	RNA binding motif protein 17
6844496	Rps10	5.038E-04	1.510	0.047	1.526	0.048	1596.16	161.05	2410.57	75.13	10.625	0.149	11.234	0.046	ribosomal protein S10
7010434	Wdr44	8.287E-03	1.510	0.139	1.538	0.141	49.72	6.79	75.07	6.89	5.609	0.197	6.218	0.132	WD repeat domain 44
6817416	Vdac2	1.035E-04	1.497	0.106	1.507	0.107	1194.88	99.48	1788.69	126.75	10.213	0.116	10.797	0.103	voltage-dependent anion channel 2
7010854	Xiap	4.250E-04	1.497	0.031	1.536	0.032	211.12	35.22	316.02	6.61	7.685	0.227	8.303	0.030	X-linked inhibitor of apoptosis
6854446	Rhbdl1	6.495E-04	1.493	0.138	1.496	0.138	107.34	4.71	160.26	14.79	6.743	0.062	7.313	0.128	rhomboid, veinlet-like 1 (Drosophila)
6880583	Snap23	1.279E-03	1.483	0.179	1.490	0.179	845.90	60.89	1254.43	151.05	9.717	0.101	10.273	0.167	synaptosomal-associated protein 23
6753594	F13b	3.400E-03	1.479	0.136	1.487	0.137	1659.13	128.01	2453.75	226.02	10.688	0.108	11.249	0.130	coagulation factor XIII, beta subunit
6823058	Dnajc9	1.712E-05	1.477	0.065	1.489	0.065	80.66	7.39	119.10	5.23	6.322	0.129	6.893	0.064	DnaJ (Hsp40) homolog, subfamily C, member 9
6974490	Agpat5	6.938E-04	1.458	0.070	1.477	0.071	69.34	8.21	101.08	4.83	6.097	0.163	6.656	0.070	1-acylglycerol-3-phosphate O-acyltransferase 5 (lysophosphatidic acid acyltransferase, epsilon)
6883643	Rbm38	6.961E-06	1.440	0.081	1.442	0.081	135.66	4.71	195.38	11.02	7.082	0.050	7.605	0.084	RNA binding motif protein 38
6966233	Mif	6.267E-04	1.437	0.147	1.446	0.148	2594.95	210.41	3728.81	381.13	11.332	0.113	11.850	0.141	macrophage migration inhibitory factor
6876023	Slc27a4	2.133E-03	1.427	0.099	1.444	0.100	308.45	33.89	440.19	30.62	8.252	0.158	8.775	0.100	solute carrier family 27 (fatty acid transporter), member 4
6849325	Spsb3	3.523E-03	1.424	0.092	1.427	0.092	119.66	5.63	170.44	11.02	6.900	0.067	7.407	0.091	splA/ryanodine receptor domain and SOCS box containing 3
6859837	Wdr36	2.723E-04	1.423	0.085	1.432	0.085	246.55	19.87	350.74	20.86	7.936	0.116	8.449	0.086	WD repeat domain 36
6882582	Ergic3	4.552E-03	1.421	0.030	1.449	0.030	884.42	121.54	1256.49	26.24	9.760	0.204	10.295	0.030	ERGIC and golgi 3
6825137	Nupl1|Mir719	1.174E-05	1.408	0.159	1.409	0.159	325.86	8.84	458.71	51.67	8.347	0.039	8.824	0.156	nucleoporin like 1 | microRNA 719
6823889	Bmpr1a	1.282E-03	1.405	0.093	1.412	0.093	394.82	27.99	554.71	36.68	8.618	0.100	9.110	0.093	bone morphogenetic protein receptor, type 1A
6983339	9130011J15Rik	6.348E-04	1.404	0.148	1.414	0.149	434.77	34.65	610.55	64.22	8.755	0.119	9.239	0.148	RIKEN cDNA 9130011J15 gene
6971017	Gga2	5.323E-03	1.404	0.119	1.426	0.121	173.32	22.68	243.27	20.67	7.414	0.179	7.916	0.123	golgi associated, gamma adaptin ear containing, ARF binding protein 2
6800973	Cox6c	1.569E-04	1.382	0.110	1.390	0.110	8165.73	598.78	#######	895.32	12.988	0.106	13.454	0.113	cytochrome c oxidase, subunit VIc

6854338	Atp6v0c	4.545E-03	1.381	0.075	1.384	0.075	2135.42	98.72	2949.67	159.27	11.057	0.067	11.522	0.080	ATPase, H+ transporting, lysosomal V0 subunit C
6747471	Rrs1	2.106E-06	1.373	0.027	1.376	0.027	143.58	5.89	197.19	3.91	7.163	0.059	7.623	0.029	RRS1 ribosome biogenesis regulator homolog (S. cerevisiae)
6890985	1700037H04Rik	4.179E-03	1.368	0.076	1.369	0.076	182.35	5.99	249.37	13.85	7.509	0.048	7.958	0.079	RIKEN cDNA 1700037H04 gene
6983698	Usp38	3.160E-03	1.366	0.080	1.373	0.080	234.35	17.34	320.03	18.71	7.865	0.103	8.317	0.083	ubiquitin specific peptidase 38
6751709	Bok	1.809E-05	1.365	0.041	1.366	0.041	284.50	5.45	388.48	11.54	8.152	0.028	8.600	0.044	BCL2-related ovarian killer protein
6881249	Cdc25b	2.696E-03	1.363	0.090	1.363	0.090	91.94	0.23	125.28	8.32	6.523	0.004	6.962	0.098	cell division cycle 25 homolog B (S. pombe)
6859415	Zfp397	2.462E-03	1.361	0.139	1.366	0.140	112.96	6.45	153.78	15.73	6.815	0.084	7.250	0.147	zinc finger protein 397
6869766	Ubtd1	3.400E-03	1.359	0.092	1.360	0.092	170.78	3.65	232.08	15.73	7.415	0.031	7.852	0.095	ubiquitin domain containing 1
6854416	Ube2i	1.671E-06	1.351	0.046	1.356	0.046	453.13	27.95	612.33	20.77	8.818	0.087	9.256	0.050	ubiquitin-conjugating enzyme E2I
6859836	Wdr36	2.498E-04	1.351	0.059	1.355	0.060	277.95	14.24	375.59	16.51	8.115	0.073	8.550	0.063	WD repeat domain 36
6880556	Pla2g4b|Jmjd7	1.067E-03	1.342	0.119	1.344	0.119	126.25	5.03	169.44	15.05	6.978	0.059	7.393	0.133	phospholipase A2, group IVB (cytosolic) | jumonji domain containing 7
6826279	Wbp4	7.278E-05	1.336	0.086	1.344	0.086	110.60	8.42	147.76	9.50	6.781	0.111	7.201	0.093	WW domain binding protein 4
6982999	1810029B16Rik	1.484E-07	1.334	0.058	1.341	0.058	71.25	5.04	95.05	4.14	6.148	0.100	6.568	0.062	RIKEN cDNA 1810029B16 gene
6847834	H3f3a|Gm12657	3.144E-03	1.334	0.054	1.340	0.054	65.74	4.63	87.66	3.52	6.032	0.099	6.452	0.057	H3 histone, family 3A | predicted gene 12657
6836979	Txn2	3.546E-04	1.320	0.059	1.326	0.059	2044.53	132.22	2699.07	119.62	10.991	0.096	11.395	0.065	thioredoxin 2
6881197	Ptpra	3.304E-04	1.317	0.051	1.327	0.052	298.51	25.84	392.99	15.28	8.210	0.129	8.616	0.055	protein tyrosine phosphatase, receptor type, A
6885733	Zdhhc12	5.614E-05	1.315	0.054	1.319	0.054	364.30	19.59	479.16	19.72	8.505	0.076	8.902	0.059	zinc finger, DHHC domain containing 12
6825888	Itm2b	1.993E-04	1.312	0.083	1.313	0.083	2447.37	69.27	3211.50	202.06	11.256	0.041	11.643	0.094	integral membrane protein 2B
6885871	Dnm1	2.525E-04	1.308	0.101	1.310	0.101	77.39	3.37	101.23	7.78	6.271	0.062	6.653	0.114	dynamin 1
6864762	Fchsd1|Rell2	4.26E-05	1.305	0.032	1.310	0.032	111.99	6.64	146.16	3.54	6.802	0.086	7.191	0.035	FCH and double SH3 domains 1 | RELT-like 2
6792297	D11Wsu99e|Cog1	6.086E-05	1.291	0.119	1.291	0.119	230.30	0.33	297.23	27.36	7.847	0.002	8.204	0.128	DNA segment, Chr 11, Wayne State University 99, expressed | component of oligomeric golgi complex 1
6818067	Parg	4.430E-03	1.287	0.040	1.289	0.040	176.86	5.79	227.70	7.01	7.465	0.048	7.830	0.044	poly (ADP-ribose) glycohydrolase
6885422	Traf2	2.336E-06	1.272	0.060	1.274	0.060	109.72	4.63	139.53	6.60	6.775	0.061	7.121	0.069	TNF receptor-associated factor 2
6885506	Surf4	1.031E-03	1.269	0.015	1.271	0.015	916.62	35.42	1163.16	13.65	9.838	0.055	10.184	0.017	surfeit gene 4
6756478	Lamb3	1.827E-03	1.257	0.059	1.258	0.059	73.26	2.23	92.05	4.31	6.194	0.044	6.521	0.068	laminin, beta 3
6769138	Bsg	1.307E-05	1.254	0.060	1.256	0.060	5298.65	211.43	6644.60	317.98	12.369	0.057	12.695	0.070	basigin
6889902	Actc1	2.711E-03	1.254	0.035	1.259	0.035	68.19	4.10	85.50	2.37	6.086	0.090	6.417	0.041	actin, alpha, cardiac muscle 1
6977687	Ddx39	4.120E-07	1.250	0.040	1.251	0.040	101.34	2.34	126.70	4.00	6.662	0.033	6.984	0.045	DEAD (Asp-Glu-Alâ--Asp) box polypeptide 39
6751505	Cops8	4.225E-04	1.242	0.065	1.248	0.065	377.49	26.73	468.95	24.48	8.553	0.099	8.869	0.076	COP9 (constitutive photomorphogenic) homolog, subunit 8 (Arabidopsis thaliana)
6855158	H2-t9|Gm8909|EG5	3.00E-05	1.222	0.078	1.251	0.080	87.08	12.49	106.45	6.78	6.411	0.227	6.728	0.090	MHC class Ib T9 | predicted gene 8909 | predicted gene, EG547347 | predicted gene 10499
6880640	Pdia3	5.543E-05	1.221	0.031	1.225	0.031	2216.53	126.64	2706.87	69.03	11.109	0.084	11.401	0.037	protein disulfide isomerase associated 3
6883273	Ddx27	3.389E-04	1.199	0.014	1.203	0.014	141.69	8.05	169.89	2.03	7.142	0.082	7.408	0.017	DEAD (Asp-Glu-Alâ--Asp) box polypeptide 27
6856232	Znrf4	1.146E-03	1.148	0.046	1.148	0.046	34.84	0.23	39.98	1.59	5.122	0.010	5.319	0.059	zinc and ring finger 4
6963163	Dub1|Usp---ps|Dub3	1.017E-03	1.143	0.035	1.143	0.035	35.36	0.30	40.41	1.25	5.144	0.012	5.335	0.044	deubiquitinating enzyme 1 | ubiquitin specific peptidase, pseudogene (USP17 homolog) | deubiquitinating enzyme 3
6861322	Rbm22	2.003E-03	1.112	0.027	1.112	0.027	257.41	3.14	286.21	6.89	8.008	0.018	8.160	0.034	RNA binding motif protein 22
6988346	Olfr969	9.165E-03	1.074	0.025	1.074	0.025	21.18	0.16	22.74	0.53	4.404	0.011	4.507	0.034	olfactory receptor 969
6843643	Tcfap4	6.963E-04	1.056	0.002	1.056	0.002	92.87	1.44	98.09	0.20	6.537	0.022	6.616	0.003	transcription factor AP4
6803226	Serpina1d|Serpina1	6.60E-09	1.030	0.159	1.032	0.159	3998.84	147.43	4120.38	635.81	11.963	0.054	11.976	0.213	serine (or cysteine) peptidase inhibitor, clade A, member 1D | member 1B | member 1E | member 1A | member 1C
7023426	Ssty2|LOC10004074	1.046E-03	0.961	0.007	0.961	0.007	22.44	0.26	21.56	0.16	4.488	0.016	4.430	0.011	spermiogenesis specific transcript on the Y 2 | similar to Ssty2 protein | y-linked testis-specific protein 1-like
6970349	Ric3	1.235E-03	0.925	0.010	0.925	0.010	38.38	0.20	35.51	0.39	5.262	0.008	5.150	0.016	resistance to inhibitors of cholinesterase 3 homolog (C. elegans)
6995454	Ncam1	2.084E-03	0.898	0.026	0.898	0.026	52.73	0.85	47.33	1.35	5.720	0.023	5.564	0.042	neural cell adhesion molecule 1
6899250	Pygo2	1.620E-07	0.885	0.011	0.885	0.011	101.30	1.40	89.61	1.10	6.662	0.020	6.485	0.018	pygopus 2
6827820	Dzip1|Cldn10	4.841E-03	0.865	0.008	0.866	0.008	46.83	1.80	40.51	0.39	5.547	0.055	5.340	0.014	DAZ interacting protein 1 | claudin 10
6995534	Sik2	3.526E-06	0.862	0.030	0.864	0.030	190.69	8.16	164.44	5.65	7.572	0.062	7.360	0.049	salt inducible kinase 2
6792496	Trim65	4.817E-06	0.859	0.028	0.860	0.028	133.02	3.89	114.25	3.73	7.054	0.042	6.835	0.048	tripartite motif-containing 65
6875804	Fam69b	7.350E-03	0.849	0.030	0.850	0.030	78.89	3.65	66.94	2.39	6.299	0.066	6.063	0.051	family with sequence similarity 69, member B
6957141	Cd4	8.192E-05	0.847	0.050	0.847	0.050	62.27	1.63	52.72	3.10	5.960	0.037	5.715	0.083	CD4 antigen
6809047	Lhfpl2	2.509E-05	0.846	0.019	0.847	0.019	124.33	4.39	105.22	2.36	6.956	0.051	6.716	0.033	lipoma HMGIC fusion partner-like 2
6996451	Tln2|Mir190	1.279E-03	0.833	0.034	0.834	0.034	67.94	2.47	56.59	2.32	6.084	0.052	5.820	0.060	talin 2 | microRNA 190
6916836	Rims3	1.079E-03	0.832	0.040	0.833	0.040	74.55	2.15	62.04	2.96	6.219	0.041	5.952	0.070	regulating synaptic membrane exocytosis 3
6934119	Hvcn1|Tctn1|Gm35	3.588E-03	0.830	0.030	0.832	0.031	57.78	3.13	47.96	1.76	5.848	0.076	5.582	0.054	hydrogen voltage-gated channel 1 | tectonic family member 1 | predicted gene 3579
6939178	Scfd2	4.321E-04	0.821	0.011	0.823	0.011	83.21	3.67	68.33	0.88	6.376	0.065	6.094	0.019	Sec1 family domain containing 2
6756130	Esrrg	7.298E-03	0.811	0.012	0.811	0.012	52.90	0.62	42.92	0.65	5.725	0.017	5.423	0.022	estrogen-related receptor gamma
6784291	Dhx8	1.021E-03	0.810	0.006	0.810	0.006	181.63	1.58	147.13	1.11	7.505	0.013	7.201	0.011	DEAH (Asp-Glu-Alâ--His) box polypeptide 8
6771662	Smarcc2	7.433E-04	0.804	0.029	0.805	0.029	380.73	14.78	306.11	10.86	8.570	0.056	8.256	0.052	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 2
6787102	Nprl3	3.357E-05	0.799	0.019	0.800	0.019	150.32	2.21	120.16	2.82	7.232	0.021	6.908	0.034	nitrogen permease regulator-like 3 (S. cerevisiae)
6812973	Kif13a	1.152E-04	0.797	0.019	0.798	0.019	104.79	2.30	83.55	1.96	6.711	0.032	6.384	0.034	kinesin family member 13A
6965979	Ccdc97	2.365E-05	0.797	0.018	0.800	0.018	356.83	19.74	284.41	6.48	8.475	0.081	8.151	0.033	coiled-coil domain containing 97
6788796	Gm16515	6.472E-03	0.794	0.055	0.797	0.055	177.40	9.71	140.93	9.73	7.466	0.081	7.132	0.097	
6782643	Phf12	3.438E-03	0.789	0.037	0.789	0.037	186.47	2.59	147.11	6.85	7.543	0.020	7.198	0.066	PHD finger protein 12
6966926	Prr12	1.387E-03	0.780	0.043	0.783	0.043	183.84	9.61	143.47	7.89	7.518	0.077	7.160	0.080	proline rich 12
6922966	Bnc2	3.634E-04	0.780	0.012	0.780	0.012	55.82	1.73	43.51	0.66	5.801	0.045	5.443	0.022	basonuclin 2
6937654	Hs3st1	8.286E-03	0.767	0.044	0.770	0.044	55.10	3.58	42.26	2.41	5.778	0.092	5.397	0.080	heparan sulfate (glucosamine) 3-O-sulfotransferase 1
6811368	A530099J19Rik	2.878E-03	0.751	0.026	0.758	0.026	37.99	3.52	28.54	0.98	5.234	0.140	4.833	0.050	RIKEN cDNA A530099J19 gene
6958439	Dennd5b	2.028E-03	0.751	0.054	0.758	0.054	465.77	45.32	349.70	25.06	8.850	0.137	8.443	0.103	DENN/MADD domain containing 5B
6813078	Phf2	3.009E-04	0.751	0.078	0.752	0.078	238.99	8.49	179.41	18.56	7.899	0.051	7.472	0.149	PHD finger protein 2
6811512	Zfp192	4.991E-03	0.746	0.013	0.747	0.013	95.56	3.03	71.28	1.26	6.577	0.046	6.155	0.025	zinc finger protein 192
6993834	Kank2	6.823E-03	0.746	0.050	0.748	0.050	227.16	10.52	169.43	11.42	7.824	0.068	7.398	0.095	KN motif and ankyrin repeat domains 2
6915650	Inadl	5.342E-05	0.745	0.007	0.748	0.007	98.18	6.22	73.13	0.73	6.612	0.089	6.192	0.014	InaD-like (Drosophila)
6989217	Dnaja4	8.737E-05	0.743	0.050	0.743	0.050	81.03	0.94	60.20	4.03	6.340	0.017	5.906	0.094	DnaJ (Hsp40) homolog, subfamily A, member 4
6782610	Myo18a	1.331E-03	0.740	0.067	0.740	0.067	249.83	3.10	184.88	16.74	7.965	0.018	7.518	0.138	myosin XVIIIA
6958147	Sox5	4.704E-07	0.735	0.006	0.736	0.006	138.85	4.91	102.09	0.86	7.116	0.051	6.674	0.012	SRY-box containing gene 5
6838386	Adcy6	2.066E-04	0.727	0.043	0.727	0.043	160.53	5.37	116.65	6.95	7.325	0.047	6.861	0.087	adenylate cyclase 6
6955879	Foxp1|9130401L11	7.422E-03	0.719	0.070	0.723	0.071	260.03	17.80	187.01	18.32	8.016	0.097	7.534	0.136	forkhead box P1 | eukaryotic translation initiation factor 4E member 3
6941150	2900026A02Rik	1.492E-05	0.695	0.047	0.696	0.047	610.53	14.12	424.61	28.70	9.253	0.033	8.723	0.101	RIKEN cDNA 2900026A02 gene
6934216	Setd1b	1.124E-04	0.693	0.034	0.704	0.034	243.24	30.43	168.50	8.20	7.904	0.180	7.393	0.070	SET domain containing 1B
6965950	Ceacam2|Ceacam1	2.756E-07	0.689	0.015	0.700	0.015	598.91	77.33	412.43	8.95	9.203	0.180	8.687	0.032	carcinoembryonic antigen-related cell adhesion molecule 2 | carcinoembryonic antigen-related cell adhesion molecule 1
6952284	Grm8	5.211E-03	0.680	0.039	0.692	0.039	48.51	6.30	32.99	1.87	5.576	0.188	5.039	0.082	glutamate receptor, metabotropic 8
6807564	Dapk1	4.083E-03	0.680	0.032	0.680	0.032	540.92	6.78	367.81	17.56	9.079	0.018	8.520	0.067	death associated protein kinase 1

6967969	Lrrk1	3.022E-03	0.679	0.057	0.684	0.057	135.42	11.15	91.99	7.69	7.071	0.124	6.513	0.125	leucine-rich repeat kinase 1
6815599	Pik3r1	5.359E-04	0.673	0.073	0.679	0.074	543.94	51.13	366.24	39.90	9.075	0.134	8.498	0.168	phosphatidylinositol 3-kinase, regulatory subunit, polypeptide 1 (p85 alpha)
6781689	Hs3st3a1|Hs3st3b1	2.654E-04	0.668	0.103	0.671	0.104	405.90	29.21	271.01	41.99	8.657	0.107	8.046	0.229	heparan sulfate (glucosamine) 3-O-sulfotransferase 3A1 | heparan sulfate (glucosamine) 3-O-sulfotransferase 3B1
6989948	Rbpms2	8.521E-04	0.667	0.043	0.671	0.043	741.66	56.28	494.59	31.85	9.527	0.106	8.944	0.091	RNA binding protein with multiple splicing 2
6908528	Palmd	4.024E-03	0.657	0.020	0.664	0.020	1146.49	123.43	752.97	22.96	10.147	0.149	9.555	0.044	palmdelphin
6952137	Cadps2	1.893E-04	0.648	0.052	0.653	0.052	71.67	6.42	46.42	3.73	6.151	0.132	5.528	0.114	Ca2+-dependent activator protein for secretion 2
6803284	Serpina3c|Serpina3	5.479E-04	0.636	0.073	0.640	0.073	236.85	20.22	150.59	17.28	7.877	0.122	7.216	0.163	serine (or cysteine) peptidase inhibitor, clade A, member 3C | serine (or cysteine) peptidase inhibitor, clade A, member 3K
6899016	Arhgef11|4933430	5.968E-03	0.636	0.075	0.637	0.075	253.83	11.59	161.32	18.95	7.985	0.065	7.313	0.174	Rho guanine nucleotide exchange factor (GEF) 11 | RIKEN cDNA 4933430H15 gene
6906749	Sema4a	5.809E-03	0.632	0.077	0.640	0.078	921.51	102.33	582.79	71.12	9.830	0.161	9.167	0.168	sema domain, immunoglobulin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 4A
6904979	Setd7	3.405E-03	0.619	0.057	0.625	0.057	128.50	11.99	79.58	7.30	6.993	0.135	6.302	0.135	SET domain containing (lysine methyltransferase) 7
6909278	Enpep	5.188E-03	0.605	0.063	0.608	0.063	603.82	41.02	365.34	38.00	9.231	0.102	8.498	0.144	glutamyl aminopeptidase
6945032	Smo	6.091E-04	0.597	0.040	0.604	0.041	270.24	27.64	161.32	10.84	8.062	0.154	7.327	0.100	smoothened homolog (Drosophila)
6820113	Gfra2	3.893E-03	0.593	0.078	0.594	0.078	122.75	4.45	72.76	9.62	6.938	0.052	6.160	0.191	glial cell line derived neurotrophic factor family receptor alpha 2
6778358	Sec14l4	1.087E-04	0.582	0.023	0.583	0.023	1751.94	74.36	1019.95	40.78	10.772	0.063	9.992	0.058	SEC14-like 4 (S. cerevisiae)
6846197	Bbx|A730021G18Ri	2.411E-03	0.579	0.037	0.581	0.037	133.90	8.31	77.52	4.98	7.060	0.088	6.271	0.091	bobby sox homolog (Drosophila) | RIKEN cDNA A730021G18 gene | RIKEN cDNA A930011E06 gene
6749933	Adam23	2.116E-03	0.560	0.107	0.562	0.107	186.41	12.13	104.40	19.90	7.536	0.092	6.646	0.304	a disintegrin and metallopeptidase domain 23
6873133	Pik3ap1	3.010E-05	0.553	0.050	0.560	0.050	1446.64	152.58	800.10	71.75	10.481	0.162	9.633	0.126	phosphoinositide-3-kinase adaptor protein 1
6949593	Slc6a12	2.004E-03	0.551	0.027	0.563	0.027	1271.79	192.93	701.01	33.92	10.282	0.208	9.450	0.072	solute carrier family 6 (neurotransmitter transporter, betaine/GABA), member 12
7016584	Dcaf12l1	1.218E-03	0.528	0.042	0.529	0.042	105.47	5.84	55.64	4.41	6.716	0.082	5.789	0.110	DDB1 and CUL4 associated factor 12-like 1
6959254	Cyp2b13|Rnf170|C	5.10E-05	0.500	0.258	0.511	0.264	1087.66	151.87	543.41	280.38	10.055	0.220	8.728	0.691	cytochrome P450, family 2, subfamily b, polypeptide 13 | polypeptide 9 | ring finger protein 170 | Dmx-like 1
6869545	Pde6c	4.61E-05	0.494	0.010	0.578	0.011	78.09	32.13	38.59	0.74	6.060	0.556	5.270	0.028	phosphodiesterase 6C, cGMP specific, cone, alpha prime
6943822	Casd1	7.208E-04	0.489	0.131	0.494	0.132	170.52	17.29	83.38	22.29	7.398	0.154	6.271	0.407	CAS1 domain containing 1
6874610	Bend7|Prc1	7.142E-04	0.435	0.059	0.438	0.059	183.28	17.22	79.69	10.74	7.506	0.130	6.288	0.206	BEN domain containing 7 | protein regulator of cytokinesis 1
6895460	Zfhx4	7.278E-03	0.435	0.046	0.455	0.048	114.07	25.31	49.57	5.26	6.767	0.304	5.616	0.147	zinc finger homeodomain 4
6900071	Ngf	8.58E-05	0.277	0.089	0.498	0.160	472.75	347.05	130.93	41.98	8.039	1.080	6.890	0.448	nerve growth factor
6932190	Csn3	4.37E-05	0.273	0.116	0.571	0.242	178.26	140.42	48.64	20.62	6.413	1.234	5.369	0.561	casein kappa
6778972	Egfr	9.10E-05	0.272	0.039	0.316	0.045	1270.58	486.28	346.00	49.65	10.094	0.562	8.407	0.198	epidermal growth factor receptor
6915847	Lepr	1.63E-05	0.177	0.007	0.316	0.013	485.46	345.43	85.84	3.55	8.087	1.106	6.421	0.060	leptin receptor
6989195	Gldn	9.62E-06	0.156	0.022	0.242	0.034	323.04	212.68	50.30	7.06	7.698	0.932	5.623	0.209	gliomedin
6938093	Ppargc1a	1.29E-05	0.131	0.043	0.182	0.059	639.76	367.73	84.11	27.25	8.849	0.807	6.226	0.505	peroxisome proliferative activated receptor, gamma, coactivator 1 alpha
6832572	Miox	1.12E-06	0.124	0.004	0.325	0.010	340.77	291.65	42.40	1.35	7.027	1.414	5.405	0.046	myo-inositol oxygenase
6964531	Dmbt1	7.43E-07	0.101	0.003	0.179	0.006	462.16	288.94	46.70	1.47	8.031	1.208	5.544	0.045	deleted in malignant brain tumors 1
7016826	Gpc3	7.66E-07	0.085	0.002	0.180	0.005	602.14	460.57	51.35	1.40	8.160	1.289	5.681	0.039	glypican 3
6810697	Akr1c18	4.14E-07	0.042	0.005	0.110	0.013	754.10	518.98	32.02	3.84	8.188	1.733	4.981	0.167	aldo-keto reductase family 1, member C18

Supporting Materials and Methods

Blood Chemistry Analysis

Hematology analysis was performed using un-clotted blood from SRSF3HKO and WT mice. Fasting blood glucose concentrations were measured using ACCU-Check glucometer (Roche). Serum triglycerides were measured using Triglyceride ELISA Kit (LabAssay from Wako Chemicals USA) following the manufacturers' instructions.

Glucose Tolerance Test (GTT) and Insulin Tolerance Test (ITT)

To assess glucose tolerance, WT and HKO mice were fasted for 6 h. Blood glucose concentrations were measured by tail bleeding using an ACCU-Check glucometer, at time 0 and indicated times thereafter, for a total of 2 h, after an ip injection of glucose of 1 gm/kg body weight. For ITTs, mice were fasted for 4 hours and insulin used for ip injection was 0.5U/ kg body weight.

Isolation of Primary Murine Hepatocytes:

Primary hepatocytes from WT and SRSF3HKO liver were obtained by two-step perfusion with liver perfusion medium (Gibco BRL 17701-038; Gibco, Detroit, MI) followed by digestion medium, L15 (Sigma L5520; Sigma, St. Louis, MO) containing 0.15 g/ml collagenase and 10 µg/ml DNase I. Liver cells were disaggregated by passing through a 40-µm-pore nylon mesh Cell Strainer (BD Falcon). The numbers of total viable cells were determined by Trypan blue staining.

Confirmation of Altered Splicing and Gene Expression.

Total RNA was reverse transcribed using random hexamers with MultiScribe MuLV reverse transcriptase (Applied Biosystems) then subjected to PCR using GoTaq polymerase (Promega). For confirmation of exon skipping, RT-PCR was done on each sample using primers on constitutive exons flanking the altered exon. To ensure a linear PCR amplification allowing semi-quantitative assessment of the spliced products, we performed PCR analysis with 25 cycles. Representative results from each group (WT and HKO) are shown in the figures. PCR products were separated on 3% agarose or 12% non-denaturing polyacrylamide gels, stained with

ethidium bromide, visualized and quantified with Kodak Electrophoresis Documentation and Analysis System (EDAS) 290.

For mRNA expression studies, real-time quantitative RT-PCR assays were performed for each sample in triplicate in a final reaction volume of 20 µl. The endogenous housekeeping gene *Gapdh* or the gene of interest was amplified using 20 ng of cDNA with iTaq SYBR Green supermix with ROX (Bio-Rad Laboratories) on Chromo4 Thermal Cyclers (Bio-Rad). The data were analyzed using the DDCt method and presented as the relative change in gene expression, normalized to *Gapdh*. All primers for qPCR were designed with Universal Probe Library (Roche).

Growth hormone treatment.

1-month-old mice were starved overnight and injected intraperitoneally with 5 mg of GH/kg BW in normal saline (0.9% NaCl) in a final volume of 0.2 ml. Animals injected with saline were used to evaluate basal conditions. The animals were sacrificed 7.5 min after injection, the livers were removed and snap frozen for protein isolation.

Analysis of Microarray data

Expression data from exon array were analyzed by two methods: 1) data were normalized by RMA and analyzed by ANOVA using Genespring (Agilent Technologies, Santa Clara, CA); 2) data were normalized by RMA and analyzed by ANOVA using Non-Coder (http://noncoder.mpi-bn.mpg.de/#); and 3) unnormalized raw data was analyzed using a Bayesian variance modeling approach in VAMPIRE. In all cases multiple testing correct was applied using a FDR q-value<0.05. Lists of significant genes by the different approaches were imported into GeneSpring for visualization and compilation. Enrichment analyses were performed on the list of altered genes using GeneGo's Metacore software (St. Joseph, MI), and on the raw data using Gene Set Enrichment Analysis (GSEA, Broad Institute, Cambridge, MA).

IGF2 and insulin treatment:

IGF2 and insulin treatment were performed using primary hepatocytes from SRSF3HKO and age matched WT mice. After plating and attachment, primary hepatocytes were serum starved for 5 hrs and then treated with IGF2 (50 or 100 ng/ml) or insulin (30 or 100 nM) for 5 minutes.

Immunoblotting and Immunohistochemistry

For immunoblotting, livers or primary hepatocytes were lysed in extraction buffer (20mM Tris, pH 7.9; 300 mM NaCl; 1% Nonidet P-40) supplemented with protease and phosphatase inhibitors. Liver/hepatocyte lysates were separated by SDS-PAGE, transferred to PVDF membranes and immunoblotted with primary antibodies followed by HRP-conjugated secondary antibodies and developed using an ECL+ kit (GE).

Antibodies used for immunoblotting : anti-phospho STAT5 (M-186) rabbit polyclonal antibody (1:1000 dilutions, Cell Signaling Technologies), anti-insulin/insulin-like growth factor -1 receptor dual phosphospecific (pYpY1162/1163) rabbit polyclonal (Biosource International, Camarilo, CA, USA), anti-Insulin receptor beta rabbit polyclonal (BD Transduction Laboratories), non-phospho (active) beta catenin (Ser33/37/Thr41)(D13A1) rabbit monoclonal antibody (Cell Signaling Technologies), phosphor-Gsk-3 Beta rabbit polyclonal antibody (Cell Signaling Technologies), anti-cyclin D1 rabbit polyclonal antibody (abcam), anti- c-Myc rabbit polyclonal antibody (Cell Signaling Technologies), anti-total/phospho-AKT (Cell Signaling Technologies), anti-total/phospho ERK1/2 rabbit polyclonal antibody (Cell Signaling Technologies), anti-STAT5 rabbit polyclonal antibody (Cell Signaling Technologies), anti-phospho-NFkB-65 rabbit polyclonal antibody (Cell Signaling Technologies), anti-phospho-JNK/SAPK rabbit polyclonal antibody (Cell Signaling Technologies).

Immunohistochemistry was performed on formalin-fixed, paraffin-embedded mouse liver sections using the following antibodies: anti-F/480 (MCA497B, AbD Serotec, UK), anti-IGF2 (abcam, ab63984), anti-SRSF3 (abcam, ab125124), anti-Laminin (abcam, ab80580). Alpha-smooth muscle actin staining was performed using Actin, α-Smooth Muscle, Immunohistology Kit (Sigma). TUNEL staining was carried out using ApopTag Peroxidase In Situ Apoptosis Detection Kit (Millipore). H&E-stained sections were analyzed for inflammation according to the following scoring system: 0, no inflammation; 1, mild lymphocytic infiltration in the portal triad; 2, severe lymphocytic infiltration in portal triad; 3, extended infiltration of lymphocytes throughout liver. Sections were scored for steatosis according to the following scale: 0, no steatosis; 1, microsteatosis; 2, microsteatosis and mild macrosteatosis; 3, severe macrosteatosis. Sirius red stained sections were analyzed for fibrosis as follows: 0, no fibrosis; 1, mild fibrosis in the portal triad; 2, severe fibrosis in portal triad; 3: bridging fibrosis.

For the human liver cancer tissue array (LV1503, US Biomax) and the pathological samples of HCC and normal liver, immunohistochemistry was performed using anti-SRSF3 rabbit polyclonal antibody (abcam, ab125124) with Super PicTure Polymer Detection Kit (Invitrogen Corporation, Frederick, MD).