Research Article

BIOMEDICAL
Journal of Scientific & Technical Research

ISSN: 2574 -1241

DOI: 10.26717/BJSTR.2023.48.007604

Ferroptosis-Related Long Non-coding RNA Model Predicts Hepatocellular Carcinoma Prognosis

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ARTICLE INFO

Received: December 22, 2022

Published: January 13, 2023

Citation: Congyue Zhang, Chaoqun Zhang, Huifang Zhou, Zhankai Hu and Dianxing Sun. Ferroptosis-Related Long Non-coding RNA Model Predicts Hepatocellular Carcinoma Prognosis. Biomed J Sci & Tech Res 48(1)-2023. BJSTR. MS.ID.007601.

ABSTRACT

Background: Hepatocellular carcinoma (HCC) is a prevalent malignancy worldwide, and ferroptosis is an iron-dependent cell death process. In addition, the aberrant expression of long noncoding RNAs (lncRNAs) that contribute to the development and progression of HCC has garnered increased interest. Materials and Methods: We collected lncRNA expression profiles associated with ferroptosis and clinicopathological information from The Cancer Genome Atlas (TCGA) and FerrDb databases. The relationship between ferroptosis-related lncRNAs (FRlncRNAs) and HCC patients' survival is determined by co-expression analysis of overall survival (OS). Using Cox regression analysis and the LASSO algorithm, a prognostic lncRNA model of 22 differentially expressed lncRNAs was developed. Results: high-risk lncRNA profile was associated with a poor prognosis in HCC, as determined by a Kaplan-Meier analysis. In predicting the prognosis of HCC, our risk assessment model outperformed conventional clinical data. GSEA uncovered immune and tumor-related pathways in high- and low-risk individuals. In addition, TCGA revealed that T cell functions, such as B cells, cytolytic macrophages, MHC-class-I, mast cells, neutrophils, NK cells, helper T cells, Type-I-IFN, and Type-II-IFN, differed significantly between high- and low-risk groups. Immune checkpoints were also differentially expressed between the risk groups, including TNFSF18, IDO2, CD276, NRP1, and TNFSF4. Conclusion: Based on lncRNAs associated with ferroptosis, our findings provide a robust prognostic and immune response prediction model for HCC patients.

Keywords: Hepatocellular Carcinoma; Lncrna; Ferroptosis; Gene; Immune

Abbreviations: FRlncRNAs: Ferroptosis-Related lncRNAs; HCC: Hepatocellular Carcinoma; lncRNAs: Long Non-Coding RNAs; TCGA: The Cancer Genome Atlas; OS: Overall Survival; ROS: Reactive Oxygen Species; KEGG: Kyoto Encyclopedia of Genes and Genomes; GO: Gene Ontology; BP: Biological Processes; MF: Molecular Function; CC: Cellular Components; DEGs: Differentially Expressed Genes; GSEA: Gene Set Enrichment Analysis; FDR: False Discovery Rate; DCA: Decision Curve Analysis; ROC: Operating Characteristic Curve; ssGSEA: Single-Sample Gene Set Enrichment Analysis; HR: Hazard Ratio; CI: Confidence Interval.

Introduction

HCC is the most prevalent pathological subtype of primary liver cancer, the fifth most prevalent malignancy globally, and the third leading cause of cancer-related mortality [1]. Multiple factors, including the chronic hepatitis virus, heavy alcohol consumption, and chronic hepatitis due to nonalcoholic fatty cirrhosis, contribute to the development of HCC [2]. Surgical resection or liver transplantation can effectively control cancer progression and prolong survival in patients with HCC at an early stage. Nonetheless, greater than two-thirds of patients will experience recurrence [3], and these patients are frequently diagnosed at an intermediate or advanced stage when recurrence occurs. Furthermore, most patients have fewer surgical options due to age or physical condition. Therefore, the effectiveness of interventional therapy, radiotherapy, targeted therapy, and local ablation is limited, and the prognosis remains dismal [4]. Consequently, it is essential to investigate the potential molecular mechanisms and cellular signaling pathways in the pathogenesis of HCC, seek early diagnosis and treatment, study the expressed genes with prognostic value, and develop a model with predictive characteristics.

In recent years, ferroptosis research has increased exponentially. It is a programmed cell death that is iron-oxidatively reactive oxygen species (ROS)-dependent and lipid peroxidation-mediated [5]. The significance of ferroptosis in regulating metabolism and redox biology has been demonstrated, influencing the pathogenesis and treatment of cancers such as prostate cancer, gastric cancer, and HCC. Recently, ferroptosis induction has emerged as a promising treatment for cancers resistant to conventional treatment. Zhang, et al. [6,7] discovered that the tumor suppressor BAP1 inhibited cystine uptake by inhibiting SLC7A11 expression, resulting in increased lipid peroxidation and ferroptosis Sun, et al. [8]. discovered that p62 expression inhibited nuclear factor degradation of erythroid 2-related factor (NRF2) and increased NRF2 nuclear accumulation via the misfiring of kelch-like ECH-associated protein 1. Liu, et al. [9]. reported the correlation between ferroptosis and the immune system and concluded that this prognostic factor could be used to screen HCC patients for immunotherapy and targeted therapies [10]. Long noncoding RNAs (LncRNAs) are noncoding transcripts longer than 200 nucleotides that can modulate the expression of numerous genes associated with cancer. Recent research by Sun et al. revealed that high levels of lncRNA GA-binding protein subunit (GABPB1) antisense RNA 1 in HCC cells enhanced erastin-induced ferroptosis by inhibiting GABPB1 translation and peroxidase-5, resulting in inhibition of cellular antioxidant capacity and cell survival [11]. Zhang et al. analyzed the relationship between ferroptosis and tumor mutations in HCC to develop a ferroptosis-related gene model that may bridge the gap between ferroptosis and nuclear tumor mutations, thereby allowing for individualized treatment of HCC patients [12]. Using the TCGA database, this study constructed a model of prognosis-related lncRNAs. The role of ferroptosis-related lncRNAs, N6-methyladenosine (m6A) mRNA, and immune response in determining the prognosis of HCC has been investigated [13].

Materials and Methods

Data Sources and Clinical Information

From the TCGA database, RNA-sequence data and associated clinical data were extracted for 424 samples, including 374 HCC tissues and 50 normal liver tissues. An overview of the relevant clinical aspects of HCC patients can be found in Supplementary (Supplementary Table 1)., with 377 clinical data available for further analysis (Table 1). The collected clinical data for patients with HCC included their gender, age, grade, TNM stage, survival status, and survival time.

Supplementary Table 1: An overview of the relevant clinical aspects of HCC patients.

	An overview of relevant clinical aspects of						HCC patients			
Id	futime	fustat	Age		Gender	Grade	Stage	T	M	N
TCGA-5R-	449		0	17	FEMALE	G3	Stage IIIA	T3a	M0	N0
TCGA-DD-	602		0	20	FEMALE	G3	Stage I	T1	M0	N0
TCGA-ED-	390		0	20	FEMALE	G3	Stage II	T2	M0	NX
TCGA-RC-	15		0	20	FEMALE	G2	Stage IVA	T1	M0	N1
TCGA-CC-	219		0	24	FEMALE	G1	Stage IIIA	T3	M0	N0
TCGA-BW-	0		0	26	FEMALE	G3	Stage IV	T2	M1	N0
TCGA-DD-	827		1	29	FEMALE	G2	Stage III	T3	M0	N0
TCGA-WX-	556		1	33	FEMALE	G2	Stage IIIA	T3a	MX	NX
TCGA-FV-	366		1	38	FEMALE	G2	Stage I	T1	MX	NX
TCGA-CC-	344		1	39	FEMALE	G3	Stage IIIA	T3	M0	N0
TCGA-XR-	1339		0	43	FEMALE	G2	Stage I	T1	MX	NX
TCGA-DD-	1085		0	43	FEMALE	G3	Stage I	T1	M0	N0

TCGA-DD-	601		1	43	FEMALE	G2	Stage II	T2	M0	NX
TCGA-DD-	555		0	45	FEMALE	G4	Stage IIIA	T3a	M0	N0
TCGA-G3-	1553		0	45	FEMALE	G2	Stage IIIA	T3	M0	N0
TCGA-EP-	596		1	46	FEMALE	G2	Stage I	T1	MX	NX
TCGA-RC-	640		0	47	FEMALE	G3	Stage I	T1	M0	N0
TCGA-ED-	6		0	48	FEMALE	G3	Stage II	T2	M0	NX
TCGA-XR-	1030		0	49	FEMALE	G3	Stage IIIB	T3	M0	N0
TCGA-DD-	608		0	49	FEMALE	G1	Stage I	T1	M0	N0
TCGA-ED-	56		1	50	FEMALE	G3	Stage IIIA	T3a	M0	N0
TCGA-FV-	1		0	51	FEMALE	G2	Stage II	T2	M0	NX
TCGA-DD-	564		0	51	FEMALE	G4	Stage I	T1	M0	N0
TCGA-BC-	2116		1	51	FEMALE	G1	unknow	T1	MX	NX
TCGA-ED-	296		1	51	FEMALE	G3	Stage IIIA	T3a	M0	N0
TCGA-CC-	279		1	51	FEMALE	G2	Stage II	T2	M0	N0
TCGA-CC-	0		0	52	FEMALE	G2	Stage IIIA	T3a	M0	N0
TCGA-EP-	627		1	52	FEMALE	G3	Stage IIIA	T3a	MX	NX
TCGA-G3-	452		1	52	FEMALE	G3	Stage I	T1	M0	N0
TCGA-BC-	770		1	52	FEMALE	G2	Stage IIIA	T3a	MX	N0
TCGA-ED-	400		0	53	FEMALE	G3	Stage II	T2	M0	N0
TCGA-G3-	65		1	53	FEMALE	G3	Stage IIIA	T3a	M0	N0
TCGA-DD-	928		0	54	FEMALE	G2	Stage II	T2	M0	N0
TCGA-2Y-	2532		1	54	FEMALE	G1	Stage I	T1	MX	NX
TCGA-DD-	2425		0	55	FEMALE	G3	Stage II	T2	M0	N0
TCGA-2Y-	1939		0	55	FEMALE	G2	Stage I	T1	MX	NX
TCGA-DD-	555		0	55	FEMALE	G2	Stage I	T1	M0	N0
TCGA-ZP-	21		0	56	FEMALE	G2	unknow	T1	MX	NX
TCGA-DD-	2746		0	56	FEMALE	G3	Stage I	T1	M0	N0
TCGA-DD-	899		1	56	FEMALE	G3	Stage I	T1	M0	N0
TCGA-DD-	394		1	57	FEMALE	G3	Stage I	T1	M0	N0
TCGA-DD-	1560		1	57	FEMALE	G2	Stage I	T1	M0	N0
TCGA-G3-	412		0	58	FEMALE	G2	Stage II	T2	M0	N0
TCGA-PD-	639		1	58	FEMALE	G2	Stage IIIB	T4	M0	N0
TCGA-DD-	141		0	59	FEMALE	G2	Stage I	T1	M0	N0
TCGA-DD-	719		0	59	FEMALE	G3	Stage I	T1	M0	N0
TCGA-ED-	406		0	59	FEMALE	G3	Stage IIIA	T3a	M0	N0
TCGA-2Y-	555		1	59	FEMALE	G3	Stage I	T1	MX	N0
TCGA-ED-	854		0	60	FEMALE	G2	Stage II	T2	M0	N0
TCGA-CC-	250		0	60	FEMALE	G2	Stage IIIC	T4	M0	N0
TCGA-ED-	408		0	60	FEMALE	G2	Stage IIIA	T3a	M0	N0
TCGA-G3-	632		0	60	FEMALE	G3	Stage I	T1	MX	NX
TCGA-KR-	951		0	61	FEMALE	G1	Stage II	T2	M0	N0
TCGA-DD-	2456		1	61	FEMALE	G2	Stage I	T1	M0	N0
TCGA-CC-	87		1	61	FEMALE	G1	Stage IIIC	T4	M0	N0
TCGA-UB-	848		0	62	FEMALE	G2	Stage II	T2b	M0	N0
TCGA-BC-	1351		0	62	FEMALE	G2	Stage IIIA	T3	M0	NX
TCGA-BC-	34	1		62	FEMALE	G2	Stage I	T1	MX	N0
TCGA-G3-	1636	0		63	FEMALE	G3	Stage I	T1	M0	N0
TCGA-DD-	171	1		63	FEMALE	G4	Stage I	T1	M0	N0

TCGA-2Y-	1731	0	64	FEMALE	G3	Stage I	T1	MX	N0
TCGA-ZP-	395	0	64	FEMALE	G1	unknow	T1	MX	NX
TCGA-WX-	615	0	64	FEMALE	G3	Stage I	T1	MX	NX
TCGA-DD-	558	1	64	FEMALE	G2	Stage IVB	T4	M1	N0
TCGA-DD-	931	1	64	FEMALE	G2	Stage IVB	T4	M1	N0
TCGA-2Y-	757	1	64	FEMALE	G3	Stage II	T2	MX	NX
TCGA-DD-	115	1	64	FEMALE	G4	Stage I	T1	M0	N0
TCGA-DD-	701	0	65	FEMALE	G1	Stage IIIA	T3a	M0	N0
TCGA-DD-	917	0	65	FEMALE	G3	Stage IIIB	T3b	M0	N0
TCGA-5R-	46	1	65	FEMALE	G2	Stage II	T2	M0	N0
TCGA-BC-	562	0	66	FEMALE	G3	Stage IIIC	T4	M0	N0
TCGA-ZP-	782	0	66	FEMALE	G1	unknow	T1	MX	NX
TCGA-BC-	8	0	66	FEMALE	G2	Stage I	T1	M0	NX
TCGA-DD-	1233	0	66	FEMALE	G3	Stage I	T1	M0	N0
TCGA-DD-	107	1	66	FEMALE	G3	Stage I	T1	M0	N0
TCGA-DD-	3125	1	66	FEMALE	G2	Stage III	T3	M0	N0
TCGA-BC-	308	1	66	FEMALE	G2	unknow	T3	MX	NX
TCGA-DD-	1008	0	67	FEMALE	G3	Stage IIIC	T2	M0	N1
TCGA-ZP-	1091	0	67	FEMALE	G1	unknow	T1	MX	NX
TCGA-2Y-	357	0	68	FEMALE	G2	Stage I	T1	MX	NX
TCGA-BC-	680	0	68	FEMALE	G3	Stage II	T2	M0	N0
TCGA-DD-	693	0	68	FEMALE	G1	Stage II	T2	MX	NX
TCGA-DD-	1049	0	68	FEMALE	G3	Stage II	T2	M0	N0
TCGA-WJ-	345	0	68	FEMALE	G2	Stage I	T1	MX	NX
TCGA-UB-	314	0	69	FEMALE	G1	Stage I	unknow	MX	NX
TCGA-DD-	1562	0	69	FEMALE	G2	Stage I	T1	M0	N0
TCGA-DD-	1066	0	70	FEMALE	G3	Stage I	T1	M0	N0
TCGA-FV-	1852	1	70	FEMALE	unknow	Stage II	T2	M0	N0
TCGA-WQ	30	0	71	FEMALE	G3	unknow	T3a	M0	NX
TCGA-DD-	1005	1	71	FEMALE	G2	Stage IIIC	T1	M0	N1
TCGA-DD-	2017	0	72	FEMALE	G2	Stage I	T1	M0	N0
TCGA-DD-	283	1	72	FEMALE	G2	Stage I	T1	M0	N0
TCGA-DD-	3258	1	72	FEMALE	G2	Stage II	T2	M0	N0
TCGA-BC-	1135	1	72	FEMALE	unknow	unknow	T2	MX	NX
TCGA-DD-	137	0	73	FEMALE	G2	Stage I	T1	M0	N0
TCGA-DD-	3478	0	73	FEMALE	G3	Stage I	T1	M0	N0
TCGA-DD-	1219	0	73	FEMALE	G2	Stage I	T1	M0	N0
TCGA-DD-	2324	0	74	FEMALE	G3	Stage I	T1	M0	N0
TCGA-RC-	22	0	74	FEMALE	G2	Stage IIIA	T3	MX	NX
TCGA-BC-	1490	1	74	FEMALE	G3	Stage IIIA	T3	M0	N0
TCGA-BD-	409	0	75	FEMALE	G2	Stage I	T1	M0	N0
TCGA-DD-	660	1	75	FEMALE	G3	Stage IIIA	T3a	M0	N0
TCGA-BC-	1397	1	75	FEMALE	G3	Stage II	T2	M0	NX
TCGA-GJ-	31	1	75	FEMALE	G2	Stage II	T2	MX	NX
TCGA-FV-	848	0	76	FEMALE	G2	Stage II	T2	M0	NX
TCGA-DD-	2131	1	76	FEMALE	G1	Stage I	T1	M0	N0
TCGA-DD-	1085	0	77	FEMALE	G1	Stage I	T1	M0	N0
TCGA-DD-	3437	0	77	FEMALE	G2	Stage II	T2	M0	N0

TCGA-DD-	1694	1	78	FEMALE	G2	Stage I	T1	M0	NX
TCGA-ZS-	1241	0	79	FEMALE	G1	Stage II	T2	MX	NX
TCGA-LG-	387	0	79	FEMALE	G2	Stage II	T2	M0	NX
TCGA-G3-	935	0	79	FEMALE	G2	Stage IIIB	T3b	M0	N0
TCGA-DD-	1210	1	80	FEMALE	G2	Stage IIIA	T3	M0	N0
TCGA-2Y-	1168	0	81	FEMALE	G2	Stage I	T1	MX	N0
TCGA-DD-	410	1	81	FEMALE	G4	Stage I	T1	MX	N0
TCGA-FV-	247	1	81	FEMALE	G2	Stage II	T2	MX	N0
TCGA-2Y-	848	1	82	FEMALE	G2	Stage II	T2	MX	NX
TCGA-G3-	27	1	83	FEMALE	G1	Stage I	T1	M0	N0
TCGA-FV-	10	0	84	FEMALE	G2	Stage I	T1	M0	NX
TCGA-DD-	9	1	85	FEMALE	G3	Stage I	T1	M0	N0
TCGA-2Y-	633	1	85	FEMALE	G2	unknow	T1	MX	NX
TCGA-HP-	752	1	90	FEMALE	unknow	unknow	TX	M0	NX
TCGA-XR-	925	0	16	MALE	G1	Stage IIIA	T3	MX	N0
TCGA-CC-	300	1	18	MALE	G1	Stage IIIC	T3	M0	N1
TCGA-DD-	1495	0	23	MALE	G3	Stage III	T3	M0	N0
TCGA-DD-	415	1	23	MALE	G3	Stage II	T2	M0	N0
TCGA-RC-	0	0	24	MALE	G3	Stage II	T2	M0	N0
TCGA-UB-	601	0	24	MALE	G3	Stage II	T2	MX	NX
TCGA-DD-	989	0	25	MALE	G2	Stage I	T1	M0	N0
TCGA-ED-	427	0	29	MALE	G2	Stage IIIA	T3a	M0	N0
TCGA-G3-	430	0	31	MALE	G1	Stage I	T1	MX	NX
TCGA-DD-	3308	0	32	MALE	G3	Stage I	T1	M0	N0
TCGA-DD-	1302	0	32	MALE	G3	Stage I	T1	M0	N0
TCGA-MR-	330	0	34	MALE	G3	Stage I	T1	MX	N0
TCGA-ED-	406	0	35	MALE	G3	Stage IIIA	T3a	M0	N0
TCGA-DD-	2317	0	35	MALE	G2	Stage I	T1	M0	N0
TCGA-CC-	129	1	35	MALE	G1	Stage IIIA	T3	M0	N0
TCGA-CC-	315	1	36	MALE	G1	Stage IIIA	T3	M0	N0
TCGA-DD-	612	1	37	MALE	G3	Stage IIIA	T3	M0	N0
TCGA-G3-	361	0	38	MALE	G2	Stage II	T2	M0	N0
TCGA-DD-	1718	0	38	MALE	G2	Stage II	T2	M0	N0
TCGA-DD-	1900	0	38	MALE	G2	Stage I	T1	M0	N0
TCGA-DD-	2728	0	38	MALE	G2	Stage I	T1	M0	N0
TCGA-DD-	1804	0	39	MALE	G3	Stage I	T1	M0	N0
TCGA-DD-	1876	0	40	MALE	G3	Stage I	T1	M0	N0
TCGA-DD-	223	1	40	MALE	G3	Stage IV	T3a	M1	N0
TCGA-RC-	468	0	42	MALE	G3	Stage II	T2	M0	N0
TCGA-DD-	1149	1	42	MALE	G3	Stage II	T2	M0	unknow
TCGA-DD-	1295	0	43	MALE	G2	Stage I	T1	M0	N0
TCGA-DD-	1424	0	43	MALE	G3	Stage I	T1	M0	N0
TCGA-DD-	2513	0	44	MALE	G2	Stage I	T1	M0	N0
TCGA-CC-	97	1	44	MALE	G2	Stage II	T2	M0	N0
TCGA-G3-	768	1	44	MALE	G2	Stage II	T2	M0	N0
TCGA-DD-	458	0	45	MALE	G3	Stage I	T1	M0	N0
TCGA-2Y-	1516	0	45	MALE	G1	Stage II	T2	MX	NX
TCGA-DD-	664	0	45	MALE	G3	Stage I	T1	M0	N0

TCGA-CC-	300	1	45	MALE	G3	Stage IIIA	T3	M0	N0
TCGA-CC-	304	1	45	MALE	G2	Stage IIIA	T3	M0	N0
TCGA-DD-	535	1	45	MALE	G2	Stage I	T1	M0	N0
TCGA-DD-	1711	0	46	MALE	G1	Stage I	T1	M0	N0
TCGA-DD-	2202	0	46	MALE	G2	Stage II	T2	M0	N0
TCGA-DD-	183	0	46	MALE	G2	Stage I	T1	M0	N0
TCGA-ED-	910	0	47	MALE	G2	Stage II	T2	M0	N0
TCGA-CC-	299	1	47	MALE	G2	Stage II	T2	M0	N0
TCGA-LG-	425	0	48	MALE	G2	Stage I	T1	M0	NX
TCGA-G3-	480	0	48	MALE	G2	Stage I	T1	M0	N0
TCGA-DD-	1769	0	48	MALE	G3	Stage II	T2	M0	N0
TCGA-QA-	94	0	48	MALE	G2	Stage II	T2	MX	NX
TCGA-DD-	2752	0	48	MALE	G1	Stage I	T1	M0	N0
TCGA-DD-	587	0	48	MALE	G3	Stage I	T1	M0	N0
TCGA-CC-	272	1	48	MALE	G2	Stage IIIB	T4	M0	N0
TCGA-CC-	129	1	48	MALE	G2	Stage II	T2	M0	N0
TCGA-DD-	381	1	48	MALE	G4	Stage I	T1	M0	N0
TCGA-2Y-	3675	0	49	MALE	G1	Stage IIIA	T3	M0	N0
TCGA-G3-	372	0	50	MALE	G1	Stage I	T1	M0	N0
TCGA-BW-	20	0	50	MALE	G2	Stage IIIA	T3a	MX	NX
TCGA-DD-	566	0	50	MALE	G2	Stage I	T1	M0	N0
TCGA-DD-	1202	0	50	MALE	G4	Stage I	T1	M0	N0
TCGA-DD-	574	0	50	MALE	G3	Stage I	T1	M0	N0
TCGA-CC-	101	1	50	MALE	G3	Stage IIIA	T3	M0	N0
TCGA-BC-	91	1	50	MALE	G3	unknow	T4	MX	NX
TCGA-DD-	432	1	50	MALE	G3	Stage II	T2	M0	N0
TCGA-DD-	763	0	51	MALE	G3	Stage I	T1	M0	N0
TCGA-DD-	1242	0	51	MALE	G4	Stage I	T1	M0	N0
TCGA-UB-	486	0	51	MALE	G2	Stage I	T1	MX	NX
TCGA-DD-	638	0	51	MALE	G3	Stage I	T1	M0	N0
TCGA-DD-	1231	0	51	MALE	G4	Stage I	T1	M0	N0
TCGA-DD-	1067	0	51	MALE	G3	Stage II	T2	M0	N0
TCGA-DD-	347	0	51	MALE	G2	Stage I	T1	M0	N0
TCGA-G3-	359	1	51	MALE	G3	Stage IIIC	T4	M0	N0
TCGA-ZP-	765	1	51	MALE	G2	unknow	T2	MX	NX
TCGA-2Y-	1624	1	51	MALE	G2	Stage I	T1	MX	NX
TCGA-G3-	594	0	52	MALE	G2	Stage II	T2	M0	N0
TCGA-FV-	12	0	52	MALE	G2	Stage I	T1	M0	NX
TCGA-DD-	552	0	52	MALE	G3	Stage I	T1	M0	N0
TCGA-DD-	469	1	52	MALE	G4	Stage II	T2	M0	N0
TCGA-G3-	780	0	53	MALE	G2	Stage IIIA	T3a	M0	N0
TCGA-RC-	588	0	53	MALE	G2	Stage II	T2	M0	N0
TCGA-DD-	1531	0	53	MALE	G3	Stage I	T1	M0	N0
TCGA-DD-	2542	1	53	MALE	G2	Stage IIIA	T3	M0	N0
TCGA-DD-	425	1	53	MALE	G3	Stage I	T1	M0	N0
TCGA-ED-	6	0	54	MALE	G2	Stage IIIA	T3a	M0	N0
TCGA-CC-	399	0	54	MALE	G3	Stage IIIA	T3	M0	N0
TCGA-CC-	363	0	54	MALE	G2	Stage IIIA	T3	M0	N0

TCGA-DD-	1345	0	54	MALE	G3	Stage I	T1	M0	N0
TCGA-DD-	2015	0	54	MALE	G2	Stage I	T1	M0	N0
TCGA-O8-	538	0	54	MALE	G2	Stage I	T1	MX	NX
TCGA-ES-	438	1	54	MALE	G2	Stage I	T1	MX	NX
TCGA-DD-	1989	0	55	MALE	G2	Stage IIIA	T3	M0	N0
TCGA-DD-	810	0	55	MALE	G4	Stage I	T1	M0	N0
TCGA-CC-	211	0	55	MALE	G2	Stage II	T2	M0	N0
TCGA-ZS-	341	0	55	MALE	G2	Stage II	T2	MX	NX
TCGA-DD-	453	0	55	MALE	G3	Stage I	T1	M0	N0
TCGA-CC-	382	0	56	MALE	G3	Stage II	T2	M0	N0
TCGA-DD-	1823	0	56	MALE	G2	Stage I	T1	M0	N0
TCGA-DD-	2455	0	56	MALE	G3	Stage II	T2	M0	N0
TCGA-DD-	1970	0	56	MALE	G2	Stage IIIA	T3	M0	N0
TCGA-UB-	214	1	56	MALE	G2	Stage IIIA	T3a	MX	NX
TCGA-5R-	520	0	57	MALE	G2	Stage II	T2	M0	N0
TCGA-CC-	0	0	57	MALE	G2	Stage IIIA	T3	M0	N0
TCGA-KR-	906	0	57	MALE	G1	Stage I	T1	M0	N0
TCGA-CC-	217	1	57	MALE	G2	Stage IIIA	T3	M0	N0
TCGA-XR-	898	0	58	MALE	G2	Stage I	T1	M0	NX
TCGA-G3-	655	0	58	MALE	G2	Stage I	T1	M0	N0
TCGA-DD-	2028	0	58	MALE	G3	Stage I	T1	M0	N0
TCGA-ED-	819	0	58	MALE	G3	Stage II	T2	M0	N0
TCGA-DD-	636	0	58	MALE	G4	Stage I	T1	M0	N0
TCGA-G3-	520	0	58	MALE	G3	Stage II	T2	M0	NX
TCGA-G3-	476	0	58	MALE	G2	Stage I	T1	M0	N0
TCGA-MR-	229	0	58	MALE	G1	Stage I	T1	MX	NX
TCGA-5C-	328	0	58	MALE	G2	Stage II	T2	M0	N0
TCGA-CC-	365	0	58	MALE	G1	Stage IIIA	T3	M0	N0
TCGA-G3-	744	0	58	MALE	G1	Stage I	T1	M0	NX
TCGA-DD-	12	1	58	MALE	G3	Stage II	T2	M0	N0
TCGA-2Y-	1229	1	58	MALE	G2	Stage I	T1	MX	NX
TCGA-2Y-	724	1	58	MALE	G2	unknow	T2	MX	NX
TCGA-UB-	500	0	59	MALE	G3	Stage IIIA	T3a	MX	N0
TCGA-DD-	436	0	59	MALE	G3	Stage II	T2	M0	N0
TCGA-GJ-	879	0	59	MALE	G2	Stage I	T1	MX	NX
TCGA-DD-	898	0	59	MALE	G4	Stage I	T1	MX	NX
TCGA-RC-	472	0	59	MALE	G3	Stage I	T1	M0	N0
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TCGA-G3-	698	0	59	MALE	G2	Stage I	T1	M0	NX
TCGA-CC-	649	1	59	MALE	G1	Stage IIIA	T3	M0	N0
TCGA-CC-	262	1	59	MALE	G3	Stage IIIA	T3	M0	N0
TCGA-ZP-	1088	1	59	MALE	G1	unknow	T1	MX	NX
TCGA-UB-	327	0	60	MALE	G2	Stage II	T2	MX	NX
TCGA-DD-	554	0	60	MALE	G3	Stage II	T2	M0	N0
TCGA-DD-	478	0	60	MALE	G2	Stage I	T1	M0	N0
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TCGA-MI-	630	0	61	MALE	G1	unknow	T2	MX	NX
TCGA-DD-	2398	0	61	MALE	G1	Stage IIIA	T3	M0	N0

TCGA-ED-	6	0	61	MALE	G2	Stage II	T2	M0	NX
TCGA-MI-	507	0	61	MALE	G2	Stage IIIC	T4	M0	N0
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TCGA-K7-	359	0	61	MALE	G2	Stage II	T2a	MX	NX
TCGA-WX-	756	0	61	MALE	G1	Stage II	T2	MX	NX
TCGA-G3-	585	0	61	MALE	G2	Stage I	T1	M0	N0
TCGA-CC-	278	1	61	MALE	G1	Stage IIIA	T3	M0	N0
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TCGA-BD-	1115	0	62	MALE	G2	Stage II	T2	MX	NX
TCGA-EP-	570	0	62	MALE	G1	Stage I	T1	MX	NX
TCGA-EP-	19	1	62	MALE	G3	Stage I	T1	MX	NX
TCGA-MI-	698	0	63	MALE	G2	Stage II	T2	M0	N0
TCGA-DD-	474	0	63	MALE	G2	Stage I	T1	M0	N0
TCGA-BW-	0	0	63	MALE	G3	Stage I	T1	MX	NX
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TCGA-ZS-	2412	0	64	MALE	G2	Stage II	T2	MX	NX
TCGA-BC-	444	0	64	MALE	G3	Stage II	T2	M0	NX
TCGA-MI-	291	0	64	MALE	G3	Stage I	T1	M0	N0
TCGA-DD-	415	0	64	MALE	G3	Stage I	T1	M0	N0
TCGA-K7-	631	0	64	MALE	G1	Stage I	T1	MX	NX
TCGA-KR-	829	0	64	MALE	G1	Stage I	T1	M0	N0
TCGA-2Y-	1271	1	64	MALE	G2	Stage I	T1	MX	N0
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TCGA-G3-	671	0	65	MALE	G2	Stage IIIB	T3b	M0	N0
TCGA-DD-	2301	0	65	MALE	G3	Stage I	T1	M0	N0
TCGA-3K-	396	0	65	MALE	G1	Stage IIIB	T3b	MX	NX
TCGA-DD-	575	0	65	MALE	G3	Stage I	T1	M0	N0
TCGA-G3-	361	0	65	MALE	G1	Stage I	T1	MX	NX
TCGA-DD-	2245	0	65	MALE	G1	Stage I	T1	M0	N0
TCGA-KR-	65	1	65	MALE	G1	Stage I	T1	M0	N0
TCGA-DD-	233	1	65	MALE	G2	Stage IIIA	T3b	M0	N0
TCGA-K7-	512	0	66	MALE	G2	Stage I	T1	MX	N0
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TCGA-DD-	44	0	66	MALE	G1	Stage I	T1	M0	N0
TCGA-RC-	579	0	66	MALE	G2	Stage I	T1	M0	N0
TCGA-2Y-	260	0	66	MALE	G2	Stage I	T1	MX	NX
TCGA-DD-	658	0	66	MALE	G2	Stage I	T1	M0	N0
TCGA-K7-	519	0	66	MALE	G1	Stage I	T1	MX	NX
TCGA-DD-	672	0	66	MALE	G3	Stage IIIA	T3a	M0	N0
TCGA-4R-	262	1	66	MALE	G2	Stage II	T2	MX	NX
TCGA-DD-	816	0	67	MALE	G2	Stage II	T2	M0	NX
TCGA-DD-	79	0	67	MALE	G3	Stage I	T1	M0	N0
TCGA-G3-	354	0	67	MALE	G2	Stage II	T2	M0	N0
TCGA-UB-	52	1	67	MALE	G3	Stage I	T1	MX	N0
TCGA-DD-	171	1	67	MALE	G3	Stage I	T1	M0	NX

TCGA-CC-	103	1	67	MALE	G1	Stage IIIC	T4	M0	N0
TCGA-DD-	419	1	67	MALE	G3	Stage IIIB	T3b	M0	N0
TCGA-DD-	2415	0	68	MALE	G2	Stage II	T2	M0	N0
TCGA-G3-	860	0	68	MALE	G2	Stage I	T1	M0	N0
TCGA-T1-	23	0	68	MALE	G2	unknow	T1	M0	NX
TCGA-CC-	248	0	68	MALE	G2	Stage IIIA	T3	M0	N0
TCGA-2Y-	1452	0	68	MALE	G2	Stage I	T1	MX	N0
TCGA-LG-	366	0	68	MALE	G2	Stage IIIA	T3a	M0	N0
TCGA-2Y-	2442	0	68	MALE	G2	Stage I	T1	MX	NX
TCGA-DD-	2301	0	68	MALE	G1	Stage I	T1	M0	N0
TCGA-GJ-	67	1	68	MALE	G2	Stage I	T1	MX	N0
TCGA-DD-	1622	1	68	MALE	G3	Stage IIIA	T3	M0	N0
TCGA-DD-	365	1	68	MALE	G3	Stage I	T1	M0	N0
TCGA-YA-	412	1	68	MALE	G3	Stage IIIA	T3a	MX	N0
TCGA-DD-	1855	0	69	MALE	G2	Stage I	T1	M0	N0
TCGA-BC-	387	0	69	MALE	G1	Stage I	T1	M0	N0
TCGA-RG-	1098	0	69	MALE	G2	Stage II	T2	M0	N0
TCGA-BD-	1363	0	69	MALE	G2	unknow	T2	MX	NX
TCGA-DD-	1633	0	69	MALE	G2	Stage I	T1	M0	N0
TCGA-DD-	1618	0	69	MALE	G3	Stage II	T2	M0	N0
TCGA-DD-	662	0	69	MALE	G3	Stage I	T1	M0	N0
TCGA-DD-	722	0	69	MALE	G3	Stage I	T1	M0	N0
TCGA-BC-	837	1	69	MALE	G2	unknow	T2	MX	NX
TCGA-BC-	547	1	69	MALE	G3	Stage IIIA	T3a	M0	NX
TCGA-DD-	195	1	69	MALE	G3	Stage II	T2	M0	N0
TCGA-2Y-	697	0	70	MALE	G2	Stage I	T1	MX	N0
TCGA-5C-	322	0	70	MALE	G2	Stage I	T1	M0	N0
TCGA-DD-	9	0	70	MALE	G2	Stage I	T1	M0	N0
TCGA-G3-	621	0	70	MALE	G2	Stage II	T2	M0	NX
TCGA-DD-	1145	0	70	MALE	G3	Stage IIIA	T3a	M0	N0
TCGA-EP-	608	0	70	MALE	G2	Stage I	T1	MX	N0
TCGA-DD-	2759	1	70	MALE	G2	Stage I	T1	M0	N0
TCGA-2Y-	36	1	70	MALE	G2	Stage II	T2	MX	NX
TCGA-G3-	56	1	70	MALE	G2	Stage IIIB	T3b	MX	NX
TCGA-DD-	785	1	70	MALE	G2	Stage I	T1	M0	NX
TCGA-DD-	728	0	71	MALE	G2	Stage I	T1	M0	N0
TCGA-G3-	180	0	71	MALE	G2	Stage I	T1	M0	N0
TCGA-CC-	102	1	71	MALE	G2	Stage IIIA	T3	M0	N0
TCGA-NI-A	1791	1	71	MALE	G1	Stage IIIA	T3	MX	NX
TCGA-DD-	644	0	72	MALE	G2	Stage I	T1	M0	N0
TCGA-ZP-	706	0	72	MALE	G1	unknow	T1	MX	NX
TCGA-DD-	1531	0	72	MALE	G2	Stage I	T1	M0	N0
TCGA-DD-	942	0	72	MALE	G2	Stage I	T1	M0	N0
TCGA-DD-	16	1	72	MALE	G3	Stage I	T1	M0	N0
TCGA-DD-	784	0	73	MALE	G2	Stage I	T1	M0	N0
TCGA-G3-	1779	0	73	MALE	G3	Stage II	T2	M0	N0
TCGA-EP-	363	0	73	MALE	G2	Stage IIIA	T3a	MX	NX
TCGA-BC-	849	0	73	MALE	G3	Stage IIIA	T3	MX	N0

TCGA-ZS-	1386	1	73	MALE	G2	Stage II	T2	MX	NX
TCGA-DD-	14	1	73	MALE	G2	Stage I	T1	M0	N0
TCGA-DD-	349	1	73	MALE	G3	Stage IIIA	T3	M0	N0
TCGA-ED-	423	0	74	MALE	G2	Stage I	T1	M0	NX
TCGA-NI-A	799	0	74	MALE	G3	Stage I	T1	MX	NX
TCGA-XR-	693	1	74	MALE	G1	Stage I	T1	MX	NX
TCGA-CC-	140	1	74	MALE	G2	Stage IIIA	T3	M0	N0
TCGA-RC-	9	0	75	MALE	G3	Stage II	T2	M0	NX
TCGA-DD-	2102	0	75	MALE	G2	Stage II	T2	M0	N0
TCGA-FV-	194	1	75	MALE	unknow	Stage I	T1	MX	NX
TCGA-FV-	581	1	75	MALE	G1	Stage I	T1	M0	N0
TCGA-DD-	11	1	75	MALE	G2	Stage II	T2	M0	N0
TCGA-EP-	303	0	76	MALE	G2	Stage I	T1	MX	NX
TCGA-G3-	447	0	76	MALE	G2	Stage I	T1	MX	NX
TCGA-BC-	711	1	76	MALE	G3	unknow	T4	MX	NX
TCGA-BC-	837	1	76	MALE	G1	unknow	T4	MX	NX
TCGA-DD-	1372	1	76	MALE	G3	Stage I	T1	M0	N0
TCGA-MI-	747	0	77	MALE	unknow	unknow	unknow	MX	NX
TCGA-DD-	643	1	77	MALE	G3	Stage II	T2	M0	NX
TCGA-DD-	802	1	77	MALE	G2	Stage IIIA	T3a	M0	NX
TCGA-HP-	91	1	78	MALE	G2	Stage I	T1	M0	NX
TCGA-FV-	2486	1	78	MALE	G2	Stage IIIA	T3	M0	NX
TCGA-G3-	673	0	80	MALE	G2	Stage I	T1	M0	N0
TCGA-FV-	729	0	80	MALE	G2	Stage I	T1	MX	N0
TCGA-ES-	688	1	80	MALE	G2	Stage I	T1	MX	NX
TCGA-BC-	153	1	80	MALE	G2	unknow	T3	MX	NX
TCGA-BC-	1423	1	81	MALE	G1	unknow	T3	MX	NX
TCGA-2V-A95S		0 unknow		MALE	G3	Stage II	T2	MX	NX

Identification of FRlncRNAs and Enrichment Analysis

The corresponding ferroptosis-related genes were downloaded from FerrDb [14], a web-based consortium offering an exhaustive and current database of ferroptosis markers, regulatory molecules, and associated diseases. We ultimately identified 382 ferroptosis-related genes (Supplementary Table 2), of which Diver comprises 150, Suppressor comprises 109, and Marker comprises 123. Pearson's test was applied to these genes to determine the relationship between FRlncRNAs and HCC. The association was deemed significant if the correlation coefficient $|R2| > 0.5$ and $p < 0.001$. First, the functions of up- and down-regulated ferroptosis-related differentially expressed genes (DEGs) were investigated. Then, we analyzed the biological pathways associated with DEGs using the Kyoto Encyclopedia of Genes and Gene Expression (KEGG) data. According to gene ontology (GO), the functions of biological processes (BP), molecular functions (MF), and cellular components (CC) regulated by differentially expressed FRlncRNAs were investigated further. Using the GO and KEGG pathways, the «cluster Profiler» R package [15] assessed the biological roles of the prognostic candidates.

Construction and Validation of a Model of FRlncRNAs

Utilizing Lasso-penalized Cox regression analysis, FRlncRNAs with prognostic value were screened. In the final cohort for analysis, 376 lncRNA-seq samples remained after excluding those with unknown survival times (n = 1) based on previous clinical data. A genetic model containing biomarkers helpful in predicting prognosis was identified using the «glmnet» package in R. A risk score was calculated for each sample in all data sets based on this model, according to the risk score = alncRNA1 × lncRNA1 expression + blncRNA2 × lncRNA2 expression +⋯ + nlncRNAn × lncRNAn expression. To evaluate the predictive ability of the model for prognostic risk, we analyzed characteristic curves (ROC) for 10-year survival using the «timeROC» function in R. Based on median scores, the RNA was split into low- and high-risk groups. Using Kaplan-Meier analysis, the prognostic significance of this model for HCC was explored. Finally, univariate and multivariate Cox regression analyses were conducted to determine whether the model had good predictive power independent of other clinicopathological characteristics.

Predictive Nomogram

The R package «regplot» was utilized to compile clinical data and develop a nomogram integrating prognostic features to predict the 1-, 3-, and 5-year OS of HCC patients.

Function Enrichment Analysis

Based on gene set enrichment analysis, potential functional pathways involved in the ferroptosis lncRNA model were identified (GSEA). GSEA was performed on the KEGG dataset c2.cp.kegg.v7.4.symbols.gmt in java GSEA4.1.0 using the optimal cut-off value to divide TCGA data and identify enrichment pathways between the high-risk and low-risk groups. Statistical significance was set at $p < 0.05$, and false discovery rate (FDR) $q < 0.25$ was deemed statistically significant.

Immunity Infiltrates Analysis and Gene Expression

In addition, the TIMER, CIBERSORT, CIBERSORT-ABS, QUANTISEQ, MCPCOUNTER, XCELL, and EPIC [16-22] algorithms were compared to evaluate FRlncRNA models between high-risk and low-risk groups based on cellular components and cellular immune responses. Heatmaps depicted the differences in immune responses under various algorithms. Moreover, single-sample gene set enrichment analysis (ssGSEA) was employed to quantify tumor-infiltrating immune cell subpopulations between the two groups and evaluate their immune function.

Cell Culture and qRT-PCR

Hepatic stellate cells LX-2 and HCC cells HepG2, Huh7 and Hep3B were cultured in DMEM medium (Gibco, China) supplemented with 10% fetal bovine serum (Gibco, China) and 1% penicillin-streptomycin (Gibco, China). The cultures were placed in a sterile incubator at 37 °C and 5% CO2. The cells were obtained in the logarithmic growth phase for subsequent experiments. Following the manufacturer's instructions, total RNA was extracted using RNAiso reagent (TaKaRa, 9108, China), and cDNA synthesis was reversed using the Prime Script RT kit (TaKaRa, RR047A, China). qPCR assays were performed using TB Green® Premix Ex Taq™ (Takara, RR420A, China). β-ACTIN was used as an endogenous reference. Relative quantification of lncRNAs was calculated using 2-ΔΔCT. The primers' sequences are listed in (Supplementary Table 3).

Supplementary Table 3: The primers' sequences.

<table>
<tr><th></th><th colspan="4">Ferroptosis associated DEGs</th><th></th></tr>
<tr><th>gene</th><th>conMean</th><th colspan="2">treatMean logFC</th><th>pValue</th><th>fdr</th></tr>
<tr><td>SLC7A11</td><td>0.030108</td><td>0.889909</td><td>4.885429</td><td colspan="2">1.65E-19 8.94E-19</td></tr>
<tr><td>AKR1C1</td><td>27.52956</td><td>64.19353</td><td>1.221446</td><td>0.000384</td><td>0.000513</td></tr>
<tr><td>AKR1C2</td><td>16.24967</td><td>50.10021</td><td>1.624406</td><td colspan="2">5.01E-06 7.68E-06</td></tr>
<tr><td>AKR1C3</td><td>17.68299</td><td>83.41396</td><td>2.237927</td><td colspan="2">1.18E-23 1.28E-22</td></tr>
<tr><td>HSPB1</td><td>71.35463</td><td>339.0672</td><td>2.248492</td><td colspan="2">7.65E-24 9.18E-23</td></tr>
<tr><td>HSF1</td><td>6.466392</td><td>17.74508</td><td>1.456387</td><td colspan="2">3.17E-25 6.23E-24</td></tr>
<tr><td>SQSTM1</td><td>29.98683</td><td>99.91757</td><td>1.736409</td><td colspan="2">9.02E-17 3.54E-16</td></tr>
<tr><td>NQO1</td><td>1.459665</td><td>57.95383</td><td>5.311194</td><td colspan="2">6.82E-16 2.58E-15</td></tr>
<tr><td>FTH1</td><td>139.0993</td><td>286.4864</td><td>1.042351</td><td colspan="2">8.93E-17 3.54E-16</td></tr>
<tr><td>MT1G</td><td>1204.511</td><td>315.6052</td><td colspan="3">-1.93225 3.78E-23 3.41E-22</td></tr>
<tr><td>FANCD2</td><td>0.131555</td><td>1.016427</td><td>2.949769</td><td colspan="2">2.65E-25 5.72E-24</td></tr>
<tr><td>HSPA5</td><td>110.1952</td><td>231.5747</td><td>1.071416</td><td colspan="2">1.04E-19 5.89E-19</td></tr>
<tr><td>HELLS</td><td>0.093803</td><td>0.861082</td><td>3.198438</td><td colspan="2">3.84E-24 5.18E-23</td></tr>
<tr><td>FADS2</td><td>9.642112</td><td>20.0576</td><td>1.056728</td><td>0.011186</td><td>0.013276</td></tr>
<tr><td>SRC</td><td>1.47643</td><td>5.368635</td><td>1.862442</td><td colspan="2">2.16E-10 4.71E-10</td></tr>
<tr><td>PML</td><td>1.502347</td><td>3.136546</td><td>1.061959</td><td colspan="2">9.29E-18 4.36E-17</td></tr>
<tr><td>TP63</td><td>0.032491</td><td>0.121942</td><td>1.908063</td><td>0.00237</td><td>0.002977</td></tr>
<tr><td>ENPP2</td><td>4.152915</td><td>9.060232</td><td>1.125424</td><td>9.16E-05</td><td>0.000128</td></tr>
<tr><td>NF2</td><td>1.559214</td><td>3.964334</td><td>1.346259</td><td colspan="2">2.04E-24 2.94E-23</td></tr>
<tr><td>PLIN2</td><td>127.362</td><td>62.57489</td><td colspan="3">-1.02528 1.68E-12 4.48E-12</td></tr>
<tr><td>AIFM2</td><td>3.506349</td><td>9.472166</td><td>1.433725</td><td colspan="2">4.82E-21 3.36E-20</td></tr>
<tr><td>ZFP36</td><td>164.7136</td><td>57.41977</td><td colspan="3">-1.52034 8.00E-18 3.84E-17</td></tr>
<tr><td>CAV1</td><td>4.222347</td><td>8.723696</td><td>1.046894</td><td colspan="2">3.25E-09 6.50E-09</td></tr>
</table>

PTGS2	0.685695	0.20982	-1.70841	5.31E-17 2.29E-16	
DUSP1	210.2614	101.3657	-1.05261 6.88E-14 2.07E-13		
NOS2	0.097262	0.402505	2.049054	5.21E-13 1.52E-12	
NCF2	1.947159	4.045334	1.054888	0.011789	0.013915
MT3	0.017155	0.505604	4.881317	0.000988	0.001278
ALB	34010.38	14088.94	-1.27141 6.53E-21 4.40E-20		
TXNRD1	6.763141	28.10662	2.055145	1.93E-17 8.71E-17	
SRXN1	0.361867	1.488914	2.040729	5.06E-15 1.73E-14	
GPX2	106.9847	267.7037	1.323232	0.010098	0.012185
DDIT4	14.47339	30.41607	1.07143	6.49E-05 9.23E-05	
ASNS	0.500574	2.570302	2.360284	2.43E-09 4.90E-09	
DDIT3	9.15751	26.01926	1.506553	3.18E-17 1.40E-16	
SLC1A4	1.912718	5.006494	1.388176	6.03E-15 2.03E-14	
SLC7A5	2.462716	5.037566	1.032477	0.026349	0.030599
ATF3	20.57439	9.029725	-1.1881 1.07E-11 2.62E-11		
ZNF419	0.285625	0.643774	1.172431	9.43E-13 2.58E-12	
ZFP69B	0.135104	0.407536	1.592859	8.39E-17 3.42E-16	
TUBE1	3.046223	1.329053	-1.19662	8.33E-21 5.45E-20	
IL6	0.867032	0.320722	-1.43476 3.10E-05 4.47E-05		
FTL	6020.631	12148.79	1.012826	7.28E-07 1.19E-06	
RPL8	211.6811	704.8365	1.735396	4.54E-21 3.27E-20	
TFRC	3.679605	10.99098	1.578697	1.93E-16 7.46E-16	
MAFG	1.056159	4.158995	1.977408	7.43E-23 6.42E-22	
HAMP	148.2531	15.96737	-3.21486	6.51E-25 1.08E-23	
STEAP3	47.67718	21.83948	-1.12636 2.11E-19 1.11E-18		
DRD4	0.155276	1.075832	2.792546	1.06E-14 3.31E-14	
SLC2A1	0.680047	2.534008	1.897715	3.92E-05 5.61E-05	
SLC2A6	0.920582	3.110677	1.75661	9.57E-08 1.68E-07	
SLC2A14	0.045282	0.17522	1.952146	0.003584	0.004423
ALOX12	0.109011	0.275266	1.336353	1.04E-12 2.81E-12	
ALOX15	0.021905	0.096189	2.134597	8.16E-06 1.23E-05	
NNMT	469.383	140.6666	-1.73849 1.15E-17 5.28E-17		
STMN1	1.902558	13.51992	2.829074	1.90E-27 1.03E-25	
RRM2	0.469399	6.378299	3.764286	3.18E-26	1.14E-24
CAPG	3.486875	13.19529	1.920016	1.95E-11 4.53E-11	
AURKA	0.65543	6.892745	3.394565	4.06E-28 2.92E-26	
CS	5.378785	13.81835	1.361233	1.45E-22 1.21E-21	
EMC2	4.26184	9.93217	1.220633	4.52E-24 5.74E-23	
NOX1	0.146418	0.415607	1.505125	9.70E-15 3.17E-14	
NOX4	0.021637	0.24261	3.487096	1.94E-28 2.10E-26	
NOX5	0.003047	0.012757	2.065801	2.62E-05 3.84E-05	
DUOX1	0.056932	0.494106	3.117501	5.88E-20 3.53E-19	
G6PD	1.311715	13.58215	3.372185	6.03E-25 1.08E-23	
ACSL4	7.321489	46.12192	2.655243	3.57E-12 9.08E-12	
NRAS	5.769457	11.90251	1.044759	7.64E-17 3.17E-16	
HRAS	4.521073	13.56737	1.585403	7.59E-25 1.17E-23	
SLC38A1	1.293731	4.376645	1.758287	3.00E-05 4.35E-05	

SLC1A5	2.729119	8.796147	1.688436	0.004123	0.005051
GLS2	4.778707	1.786804	-1.41924 1.24E-15 4.63E-15		
ALOX15B	0.142067	1.817888	3.677623	7.72E-07 1.25E-06	
MAPK3	3.657011	9.508188	1.378505	5.73E-26 1.77E-24	
CDKN2A	0.162719	4.09759	4.65432	1.87E-25 4.49E-24	
MYB	0.046398	0.13344	1.524058	7.29E-08 1.29E-07	
PRKAA2	0.279372	1.628446	2.543237	2.30E-10 4.97E-10	
BAP1	7.278584	15.18776	1.061179	1.68E-23 1.72E-22	
ABCC1	0.707154	2.380374	1.751092	3.82E-06 5.94E-06	
YY1AP1	3.836373	9.089088	1.244393	1.04E-23 1.19E-22	
EGLN2	1.596814	3.789287	1.24673	1.96E-20 1.21E-19	
MIOX	0.025308	0.730526	4.851295	1.25E-11 3.03E-11	
TAZ	1.723546	5.520824	1.679503	7.52E-29 1.62E-26	
DNAJB6	1.465015	3.293092	1.168527	2.68E-26	1.14E-24

Statistical Analysis

All statistical analyses were conducted using the R programming language and associated software packages. Using ROC and decision curve analysis (DCA), [23] evaluated the relationship between the model and its clinicopathological performance. The statistical significance level for each analysis was set at $p < 0.05$.

Results

Enrichment Analysis of Ferroptosis-Related Genes

(Figure 1) depicts the study's workflow. Supplementarily, we identified 84 DEGs associated with ferroptosis (13 downregulated and 71 upregulated; (Supplementary Table 4). GO enrichment analysis revealed that BP was involved in the cellular response to chemical and oxidative stress. The production of the apical portion of cells, focal adhesion, melanosomes, and pigment granules was primarily regulated by MF. NAD(P)H oxidoreductase activity, organic anion transmembrane transporter activity, and antioxidant activity were primarily upregulated in CC. KEGG pathway analysis revealed that the over-expressed genes were primarily involved in neurodegeneration and multiple disease pathways, chemical carcinogenesis and reactive oxygen species, microRNAs in cancer, lipid and atherosclerosis, central carbon metabolism in cancer, serotonergic synapse, fluid shear stress and atherosclerosis, and ferroptosis [24] (Figure 2a, 2b) and (Supplementary Table 5).

Supplementary Table 4: Ferroptosis-associated DEGs.

GO and KEGG pathway anaysis								
ONTO-LOG ID	Description	GeneRatio BgRatio		pvalue	p.adjust	qvalue	geneID	Count
BP	GO:006219 cellular response to chemical stress	25/83	347/18862	7.20E-24	2.00E-20	1.38E-20	SLC7A11/A	25
BP	GO:000697 response to oxidative stress	25/83	444/18862	3.11E-21	3.12E-18	2.15E-18	SLC7A11/A	25
BP	GO:003459 cellular response to oxidative stress	22/83	299/18862	3.37E-21	3.12E-18	2.15E-18	SLC7A11/A	22
BP	GO:007259 reactive oxygen species metabolic process	15/83	281/18862	1.34E-12	9.29E-10	6.40E-10	AKR1C3/N	15

BP	GO:003166 response to nutrient levels	17/83	451/18862	9.68E-12	5.38E-09	3.71E-09	AKR1C3/H	17
BP	GO:000680 superoxide metabolic process	9/83	70/18862	2.07E-11	9.29E-09	6.40E-09	NQO1/NO	9
BP	GO:000999 response to extracellular stimulus	17/83	477/18862	2.34E-11	9.29E-09	6.40E-09	AKR1C3/H	17
BP	GO:000963 response to toxic substance	12/83	239/18862	5.69E-10	1.98E-07	1.36E-07	SLC7A11/N	12
BP	GO:004259 response to starvation	11/83	196/18862	9.68E-10	2.99E-07	2.06E-07	AKR1C3/H	11
BP	GO:001584 organic acid transport	13/83	324/18862	1.60E-09	4.46E-07	3.07E-07	SLC7A11/A	13
BP	GO:003355 unsaturated fatty acid metabolic process	9/83	115/18862	1.91E-09	4.83E-07	3.33E-07	AKR1C1/AK	9
BP	GO:012025 olefinic compound metabolic process	9/83	119/18862	2.59E-09	6.00E-07	4.14E-07	AKR1C1/AK	9
BP	GO:000669 icosanoid metabolic process	9/83	123/18862	3.48E-09	7.43E-07	5.12E-07	AKR1C1/AK	9
BP	GO:001003 response to metal ion	13/83	352/18862	4.36E-09	8.65E-07	5.96E-07	AKR1C3/H	13
BP	GO:004255 superoxide anion generation	6/83	35/18862	8.86E-09	1.57E-06	1.08E-06	NCF2/ALO	6
BP	GO:001571 organic anion transport	13/83	376/18862	9.58E-09	1.57E-06	1.08E-06	SLC7A11/A	13
BP	GO:009875 detoxification	9/83	138/18862	9.60E-09	1.57E-06	1.08E-06	NQO1/MT	9
BP	GO:000686 lipid transport	14/83	461/18862	1.26E-08	1.86E-06	1.28E-06	SLC7A11/A	14
BP	GO:007048 response to oxygen levels	13/83	385/18862	1.27E-08	1.86E-06	1.28E-06	HSF1/SRC/	13
BP	GO:009886 cellular oxidant detoxification	8/83	102/18862	1.56E-08	2.17E-06	1.50E-06	NQO1/PTG	8

BP	GO:007099 neuron death	12/83	342/18862	3.18E-08	4.09E-06	2.82E-06	SLC7A11/H	12
BP	GO:004545 cell redox homeostasis	6/83	43/18862	3.23E-08	4.09E-06	2.82E-06	NQO1/NO	6
BP	GO:000166 response to hypoxia	12/83	348/18862	3.85E-08	4.66E-06	3.21E-06	HSF1/SRC/	12
BP	GO:199074 cellular detoxification	8/83	115/18862	4.02E-08	4.66E-06	3.21E-06	NQO1/PTG	8
BP	GO:003629 response to decreased oxygen levels	12/83	360/18862	5.58E-08	5.99E-06	4.12E-06	HSF1/SRC/	12
BP	GO:000167 long-chain fatty acid metabolic process	8/83	120/18862	5.62E-08	5.99E-06	4.12E-06	AKR1C3/FA	8
BP	GO:003600positive regulation of transcription from RNA polymer	5/83	24/18862	5.81E-08	5.99E-06	4.12E-06	HSF1/HSPA	5
BP	GO:009723 cellular response to toxic substance	8/83	122/18862	6.39E-08	6.35E-06	4.37E-06	NQO1/PTG	8
BP	GO:000663 unsaturated fatty acid biosynthetic process	6/83	51/18862	9.29E-08	8.91E-06	6.14E-06	AKR1C3/FA	6
BP	GO:015010 transport across blood-brain barrier	7/83	87/18862	1.09E-07	1.01E-05	6.94E-06	SLC1A4/SL	7
BP	GO:001033 response to gamma radiation	6/83	53/18862	1.18E-07	1.02E-05	7.04E-06	HSF1/FANC	6
BP	GO:001023 vascular transport	7/83	88/18862	1.18E-07	1.02E-05	7.04E-06	SLC1A4/SL	7
BP	GO:000663 fatty acid metabolic process	12/83	392/18862	1.41E-07	1.19E-05	8.17E-06	AKR1C1/AK	12
BP	GO:007124 cellular response to metal ion	9/83	189/18862	1.46E-07	1.19E-05	8.23E-06	AKR1C3/H	9
BP	GO:190165 response to ketone	9/83	193/18862	1.75E-07	1.36E-05	9.36E-06	AKR1C2/AK	9

BP	GO:005507 transition metal ion homeostasis	8/83	139/18862	1.76E-07	1.36E-05	9.36E-06	FTH1/MT1	8
BP	GO:001936 arachidonic acid metabolic process	6/83	59/18862	2.26E-07	1.70E-05	1.17E-05	AKR1C3/PT	6
BP	GO:190503 carboxylic acid transmembrane transport	8/83	154/18862	3.87E-07	2.83E-05	1.95E-05	SLC7A11/S	8
BP	GO:190382 organic acid transmembrane transport	8/83	155/18862	4.06E-07	2.90E-05	1.99E-05	SLC7A11/S	8
BP	GO:000926 cellular response to starvation	8/83	157/18862	4.48E-07	3.07E-05	2.11E-05	AKR1C3/H	8
BP	GO:007124 cellular response to inorganic substance	9/83	216/18862	4.52E-07	3.07E-05	2.11E-05	AKR1C3/H	9
BP	GO:004694 carboxylic acid transport	10/83	284/18862	4.72E-07	3.13E-05	2.15E-05	SLC7A11/A	10
BP	GO:003461 cellular response to reactive oxygen species	8/83	159/18862	4.93E-07	3.19E-05	2.20E-05	AKR1C3/H	8
BP	GO:001937 lipoxygenase pathway	4/83	16/18862	6.09E-07	3.79E-05	2.61E-05	PTGS2/ALO	4
BP	GO:000030 response to reactive oxygen species	9/83	224/18862	6.14E-07	3.79E-05	2.61E-05	AKR1C3/H	9
BP	GO:007127 cellular response to cadmium ion	5/83	38/18862	6.54E-07	3.95E-05	2.72E-05	AKR1C3/H	5
BP	GO:005140 neuron apoptotic process	9/83	230/18862	7.66E-07	4.53E-05	3.12E-05	NQO1/HSP	9
BP	GO:190121 regulation of neuron death	10/83	302/18862	8.27E-07	4.79E-05	3.30E-05	SLC7A11/H	10

BP	GO:007121 cellular response to biotic stimulus	9/83	233/18862	8.53E-07	4.84E-05	3.33E-05	HSF1/HSPA	9
BP	GO:004691 cellular transition metal ion homeostasis	7/83	118/18862	8.79E-07	4.89E-05	3.37E-05	FTH1/MT1	7
BP	GO:000301 vascular process in circulatory system	9/83	245/18862	1.29E-06	6.95E-05	4.79E-05	SRC/CAV1/	9
BP	GO:000682 iron ion transport	6/83	79/18862	1.30E-06	6.95E-05	4.79E-05	FTH1/FTL/T	6
BP	GO:000004 transition metal ion transport	7/83	127/18862	1.44E-06	7.57E-05	5.21E-05	FTH1/MT3/	7
BP	GO:004218 cellular ketone metabolic process	9/83	254/18862	1.74E-06	8.98E-05	6.19E-05	SLC7A11/A	9
BP	GO:004873 gland development	11/83	413/18862	1.90E-06	9.63E-05	6.63E-05	SRC/PML/T	11
BP	GO:004365 linoleic acid metabolic process	4/83	21/18862	1.97E-06	9.79E-05	6.74E-05	FADS2/ALO	4
BP	GO:005507 iron ion homeostasis	6/83	86/18862	2.15E-06	0.00011	7.21E-05	FTH1/FTL/T	6
BP	GO:003649 PERK-mediated unfolded protein response	4/83	23/18862	2.90E-06	0.00014	9.57E-05	HSPA5/AS	4
BP	GO:001021 response to ionizing radiation	7/83	142/18862	3.04E-06	0.00014	9.88E-05	HSF1/FANC	7
BP	GO:004249 response to drug	10/83	359/18862	3.90E-06	0.00018	0.00013	HSF1/NQO	10

BP	GO:003166 cellular response to nutrient levels	8/83	210/18862	3.98E-06	0.00018	0.00013	AKR1C3/H	8
BP	GO:009719 intrinsic apoptotic signaling pathway	9/83	283/18862	4.23E-06	0.00019	0.00013	HSPB1/SRC	9
BP	GO:001590 fatty acid transport	7/83	150/18862	4.38E-06	0.00019	0.00013	SLC7A11/P	7
BP	GO:014046 integrated stress response signaling	4/83	27/18862	5.66E-06	0.00025	0.00017	HSPA5/AS	4
BP	GO:007148 cellular response to gamma radiation	4/83	28/18862	6.58E-06	0.00028	0.00019	HSF1/HSPA	4
BP	GO:004668 response to cadmium ion	5/83	61/18862	7.16E-06	0.0003	0.00021	AKR1C3/H	5
BP	GO:000756 aging	9/83	304/18862	7.54E-06	0.00031	0.00022	NQO1/PM	9
BP	GO:009865 import into cell	8/83	230/18862	7.78E-06	0.00032	0.00022	SLC7A11/S	8

BP	GO:003569 cellular response to drug	5/83	63/18862	8.40E-06	0.00033	0.00023	HSF1/HSPA	5
BP	GO:190247 L-alpha-amino acid transmembrane transport	5/83	63/18862	8.40E-06	0.00033	0.00023	SLC7A11/S	5
BP	GO:004361regulation of transcription from RNA polymerase II pro	6/83	109/18862	8.53E-06	0.00033	0.00023	HSF1/HSPA	6
BP	GO:003166 cellular response to extracellular stimulus	8/83	235/18862	9.10E-06	0.00035	0.00024	AKR1C3/H	8
BP	GO:000663 fatty acid biosynthetic process	7/83	168/18862	9.23E-06	0.00035	0.00024	AKR1C3/FA	7
BP	GO:003064 aminoglycoside antibiotic metabolic process	3/83	10/18862	9.64E-06	0.00036	0.00025	AKR1C1/AK	3
BP	GO:007147 cellular response to ionizing radiation	5/83	65/18862	9.81E-06	0.00036	0.00025	HSF1/HSPA	5

BP	GO:001580 L-amino acid transport	5/83	66/18862	1.06E-05	0.00039	0.00027	SLC7A11/S	5
BP	GO:005123 maintenance of location	9/83	319/18862	1.11E-05	0.0004	0.00028	FTH1/HSPA	9
BP	GO:004362regulation of DNA-templated transcription in response	6/83	115/18862	1.16E-05	0.00041	0.00029	HSF1/HSPA	6
BP	GO:004275 long-chain fatty acid biosynthetic process	4/83	33/18862	1.29E-05	0.00046	0.00031	PTGS2/ALO	4
BP	GO:199044positive regulation of transcription from RNA polymer	3/83	11/18862	1.32E-05	0.00046	0.00032	HSPA5/DD	3
BP	GO:001571 monocarboxylic acid transport	7/83	178/18862	1.34E-05	0.00046	0.00032	SLC7A11/A	7
BP	GO:004639 carboxylic acid biosynthetic process	9/83	327/18862	1.35E-05	0.00046	0.00032	AKR1C3/FA	9
BP	GO:000687 cellular iron ion homeostasis	5/83	70/18862	1.41E-05	0.00047	0.00033	FTH1/FTL/T	5

BP	GO:004854 response to steroid hormone	9/83	330/18862	1.45E-05	0.00047	0.00033	AKR1C3/SR	9
BP	GO:014035 lipid import into cell	4/83	34/18862	1.46E-05	0.00047	0.00033	SLC7A11/S	4
BP	GO:190166 quinone metabolic process	4/83	34/18862	1.46E-05	0.00047	0.00033	AKR1C1/AK	4
BP	GO:001605 organic acid biosynthetic process	9/83	335/18862	1.64E-05	0.00052	0.00036	AKR1C3/FA	9
BP	GO:190340 reactive oxygen species biosynthetic process	6/83	123/18862	1.70E-05	0.00054	0.00037	NQO1/CAV	6
BP	GO:007258 caveolin-mediated endocytosis	3/83	12/18862	1.76E-05	0.00055	0.00038	SRC/CAV1/	3
BP	GO:200123 positive regulation of apoptotic signaling pathway	6/83	126/18862	1.95E-05	0.0006	0.00042	PML/TP63/	6

BP	GO:006201 regulation of small molecule metabolic process	10/83	437/18862	2.16E-05	0.00066	0.00046	SLC7A11/A	10
BP	GO:007139 cellular response to fatty acid	4/83	38/18862	2.30E-05	0.00069	0.00048	AKR1C1/AK	4
BP	GO:004352 regulation of neuron apoptotic process	7/83	197/18862	2.59E-05	0.00077	0.00053	NQO1/MT	7
BP	GO:007122 cellular response to lipopolysaccharide	7/83	197/18862	2.59E-05	0.00077	0.00053	HSF1/SRC/	7
BP	GO:000931 response to radiation	10/83	447/18862	2.62E-05	0.00077	0.00053	SLC7A11/H	10
BP	GO:004254 response to hydrogen peroxide	6/83	135/18862	2.89E-05	0.00084	0.00058	HSF1/NQO	6

BP	GO:005118 vitamin transport	4/83	41/18862	3.12E-05	0.00089	0.00062	SLC2A1/SL	4
BP	GO:004328regulation of cysteine-type endopeptidase activity invo	7/83	205/18862	3.34E-05	0.00095	0.00065	HSF1/SRC/	7
BP	GO:008971 amino acid import across plasma membrane	4/83	42/18862	3.43E-05	0.00097	0.00067	SLC7A11/S	4
BP	GO:004244 progesterone metabolic process	3/83	15/18862	3.60E-05	0.001	0.00069	AKR1C1/AK	3
BP	GO:005165 maintenance of location in cell	7/83	209/18862	3.78E-05	0.00103	0.00071	FTH1/HSPA	7
BP	GO:007121 cellular response to molecule of bacterial origin	7/83	209/18862	3.78E-05	0.00103	0.00071	HSF1/SRC/	7
BP	GO:001580 neutral amino acid transport	4/83	44/18862	4.14E-05	0.00111	0.00076	SLC1A4/SL	4

BP	GO:004512 regulation of bone resorption	4/83	44/18862	4.14E-05	0.00111	0.00076	SRC/IL6/TF	4
BP	GO:000226 myeloid cell homeostasis	6/83	145/18862	4.32E-05	0.00113	0.00078	SLC7A11/Z	6
BP	GO:005159 response to calcium ion	6/83	145/18862	4.32E-05	0.00113	0.00078	AKR1C3/H	6
BP	GO:007030 cellular response to hydrogen peroxide	5/83	90/18862	4.79E-05	0.00124	0.00086	HSF1/NQO	5
BP	GO:190165 cellular response to ketone	5/83	92/18862	5.32E-05	0.00137	0.00094	AKR1C2/AK	5
BP	GO:007149 cellular response to external stimulus	8/83	303/18862	5.61E-05	0.0014	0.00097	AKR1C3/H	8
BP	GO:000686 amino acid transport	6/83	152/18862	5.62E-05	0.0014	0.00097	SLC7A11/S	6

BP	GO:003196 response to corticosteroid	6/83	152/18862	5.62E-05	0.0014	0.00097	AKR1C3/SR	6
BP	GO:000669 prostanoid metabolic process	4/83	48/18862	5.85E-05	0.0014	0.00097	AKR1C1/AK	4
BP	GO:000669 prostaglandin metabolic process	4/83	48/18862	5.85E-05	0.0014	0.00097	AKR1C1/AK	4
BP	GO:004214 cellular response to glucose starvation	4/83	48/18862	5.85E-05	0.0014	0.00097	HSPA5/AS	4
BP	GO:004309 amino acid import	4/83	48/18862	5.85E-05	0.0014	0.00097	SLC7A11/S	4
BP	GO:007233 monocarboxylic acid biosynthetic process	7/83	224/18862	5.86E-05	0.0014	0.00097	AKR1C3/FA	7

BP	GO:009750 stress response to metal ion	3/83	18/18862	6.39E-05	0.00152	0.00105	MT1G/HSP	3
BP	GO:000333 amino acid transmembrane transport	5/83	96/18862	6.52E-05	0.00154	0.00106	SLC7A11/S	5
BP	GO:001810 peptidyl-serine phosphorylation	8/83	310/18862	6.59E-05	0.001539	0.00106	SRC/CAV1/	8
BP	GO:003016 platelet activation	6/83	157/18862	6.72E-05	0.001558	0.00107	SLC7A11/H	6
BP	GO:200011 regulation of cysteine-type endopeptidase activity	7/83	230/18862	6.92E-05	0.00159	0.0011	HSF1/SRC/	7
BP	GO:004685 regulation of bone remodeling	4/83	51/18862	7.44E-05	0.0017	0.00117	SRC/IL6/TF	4

BP	GO:009730 response to alcohol	7/83	233/18862	7.50E-05	0.001697	0.00117	AKR1C2/AK	7
BP	GO:000705 cell cycle arrest	7/83	235/18862	7.92E-05	0.00178	0.00122	PML/DUSP	7
BP	GO:000698 ER-nucleus signaling pathway	4/83	53/18862	8.66E-05	0.00193	0.00133	HSPA5/AS	4
BP	GO:000692 inflammatory cell apoptotic process	3/83	20/18862	8.87E-05	0.00193	0.00133	SLC7A11/IL	3
BP	GO:007137 cellular response to prostaglandin stimulus	3/83	20/18862	8.87E-05	0.00193	0.00133	AKR1C2/AK	3
BP	GO:190264 tertiary alcohol metabolic process	3/83	20/18862	8.87E-05	0.00193	0.00133	AKR1C1/AK	3
BP	GO:007121 cellular response to abiotic stimulus	8/83	330/18862	0.0001	0.00218	0.0015	HSF1/HSPA	8

BP	GO:010400 cellular response to environmental stimulus	8/83	330/18862	0.0001	0.00218	0.0015	HSF1/HSPA	8
BP	GO:001613 glycoside metabolic process	3/83	21/18862	0.0001	0.00219	0.00151	AKR1C1/AK	3
BP	GO:001974 secondary metabolic process	4/83	56/18862	0.00011	0.00227	0.00156	SLC7A11/A	4
BP	GO:001820 peptidyl-serine modification	8/83	333/18862	0.00011	0.00227	0.00156	SRC/CAV1/	8
BP	GO:190161 organic hydroxy compound biosynthetic process	7/83	251/18862	0.00012	0.00248	0.00171	SLC7A11/A	7
BP	GO:000181 positive regulation of cytokine production	9/83	437/18862	0.00013	0.00263	0.00181	HSPB1/PTG	9

BP	GO:002261 gland morphogenesis	5/83	111/18862	0.00013	0.00264	0.00182	SRC/PML/T	5
BP	GO:000759 blood coagulation	8/83	342/18862	0.00013	0.00264	0.00182	SLC7A11/H	8
BP	GO:190438 cellular response to angiotensin	3/83	23/18862	0.00014	0.00275	0.0019	HSF1/SRC/	3
BP	GO:000759 hemostasis	8/83	346/18862	0.00014	0.00282	0.00194	SLC7A11/H	8
BP	GO:005081 coagulation	8/83	347/18862	0.00014	0.00286	0.00197	SLC7A11/H	8
BP	GO:200123 regulation of apoptotic signaling pathway	8/83	348/18862	0.00015	0.00289	0.00199	HSPB1/SRC	8
BP	GO:000189 tissue homeostasis	7/83	260/18862	0.00015	0.00291	0.002	HSPB1/SRC	7
BP	GO:007054 response to fatty acid	4/83	61/18862	0.00015	0.00292	0.00201	AKR1C1/AK	4
BP	GO:000756 cell aging	5/83	115/18862	0.00015	0.00296	0.00204	PML/TP63/	5

BP	GO:006143 establishment of skin barrier	3/83	24/18862	0.00016	0.00296	0.00204	TP63/ALOX	3
BP	GO:005073 regulation of peptidyl-tyrosine phosphorylation	7/83	262/18862	0.00016	0.00296	0.00204	HSF1/SRC/	7
BP	GO:000989 positive regulation of catabolic process	9/83	450/18862	0.00016	0.00297	0.00205	HSF1/ZFP3	9
BP	GO:004545 bone resorption	4/83	62/18862	0.00016	0.00297	0.00205	SRC/IL6/TF	4
BP	GO:004560 regulation of epidermal cell differentiation	4/83	62/18862	0.00016	0.00297	0.00205	TP63/ZFP3	4
BP	GO:190157 fatty acid derivative biosynthetic process	4/83	62/18862	0.00016	0.00297	0.00205	ALOX12/A	4

BP	GO:000698 response to unfolded protein	6/83	185/18862	0.00017	0.00303	0.00209	HSPB1/HSF	6
BP	GO:001056 regulation of cellular ketone metabolic process	6/83	185/18862	0.00017	0.00303	0.00209	SLC7A11/A	6
BP	GO:199077 response to angiotensin	3/83	25/18862	0.00018	0.0032	0.00221	HSF1/SRC/	3
BP	GO:003356 regulation of water loss via skin	3/83	26/18862	0.0002	0.00359	0.00247	TP63/ALOX	3
BP	GO:200037regulation of reactive oxygen species metabolic proce	6/83	192/18862	0.0002	0.00364	0.00251	AKR1C3/CA	6
BP	GO:003052 intracellular receptor signaling pathway	7/83	274/18862	0.00021	0.00365	0.00252	AKR1C3/SR	7
BP	GO:006024 anatomical structure homeostasis	9/83	466/18862	0.00021	0.00366	0.00252	HSPB1/SRC	9

BP	GO:001810 peptidyl-tyrosine phosphorylation	8/83	369/18862	0.00022	0.00385	0.00265	HSF1/SRC/	8
BP	GO:001821 peptidyl-tyrosine modification	8/83	372/18862	0.00023	0.00404	0.00278	HSF1/SRC/	8
BP	GO:005105 positive regulation of DNA metabolic process	6/83	198/18862	0.00024	0.00416	0.00287	HSF1/SRC/	6
BP	GO:004568 regulation of epidermis development	4/83	69/18862	0.00024	0.00419	0.00289	TP63/ZFP3	4
BP	GO:001057positive regulation of vascular endothelial growth facto	3/83	28/18862	0.00025	0.00422	0.0029	PTGS2/IL6/	3
BP	GO:003302 myeloid cell apoptotic process	3/83	28/18862	0.00025	0.00422	0.0029	SLC7A11/IL	3
BP	GO:007128 cellular response to copper ion	3/83	28/18862	0.00025	0.00422	0.0029	HSF1/MT1	3

BP	GO:007138 cellular response to steroid hormone stimulus	6/83	201/18862	0.00026	0.00437	0.00301	AKR1C3/SR	6
BP	GO:004668 response to organophosphorus	5/83	130/18862	0.00027	0.00455	0.00314	AKR1C1/H	5
BP	GO:007233 modified amino acid transport	3/83	29/18862	0.00028	0.0046	0.00317	SLC7A11/S	3
BP	GO:001590 long-chain fatty acid transport	4/83	72/18862	0.00029	0.00471	0.00324	PLIN2/DRD	4
BP	GO:003133 positive regulation of cellular catabolic process	8/83	384/18862	0.00029	0.00471	0.00324	HSF1/ZFP3	8
BP	GO:003596 response to topologically incorrect protein	6/83	206/18862	0.0003	0.00484	0.00334	HSPB1/HSF	6

BP	GO:000680 nitric oxide biosynthetic process	4/83	73/18862	0.0003	0.00487	0.00335	NQO1/CAV	4
BP	GO:003110 animal organ regeneration	4/83	73/18862	0.0003	0.00487	0.00335	IL6/HAMP/	4
BP	GO:003469 response to prostaglandin	3/83	30/18862	0.00031	0.00492	0.00339	AKR1C2/AK	3
BP	GO:190382 positive regulation of cellular protein localization	7/83	295/18862	0.00032	0.00513	0.00353	SQSTM1/S	7
BP	GO:003497 response to endoplasmic reticulum stress	7/83	296/18862	0.00033	0.00517	0.00356	HSPA5/PM	7
BP	GO:005134 negative regulation of transferase activity	7/83	296/18862	0.00033	0.00517	0.00356	HSPB1/SRC	7

BP	GO:000906 glutamine family amino acid metabolic process	4/83	75/18862	0.00033	0.00525	0.00362	SLC7A11/N	4
BP	GO:009742 liver regeneration	3/83	31/18862	0.00034	0.00528	0.00364	IL6/HAMP/	3
BP	GO:000188 liver development	5/83	138/18862	0.00036	0.00557	0.00383	ASNS/IL6/H	5
BP	GO:007037 regulation of ERK1 and ERK2 cascade	7/83	301/18862	0.00036	0.0056	0.00385	SRC/DUSP	7
BP	GO:004620 nitric oxide metabolic process	4/83	77/18862	0.00037	0.00566	0.0039	NQO1/CAV	4
BP	GO:003133negative regulation of protein-containing complex ass	5/83	139/18862	0.00037	0.00566	0.0039	HSF1/HSPA	5
BP	GO:006100 hepaticobiliary system development	5/83	140/18862	0.00038	0.00582	0.00401	ASNS/IL6/H	5

BP	GO:200105 reactive nitrogen species metabolic process	4/83	78/18862	0.00039	0.00587	0.00404	NQO1/CAV	4
BP	GO:007127 cellular response to calcium ion	4/83	82/18862	0.00047	0.00702	0.00484	AKR1C3/H	4
BP	GO:190156 fatty acid derivative metabolic process	4/83	82/18862	0.00047	0.00702	0.00484	ALOX12/A	4
BP	GO:000673 NADP metabolic process	3/83	35/18862	0.00049	0.00722	0.00498	NQO1/NO	3
BP	GO:003462 cellular response to unfolded protein	5/83	149/18862	0.00051	0.00753	0.00519	HSF1/HSPA	5
BP	GO:190040 regulation of cellular response to oxidative stress	4/83	84/18862	0.00052	0.00757	0.00522	SLC7A11/H	4

BP	GO:007037 ERK1 and ERK2 cascade	7/83	320/18862	0.00052	0.00764	0.00526	SRC/DUSP	7
BP	GO:000669 leukotriene metabolic process	3/83	36/18862	0.00053	0.00769	0.0053	ALOX12/A	3
BP	GO:004250regulation of tyrosine phosphorylation of STAT protein	4/83	85/18862	0.00054	0.0078	0.00537	HSF1/NF2/	4
BP	GO:007145 cellular response to oxygen levels	6/83	231/18862	0.00054	0.00784	0.0054	SRC/CAV1/	6
BP	GO:003410 regulation of tissue remodeling	4/83	86/18862	0.00056	0.00807	0.00556	SRC/IL6/TF	4
BP	GO:003249 response to lipopolysaccharide	7/83	326/18862	0.00058	0.00831	0.00573	HSF1/SRC/	7
BP	GO:000726 tyrosine phosphorylation of STAT protein	4/83	88/18862	0.00061	0.00871	0.006	HSF1/NF2/	4

BP	GO:003085 regulation of epithelial cell differentiation	5/83	156/18862	0.00063	0.00885	0.0061	TP63/ZFP3	5
BP	GO:003647 cell death in response to oxidative stress	4/83	89/18862	0.00064	0.00895	0.00617	SLC7A11/H	4
BP	GO:004684 bone remodeling	4/83	89/18862	0.00064	0.00895	0.00617	SRC/IL6/TF	4
BP	GO:001657 histone phosphorylation	3/83	39/18862	0.00067	0.00927	0.00638	AURKA/MA	3
BP	GO:003266 regulation of interleukin-17 production	3/83	39/18862	0.00067	0.00927	0.00638	DDIT3/SLC	3
BP	GO:002240 regulation of cell-cell adhesion	8/83	437/18862	0.00067	0.00927	0.00638	SRC/NF2/C	8

BP	GO:200124 regulation of intrinsic apoptotic signaling pathway	5/83	160/18862	0.0007	0.00963	0.00664	HSPB1/SRC	5
BP	GO:000820 C21-steroid hormone metabolic process	3/83	40/18862	0.00072	0.0097	0.00668	AKR1C1/AK	3
BP	GO:004290 xenobiotic transport	3/83	40/18862	0.00072	0.0097	0.00668	SLC7A5/SL	3
BP	GO:006044 mammary gland morphogenesis	3/83	40/18862	0.00072	0.0097	0.00668	SRC/PML/C	3
BP	GO:009873 import across plasma membrane	5/83	161/18862	0.00072	0.0097	0.00668	SLC7A11/S	5
BP	GO:190121 positive regulation of neuron death	4/83	92/18862	0.00073	0.0097	0.00668	NQO1/DDI	4

BP	GO:004592 negative regulation of growth	6/83	245/18862	0.00074	0.00985	0.00679	MT1G/PML	6
BP	GO:000683 dicarboxylic acid transport	4/83	93/18862	0.00076	0.00992	0.00683	SLC7A11/S	4
BP	GO:005159 response to cAMP	4/83	93/18862	0.00076	0.00992	0.00683	HSPA5/DU	4
BP	GO:190288 regulation of response to oxidative stress	4/83	93/18862	0.00076	0.00992	0.00683	SLC7A11/H	4
BP	GO:000195 negative regulation of cell-matrix adhesion	3/83	41/18862	0.00078	0.01009	0.00695	SRC/NF2/C	3
BP	GO:003357 response to testosterone	3/83	41/18862	0.00078	0.01009	0.00695	HSF1/NQO	3
BP	GO:004887 homeostasis of number of cells	6/83	249/18862	0.00081	0.0104	0.00716	SLC7A11/Z	6

BP	GO:000758 response to nutrient	5/83	165/18862	0.00081	0.0104	0.00716	AKR1C3/H	5
BP	GO:000223 response to molecule of bacterial origin	7/83	346/18862	0.00083	0.01049	0.00723	HSF1/SRC/	7
BP	GO:000725 receptor signaling pathway via JAK-STAT	5/83	166/18862	0.00083	0.01049	0.00723	HSF1/NF2/	5
BP	GO:004561 regulation of keratinocyte differentiation	3/83	42/18862	0.00083	0.01049	0.00723	TP63/ZFP3	3
BP	GO:004668 response to copper ion	3/83	42/18862	0.00083	0.01049	0.00723	HSF1/MT1	3
BP	GO:003232 serine transport	2/83	10/18862	0.00084	0.01049	0.00723	SLC1A4/SL	2
BP	GO:003650 ATF6-mediated unfolded protein response	2/83	10/18862	0.00084	0.01049	0.00723	HSPA5/DD	2

BP	GO:190251 regulation of apoptotic DNA fragmentation	2/83	10/18862	0.00084	0.01049	0.00723	HSF1/IL6	2
BP	GO:004801vascular endothelial growth factor receptor signaling p	4/83	96/18862	0.00085	0.01052	0.00725	HSPB1/SRC	4
BP	GO:004866 positive regulation of smooth muscle cell proliferation	4/83	96/18862	0.00085	0.01052	0.00725	IL6/ALOX1	4
BP	GO:005254 regulation of peptidase activity	8/83	455/18862	0.00088	0.01073	0.00739	HSF1/SRC/	8
BP	GO:003596 cellular response to topologically incorrect protein	5/83	168/18862	0.00088	0.01073	0.00739	HSF1/HSPA	5
BP	GO:003262 interleukin-17 production	3/83	43/18862	0.00089	0.01089	0.0075	DDIT3/SLC	3
BP	GO:005105 regulation of DNA metabolic process	7/83	353/18862	0.00093	0.01129	0.00778	HSF1/SRC/	7

BP	GO:000863intrinsic apoptotic signaling pathway in response to ox	3/83	44/18862	0.00096	0.0115	0.00792	HSPB1/PM	3
BP	GO:004277intrinsic apoptotic signaling pathway in response to DN	3/83	44/18862	0.00096	0.0115	0.00792	PML/TP63/	3
BP	GO:005109 regulation of binding	7/83	357/18862	0.00099	0.0119	0.0082	HSF1/SRC/	7
BP	GO:001937 cyclooxygenase pathway	2/83	11/18862	0.00103	0.01203	0.00829	AKR1C3/PT	2
BP	GO:003540 histone-serine phosphorylation	2/83	11/18862	0.00103	0.01203	0.00829	AURKA/PR	2
BP	GO:007077 L-aspartate transmembrane transport	2/83	11/18862	0.00103	0.01203	0.00829	SLC1A4/SL	2
BP	GO:009008 negative regulation of inclusion body assembly	2/83	11/18862	0.00103	0.01203	0.00829	HSF1/DNA	2

BP	GO:200039 regulation of lamellipodium morphogenesis	2/83	11/18862	0.00103	0.01203	0.00829	SRC/ENPP2	2
BP	GO:001063 positive regulation of epithelial cell migration	5/83	175/18862	0.00105	0.01213	0.00836	HSPB1/SRC	5
BP	GO:004877 tissue remodeling	5/83	175/18862	0.00105	0.01213	0.00836	SRC/CAV1/	5
BP	GO:005212 movement in host environment	5/83	175/18862	0.00105	0.01213	0.00836	SRC/PML/C	5
BP	GO:009769 receptor signaling pathway via STAT	5/83	175/18862	0.00105	0.01213	0.00836	HSF1/NF2/	5
BP	GO:003134 positive regulation of defense response	7/83	361/18862	0.00106	0.01217	0.00839	SRC/PTGS2	7
BP	GO:001604 cell growth	8/83	470/18862	0.00108	0.01233	0.00849	PML/MT3/	8

BP	GO:000695 acute-phase response	3/83	46/18862	0.00109	0.01235	0.00851	PTGS2/IL6/	3
BP	GO:007135 cellular response to interleukin-6	3/83	46/18862	0.00109	0.01235	0.00851	SRC/IL6/HA	3
BP	GO:005072 regulation of inflammatory response	7/83	366/18862	0.00115	0.01287	0.00887	FANCD2/P	7
BP	GO:003003 contractile actin filament bundle assembly	4/83	104/18862	0.00115	0.01287	0.00887	SRC/NF2/S	4
BP	GO:004314 stress fiber assembly	4/83	104/18862	0.00115	0.01287	0.00887	SRC/NF2/S	4
BP	GO:190379 positive regulation of anion transport	8/83	478/18862	0.0012	0.0134	0.00923	SRC/TP63/	8
BP	GO:000698 ER overload response	2/83	12/18862	0.00123	0.01349	0.00929	HSPA5/DD	2

BP	GO:003567 oligopeptide transmembrane transport	2/83	12/18862	0.00123	0.01349	0.00929	SLC7A11/A	2
BP	GO:190362 regulation of DNA catabolic process	2/83	12/18862	0.00123	0.01349	0.00929	HSF1/IL6	2
BP	GO:001400 glial cell proliferation	3/83	48/18862	0.00123	0.01349	0.00929	NF2/IL6/M	3
BP	GO:200123positive regulation of extrinsic apoptotic signaling path	3/83	48/18862	0.00123	0.01349	0.00929	PML/CAV1	3
BP	GO:000606 alcohol metabolic process	7/83	373/18862	0.00128	0.01395	0.00961	AKR1C1/AK	7
BP	GO:007234 sulfur compound transport	3/83	49/18862	0.00131	0.01421	0.00979	SLC7A11/S	3
BP	GO:002240 positive regulation of cell-cell adhesion	6/83	276/18862	0.00137	0.0148	0.0102	SRC/CAV1/	6

BP	GO:000293 response to ischemia	3/83	50/18862	0.00139	0.01484	0.01022	SQSTM1/N	3
BP	GO:007074 response to interleukin-6	3/83	50/18862	0.00139	0.01484	0.01022	SRC/IL6/HA	3
BP	GO:190200 fatty acid transmembrane transport	3/83	50/18862	0.00139	0.01484	0.01022	SLC7A11/S	3
BP	GO:007190 regulation of protein serine/ threonine kinase activity	8/83	492/18862	0.00144	0.01535	0.01057	HSPB1/SRC	8
BP	GO:000685 oligopeptide transport	2/83	13/18862	0.00145	0.01535	0.01057	SLC7A11/A	2
BP	GO:007171 icosanoid transport	3/83	51/18862	0.00147	0.01554	0.0107	NOS2/DRD	3
BP	GO:007147 cellular response to radiation	5/83	191/18862	0.00155	0.01626	0.0112	HSF1/HSPA	5

BP	GO:190160 alpha-amino acid metabolic process	5/83	191/18862	0.00155	0.01626	0.0112	SLC7A11/N	5
BP	GO:005073positive regulation of peptidyl-tyrosine phosphorylatio	5/83	193/18862	0.00162	0.01694	0.01167	HSF1/SRC/	5
BP	GO:003297 regulation of actin filament-based process	7/83	389/18862	0.00163	0.01694	0.01167	NF2/CAV1	7
BP	GO:000178 neutrophil homeostasis	2/83	14/18862	0.00168	0.01714	0.01181	SLC7A11/IL	2
BP	GO:003435NAD biosynthesis via nicotinamide riboside salvage pa	2/83	14/18862	0.00168	0.01714	0.01181	PTGS2/NN	2
BP	GO:003535regulation of peroxisome proliferator activated recepto	2/83	14/18862	0.00168	0.01714	0.01181	ALOX15/A	2
BP	GO:003629 cellular response to increased oxygen levels	2/83	14/18862	0.00168	0.01714	0.01181	CAV1/NOX	2

BP	GO:003816 angiotensin-activated signaling pathway	2/83	14/18862	0.00168	0.01714	0.01181	SRC/CAV1	2
BP	GO:008610G protein-coupled receptor signaling pathway involve	2/83	14/18862	0.00168	0.01714	0.01181	SRC/CAV1	2
BP	GO:004352 positive regulation of neuron apoptotic process	3/83	54/18862	0.00173	0.01755	0.01209	NQO1/DDI	3
BP	GO:004339 regulation of protein binding	5/83	196/18862	0.00174	0.01755	0.01209	HSF1/SRC/	5
BP	GO:004616 alcohol catabolic process	3/83	55/18862	0.00183	0.01842	0.01269	AKR1C3/M	3
BP	GO:004851 rhythmic process	6/83	294/18862	0.00188	0.01891	0.01303	HSPA5/SRC	6
BP	GO:001027 detoxification of copper ion	2/83	15/18862	0.00194	0.01915	0.0132	MT1G/MT3	2

BP	GO:003563 entry of bacterium into host cell	2/83	15/18862	0.00194	0.01915	0.0132	SRC/CAV1	2
BP	GO:004257 retinal metabolic process	2/83	15/18862	0.00194	0.01915	0.0132	AKR1C1/AK	2
BP	GO:199016 stress response to copper ion	2/83	15/18862	0.00194	0.01915	0.0132	MT1G/MT3	2
BP	GO:190054 regulation of purine nucleotide metabolic process	4/83	120/18862	0.00194	0.01917	0.01321	NOS2/DDI	4
BP	GO:001921 regulation of lipid metabolic process	7/83	402/18862	0.00196	0.01926	0.01326	AKR1C3/SR	7
BP	GO:001004 response to zinc ion	3/83	57/18862	0.00203	0.01977	0.01362	MT1G/MT3	3

BP	GO:003052 intracellular estrogen receptor signaling pathway	3/83	57/18862	0.00203	0.01977	0.01362	SRC/TP63/	3
BP	GO:000614 regulation of nucleotide metabolic process	4/83	122/18862	0.00207	0.02008	0.01383	NOS2/DDI	4
BP	GO:000155 regulation of cell growth	7/83	406/18862	0.00207	0.02008	0.01383	PML/MT3/	7
BP	GO:001057regulation of vascular endothelial growth factor produ	3/83	58/18862	0.00213	0.02056	0.01417	PTGS2/IL6/	3
BP	GO:004577 negative regulation of bone resorption	2/83	16/18862	0.00221	0.02093	0.01442	IL6/HAMP	2
BP	GO:005123 sequestering of metal ion	2/83	16/18862	0.00221	0.02093	0.01442	FTH1/FTL	2
BP	GO:007267 lamellipodium morphogenesis	2/83	16/18862	0.00221	0.02093	0.01442	SRC/ENPP2	2

BP	GO:009008 regulation of inclusion body assembly	2/83	16/18862	0.00221	0.02093	0.01442	HSF1/DNA	2
BP	GO:190207 response to salt	2/83	16/18862	0.00221	0.02093	0.01442	HSF1/HSPA	2
BP	GO:004547 response to ethanol	4/83	126/18862	0.00232	0.0219	0.01509	NQO1/HA	4
BP	GO:004340 regulation of MAP kinase activity	6/83	307/18862	0.00234	0.0219	0.01509	SRC/CAV1/	6
BP	GO:007037 positive regulation of ERK1 and ERK2 cascade	5/83	210/18862	0.00234	0.0219	0.01509	SRC/MT3/A	5
BP	GO:007138 cellular response to corticosteroid stimulus	3/83	60/18862	0.00235	0.0219	0.01509	AKR1C3/ZF	3
BP	GO:200124positive regulation of intrinsic apoptotic signaling path	3/83	60/18862	0.00235	0.0219	0.01509	CAV1/DDIT	3

BP	GO:003096 endoplasmic reticulum unfolded protein response	4/83	127/18862	0.00239	0.02223	0.01531	HSPA5/AS	4
BP	GO:005087 positive regulation of T cell activation	5/83	212/18862	0.00244	0.02264	0.0156	SRC/CAV1/	5
BP	GO:004253negative regulation of tyrosine phosphorylation of STA	2/83	17/18862	0.00249	0.02288	0.01576	NF2/CAV1	2
BP	GO:006168 detoxification of inorganic compound	2/83	17/18862	0.00249	0.02288	0.01576	MT1G/MT3	2
BP	GO:200081 negative regulation of anoikis	2/83	17/18862	0.00249	0.02288	0.01576	SRC/CAV1	2
BP	GO:000991 hormone transport	6/83	312/18862	0.00254	0.02319	0.01598	NOS2/SLC	6

BP	GO:001057 vascular endothelial growth factor production	3/83	62/18862	0.00258	0.02342	0.01614	PTGS2/IL6/	3
BP	GO:007052 platelet aggregation	3/83	62/18862	0.00258	0.02342	0.01614	SLC7A11/H	3
BP	GO:006104 regulation of wound healing	4/83	131/18862	0.00267	0.02422	0.01668	CAV1/ALO	4
BP	GO:200037negative regulation of reactive oxygen species metabo	3/83	63/18862	0.0027	0.02436	0.01678	CAV1/MT3	3
BP	GO:005254 regulation of endopeptidase activity	7/83	426/18862	0.00271	0.0244	0.01681	HSF1/SRC/	7
BP	GO:005067 epithelial cell proliferation	7/83	428/18862	0.00278	0.02465	0.01698	TP63/ZFP3	7
BP	GO:003274 positive regulation of interleukin-17 production	2/83	18/18862	0.0028	0.02465	0.01698	SLC7A5/IL6	2

BP	GO:004685 negative regulation of bone remodeling	2/83	18/18862	0.0028	0.02465	0.01698	IL6/HAMP	2
BP	GO:006025 positive regulation of glial cell proliferation	2/83	18/18862	0.0028	0.02465	0.01698	IL6/MYB	2
BP	GO:007124 cellular response to arsenic-containing substance	2/83	18/18862	0.0028	0.02465	0.01698	HSF1/ATF3	2
BP	GO:200064regulation of early endosome to late endosome transp	2/83	18/18862	0.0028	0.02465	0.01698	SRC/MAPK	2
BP	GO:000269 positive regulation of immune effector process	5/83	219/18862	0.00281	0.02465	0.01698	NOS2/SLC	5

BP	GO:005170 biological process involved in interaction with host	5/83	219/18862	0.00281	0.02465	0.01698	SRC/PML/C	5
BP	GO:003250 maintenance of protein location in cell	3/83	64/18862	0.00282	0.02467	0.017	HSPA5/PM	3
BP	GO:005138 response to glucocorticoid	4/83	135/18862	0.00298	0.02598	0.0179	ZFP36/DUS	4
BP	GO:004559 regulation of fat cell differentiation	4/83	136/18862	0.00306	0.02659	0.01832	ZFP36/PTG	4
BP	GO:005190 regulation of mitochondrial depolarization	2/83	19/18862	0.00312	0.027	0.0186	SRC/ALOX	2
BP	GO:005086 regulation of T cell activation	6/83	327/18862	0.0032	0.02761	0.01902	FANCD2/S	6

BP	GO:001081 negative regulation of cell-substrate adhesion	3/83	67/18862	0.00321	0.02767	0.01906	SRC/NF2/C	3
BP	GO:000820 steroid metabolic process	6/83	329/18862	0.00329	0.02828	0.01948	AKR1C1/AK	6
BP	GO:190001regulation of cytokine production involved in inflamma	3/83	68/18862	0.00335	0.02859	0.01969	NOS2/IL6/	3
BP	GO:190320 regulation of oxidative stress-induced cell death	3/83	68/18862	0.00335	0.02859	0.01969	SLC7A11/H	3
BP	GO:000652 cellular amino acid metabolic process	6/83	331/18862	0.00339	0.02886	0.01988	SLC7A11/N	6
BP	GO:005109regulation of DNA-binding transcription factor activity	7/83	444/18862	0.00341	0.02889	0.0199	FANCD2/C	7

BP	GO:003410 negative regulation of tissue remodeling	2/83	20/18862	0.00345	0.02908	0.02004	IL6/HAMP	2
BP	GO:006044branching involved in mammary gland duct morphoge	2/83	20/18862	0.00345	0.02908	0.02004	SRC/PML	2
BP	GO:006201positive regulation of small molecule metabolic proces	4/83	141/18862	0.00348	0.02908	0.02004	SRC/PTGS2	4
BP	GO:000253cytokine production involved in inflammatory respons	3/83	69/18862	0.00349	0.02908	0.02004	NOS2/IL6/	3
BP	GO:001482 response to activity	3/83	69/18862	0.00349	0.02908	0.02004	HSF1/IL6/P	3
BP	GO:004325 regulation of protein-containing complex assembly	7/83	446/18862	0.00349	0.02908	0.02004	HSF1/HSPA	7
BP	GO:003313 regulation of peptidyl-serine phosphorylation	4/83	143/18862	0.00366	0.03041	0.02095	CAV1/DDIT	4

BP	GO:190303 positive regulation of leukocyte cell-cell adhesion	5/83	234/18862	0.00373	0.03086	0.02126	SRC/CAV1/	5
BP	GO:001407 response to purine-containing compound	4/83	144/18862	0.00376	0.03099	0.02135	HSPA5/DU	4
BP	GO:003535peroxisome proliferator activated receptor signaling p	2/83	21/18862	0.00381	0.03112	0.02144	ALOX15/A	2
BP	GO:003808 peptidyl-tyrosine autophosphorylation	2/83	21/18862	0.00381	0.03112	0.02144	CAV1/MAP	2
BP	GO:007163positive regulation of transforming growth factor beta	2/83	21/18862	0.00381	0.03112	0.02144	PTGS2/MY	2
BP	GO:007190negative regulation of protein serine/threonine kinase	4/83	145/18862	0.00385	0.03139	0.02162	HSPB1/CA	4
BP	GO:004315negative regulation of cysteine-type endopeptidase ac	3/83	72/18862	0.00394	0.03184	0.02193	SRC/MT3/D	3

BP	GO:004870 astrocyte differentiation	3/83	72/18862	0.00394	0.03184	0.02193	MT3/IL6/M	3
BP	GO:005089 multicellular organismal water homeostasis	3/83	72/18862	0.00394	0.03184	0.02193	TP63/ALOX	3
BP	GO:003128 positive regulation of cyclase activity	2/83	22/18862	0.00417	0.03344	0.02304	NOS2/MAP	2
BP	GO:005188 mitochondrial depolarization	2/83	22/18862	0.00417	0.03344	0.02304	SRC/ALOX	2
BP	GO:005509 response to hyperoxia	2/83	22/18862	0.00417	0.03344	0.02304	CAV1/NOX	2
BP	GO:001656 covalent chromatin modification	7/83	461/18862	0.00418	0.03344	0.02304	HELLS/MT3	7

BP	GO:000646 negative regulation of protein kinase activity	5/83	243/18862	0.00437	0.03486	0.02401	HSPB1/NF2	5
BP	GO:004353positive regulation of blood vessel endothelial cell mig	3/83	75/18862	0.00442	0.035	0.02411	HSPB1/PTG	3
BP	GO:007233intrinsic apoptotic signaling pathway by p53 class med	3/83	75/18862	0.00442	0.035	0.02411	PML/TP63/	3
BP	GO:000654 glutamine metabolic process	2/83	23/18862	0.00456	0.03551	0.02446	ASNS/GLS2	2
BP	GO:001943 removal of superoxide radicals	2/83	23/18862	0.00456	0.03551	0.02446	NQO1/MT	2
BP	GO:003303 regulation of myeloid cell apoptotic process	2/83	23/18862	0.00456	0.03551	0.02446	SLC7A11/C	2

BP	GO:006054 negative regulation of necrotic cell death	2/83	23/18862	0.00456	0.03551	0.02446	CAV1/MT3	2
BP	GO:006105regulation of cell growth involved in cardiac muscle ce	2/83	23/18862	0.00456	0.03551	0.02446	HAMP/G6P	2
BP	GO:007084 inclusion body assembly	2/83	23/18862	0.00456	0.03551	0.02446	HSF1/DNA	2
BP	GO:003295 regulation of actin cytoskeleton organization	6/83	352/18862	0.00458	0.03555	0.02449	NF2/ALOX	6
BP	GO:004440 entry into host	4/83	153/18862	0.00466	0.03607	0.02485	SRC/CAV1/	4
BP	GO:003323 regulation of cellular amine metabolic process	3/83	77/18862	0.00476	0.03651	0.02515	SLC7A11/N	3

BP	GO:190161 organic hydroxy compound catabolic process	3/83	77/18862	0.00476	0.03651	0.02515	AKR1C3/M	3
BP	GO:005101 actin filament bundle assembly	4/83	154/18862	0.00477	0.03651	0.02515	SRC/NF2/S	4
BP	GO:200123 regulation of extrinsic apoptotic signaling pathway	4/83	154/18862	0.00477	0.03651	0.02515	SRC/PML/C	4
BP	GO:000630 apoptotic DNA fragmentation	2/83	24/18862	0.00496	0.03757	0.02588	HSF1/IL6	2
BP	GO:001574 C4-dicarboxylate transport	2/83	24/18862	0.00496	0.03757	0.02588	SLC1A4/SL	2
BP	GO:007129 cellular response to zinc ion	2/83	24/18862	0.00496	0.03757	0.02588	MT1G/MT3	2

BP	GO:200020 regulation of anoikis	2/83	24/18862	0.00496	0.03757	0.02588	SRC/CAV1	2
BP	GO:007156cellular response to transforming growth factor beta st	5/83	251/18862	0.00501	0.03778	0.02603	HSPA5/SRC	5
BP	GO:000961 response to virus	6/83	359/18862	0.00503	0.03778	0.02603	HSPB1/SRC	6
BP	GO:000177 leukocyte homeostasis	3/83	79/18862	0.00511	0.03778	0.02603	SLC7A11/IL	3
BP	GO:000611 regulation of glycolytic process	3/83	79/18862	0.00511	0.03778	0.02603	DDIT4/SLC	3
BP	GO:003010 water homeostasis	3/83	79/18862	0.00511	0.03778	0.02603	TP63/ALOX	3
BP	GO:003220 regulation of telomere maintenance	3/83	79/18862	0.00511	0.03778	0.02603	SRC/PML/M	3

BP	GO:004814 regulation of fibroblast proliferation	3/83	79/18862	0.00511	0.03778	0.02603	FTH1/PML/	3
BP	GO:009039 cellular senescence	3/83	79/18862	0.00511	0.03778	0.02603	PML/HRAS	3
BP	GO:190003 regulation of cellular response to heat	3/83	79/18862	0.00511	0.03778	0.02603	HSF1/MAP	3
BP	GO:006157 actin filament bundle organization	4/83	158/18862	0.00522	0.03847	0.0265	SRC/NF2/S	4
BP	GO:000193 negative regulation of protein phosphorylation	6/83	362/18862	0.00524	0.03852	0.02653	HSPB1/NF2	6
BP	GO:000189 retina homeostasis	3/83	80/18862	0.00529	0.03852	0.02653	HSPB1/ALB	3

BP	GO:001066 regulation of muscle cell apoptotic process	3/83	80/18862	0.00529	0.03852	0.02653	HSF1/ALOX	3
BP	GO:004814 fibroblast proliferation	3/83	80/18862	0.00529	0.03852	0.02653	FTH1/PML/	3
BP	GO:200011negative regulation of cysteine-type endopeptidase ac	3/83	80/18862	0.00529	0.03852	0.02653	SRC/MT3/D	3
BP	GO:000709 mitotic cell cycle checkpoint	4/83	159/18862	0.00533	0.03852	0.02654	FANCD2/P	4
BP	GO:005110 negative regulation of binding	4/83	159/18862	0.00533	0.03852	0.02654	CAV1/DDIT	4
BP	GO:200024 regulation of reproductive process	4/83	159/18862	0.00533	0.03852	0.02654	SRC/DUSP	4

BP	GO:001044 response to acidic pH	2/83	25/18862	0.00537	0.03852	0.02654	SRC/NOX1	2
BP	GO:007145 cellular response to oxygen radical	2/83	25/18862	0.00537	0.03852	0.02654	NQO1/MT	2
BP	GO:007145 cellular response to super-oxide	2/83	25/18862	0.00537	0.03852	0.02654	NQO1/MT	2
BP	GO:004346regulation of generation of precursor metabolites and	4/83	160/18862	0.00545	0.03885	0.02677	NOS2/DDI	4
BP	GO:004866 regulation of smooth muscle cell proliferation	4/83	160/18862	0.00545	0.03885	0.02677	IL6/ALOX1	4
BP	GO:014035 lipid export from cell	3/83	81/18862	0.00548	0.03885	0.02677	NOS2/GLS	3
BP	GO:190589regulation of response to endoplasmic reticulum stress	3/83	81/18862	0.00548	0.03885	0.02677	HSPA5/CA	3

BP	GO:007155 response to transforming growth factor beta	5/83	257/18862	0.00553	0.03915	0.02697	HSPA5/SRC	5
BP	GO:000930 protein secretion	6/83	367/18862	0.00559	0.03937	0.02712	NOS2/IL6/	6
BP	GO:004586 positive regulation of proteolysis	6/83	367/18862	0.00559	0.03937	0.02712	HSF1/SRC/	6
BP	GO:003559establishment of protein localization to extracellular re	6/83	368/18862	0.00567	0.03978	0.02741	NOS2/IL6/	6
BP	GO:004865 smooth muscle cell proliferation	4/83	162/18862	0.00569	0.03989	0.02748	IL6/ALOX1	4
BP	GO:000018 inactivation of MAPK activity	2/83	26/18862	0.00581	0.04047	0.02788	CAV1/DUS	2
BP	GO:004688 regulation of hormone secretion	5/83	260/18862	0.00581	0.04047	0.02788	NOS2/IL6/	5

BP	GO:005140 stress-activated MAPK cascade	5/83	261/18862	0.0059	0.04101	0.02825	ZFP36/DUS	5
BP	GO:190303 regulation of response to wounding	4/83	164/18862	0.00594	0.04122	0.0284	CAV1/ALO	4
BP	GO:001065 muscle cell apoptotic process	3/83	84/18862	0.00606	0.04192	0.02888	HSF1/ALOX	3
BP	GO:007233 signal transduction by p53 class mediator	5/83	263/18862	0.00609	0.04202	0.02895	PML/TP63/	5
BP	GO:000916 nucleotide biosynthetic process	5/83	264/18862	0.00619	0.04236	0.02918	PTGS2/NO	5
BP	GO:007169 protein localization to extracellular region	6/83	375/18862	0.0062	0.04236	0.02918	NOS2/IL6/	6

BP	GO:000267 positive regulation of acute inflammatory response	2/83	27/18862	0.00625	0.04236	0.02918	PTGS2/IL6	2
BP	GO:000906 glutamine family amino acid catabolic process	2/83	27/18862	0.00625	0.04236	0.02918	NOS2/GLS	2
BP	GO:001594nucleobase-containing small molecule interconversion	2/83	27/18862	0.00625	0.04236	0.02918	TXNRD1/R	2
BP	GO:190364 regulation of cytoplasmic transport	2/83	27/18862	0.00625	0.04236	0.02918	SRC/MAPK	2
BP	GO:001991 lipid storage	3/83	85/18862	0.00626	0.04236	0.02918	PLIN2/CAV	3
BP	GO:003410 homotypic cell-cell adhesion	3/83	85/18862	0.00626	0.04236	0.02918	SLC7A11/H	3

BP	GO:003367 negative regulation of kinase activity	5/83	267/18862	0.00648	0.04364	0.03007	HSPB1/NF2	5
BP	GO:190129 nucleoside phosphate biosynthetic process	5/83	267/18862	0.00648	0.04364	0.03007	PTGS2/NO	5
BP	GO:005189 membrane depolarization	3/83	87/18862	0.00668	0.04446	0.03063	SRC/CAV1/	3
BP	GO:190406negative regulation of cation transmembrane transpor	3/83	87/18862	0.00668	0.04446	0.03063	CAV1/HAM	3
BP	GO:000030 response to superoxide	2/83	28/18862	0.00671	0.04446	0.03063	NQO1/MT	2
BP	GO:001003 response to iron ion	2/83	28/18862	0.00671	0.04446	0.03063	HAMP/G6P	2
BP	GO:004642negative regulation of receptor signaling pathway via J	2/83	28/18862	0.00671	0.04446	0.03063	NF2/CAV1	2

BP	GO:006060 mammary gland duct morphogenesis	2/83	28/18862	0.00671	0.04446	0.03063	SRC/PML	2
BP	GO:190217regulation of oxidative stress-induced intrinsic apopto	2/83	28/18862	0.00671	0.04446	0.03063	HSPB1/NO	2
BP	GO:004217 regulation of protein catabolic process	6/83	383/18862	0.00685	0.04523	0.03116	PML/CAV1	6
BP	GO:000165 temperature homeostasis	4/83	171/18862	0.00688	0.0453	0.03121	HSF1/CAV1	4
BP	GO:000253production of molecular mediator involved in inflamm	3/83	88/18862	0.00689	0.0453	0.03121	NOS2/IL6/	3
BP	GO:003304 regulation of chromosome organization	5/83	273/18862	0.0071	0.04619	0.03182	SRC/PML/D	5
BP	GO:004349 protein kinase B signaling	5/83	273/18862	0.0071	0.04619	0.03182	AKR1C2/AK	5

BP	GO:011005 regulation of actin filament organization	5/83	273/18862	0.0071	0.04619	0.03182	NF2/ALOX	5
BP	GO:005149 regulation of stress fiber assembly	3/83	89/18862	0.00711	0.04619	0.03182	NF2/STMN	3
BP	GO:009730 cellular response to alcohol	3/83	89/18862	0.00711	0.04619	0.03182	AKR1C2/AK	3
BP	GO:000030 response to oxygen radical	2/83	29/18862	0.00719	0.04619	0.03182	NQO1/MT	2
BP	GO:000943 NAD biosynthetic process	2/83	29/18862	0.00719	0.04619	0.03182	PTGS2/NN	2
BP	GO:003629 response to increased oxygen levels	2/83	29/18862	0.00719	0.04619	0.03182	CAV1/NOX	2

BP	GO:190002 regulation of ruffle assembly	2/83	29/18862	0.00719	0.04619	0.03182	CAV1/HRA	2
BP	GO:200063 positive regulation of gene silencing by miRNA	2/83	29/18862	0.00719	0.04619	0.03182	ZFP36/IL6	2
BP	GO:004347 regulation of carbohydrate catabolic process	3/83	90/18862	0.00733	0.04698	0.03236	DDIT4/SLC	3
BP	GO:003109 stress-activated protein kinase signaling cascade	5/83	276/18862	0.00743	0.04749	0.03272	ZFP36/DUS	5
BP	GO:003313negative regulation of peptidyl-serine phosphorylation	2/83	30/18862	0.00768	0.04867	0.03353	CAV1/DDIT	2
BP	GO:004668 response to arsenic-containing substance	2/83	30/18862	0.00768	0.04867	0.03353	HSF1/ATF3	2

BP	GO:006014positive regulation of post-transcriptional gene silencin	2/83	30/18862	0.00768	0.04867	0.03353	ZFP36/IL6	2
BP	GO:007010 interleukin-6-mediated signaling pathway	2/83	30/18862	0.00768	0.04867	0.03353	SRC/IL6	2
BP	GO:190179regulation of signal transduction by p53 class mediato	4/83	177/18862	0.00775	0.04897	0.03373	PML/TP63/	4
BP	GO:005070 regulation of protein secretion	5/83	279/18862	0.00777	0.04897	0.03373	NOS2/IL6/	5
BP	GO:004518 maintenance of protein location	3/83	92/18862	0.00779	0.049	0.03375	HSPA5/PM	3
BP	GO:002290 electron transport chain	4/83	178/18862	0.0079	0.04948	0.03408	AIFM2/NCF	4
BP	GO:005079 regulation of insulin secretion	4/83	178/18862	0.0079	0.04948	0.03408	NOS2/IL6/	4

BP	GO:001401 regulation of gliogenesis	3/83	93/18862	0.00802	0.05013	0.03454	NF2/IL6/M	3
BP	GO:000073 DNA catabolic process, endo-nucleolytic	2/83	31/18862	0.00819	0.05071	0.03493	HSF1/IL6	2
BP	GO:000151 prostaglandin biosynthetic process	2/83	31/18862	0.00819	0.05071	0.03493	AKR1C3/PT	2
BP	GO:004645 prostanoid biosynthetic process	2/83	31/18862	0.00819	0.05071	0.03493	AKR1C3/PT	2
BP	GO:007030 lens fiber cell differentiation	2/83	31/18862	0.00819	0.05071	0.03493	SLC7A11/N	2
BP	GO:004206 gliogenesis	5/83	283/18862	0.00823	0.05071	0.03493	NF2/MT3/I	5
BP	GO:003430 primary alcohol metabolic process	3/83	94/18862	0.00826	0.05071	0.03493	AKR1C1/AK	3

BP	GO:006109 regulation of protein tyrosine kinase activity	3/83	94/18862	0.00826	0.05071	0.03493	SRC/CAV1/	3
BP	GO:190403 regulation of epithelial cell apoptotic process	3/83	94/18862	0.00826	0.05071	0.03493	AKR1C3/ZF	3
BP	GO:003287 regulation of stress-activated MAPK cascade	4/83	181/18862	0.00837	0.05114	0.03523	DUSP1/NO	4
BP	GO:004340 negative regulation of MAPK cascade	4/83	181/18862	0.00837	0.05114	0.03523	NF2/CAV1	4
BP	GO:000269 positive regulation of leukocyte activation	6/83	401/18862	0.00849	0.05163	0.03557	SRC/CAV1/	6
BP	GO:000279 peptide secretion	6/83	401/18862	0.00849	0.05163	0.03557	NOS2/IL6/	6

BP	GO:003064 regulation of cellular pH	3/83	95/18862	0.0085	0.05163	0.03557	MAFG/NO	3
BP	GO:001935 nicotinamide nucleotide biosynthetic process	2/83	32/18862	0.00871	0.05221	0.03596	PTGS2/NN	2
BP	GO:001936 pyridine nucleotide biosynthetic process	2/83	32/18862	0.00871	0.05221	0.03596	PTGS2/NN	2
BP	GO:003267 regulation of interleukin-4 production	2/83	32/18862	0.00871	0.05221	0.03596	DDIT3/SLC	2
BP	GO:004801 neurotrophin TRK receptor signaling pathway	2/83	32/18862	0.00871	0.05221	0.03596	SRC/DDIT4	2
BP	GO:004838 retinoic acid receptor signaling pathway	2/83	32/18862	0.00871	0.05221	0.03596	AKR1C3/PM	2

BP	GO:007135 cellular response to interleukin-4	2/83	32/18862	0.00871	0.05221	0.03596	HSPA5/PM	2
BP	GO:003209 negative regulation of protein binding	3/83	96/18862	0.00875	0.05233	0.03605	CAV1/AUR	3
BP	GO:007030regulation of stress-activated protein kinase signaling	4/83	184/18862	0.00885	0.05283	0.0364	DUSP1/NO	4
BP	GO:004860 reproductive structure development	6/83	405/18862	0.00889	0.05295	0.03648	AKR1C3/H	6
BP	GO:003030 negative regulation of cell growth	4/83	185/18862	0.00902	0.05359	0.03692	PML/MT3/	4
BP	GO:004232 negative regulation of phosphorylation	6/83	407/18862	0.0091	0.05363	0.03694	HSPB1/NF2	6
BP	GO:006145 reproductive system development	6/83	408/18862	0.0092	0.05363	0.03694	AKR1C3/H	6

BP	GO:000329 physiological muscle hypertrophy	2/83	33/18862	0.00925	0.05363	0.03694	HAMP/G6P	2
BP	GO:000330 physiological cardiac muscle hypertrophy	2/83	33/18862	0.00925	0.05363	0.03694	HAMP/G6P	2
BP	GO:000653 glutamate metabolic process	2/83	33/18862	0.00925	0.05363	0.03694	SLC7A11/G	2
BP	GO:003026 apoptotic nuclear changes	2/83	33/18862	0.00925	0.05363	0.03694	HSF1/IL6	2
BP	GO:003263 interleukin-4 production	2/83	33/18862	0.00925	0.05363	0.03694	DDIT3/SLC	2
BP	GO:006025 regulation of glial cell proliferation	2/83	33/18862	0.00925	0.05363	0.03694	IL6/MYB	2
BP	GO:006104cell growth involved in cardiac muscle cell developmen	2/83	33/18862	0.00925	0.05363	0.03694	HAMP/G6P	2

BP	GO:190489negative regulation of receptor signaling pathway via	2/83	33/18862	0.00925	0.05363	0.03694	NF2/CAV1	2
BP	GO:001921 regulation of fatty acid metabolic process	3/83	98/18862	0.00926	0.05363	0.03694	CAV1/PTG	3
BP	GO:011002 regulation of actomyosin structure organization	3/83	98/18862	0.00926	0.05363	0.03694	NF2/STMN	3
BP	GO:001063 regulation of epithelial cell migration	5/83	293/18862	0.00948	0.05479	0.03774	HSPB1/SRC	5
BP	GO:000270positive regulation of production of molecular mediato	3/83	99/18862	0.00952	0.05479	0.03774	SLC7A5/IL6	3
BP	GO:004327 response to alkaloid	3/83	99/18862	0.00952	0.05479	0.03774	NQO1/HSP	3

BP	GO:005086 positive regulation of cell activation	6/83	412/18862	0.00963	0.05531	0.0381	SRC/CAV1/	6
BP	GO:190595 regulation of lipid localization	4/83	189/18862	0.0097	0.05564	0.03833	PLIN2/CAV	4
BP	GO:000716 negative regulation of cell adhesion	5/83	295/18862	0.00974	0.05571	0.03838	SRC/NF2/D	5
BP	GO:000863intrinsic apoptotic signaling pathway in response to DN	3/83	100/18862	0.00978	0.05571	0.03838	PML/TP63/	3
BP	GO:004327 anoikis	2/83	34/18862	0.0098	0.05571	0.03838	SRC/CAV1	2
BP	GO:200075 positive regulation of peptidyl-lysine acetylation	2/83	34/18862	0.0098	0.05571	0.03838	MAPK3/PR	2
BP	GO:004358 skin development	6/83	415/18862	0.00995	0.05649	0.03891	AKR1C3/TP	6
BP	GO:004642regulation of receptor signaling pathway via JAK-STAT	3/83	101/18862	0.01005	0.05673	0.03908	NF2/CAV1	3

BP	GO:200037positive regulation of reactive oxygen species metabol	3/83	101/18862	0.01005	0.05673	0.03908	AKR1C3/PT	3
BP	GO:003103 actomyosin structure organization	4/83	191/18862	0.01006	0.05673	0.03908	SRC/NF2/S	4
BP	GO:003109 regeneration	4/83	192/18862	0.01024	0.05694	0.03923	IL6/HAMP/	4
BP	GO:003223 regulation of actin filament bundle assembly	3/83	102/18862	0.01032	0.05694	0.03923	NF2/STMN	3
BP	GO:004320 response to amino acid	3/83	102/18862	0.01032	0.05694	0.03923	HSF1/NQO	3
BP	GO:004477 mitotic DNA damage checkpoint	3/83	102/18862	0.01032	0.05694	0.03923	FANCD2/P	3

BP	GO:007188 leukocyte apoptotic process	3/83	102/18862	0.01032	0.05694	0.03923	SLC7A11/IL	3
BP	GO:000692cellular component disassembly involved in execution	2/83	35/18862	0.01036	0.05694	0.03923	HSF1/IL6	2
BP	GO:001936 pyridine nucleotide metabolic process	2/83	35/18862	0.01036	0.05694	0.03923	PTGS2/NN	2
BP	GO:003214 activation of protein kinase B activity	2/83	35/18862	0.01036	0.05694	0.03923	SRC/MT3	2
BP	GO:004649 nicotinamide nucleotide metabolic process	2/83	35/18862	0.01036	0.05694	0.03923	PTGS2/NN	2
BP	GO:005135 negative regulation of oxidoreductase activity	2/83	35/18862	0.01036	0.05694	0.03923	CAV1/MT3	2

BP	GO:007067 response to interleukin-4	2/83	35/18862	0.01036	0.05694	0.03923	HSPA5/PM	2
BP	GO:007252 pyridine-containing compound biosynthetic process	2/83	35/18862	0.01036	0.05694	0.03923	PTGS2/NN	2
BP	GO:190589positive regulation of response to endoplasmic reticulu	2/83	35/18862	0.01036	0.05694	0.03923	CAV1/DDIT	2
BP	GO:003009 myeloid cell differentiation	6/83	419/18862	0.0104	0.05706	0.03931	MT1G/SRC	6
BP	GO:000688 regulation of pH	3/83	103/18862	0.0106	0.0576	0.03968	MAFG/NO	3
BP	GO:003263 interleukin-8 production	3/83	103/18862	0.0106	0.0576	0.03968	NOS2/DDI	3
BP	GO:003265 regulation of interleukin-1 beta production	3/83	103/18862	0.0106	0.0576	0.03968	HSPB1/PM	3

BP	GO:007049 interleukin-1-mediated signaling pathway	3/83	103/18862	0.0106	0.0576	0.03968	SQSTM1/IL	3
BP	GO:190547 regulation of protein localization to membrane	4/83	194/18862	0.0106	0.0576	0.03968	SLC7A11/S	4
BP	GO:004687 hormone secretion	5/83	302/18862	0.0107	0.05803	0.03997	NOS2/IL6/	5
BP	GO:190121 negative regulation of neuron death	4/83	195/18862	0.01079	0.05838	0.04022	SLC7A11/H	4
BP	GO:003357 transferrin transport	2/83	36/18862	0.01094	0.05896	0.04061	TFRC/STEA	2
BP	GO:004573 respiratory burst	2/83	36/18862	0.01094	0.05896	0.04061	NCF2/NOX	2
BP	GO:004578 positive regulation of cell adhesion	6/83	425/18862	0.0111	0.05972	0.04114	SRC/CAV1/	6

BP	GO:001605 carbohydrate catabolic process	4/83	197/18862	0.01117	0.05997	0.04131	DDIT4/SLC	4
BP	GO:006032 cell chemotaxis	5/83	306/18862	0.01128	0.06046	0.04165	HSPB1/DU	5
BP	GO:001895 phenol-containing compound metabolic process	3/83	106/18862	0.01145	0.06112	0.0421	SLC7A11/D	3
BP	GO:004477 mitotic DNA integrity check-point	3/83	106/18862	0.01145	0.06112	0.0421	FANCD2/P	3
BP	GO:000009 sulfur amino acid metabolic process	2/83	37/18862	0.01153	0.0612	0.04216	SLC7A11/N	2
BP	GO:001083 regulation of keratinocyte proliferation	2/83	37/18862	0.01153	0.0612	0.04216	TP63/ZFP3	2

BP	GO:190274 positive regulation of lamellipodium organization	2/83	37/18862	0.01153	0.0612	0.04216	SRC/ENPP2	2
BP	GO:000279 regulation of peptide secretion	5/83	308/18862	0.01158	0.06134	0.04226	NOS2/IL6/	5
BP	GO:000252 acute inflammatory response	3/83	107/18862	0.01174	0.06168	0.04249	PTGS2/IL6/	3
BP	GO:003264 regulation of interferon-gamma production	3/83	107/18862	0.01174	0.06168	0.04249	DDIT3/SLC	3
BP	GO:003313 positive regulation of peptidyl-serine phosphorylation	3/83	107/18862	0.01174	0.06168	0.04249	CAV1/IL6/T	3
BP	GO:200027 regulation of DNA biosynthetic process	3/83	107/18862	0.01174	0.06168	0.04249	SRC/DUSP	3

BP	GO:001095 positive regulation of peptidase activity	4/83	200/18862	0.01176	0.06168	0.04249	HSF1/PML/	4
BP	GO:003261 interleukin-1 beta production	3/83	108/18862	0.01204	0.0629	0.04333	HSPB1/PM	3
BP	GO:000150 neurotransmitter uptake	2/83	38/18862	0.01214	0.0629	0.04333	DRD4/SLC3	2
BP	GO:000688 cellular zinc ion homeostasis	2/83	38/18862	0.01214	0.0629	0.04333	MT1G/MT3	2
BP	GO:003209 response to food	2/83	38/18862	0.01214	0.0629	0.04333	MT3/G6PD	2
BP	GO:003817 neurotrophin signaling pathway	2/83	38/18862	0.01214	0.0629	0.04333	SRC/DDIT4	2
BP	GO:000717transforming growth factor beta receptor signaling pa	4/83	202/18862	0.01216	0.0629	0.04333	HSPA5/SRC	4
BP	GO:000961 response to mechanical stimulus	4/83	202/18862	0.01216	0.0629	0.04333	SRC/ASNS/	4

BP	GO:000989 negative regulation of catabolic process	5/83	312/18862	0.01219	0.0629	0.04333	PML/ZFP36	5
BP	GO:005122 positive regulation of protein transport	5/83	312/18862	0.01219	0.0629	0.04333	SRC/TP63/	5
BP	GO:000701 actin filament organization	6/83	435/18862	0.01234	0.06345	0.04371	SRC/NF2/A	6
BP	GO:190465 glucose transmembrane transport	3/83	109/18862	0.01234	0.06345	0.04371	SLC2A1/SL	3
BP	GO:003444 lipid oxidation	3/83	110/18862	0.01265	0.06479	0.04463	ALOX12/A	3
BP	GO:190489 regulation of receptor signaling pathway via STAT	3/83	110/18862	0.01265	0.06479	0.04463	NF2/CAV1	3

BP	GO:003314regulation of intracellular estrogen receptor signaling	2/83	39/18862	0.01276	0.06498	0.04476	SRC/TP63	2
BP	GO:005089 intestinal absorption	2/83	39/18862	0.01276	0.06498	0.04476	AKR1C1/H	2
BP	GO:200027 negative regulation of DNA biosynthetic process	2/83	39/18862	0.01276	0.06498	0.04476	SRC/DUSP	2
BP	GO:003162 receptor internalization	3/83	111/18862	0.01296	0.06529	0.04498	CAV1/TFRC	3
BP	GO:004666 female sex differentiation	3/83	111/18862	0.01296	0.06529	0.04498	HSPA5/SRC	3
BP	GO:190595 positive regulation of lipid localization	3/83	111/18862	0.01296	0.06529	0.04498	PLIN2/CAV	3

BP	GO:000610 regulation of carbohydrate metabolic process	4/83	206/18862	0.01298	0.06529	0.04498	SRC/DDIT4	4
BP	GO:003010 regulation of endocytosis	4/83	206/18862	0.01298	0.06529	0.04498	SRC/CAV1/	4
BP	GO:007055 response to interleukin-1	4/83	206/18862	0.01298	0.06529	0.04498	SQSTM1/S	4
BP	GO:007145 cellular response to hypoxia	4/83	206/18862	0.01298	0.06529	0.04498	SRC/PTGS2	4
BP	GO:003007 insulin secretion	4/83	207/18862	0.0132	0.06624	0.04563	NOS2/IL6/	4
BP	GO:000864 hexose transmembrane transport	3/83	112/18862	0.01328	0.06626	0.04565	SLC2A1/SL	3
BP	GO:003260 interferon-gamma production	3/83	112/18862	0.01328	0.06626	0.04565	DDIT3/SLC	3

BP	GO:000630 DNA catabolic process	2/83	40/18862	0.01339	0.06626	0.04565	HSF1/IL6	2
BP	GO:004502 early endosome to late endosome transport	2/83	40/18862	0.01339	0.06626	0.04565	SRC/MAPK	2
BP	GO:005506 zinc ion homeostasis	2/83	40/18862	0.01339	0.06626	0.04565	MT1G/MT3	2
BP	GO:007163regulation of transforming growth factor beta product	2/83	40/18862	0.01339	0.06626	0.04565	PTGS2/MY	2
BP	GO:015007 regulation of neuroinflammatory response	2/83	40/18862	0.01339	0.06626	0.04565	PTGS2/IL6	2
BP	GO:190403 positive regulation of epithelial cell apoptotic process	2/83	40/18862	0.01339	0.06626	0.04565	AKR1C3/IL	2
BP	GO:003051intracellular steroid hormone receptor signaling pathw	3/83	113/18862	0.0136	0.06693	0.04611	SRC/TP63/	3

BP	GO:000007 cell cycle checkpoint	4/83	209/18862	0.01363	0.06693	0.04611	FANCD2/P	4
BP	GO:000633 chromatin remodeling	4/83	209/18862	0.01363	0.06693	0.04611	HELLS/TP6	4
BP	GO:009027 regulation of peptide hormone secretion	4/83	209/18862	0.01363	0.06693	0.04611	NOS2/IL6/	4
BP	GO:004593 negative regulation of mitotic cell cycle	5/83	321/18862	0.01365	0.06693	0.04611	FANCD2/P	5
BP	GO:000222 stimulatory C-type lectin receptor signaling pathway	3/83	114/18862	0.01392	0.06777	0.04669	SRC/NRAS	3
BP	GO:000609 glycolytic process	3/83	114/18862	0.01392	0.06777	0.04669	DDIT4/SLC	3

BP	GO:001574 monosaccharide transmembrane transport	3/83	114/18862	0.01392	0.06777	0.04669	SLC2A1/SL	3
BP	GO:000225 organ or tissue specific immune response	2/83	41/18862	0.01404	0.06777	0.04669	NOS2/IL6	2
BP	GO:000926 response to pH	2/83	41/18862	0.01404	0.06777	0.04669	SRC/NOX1	2
BP	GO:001093 regulation of necrotic cell death	2/83	41/18862	0.01404	0.06777	0.04669	CAV1/MT3	2
BP	GO:003085 prostate gland development	2/83	41/18862	0.01404	0.06777	0.04669	TP63/ALOX	2
BP	GO:005160 response to electrical stimulus	2/83	41/18862	0.01404	0.06777	0.04669	NQO1/SRC	2

BP	GO:007252 pyridine-containing compound metabolic process	2/83	41/18862	0.01404	0.06777	0.04669	PTGS2/NN	2
BP	GO:001657 histone modification	6/83	448/18862	0.0141	0.06794	0.04681	MT3/AURK	6
BP	GO:000170 formation of primary germ layer	3/83	115/18862	0.01425	0.06832	0.04706	NF2/DUSP	3
BP	GO:000675 ATP generation from ADP	3/83	115/18862	0.01425	0.06832	0.04706	DDIT4/SLC	3
BP	GO:003000 cellular monovalent inorganic cation homeostasis	3/83	115/18862	0.01425	0.06832	0.04706	MAFG/NO	3
BP	GO:000762 circadian rhythm	4/83	212/18862	0.01429	0.06841	0.04713	PML/NOS2	4

BP	GO:003421 carbohydrate transmembrane transport	3/83	116/18862	0.01458	0.06951	0.04789	SLC2A1/SL	3
BP	GO:190401 epithelial cell apoptotic process	3/83	116/18862	0.01458	0.06951	0.04789	AKR1C3/ZF	3
BP	GO:001400 astrocyte development	2/83	42/18862	0.0147	0.06951	0.04789	MT3/IL6	2
BP	GO:001407 response to amine	2/83	42/18862	0.0147	0.06951	0.04789	NQO1/DRD	2
BP	GO:003296 regulation of collagen biosynthetic process	2/83	42/18862	0.0147	0.06951	0.04789	IL6/MYB	2
BP	GO:007160 transforming growth factor beta production	2/83	42/18862	0.0147	0.06951	0.04789	PTGS2/MY	2

BP	GO:007259 maintenance of protein localization in organelle	2/83	42/18862	0.0147	0.06951	0.04789	HSPA5/PM	2
BP	GO:003629 cellular response to decreased oxygen levels	4/83	214/18862	0.01475	0.06962	0.04796	SRC/PTGS2	4
BP	GO:001050 regulation of autophagy	5/83	328/18862	0.01485	0.0699	0.04815	HSPB1/MT	5
BP	GO:190495positive regulation of establishment of protein localiza	5/83	328/18862	0.01485	0.0699	0.04815	SRC/TP63/	5
BP	GO:003053 adult behavior	3/83	117/18862	0.01492	0.07008	0.04828	SLC7A11/M	3
BP	GO:190303 regulation of leukocyte cell-cell adhesion	5/83	330/18862	0.01521	0.07113	0.049	SRC/CAV1/	5
BP	GO:000222innate immune response activating cell surface recepto	3/83	118/18862	0.01526	0.07113	0.048998 SRC/NRAS		3

BP	GO:004275 regulation of circadian rhythm	3/83	118/18862	0.01526	0.07113	0.049	PML/DRD4	3
BP	GO:002176 substantia nigra development	2/83	43/18862	0.01537	0.07113	0.049	HSPA5/G6	2
BP	GO:002260 ovulation cycle process	2/83	43/18862	0.01537	0.07113	0.049	HSPA5/SRC	2
BP	GO:003230 icosanoid secretion	2/83	43/18862	0.01537	0.07113	0.049	NOS2/DRD	2
BP	GO:004222 response to cocaine	2/83	43/18862	0.01537	0.07113	0.049	HSPA5/DR	2
BP	GO:009717 ruffle assembly	2/83	43/18862	0.01537	0.07113	0.049	CAV1/HRA	2
BP	GO:009892vesicle-mediated transport between endosomal comp	2/83	43/18862	0.01537	0.07113	0.049	SRC/MAPK	2
BP	GO:009719 extrinsic apoptotic signaling pathway	4/83	217/18862	0.01544	0.07126	0.04909	SRC/PML/C	4

BP	GO:000110 response to acid chemical	3/83	119/18862	0.01561	0.07126	0.04909	HSF1/NQO	3
BP	GO:000268 regulation of leukocyte chemotaxis	3/83	119/18862	0.01561	0.07126	0.04909	DUSP1/IL6	3
BP	GO:000275innate immune response-activating signal transductio	3/83	119/18862	0.01561	0.07126	0.049089 SRC/NRAS		3
BP	GO:003265 regulation of interleukin-1 production	3/83	119/18862	0.01561	0.07126	0.04909	HSPB1/PM	3
BP	GO:003476 negative regulation of ion transmembrane transport	3/83	119/18862	0.01561	0.07126	0.04909	CAV1/HAM	3
BP	GO:190357 regulation of ATP metabolic process	3/83	119/18862	0.01561	0.07126	0.04909	DDIT4/SLC	3
BP	GO:200013negative regulation of G1/S transition of mitotic cell cy	3/83	119/18862	0.01561	0.07126	0.04909	PML/AURK	3

BP	GO:001081 regulation of cell-substrate adhesion	4/83	218/18862	0.01568	0.07137	0.04917	SRC/NF2/A	4
BP	GO:004244 hormone metabolic process	4/83	218/18862	0.01568	0.07137	0.04917	AKR1C1/AK	4
BP	GO:003460 cellular response to heat	3/83	120/18862	0.01596	0.07238	0.04986	HSF1/MAP	3
BP	GO:003476 negative regulation of transmembrane transport	3/83	120/18862	0.01596	0.07238	0.04986	CAV1/HAM	3
BP	GO:000263 positive regulation of immunoglobulin production	2/83	44/18862	0.01606	0.07249	0.04994	IL6/TFRC	2
BP	GO:000325 regulation of membrane depolarization	2/83	44/18862	0.01606	0.07249	0.04994	SRC/ALOX	2

BP	GO:015007 neuroinflammatory response	2/83	44/18862	0.01606	0.07249	0.04994	PTGS2/IL6	2
CC	GO:004302 NADPH oxidase complex	4/83	12/19520	1.47E-07	3.15E-05	2.58E-05 NCF2/NOX		4
CC	GO:000576 secondary lysosome	4/83	16/19520	5.32E-07	5.72E-05	4.68E-05 SQSTM1/F		4
CC	GO:004247 melanosome	6/83	106/19520	5.98E-06	0.00032	0.00026	HSPA5/SLC	6
CC	GO:004877 pigment granule	6/83	106/19520	5.98E-06	0.00032	0.00026	HSPA5/SLC	6
CC	GO:004475 autolysosome	3/83	10/19520	8.71E-06	0.00037	0.000306 SQSTM1/F		3
CC	GO:000581 lipid droplet	5/83	95/19520	5.28E-05	0.00189	0.00155	PLIN2/AIFM	5
CC	GO:004517 apical part of cell	9/83	414/19520	6.54E-05	0.00201	0.00164	SLC7A11/N	9
CC	GO:000079 heterochromatin	4/83	72/19520	0.00025	0.00674	0.00551	HSF1/HELL	4
CC	GO:000590 caveola	4/83	80/19520	0.00038	0.00836	0.00684	SRC/CAV1/	4

CC	GO:000592 focal adhesion	8/83	416/19520	0.00039	0.00836	0.00684	HSPB1/HSP	8
CC	GO:003005 cell-substrate junction	8/83	423/19520	0.00043	0.00849	0.00694	HSPB1/HSP	8
CC	GO:000992 basal plasma membrane	6/83	240/19520	0.00056	0.00996	0.00815	SLC7A5/TF	6
CC	GO:004517 basal part of cell	6/83	258/19520	0.00081	0.01342	0.01097	SLC7A5/TF	6
CC	GO:004512 pronucleus	2/83	12/19520	0.00115	0.01731	0.01416	SLC2A1/AU	2
CC	GO:004485 plasma membrane raft	4/83	111/19520	0.00129	0.01731	0.01416	SRC/CAV1/	4
CC	GO:199020 oxidoreductase complex	4/83	111/19520	0.00129	0.01731	0.01416	NCF2/NOX	4
CC	GO:001632 basolateral plasma membrane	5/83	211/19520	0.00206	0.0261	0.02134	SLC7A5/TF	5

CC	GO:001632 apical plasma membrane	6/83	351/19520	0.00383	0.04376	0.03578	SLC7A5/SL	6
CC	GO:001623 inclusion body	3/83	74/19520	0.00387	0.04376	0.03578	SQSTM1/M	3
CC	GO:000576 early endosome	6/83	378/19520	0.00547	0.05881	0.04808	PML/NF2/C	6
MF	GO:001665 oxidoreductase activity, acting on NAD(P)H	12/83	102/18337	3.15E-14	1.07E-11	7.96E-12	AKR1C1/AK	12
MF	GO:001617 superoxide-generating NAD(P)H oxidase activity	5/83	11/18337	7.60E-10	1.29E-07	9.61E-08	NCF2/NOX	5
MF	GO:001620 antioxidant activity	8/83	86/18337	4.98E-09	5.64E-07	4.19E-07	NQO1/PTG	8
MF	GO:005066oxidoreductase activity, acting on NAD(P)H, oxygen as	5/83	16/18337	7.06E-09	6.00E-07	4.46E-07	NCF2/NOX	5

MF	GO:000851 organic anion transmembrane transporter activity	9/83	177/18337	1.06E-07	7.18E-06	5.34E-06	SLC7A11/S	9
MF	GO:001517neutral amino acid transmembrane transporter activity	5/83	34/18337	4.22E-07	2.39E-05	1.78E-05	SLC7A11/S	5
MF	GO:005066 NADP binding	5/83	53/18337	4.07E-06	0.0002	0.00015	NOS2/NOX	5
MF	GO:001670oxidoreductase activity, acting on single donors with in	4/83	25/18337	4.59E-06	0.0002	0.00015	ALOX12/A	4
MF	GO:000550 iron ion binding	7/83	150/18337	5.26E-06	0.0002	0.00015	FTH1/FTL/A	7
MF	GO:000403 aldo-keto reductase (NADP) activity	4/83	27/18337	6.33E-06	0.00021	0.00015	AKR1C1/AK	4
MF	GO:001517 L-amino acid transmembrane transporter activity	5/83	59/18337	6.95E-06	0.00021	0.00015	SLC7A11/S	5

MF	GO:001665oxidoreductase activity, acting on NAD(P)H, quinone o	5/83	60/18337	7.56E-06	0.00021	0.00015	AKR1C1/AK	5
MF	GO:001670oxidoreductase activity, acting on paired donors, with	7/83	160/18337	8.04E-06	0.00021	0.00015	AKR1C1/AK	7
MF	GO:009048 vitamin transmembrane transporter activity	4/83	29/18337	8.50E-06	0.00021	0.00015	SLC2A1/SL	4
MF	GO:000819 ferric iron binding	3/83	10/18337	1.05E-05	0.00024	0.00018	FTH1/FTL/	3
MF	GO:003205 bile acid binding	3/83	11/18337	1.44E-05	0.00031	0.00023	AKR1C1/AK	3
MF	GO:000403 alditol:NADP+ 1-oxidoreductase activity	3/83	12/18337	1.91E-05	0.00038	0.00028	AKR1C1/AK	3
MF	GO:001517 amino acid transmembrane transporter activity	5/83	81/18337	3.29E-05	0.00059	0.00044	SLC7A11/S	5

MF	GO:005066 flavin adenine dinucleotide binding	5/83	81/18337	3.29E-05	0.00059	0.00044	AIFM2/NO	5
MF	GO:002003 heme binding	6/83	140/18337	4.14E-05	0.0007	0.00052	SRC/PTGS2	6
MF	GO:001517 acidic amino acid transmembrane transporter activity	3/83	16/18337	4.80E-05	0.00078	0.00058	SLC7A11/S	3
MF	GO:005121 dioxygenase activity	5/83	89/18337	5.18E-05	0.0008	0.0006	PTGS2/ALO	5
MF	GO:004690 tetrapyrrole binding	6/83	150/18337	6.09E-05	0.0009	0.00067	SRC/PTGS2	6
MF	GO:001670oxidoreductase activity, acting on paired donors, with	4/83	48/18337	6.52E-05	0.00092	0.00069	AKR1C1/AK	4
MF	GO:000430 estradiol 17-beta-dehydrogenase activity	3/83	18/18337	6.95E-05	0.00095	0.0007	AKR1C1/AK	3
MF	GO:004694 carboxylic acid transmembrane transporter activity	6/83	157/18337	7.85E-05	0.001	0.00074	SLC7A11/S	6

MF	GO:000534 organic acid transmembrane transporter activity	6/83	158/18337	8.13E-05	0.001	0.00074	SLC7A11/S	6
MF	GO:001672 oxidoreductase activity, acting on metal ions	3/83	19/18337	8.22E-05	0.001	0.00074	FTH1/STEA	3
MF	GO:000535 glucose transmembrane transporter activity	3/83	21/18337	0.00011	0.00119	0.00089	SLC2A1/SL	3
MF	GO:000810 alcohol dehydrogenase (NADP+) activity	3/83	21/18337	0.00011	0.00119	0.00089	AKR1C1/AK	3
MF	GO:001514 hexose transmembrane transporter activity	3/83	21/18337	0.00011	0.00119	0.00089	SLC2A1/SL	3

MF	GO:007234modified amino acid transmembrane transporter activ	3/83	21/18337	0.00011	0.00119	0.00089	SLC7A11/S	3
MF	GO:001514 monosaccharide transmembrane transporter activity	3/83	23/18337	0.00015	0.00153	0.00114	SLC2A1/SL	3
MF	GO:001670oxidoreductase activity, acting on single donors with in	3/83	24/18337	0.00017	0.00169	0.00126	ALOX12/A	3
MF	GO:003140 carboxylic acid binding	6/83	184/18337	0.00019	0.00181	0.00134	AKR1C1/AK	6
MF	GO:005111 sugar transmembrane transporter activity	3/83	25/18337	0.00019	0.00181	0.00134	SLC2A1/SL	3
MF	GO:001661oxidoreductase activity, acting on the CH-OH group o	5/83	120/18337	0.00021	0.00188	0.0014	AKR1C1/AK	5
MF	GO:000819 ferrous iron binding	3/83	26/18337	0.00022	0.00188	0.0014	FTH1/FTL/E	3
MF	GO:001662oxidoreductase activity, acting on the CH-CH group of	3/83	26/18337	0.00022	0.00188	0.0014	AKR1C1/AK	3

MF	GO:000850 anion transmembrane transporter activity	9/83	459/18337	0.00023	0.00193	0.00144	SLC7A11/S	9
MF	GO:003329 monocarboxylic acid binding	4/83	71/18337	0.0003	0.0025	0.00186	AKR1C1/AK	4
MF	GO:001661oxidoreductase activity, acting on CH-OH group of do 5/83		130/18337	0.00031	0.0025	0.00186	AKR1C1/AK	5
MF	GO:003376steroid dehydrogenase activity, acting on the CH-OH	3/83	30/18337	0.00033	0.00263	0.00195	AKR1C1/AK	3
MF	GO:001622 steroid dehydrogenase activity	3/83	34/18337	0.00048	0.00374	0.00278	AKR1C1/AK	3
MF	GO:001514 carbohydrate transmembrane transporter activity	3/83	37/18337	0.00062	0.0047	0.00349	SLC2A1/SL	3

MF	GO:001982 oxygen binding	3/83	39/18337	0.00073	0.00537	0.00399	ALB/NOX4	3
MF	GO:000531 lipid transporter activity	5/83	162/18337	0.00084	0.0061	0.00453	SLC7A11/S	5
MF	GO:001680 ether hydrolase activity	2/83	10/18337	0.00089	0.00617	0.00459	ALOX12/A	2
MF	GO:003028 testosterone dehydrogenase [NAD(P)] activity	2/83	10/18337	0.00089	0.00617	0.00459	AKR1C1/AK	2
MF	GO:000471 protein serine/threonine/ tyrosine kinase activity	3/83	44/18337	0.00104	0.00704	0.00523	AURKA/MA	3
MF	GO:001680 hydrolase activity, acting on ether bonds	2/83	11/18337	0.00108	0.00709	0.00527	ALOX12/A	2
MF	GO:014029 small molecule sensor activity	2/83	11/18337	0.00108	0.00709	0.00527	NOX4/EGL	2

MF	GO:000449 monooxygenase activity	4/83	101/18337	0.00114	0.00732	0.00544	AKR1C1/AK	4
MF	GO:190168 sulfur compound transmembrane transporter activity	3/83	48/18337	0.00134	0.00841	0.00625	SLC7A11/S	3
MF	GO:000460 peroxidase activity	3/83	53/18337	0.00178	0.011	0.00817	PTGS2/GPX	3
MF	GO:000508 protein kinase C binding	3/83	54/18337	0.00188	0.0114	0.00847	HSPB1/SQ	3
MF	GO:001668oxidoreductase activity, acting on peroxide as accepto	3/83	57/18337	0.00219	0.01309	0.00972	PTGS2/GPX	3
MF	GO:001555 C4-dicarboxylate transmembrane transporter activity	2/83	16/18337	0.00233	0.01334	0.00992	SLC1A4/SL	2
MF	GO:003517 histone kinase activity	2/83	16/18337	0.00233	0.01334	0.00992	AURKA/PR	2

MF	GO:003107 heat shock protein binding	4/83	123/18337	0.00236	0.01334	0.00992	HSF1/HSPA	4
MF	GO:001662oxidoreductase activity, acting on the CH-CH group of	3/83	59/18337	0.00242	0.01337	0.00994	AKR1C1/AK	3
MF	GO:002280 active transmembrane transporter activity	6/83	301/18337	0.00244	0.01337	0.00994	SLC7A11/S	6
MF	GO:000550 copper ion binding	3/83	60/18337	0.00254	0.01371	0.01019	MT3/ALB/H	3
MF	GO:004698 protein heterodimerization activity	6/83	324/18337	0.00351	0.01863	0.01384	HSF1/CAV1	6
MF	GO:000905 electron transfer activity	4/83	138/18337	0.00356	0.01865	0.01385	AIFM2/NCF	4
MF	GO:001529 secondary active transmembrane transporter activity	5/83	239/18337	0.00459	0.02365	0.01757	SLC7A11/S	5

MF	GO:014027 exogenous protein binding	3/83	77/18337	0.00514	0.02609	0.01938	ALB/TFRC/	3
MF	GO:000531 dicarboxylic acid transmembrane transporter activity	2/83	30/18337	0.00811	0.03996	0.0297	SLC1A4/SL	2
MF	GO:004291 xenobiotic transmembrane transporter activity	2/83	30/18337	0.00811	0.03996	0.0297	SLC2A1/AB	2
MF	GO:007188 14-3-3 protein binding	2/83	31/18337	0.00864	0.04199	0.0312	ZFP36/DDI	2
MF	GO:003029 protein serine/threonine kinase inhibitor activity	2/83	32/18337	0.00919	0.04403	0.03271	HSPB1/CD	2
MF	GO:003162 ubiquitin protein ligase binding	5/83	293/18337	0.01061	0.0498	0.037	SQSTM1/H	5
MF	GO:003218 ubiquitin-like protein binding	3/83	101/18337	0.01084	0.0498	0.037	HSPB1/SQ	3
MF	GO:005108 chaperone binding	3/83	101/18337	0.01084	0.0498	0.037	HSPA5/ALB	3
MF	GO:004418 protein folding chaperone	2/83	36/18337	0.01154	0.05232	0.03888	HSPB1/HSP	2
MF	GO:004216 SH2 domain binding	2/83	38/18337	0.01281	0.05728	0.04256	SQSTM1/S	2

MF	GO:004438 ubiquitin-like protein ligase binding	5/83	312/18337	0.01363	0.06018	0.04471	SQSTM1/H	5
KEGG	hsa04216 Ferroptosis	7/68	41/8101	3.84E-08	8.49E-06	5.74E-06	SLC7A11/F	7
KEGG	hsa05230 Central carbon metabolism in cancer	Aug-68	70/8101	1.01E-07	1.12E-05	7.55E-06	SLC7A5/SL	8
KEGG	hsa05208 Chemical carcinogenesis - reactive oxygen species	11/68	223/8101	2.07E-06	0.00015	0.0001	AKR1C1/AK	11
KEGG	hsa04726 Serotonergic synapse	8/68	115/8101	4.70E-06	0.00026	0.00018	PTGS2/DU	8
KEGG	hsa04370 VEGF signaling pathway	6/68	59/8101	8.88E-06	0.00039	0.00027	HSPB1/SRC	6
KEGG	hsa00590 Arachidonic acid metabolism	6/68	61/8101	1.08E-05	0.0004	0.00027	AKR1C3/PT	6
KEGG	hsa05418 Fluid shear stress and atherosclerosis	8/68	139/8101	1.91E-05	0.00059	0.0004	SQSTM1/N	8
KEGG	hsa05219 Bladder cancer	5/68	41/8101	2.13E-05	0.00059	0.0004	SRC/NRAS	5
KEGG	hsa05417 Lipid and atherosclerosis	9/68	215/8101	6.99E-05	0.00172	0.00116	HSPA5/SRC	9

KEGG	hsa04933 AGE-RAGE signaling pathway in diabetic complication	6/68	100/8101	0.00018	0.00397	0.00268	IL6/NOX1/	6
KEGG	hsa04625 C-type lectin receptor signaling pathway	6/68	104/8101	0.00022	0.00434	0.00293	SRC/PTGS2	6
KEGG	hsa05206 MicroRNAs in cancer	10/68	310/8101	0.00024	0.00434	0.00293	TP63/PTGS	10
KEGG	hsa05211 Renal cell carcinoma	5/68	69/8101	0.00027	0.00453	0.00306	SLC2A1/NR	5
KEGG	hsa04066 HIF-1 signaling pathway	6/68	109/8101	0.00029	0.00454	0.00307	NOS2/IL6/	6
KEGG	hsa01521 EGFR tyrosine kinase inhibitor resistance	5/68	79/8101	0.0005	0.00726	0.00491	SRC/IL6/NR	5
KEGG	hsa05022 Pathways of neurodegeneration - multiple diseases	12/68	476/8101	0.00053	0.00726	0.00491	SQSTM1/H	12
KEGG	hsa04140 Autophagy - animal	6/68	141/8101	0.00113	0.01403	0.00949	SQSTM1/D	6
KEGG	hsa05167 Kaposi sarcoma-associated herpesvirus infection	7/68	194/8101	0.00114	0.01403	0.00949	SRC/ZFP36	7
KEGG	hsa01522 Endocrine resistance	5/68	98/8101	0.00134	0.01552	0.0105	SRC/NRAS	5

KEGG	hsa04921 Oxytocin signaling pathway	6/68	154/8101	0.00177	0.01903	0.01287	SRC/PTGS2	6
KEGG	hsa04150 mTOR signaling pathway	6/68	155/8101	0.00183	0.01903	0.01287	DDIT4/SLC	6
KEGG	hsa04218 Cellular senescence	6/68	156/8101	0.0019	0.01903	0.01287	SQSTM1/IL	6
KEGG	hsa01523 Antifolate resistance	3/68	31/8101	0.00215	0.02065	0.01397	IL6/ALOX1	3
KEGG	hsa05221 Acute myeloid leukemia	4/68	67/8101	0.00234	0.02154	0.01457	PML/NRAS	4
KEGG	hsa05166 Human T-cell leukemia virus 1 infection	7/68	222/8101	0.00248	0.02169	0.01467	ZFP36/IL6/	7
KEGG	hsa05163 Human cytomegalovirus infection	7/68	225/8101	0.00267	0.02169	0.01467	SRC/PTGS2	7
KEGG	hsa04917 Prolactin signaling pathway	4/68	70/8101	0.00275	0.02169	0.01467	SRC/NRAS	4
KEGG	hsa05225 Hepatocellular carcinoma	6/68	168/8101	0.00275	0.02169	0.01467	NQO1/TXN	6

KEGG	hsa04137 Mitophagy - animal	4/68	72/8101	0.00304	0.02169	0.01467	SQSTM1/S	4
KEGG	hsa05218 Melanoma	4/68	72/8101	0.00304	0.02169	0.01467	NRAS/HRA	4
KEGG	hsa05223 non-small cell lung cancer	4/68	72/8101	0.00304	0.02169	0.01467	NRAS/HRA	4
KEGG	hsa04115 p53 signaling pathway	4/68	73/8101	0.0032	0.022	0.01488	AIFM2/STE	4
KEGG	hsa04919 Thyroid hormone signaling pathway	5/68	121/8101	0.00337	0.022	0.01488	SRC/SLC2A	5
KEGG	hsa04918 Thyroid hormone synthesis	4/68	75/8101	0.00353	0.022	0.01488	HSPA5/ALB	4
KEGG	hsa05214 Glioma	4/68	75/8101	0.00353	0.022	0.01488	NRAS/HRA	4
KEGG	hsa05216 Thyroid cancer	3/68	37/8101	0.00358	0.022	0.01488	NRAS/HRA	3
KEGG	hsa05220 Chronic myeloid leukemia	4/68	76/8101	0.0037	0.02211	0.01495	NRAS/HRA	4

KEGG	hsa05140 Leishmaniasis	4/68	77/8101	0.00388	0.02256	0.01526	PTGS2/NO	4
KEGG	hsa04926 Relaxin signaling pathway	5/68	129/8101	0.00443	0.02507	0.01696	SRC/NOS2	5
KEGG	hsa05010 Alzheimer disease	9/68	384/8101	0.00454	0.02507	0.01696	PTGS2/NO	9
KEGG	hsa04068 FoxO signaling pathway	5/68	131/8101	0.00473	0.02549	0.01724	IL6/NRAS/	5
KEGG	hsa04012 ErbB signaling pathway	4/68	85/8101	0.00552	0.02905	0.01965	SRC/NRAS	4
KEGG	hsa04371 Apelin signaling pathway	5/68	139/8101	0.00607	0.0312	0.0211	NOS2/NRA	5
KEGG	hsa04540 Gap junction	4/68	88/8101	0.00624	0.03134	0.0212	SRC/NRAS	4
KEGG	hsa04912 GnRH signaling pathway	4/68	93/8101	0.00757	0.03719	0.02516	SRC/NRAS	4
KEGG	hsa04010 MAPK signaling pathway	7/68	294/8101	0.01127	0.05352	0.0362	HSPB1/DU	7
KEGG	hsa05161 Hepatitis B	5/68	162/8101	0.01138	0.05352	0.0362	SRC/IL6/NR	5
KEGG	hsa00480 Glutathione metabolism	3/68	58/8101	0.01256	0.05665	0.03832	GPX2/RRM	3

KEGG	hsa05213 Endometrial cancer	3/68	58/8101	0.01256	0.05665	0.03832	NRAS/HRA	3
KEGG	hsa04730 Long-term depression	3/68	60/8101	0.01377	0.05965	0.04035	NRAS/HRA	3
KEGG	hsa04978 Mineral absorption	3/68	60/8101	0.01377	0.05965	0.04035	FTH1/MT1	3
KEGG	hsa00220 Arginine biosynthesis	2/68	22/8101	0.01439	0.06002	0.04059	NOS2/GLS	2
KEGG	hsa00140 Steroid hormone biosynthesis	3/68	61/8101	0.01439	0.06002	0.040591 AKR1C1/AK	3	
KEGG	hsa04213 Longevity regulating pathway - multiple species	3/68	62/8101	0.01504	0.06153	0.041618 NRAS/HRA	3	
KEGG	hsa04929 GnRH secretion	3/68	64/8101	0.01637	0.06577	0.044485 NRAS/HRA	3	
KEGG	hsa04071 Sphingolipid signaling pathway	4/68	119/8101	0.01752	0.06914	0.046764 NRAS/HRA	4	
KEGG	hsa04720 Long-term potentiation	3/68	67/8101	0.01849	0.07169	0.048485 NRAS/HRA	3	

KEGG	hsa04664 Fc epsilon RI signaling pathway	3/68	68/8101	0.01923	0.07327	0.049555 NRAS/HRA	3	

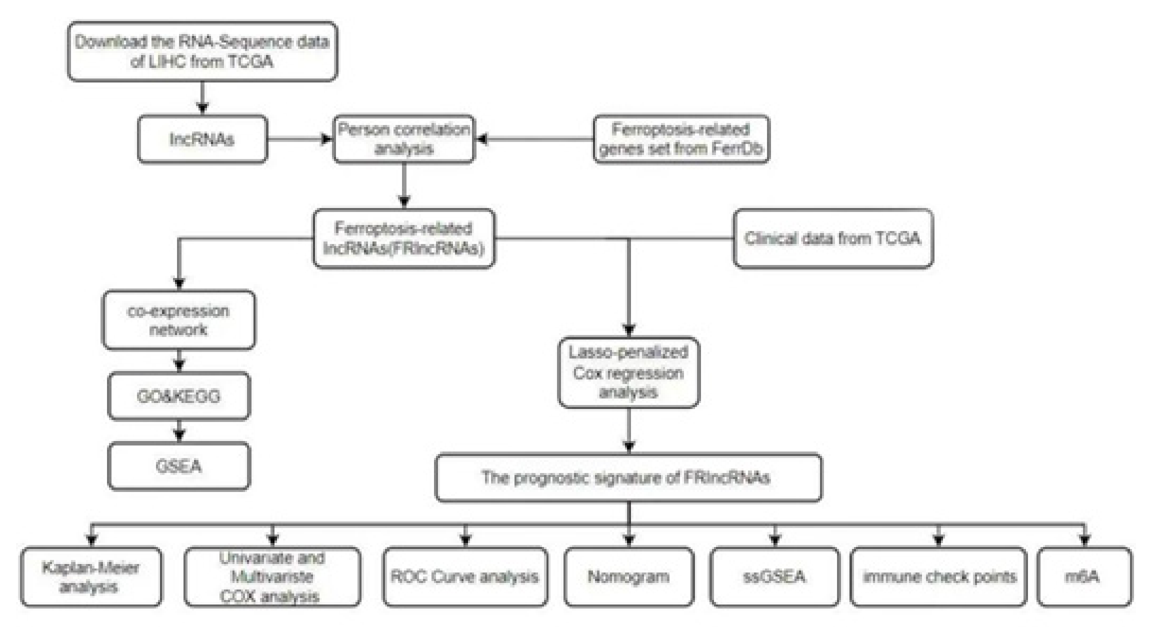


Figure 1: The study's flow chart. TCGA: The Cancer Genome Atlas; ROC: operating haracteristic curve; KEGG: Kyoto Encyclopedia of Genes and Genomes; GO: Gene ontology; GSEA: Gene set enrichment analysis; ssGSEA: single-sample gene set enrichment analysis.

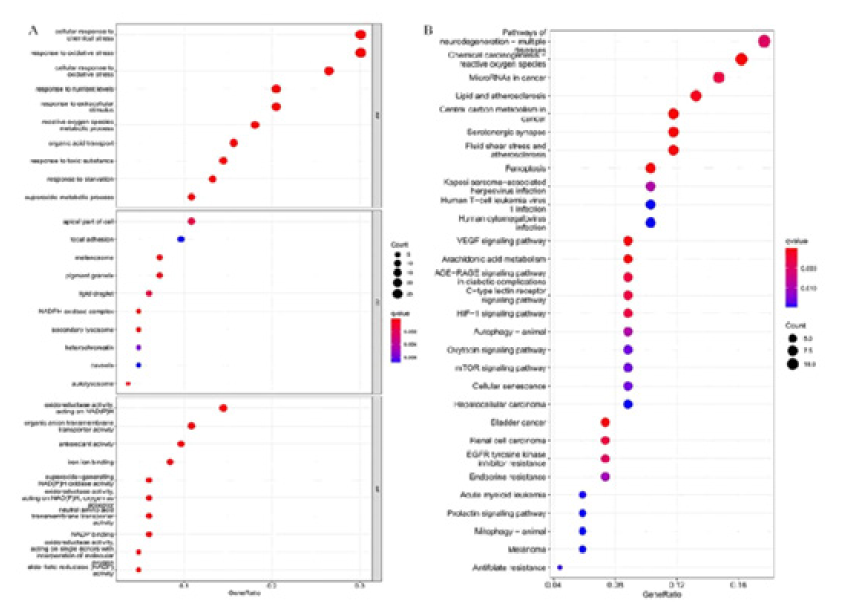


Figure 2: GO and b KEGG enrichment analysis of differentially expressed genes associated with ferroptosis.

Prognostic Characteristics and Prognostic Value of the Model

We identified 1072 lncRNAs associated with ferroptosis (Supplementary Table 5). Univariate COX analysis established 58 significant FRlncRNAs included in multivariate Cox analysis. Twenty-two DE-lncRNAs (AC091057.1, AL357079.1, SNHG4, AL671710.1, KDM4A-AS1, PTOV1-AS1, AC022007.1, MKLN1-AS, AC099850.3, Z95115.1, PRRT3-AS1 SNHG12, LINC01224, SREBF2-AS1, LINC00205, NRAV, AC145207.5, MIR4435-2HG, MIR210HG, ZFPM2-AS1, AL050341.2, LUCAT1) were determined as independent prognostic predictors of HCC (Supplementary Table 6). Consequently, we calculated the risk scores and constructed prognostic signatures for lncRNAs. Kaplan-Meier analysis confirmed that patients in the high-risk group with TCGA-LIHC had significantly shorter survival times at 1, 3, and 5 years compared to those in the low-risk group ($p < 0.001$, (Figure 3a)). In addition, the time-dependent ROC curve for survival prediction of the risk score model had an AUC of 0.811 at one year, which was more specific and sensitive in predicting the prognosis of HCC than conventional clinicopathological features (Figures 3b, 3e). In addition, time-dependent ROC analysis demonstrated that the AUC predictive value of the novel model for the 1-, 3-, and 5-year survival rate was 0.811, 0.752, and 0.692, respectively (Figure 3d). The risk score and survival status of each HCC patient were represented using prognostic curves and scatter plots. Using patient risk survival status plots, we determined that patient risk score was negatively correlated with HCC patient survival and that most deaths occurred in the high-risk group (Figure 3c). Next, univariate Cox analysis revealed that lncRNA-based characteristics (HR: 1.106, 95% CI: 1.081-1.132) and tumor stage (HR: 1.680, 95% CI: 1.369-2.062) were independent prognostic factors in HCC patients (Figure 4a). Multivariate Cox analysis indicated that lncRNA characteristics (HR: 1.098, 95% CI: 1.072-1.125) and tumor stage (HR: 1.585, 95% CI: 1.282-1.958) were likewise independent prognostic risk factors for HCC patients (Figure 4b). (Figure 5a) depicts the relationship between lncRNAs and mRNAs. Additionally, we examined the association heatmap between prognostic characteristics and clinicopathological manifestations of FRlncRNAs (Figure 5b). In this combined nomogram, the risk score model was found to play the best role in these clinically significant variables and can therefore be used in the clinical prognostic assessment of HCC patients (Additional Figure 1). These studies demonstrate that this novel model of lncRNAs associated with ferroptosis is a reliable, independent prognostic factor for patients with HCC.

Supplementary Table 5: GO and KEGG pathway analyses.

Ferroptosis associated lncRNAs				
ferrGene	**lncRNA**	**cor**	**pvalue**	**Regulation**
BECN1	ABALON	0.52906	2.31E-28	postive
CS	ABALON	0.59677	1.88E-37	postive
SLC38A1	ABALON	0.56645	4.02E-33	postive
SP1	ABALON	0.58957	2.21E-36	postive
DNAJB6	AC000123.	0.52344	1.07E-27	postive
FANCD2	AC002116.	0.55063	4.91E-31	postive

STMN1	AC002116.	0.52665	4.48E-28	postive
EGLN2	AC002398.	0.54417	3.26E-30	postive
OTUB1	AC002398.	0.5371	2.46E-29	postive
HBA1	AC002398.	0.72638	1.49E-62	postive
PLIN4	AC002398.	0.8438	1.37E-102	postive
MUC1	AC003070.	0.57837	9.05E-35	postive
PTGS2	AC003070.	0.67439	6.10E-51	postive
PLIN4	AC004130.	0.57801	1.01E-34	postive
ALOX5	AC004540.	0.53782	2.01E-29	postive
CA9	AC004540.	0.52408	9.01E-28	postive
CS	AC004540.	0.55658	8.31E-32	postive
CYBB	AC004585.	0.65245	1.00E-46	postive
IFNG	AC004585.	0.58332	1.78E-35	postive
KRAS	AC004803.	0.50083	3.85E-25	postive
ABCC1	AC004812.	0.50867	5.25E-26	postive
OTUB1	AC004812.	0.51907	3.46E-27	postive

FANCD2	AC004816.	0.56008	2.87E-32	postive
STMN1	AC004816.	0.59128	1.24E-36	postive
PCK2	AC004832.	0.51465	1.11E-26	postive
SCP2	AC004832.	0.58974	2.09E-36	postive
ATM	AC004908.	0.58755	4.37E-36	postive
CYBB	AC004921.	0.61331	5.15E-40	postive
FANCD2	AC004943.	0.53973	1.17E-29	postive
NRAS	AC004943.	0.50199	2.88E-25	postive
PIK3CA	AC004943.	0.5125	1.95E-26	postive
ANO6	AC005034.	0.54445	3.00E-30	postive
IREB2	AC005034.	0.54454	2.92E-30	postive
KLHL24	AC005034.	0.5098	3.93E-26	postive
PIK3CA	AC005034.	0.53309	7.57E-29	postive
ZEB1	AC005034.	0.50547	1.19E-25	postive
PLIN4	AC005046.	0.58305	1.95E-35	postive

HSPB1	AC005076.	0.52377	9.80E-28	postive
ATG16L1	AC005104.	0.50262	2.46E-25	postive
ATM	AC005104.	0.55138	3.94E-31	postive
SETD1B	AC005104.	0.52081	2.17E-27	postive
ATM	AC005253.	0.5377	2.08E-29	postive
SETD1B	AC005253.	0.52516	6.73E-28	postive
SP1	AC005253.	0.56262	1.32E-32	postive
NF2	AC005261.	0.52065	2.27E-27	postive
ZNF419	AC005261.	0.64276	5.67E-45	postive
EGLN2	AC005261.	0.52106	2.03E-27	postive
ALOX12	AC005288.	0.52124	1.94E-27	postive
ATG16L1	AC005288.	0.59963	6.95E-38	postive
ATM	AC005288.	0.6472	9.08E-46	postive

BACH1	AC005288.	0.55607	9.68E-32	postive
BECN1	AC005288.	0.7254	2.61E-62	postive
CHMP5	AC005288.	0.5451	2.48E-30	postive
CS	AC005288.	0.53009	1.74E-28 postive	postive
HIF1A	AC005288.	0.55227	3.03E-31 postive	postive
IREB2	AC005288.	0.6858	2.79E-53 postive	postive
MAPK1	AC005288.	0.68514	3.84E-53	postive
MAPK8	AC005288.	0.57206	6.87E-34	postive
MAPK9	AC005288.	0.53792	1.95E-29	postive
NRAS	AC005288.	0.60346	1.80E-38	postive
OXSR1	AC005288.	0.6207	3.29E-41	postive

PIK3CA	AC005288.	0.68643	2.06E-53	postive
PRKAA1	AC005288.	0.52399	9.23E-28	postive
RB1	AC005288.	0.53321	7.32E-29	postive
SETD1B	AC005288.	0.64516	2.12E-45	postive
SIRT1	AC005288.	0.53436	5.32E-29	postive
SNX4	AC005288.	0.5593	3.65E-32	postive
SP1	AC005288.	0.74009	4.46E-66	postive
ZEB1	AC005288.	0.57629	1.77E-34	postive

ZFP69B	AC005288.	0.53961	1.21E-29	postive
WIPI1	AC005332.	0.51355	1.48E-26	postive
EGLN2	AC005393.	0.5097	4.03E-26	postive
BECN1	AC005670.	0.54141	7.20E-30	postive
ALOX12	AC005696.	0.52671	4.40E-28	postive
CS	AC005696.	0.57533	2.42E-34	postive

HBA1	AC005785.	0.56646	4.01E-33	postive
PLIN4	AC005785.	0.68341	8.81E-53	postive
ACO1	AC005920.	0.50947	4.28E-26	postive
GLS2	AC005920.	0.5066	8.94E-26	postive
EGLN2	AC006213.	0.57424	3.42E-34	postive
ZNF419	AC006213.	0.55283	2.56E-31	postive
HELLS	AC006213.	0.55714	7.02E-32	postive
HSPB1	AC006273.	0.58796	3.80E-36	postive

ALOX12	AC006435.	0.50141	3.33E-25	postive
ZNF419	AC007066.	0.56301	1.17E-32	postive
SOCS1	AC007220.	0.5154	9.14E-27	postive
ALOX12	AC007406.	0.52835	2.82E-28	postive
ATG16L1	AC007406.	0.56596	4.68E-33	postive
ATM	AC007406.	0.63381	2.08E-43	postive
IREB2	AC007406.	0.61989	4.47E-41	postive

MAPK1	AC007406.	0.61261	6.66E-40	postive
MAPK8	AC007406.	0.50498	1.35E-25	postive
OXSR1	AC007406.	0.50537	1.22E-25	postive
PIK3CA	AC007406.	0.55091	4.53E-31	postive
RB1	AC007406.	0.51266	1.87E-26	postive
SETD1B	AC007406.	0.58247	2.36E-35	postive

SIRT1	AC007406.	0.54222	5.72E-30	postive
SP1	AC007406.	0.66956	5.54E-50	postive
ZEB1	AC007406.	0.53033	1.63E-28	postive
IREB2	AC007637.	0.55491	1.37E-31	postive
HRAS	AC007773.	0.59364	5.54E-37	postive
HSPB1	AC007773.	0.59254	8.06E-37	postive
ABCC1	AC008074.	0.50798	6.28E-26	postive

CYBB	AC008105.	0.55833	4.90E-32	postive
ALOX12	AC008124.	0.50302	2.22E-25	postive
ATM	AC008124.	0.50709	7.89E-26	postive
GABPB1	AC008124.	0.58029	4.83E-35	postive
SP1	AC008124.	0.55506	1.31E-31	postive
HRAS	AC008443.	0.53395	5.96E-29	postive
HSPB1	AC008443.	0.57848	8.71E-35	postive

DPP4	AC008549.	0.53428	5.43E-29	postive
PANX1	AC008549.	0.58801	3.74E-36	postive
PEBP1	AC008549.	0.53272	8.39E-29	postive
HRAS	AC008608.	0.53479	4.71E-29	postive
HSPB1	AC008608.	0.55883	4.21E-32	postive
RPL8	AC008608.	0.51461	1.12E-26	postive
HRAS	AC008610.	0.61003	1.71E-39	postive

HSPB1	AC008610.	0.66542	3.57E-49	postive
NOS2	AC008708.	0.57717	1.33E-34	postive
ZNF419	AC008735.	0.51707	5.88E-27	postive
SETD1B	AC008735.	0.51575	8.32E-27	postive
DUOX2	AC008736.	0.86698	1.44E-114	postive
MUC1	AC008736.	0.64536	1.95E-45	postive
IREB2	AC008764.	0.52463	7.77E-28	postive
MAPK1	AC008764.	0.50908	4.73E-26	postive
ATM	AC008770.	0.53258	8.73E-29	postive

IREB2	AC008770.	0.52636	4.85E-28	postive
EGLN2	AC008915.	0.55933	3.61E-32	postive
HRAS	AC008915.	0.52564	5.89E-28	postive
SLC40A1	AC008966.	0.50754	7.03E-26	postive
CYBB	AC008972.	0.50731	7.46E-26	postive
EGLN2	AC009065.	0.52286	1.25E-27	postive

HRAS	AC009065.	0.62825	1.84E-42	postive
HSPB1	AC009065.	0.59141	1.19E-36	postive
ABCC1	AC009120.	0.5007	3.98E-25	postive
ABCC1	AC009133.	0.50498	1.35E-25	postive
HRAS	AC009275.	0.52372	9.94E-28	postive
HSPB1	AC009275.	0.54035	9.76E-30	postive
KRAS	AC009318.	0.50943	4.32E-26	postive
HRAS	AC009686.	0.54023	1.01E-29	postive

HSPB1	AC009686.	0.61578	2.07E-40	postive
ATM	AC010186.	0.53349	6.79E-29	postive
PCK2	AC010205.	0.54238	5.46E-30	postive
ZNF419	AC010326.	0.60006	5.97E-38	postive
PCK2	AC010336.	0.59258	7.95E-37	postive
ATG4D	AC010503.	0.53699	2.53E-29	postive
DPP4	AC010531.	0.58194	2.81E-35	postive
HRAS	AC010531.	0.54206	5.98E-30	postive

HSPB1	AC010531.	0.61488	2.89E-40	postive
RGS4	AC010547.	0.5577	5.93E-32	postive
HRAS	AC010618.	0.53364	6.50E-29	postive
ALOX12	AC010834.	0.51908	3.45E-27	postive
ATM	AC010834.	0.61861	7.22E-41	postive
IREB2	AC010834.	0.54908	7.78E-31	postive

MAPK1	AC010834.	0.51021	3.53E-26	postive
MAPK8	AC010834.	0.50154	3.22E-25	postive
PIK3CA	AC010834.	0.53134	1.23E-28	postive
SETD1B	AC010834.	0.58973	2.09E-36	postive
SP1	AC010834.	0.62407	9.15E-42	postive
EGLN2	AC010969.	0.50789	6.42E-26	postive

EGLN2	AC011445.	0.61355	4.71E-40	postive
ABCC1	AC011462.	0.51502	1.01E-26	postive
EGLN2	AC011468.	0.57506	2.64E-34	postive
ZNF419	AC011468.	0.59244	8.34E-37	postive
HBA1	AC011472.	0.52151	1.80E-27	postive
DUOX1	AC011477.	0.51201	2.21E-26	postive

SLC2A1	AC012615.	0.55965	3.28E-32	postive
ALOX12	AC012615.	0.52479	7.43E-28	postive
SETD1B	AC012615.	0.50487	1.39E-25	postive
HSF1	AC012676.	0.54683	1.50E-30	postive
RPL8	AC012676.	0.51927	3.28E-27	postive
CYBB	AC015819.	0.55461	1.50E-31	postive

ATM	AC015849.	0.53781	2.01E-29	postive
SETD1B	AC015849.	0.575	2.68E-34	postive
GABPB1	AC015871.	0.51861	3.91E-27	postive
HRAS	AC015912.	0.62917	1.28E-42	postive
HSPB1	AC015912.	0.67763	1.35E-51	postive
PTGS2	AC015922.	0.57361	4.20E-34	postive

GABPB1	AC016355.	0.58161	3.14E-35	postive
HSPB1	AC016405.	0.53295	7.89E-29	postive
RPL8	AC016405.	0.60644	6.22E-39	postive
PROM2	AC016590.	0.52131	1.90E-27	postive
RGS4	AC016735.	0.64148	9.59E-45	postive
DRD4	AC018638.	0.74099	2.57E-66	postive
FANCD2	AC018690.	0.50442	1.56E-25	postive

OXSR1	AC018690.	0.51022	3.52E-26	postive
ATF4	AC018904.	0.50089	3.79E-25	postive
PLIN4	AC019197.	0.5107	3.11E-26	postive
DUOX1	AC020907.	0.51146	2.56E-26	postive
GLS2	AC020978.	0.60354	1.75E-38	postive
PROM2	AC021016.	0.5191	3.43E-27	postive

FANCD2	AC022007.	0.55393	1.85E-31	postive
SP1	AC022150.	0.51953	3.06E-27	postive
ZNF419	AC022150.	0.54776	1.14E-30	postive
KRAS	AC022364.	0.61822	8.35E-41	postive
ATF4	AC024060.	0.53034	1.63E-28	postive
ATM	AC024075.	0.51256	1.92E-26	postive
IREB2	AC024075.	0.5815	3.25E-35	postive

MAPK1	AC024075.	0.548	1.07E-30	postive
SETD1B	AC024075.	0.52642	4.77E-28	postive
SP1	AC024075.	0.51543	9.07E-27	postive
HRAS	AC025048.	0.6505	2.29E-46	postive
HSPB1	AC025048.	0.56465	7.03E-33	postive
HIF1A	AC026356.	0.56214	1.53E-32	postive

SLC38A1	AC026356.	0.55378	1.93E-31	postive
CDKN2A	AC026401.	0.61101	1.19E-39	postive
FANCD2	AC026401.	0.58273	2.17E-35	postive
G6PD	AC026401.	0.53328	7.18E-29	postive
MAPK3	AC026401.	0.60905	2.44E-39	postive
PHKG2	AC026401.	0.55034	5.36E-31	postive
SLC1A5	AC026401.	0.59242	8.39E-37	postive

STMN1	AC026401.	0.64747	8.13E-46	postive
MT1G	AC026461.	0.80386	6.07E-86	postive
EGLN2	AC026803.	0.55259	2.75E-31	postive
HRAS	AC026803.	0.51733	5.49E-27	postive
HRAS	AC026979.	0.58362	1.62E-35	postive
HSPB1	AC026979.	0.62806	1.97E-42	postive

ATM	AC027097.	0.50668	8.76E-26	postive
EGLN2	AC027644.	0.6068	5.47E-39	postive
HRAS	AC027644.	0.62464	7.36E-42	postive
HSPB1	AC027644.	0.56635	4.15E-33	postive
GABPB1	AC034236.	0.50839	5.65E-26	postive
PEBP1	AC036176.	0.50146	3.28E-25	postive

ATM	AC037459.	0.59719	1.63E-37	postive
PIK3CA	AC037459.	0.50822	5.91E-26	postive
SP1	AC037459.	0.53073	1.46E-28	postive
EGLN2	AC046143.	0.59923	8.01E-38	postive
HRAS	AC046143.	0.5743	3.36E-34	postive
GCLC	AC055720.	0.50399	1.74E-25	postive
ATF4	AC055822.	0.50091	3.77E-25	postive

SP1	AC055855.	0.51489	1.04E-26	postive
ABCC1	AC060766.	0.52154	1.79E-27	postive
CAV1	AC060766.	0.53333	7.08E-29	postive
ABCC1	AC060766.	0.57982	5.63E-35	postive
CAV1	AC060766.	0.55603	9.83E-32	postive
PML	AC060766.	0.51908	3.45E-27	postive
DUOX1	AC061975.	0.51292	1.75E-26	postive

ASNS	AC061992.	0.53754	2.17E-29	postive
BECN1	AC067852.	0.67885	7.65E-52	postive
FANCD2	AC068756.	0.51627	7.27E-27	postive
HRAS	AC069281.	0.56093	2.21E-32	postive
HSPB1	AC069281.	0.60437	1.30E-38	postive
ANO6	AC073046.	0.50255	2.50E-25	postive
ATM	AC073046.	0.6218	2.17E-41	postive

BACH1	AC073046.	0.50901	4.81E-26	postive
IREB2	AC073046.	0.64447	2.81E-45	postive
MAPK1	AC073046.	0.61606	1.87E-40	postive
PIK3CA	AC073046.	0.58572	8.03E-36	postive
PRKAA1	AC073046.	0.50502	1.34E-25	postive
SETD1B	AC073046.	0.5983	1.10E-37	postive

SP1	AC073046.	0.61699	1.32E-40	postive
ZEB1	AC073046.	0.51945	3.13E-27	postive
SETD1B	AC073575.	0.5053	1.24E-25	postive
EGLN2	AC073896.	0.54227	5.64E-30	postive
HRAS	AC073896.	0.65339	6.73E-47	postive
HSPB1	AC073896.	0.60132	3.84E-38	postive
EGLN2	AC074212.	0.58985	2.01E-36	postive

RPL8	AC074212.	0.52159	1.76E-27	postive
HSPB1	AC078846.	0.52034	2.47E-27	postive
DRD4	AC078909.	0.54586	1.99E-30	postive
DPP4	AC078993.	0.52838	2.79E-28	postive
PANX1	AC078993.	0.55542	1.18E-31	postive
CYBB	AC079015.	0.64377	3.76E-45	postive
PML	AC079015.	0.51392	1.35E-26	postive

IL33	AC079305.	0.50241	2.59E-25	postive
SCP2	AC079848.	0.51076	3.07E-26	postive
ATM	AC084018.	0.51463	1.12E-26	postive
SETD1B	AC084018.	0.61281	6.20E-40	postive
SP1	AC084018.	0.51342	1.54E-26	postive
ULK1	AC084018.	0.55328	2.24E-31	postive
SLC1A5	AC087501.	0.56348	1.01E-32	postive

CHMP6	AC087741.	0.55983	3.10E-32	postive
HRAS	AC087741.	0.5163	7.21E-27	postive
PANX1	AC090150.	0.50015	4.56E-25	postive
GABPB1	AC090517.	0.57653	1.64E-34	postive
ATG7	AC090559.	0.50981	3.92E-26	postive
CYBB	AC090559.	0.82545	2.04E-94	postive
HIF1A	AC090559.	0.58643	6.35E-36	postive

JDP2	AC090559.	0.52982	1.88E-28	postive
PML	AC090559.	0.56932	1.64E-33	postive
RB1	AC090559.	0.51851	4.01E-27	postive
TLR4	AC090559.	0.62506	6.28E-42	postive
YWHAE	AC090617.	0.53894	1.46E-29	postive
ATM	AC091057.	0.5134	1.54E-26	postive

ELAVL1	AC091057.	0.50707	7.92E-26	postive
FANCD2	AC091057.	0.76357	1.18E-72	postive
HELLS	AC091057.	0.6887	6.82E-54	postive
HMGB1	AC091057.	0.5581	5.24E-32	postive
MAPK1	AC091057.	0.52123	1.94E-27	postive
MAPK8	AC091057.	0.50619	9.91E-26	postive
OXSR1	AC091057.	0.52476	7.50E-28	postive

RRM2	AC091057.	0.5908	1.46E-36	postive
SETD1B	AC091057.	0.54959	6.69E-31	postive
SP1	AC091057.	0.60494	1.07E-38	postive
STMN1	AC091057.	0.63241	3.62E-43	postive
VEGFA	AC091057.	0.52581	5.64E-28	postive
YY1AP1	AC091057.	0.51252	1.94E-26	postive
HSPB1	AC091488.	0.50995	3.78E-26	postive

NQO1	AC092115.	0.70426	2.64E-57	postive
ABCC1	AC092118.	0.544	3.42E-30	postive
NF2	AC092171.	0.53923	1.34E-29	postive
LPCAT3	AC092941.	0.53671	2.75E-29	postive
DUOX2	AC093001.	0.55818	5.12E-32	postive
PROM2	AC093010.	0.53348	6.80E-29	postive

ATM	AC093227.	0.52927	2.18E-28	postive
MAPK1	AC093227.	0.51239	2.01E-26	postive
MAPK8	AC093227.	0.58043	4.61E-35	postive
SIRT1	AC093227.	0.52673	4.39E-28	postive
SP1	AC093227.	0.55771	5.92E-32	postive
ZNF419	AC093227.	0.51112	2.79E-26	postive
EPAS1	AC093278.	0.55176	3.52E-31	postive

ZEB1	AC093278.	0.51483	1.06E-26	postive
IREB2	AC093752.	0.55697	7.39E-32	postive
NRAS	AC098484.	0.55466	1.48E-31	postive
SCP2	AC099508.	0.52984	1.87E-28	postive
ATG3	AC099850.	0.53013	1.72E-28	postive

ATG5	AC099850.	0.50103	3.66E-25	postive
AURKA	AC099850.	0.51376	1.40E-26	postive
ELAVL1	AC099850.	0.54417	3.26E-30	postive
FANCD2	AC099850.	0.73169	6.82E-64	postive
HELLS	AC099850.	0.63885	2.77E-44	postive
HMGB1	AC099850.	0.50816	5.99E-26	postive

MAPK1	AC099850.	0.51511	9.84E-27	postive
NRAS	AC099850.	0.61429	3.59E-40	postive
OXSR1	AC099850.	0.54092	8.30E-30	postive
PIK3CA	AC099850.	0.5439	3.52E-30	postive
RRM2	AC099850.	0.71951	7.17E-61	postive
SLC1A5	AC099850.	0.52483	7.36E-28	postive

SP1	AC099850.	0.54085	8.46E-30	postive
STMN1	AC099850.	0.64402	3.39E-45	postive
ZFP69B	AC099850.	0.5782	9.54E-35	postive
HBA1	AC100793.	0.65826	8.30E-48	postive
PLIN4	AC100793.	0.79654	2.62E-83	postive
HBA1	AC104463.	0.54148	7.07E-30	postive
PLIN4	AC104463.	0.59676	1.89E-37	postive

ATM	AC104532.	0.53781	2.01E-29	postive
SIRT1	AC104532.	0.50509	1.31E-25	postive
SP1	AC104532.	0.50274	2.38E-25	postive
MT3	AC105118.	0.60852	2.95E-39	postive
PHKG2	AC106820.	0.50731	7.46E-26	postive
PLIN4	AC106897.	0.52468	7.66E-28	postive
MAPK1	AC107027.	0.52528	6.50E-28	postive

SNX4	AC107027.	0.50186	2.97E-25	postive
SP1	AC107027.	0.53905	1.42E-29	postive
SLC38A1	AC107959.	0.57992	5.46E-35	postive
ATM	AC108010.	0.57129	8.79E-34	postive
IREB2	AC108010.	0.62464	7.37E-42	postive
PIK3CA	AC108010.	0.5488	8.45E-31	postive

SETD1B	AC108010.	0.52307	1.18E-27	postive
SP1	AC108010.	0.53727	2.35E-29	postive
ZEB1	AC108010.	0.52342	1.08E-27	postive
EGLN2	AC108047.	0.5216	1.76E-27	postive
HRAS	AC108047.	0.55151	3.79E-31	postive
HSPB1	AC108047.	0.55564	1.10E-31	postive

CYBB	AC108134.	0.61385	4.22E-40	postive
ATM	AC108449.	0.55891	4.10E-32	postive
IREB2	AC108449.	0.60294	2.17E-38	postive
MAPK1	AC108449.	0.53321	7.33E-29	postive
PIK3CA	AC108449.	0.60324	1.95E-38	postive
RB1	AC108449.	0.52305	1.19E-27	postive

SP1	AC108449.	0.53559	3.76E-29	postive
ZEB1	AC108449.	0.54695	1.45E-30	postive
IL6	AC108451.	0.54134	7.35E-30	postive
KRAS	AC108451.	0.54812	1.03E-30	postive
ABCC1	AC108463.	0.52951	2.05E-28	postive
VLDLR	AC108463.	0.51933	3.23E-27	postive

EGLN2	AC108673.	0.52388	9.51E-28	postive
HRAS	AC109322.	0.62026	3.88E-41	postive
HSF1	AC109322.	0.55663	8.18E-32	postive
HSPB1	AC109322.	0.63779	4.25E-44	postive
RPL8	AC109322.	0.74472	2.57E-67	postive
ATM	AC109460.	0.60407	1.45E-38	postive
IREB2	AC109460.	0.51523	9.54E-27	postive
PIK3CA	AC109460.	0.53848	1.66E-29	postive

PRKAA1	AC109460.	0.55829	4.96E-32	postive
SETD1B	AC109460.	0.58114	3.66E-35	postive
SP1	AC109460.	0.56894	1.84E-33	postive
CYBB	AC110995.	0.55961	3.32E-32	postive
OXSR1	AC112220.	0.52612	5.18E-28	postive
EGLN2	AC112491.	0.59673	1.91E-37	postive
WIPI2	AC113145.	0.55936	3.58E-32	postive

ABCC1	AC116351.	0.69181	1.47E-54	postive
SLC38A1	AC116351.	0.56806	2.43E-33	postive
TP53	AC116914.	0.50028	4.42E-25	postive
HRAS	AC117386.	0.50664	8.83E-26	postive
HSPB1	AC117386.	0.50028	4.41E-25	postive
ZNF419	AC120053.	0.54466	2.83E-30	postive
ELAVL1	AC124045.	0.51968	2.94E-27	postive

DDIT3	AC124798.	0.50175	3.05E-25	postive
SLC38A1	AC124798.	0.52833	2.83E-28	postive
SP1	AC125257.	0.50473	1.44E-25	postive
HELLS	AC127024.	0.5489	8.19E-31	postive
SETD1B	AC127024.	0.55511	1.30E-31	postive
SP1	AC127024.	0.50912	4.68E-26	postive
ATF4	AC127024.	0.50169	3.10E-25	postive

FANCD2	AC127024.	0.5109	2.95E-26	postive
ZNF419	AC127024.	0.52576	5.71E-28	postive
CS	AC127521.	0.51293	1.74E-26	postive
PROM2	AC127521.	0.50076	3.92E-25	postive
RGS4	AC127521.	0.56282	1.24E-32	postive
SLC38A1	AC129510.	0.50651	9.14E-26	postive
SP1	AC129510.	0.55899	4.01E-32	postive

HRAS	AC131009.	0.56408	8.40E-33	postive
HSPB1	AC131009.	0.62876	1.50E-42	postive
FANCD2	AC132807.	0.50794	6.33E-26	postive
HELLS	AC132938.	0.50734	7.40E-26	postive
ALOX5	AC133644.	0.52133	1.89E-27	postive
IREB2	AC135050.	0.53287	8.05E-29	postive

PLIN4	AC135507.	0.54932	7.24E-31	postive
SCP2	AC137056.	0.5089	4.96E-26	postive
ATM	AC138028.	0.55312	2.35E-31	postive
EGLN2	AC138207.	0.51184	2.31E-26	postive
HRAS	AC138207.	0.56594	4.71E-33	postive
CAV1	AC138207.	0.51903	3.50E-27	postive
CYBB	AC138207.	0.55847	4.69E-32	postive

PML	AC138207.	0.58374	1.55E-35	postive
CYBB	AC138207.	0.70111	1.35E-56	postive
PML	AC138207.	0.60056	5.02E-38	postive
GPX4	AC138696.	0.56595	4.71E-33	postive
HSPB1	AC138696.	0.53537	4.00E-29	postive
CHMP6	AC139530.	0.58514	9.76E-36	postive
HRAS	AC139530.	0.55539	1.19E-31	postive
ATM	AC145098.	0.56335	1.05E-32	postive

CAPG	AC145098.	0.56327	1.08E-32	postive
CYBB	AC145098.	0.78164	2.89E-78	postive
PML	AC145098.	0.54132	7.40E-30	postive
TLR4	AC145098.	0.52759	3.47E-28	postive
HELLS	AC145207.	0.50895	4.89E-26	postive
SRXN1	AC145207.	0.59598	2.47E-37	postive
TXNRD1	AC145207.	0.56179	1.71E-32	postive

PLIN4	AC145423.	0.57336	4.54E-34	postive
DPP4	AC231981.	0.51473	1.09E-26	postive
ALOX12	AC232271.	0.5026	2.47E-25	postive
ATM	AC232271.	0.50754	7.02E-26	postive
SP1	AC232271.	0.51633	7.15E-27	postive
ATM	AC243960.	0.56948	1.55E-33	postive

CYBB	AC243960.	0.52613	5.17E-28	postive
IFNG	AC243960.	0.5842	1.33E-35	postive
ATG4D	AC245041.	0.50949	4.26E-26	postive
DUOX2	AC245041.	0.60043	5.25E-38	postive
MUC1	AC245041.	0.50088	3.80E-25	postive
ABCC1	AC245041.	0.63704	5.75E-44	postive
PROM2	AC245041.	0.73985	5.15E-66	postive

ABCC1	AF131215.	0.59627	2.23E-37	postive
PROM2	AF131215.	0.53083	1.42E-28	postive
CAV1	AGAP2-AS	0.52163	1.74E-27	postive
HIC1	AGAP2-AS	0.52543	6.24E-28	postive
PLIN4	AGAP2-AS	0.64473	2.53E-45	postive
ATM	AL031600.	0.51378	1.40E-26	postive
SETD1B	AL031600.	0.56008	2.87E-32	postive
ATM	AL031714.	0.58216	2.61E-35	postive

FBXW7	AL031714.	0.50412	1.68E-25	postive
SETD1B	AL031714.	0.56262	1.32E-32	postive
SP1	AL031714.	0.54927	7.36E-31	postive
NRAS	AL031985.	0.53828	1.76E-29	postive
ZFP69B	AL031985.	0.84786	1.54E-104	postive
AKR1C2	AL033397.	0.50114	3.56E-25	postive

SRXN1	AL033397.	0.50646	9.25E-26	postive
TXNRD1	AL033397.	0.5462	1.80E-30	postive
ATF4	AL035071.	0.51579	8.24E-27	postive
OTUB1	AL035071.	0.52049	2.37E-27	postive
SLC1A5	AL035446.	0.51084	3.00E-26	postive
VLDLR	AL035446.	0.64856	5.17E-46	postive

EGLN2	AL035461.	0.53252	8.89E-29	postive
FANCD2	AL035461.	0.54009	1.05E-29	postive
NF2	AL035461.	0.52546	6.20E-28	postive
SLC1A5	AL035461.	0.53832	1.74E-29	postive
STMN1	AL035461.	0.58375	1.55E-35	postive
PROM2	AL049555.	0.6162	1.77E-40	postive
PROM2	AL049629.	0.55574	1.07E-31	postive

ATM	AL049840.	0.56877	1.94E-33	postive
FBXW7	AL049840.	0.51971	2.92E-27	postive
SETD1B	AL049840.	0.50535	1.23E-25	postive
ATG16L1	AL049840.	0.51045	3.32E-26	postive
MAPK1	AL049840.	0.55042	5.23E-31	postive
ATG16L1	AL049840.	0.50653	9.09E-26	postive
ATM	AL049840.	0.51438	1.19E-26	postive

MAPK1	AL049840.	0.54306	4.49E-30	postive
SETD1B	AL049840.	0.56626	4.27E-33	postive
FANCD2	AL050341.	0.51293	1.74E-26	postive
GABPB1	AL050341.	0.58897	2.70E-36	postive
STMN1	AL050341.	0.52796	3.13E-28	postive
DRD4	AL109615.	0.61869	7.01E-41	postive

ALOX12	AL118506.	0.51359	1.47E-26	postive
IREB2	AL118506.	0.54363	3.81E-30	postive
PIK3CA	AL118506.	0.53224	9.61E-29	postive
SP1	AL118506.	0.50475	1.43E-25	postive
PLIN4	AL118558.	0.62818	1.88E-42	postive
PLIN4	AL118558.	0.51479	1.07E-26	postive
EGLN2	AL121832.	0.55757	6.17E-32	postive
RPL8	AL121832.	0.5652	5.94E-33	postive

DUOX2	AL122035.	0.51613	7.54E-27	postive
HIF1A	AL122035.	0.67391	7.61E-51	postive
IREB2	AL132639.	0.52598	5.38E-28	postive
ATM	AL132989.	0.56574	5.02E-33	postive
IREB2	AL132989.	0.50774	6.68E-26	postive
SETD1B	AL132989.	0.53182	1.08E-28	postive
SP1	AL132989.	0.57653	1.64E-34	postive

ALOX12	AL133355.	0.53156	1.16E-28	postive
ATG4D	AL133355.	0.51419	1.25E-26	postive
CS	AL133355.	0.59318	6.48E-37	postive
SP1	AL133355.	0.54659	1.61E-30	postive
CYBB	AL133371.	0.7208	3.50E-61	postive
PML	AL133371.	0.52076	2.20E-27	postive

TLR4	AL133371.	0.50235	2.63E-25	postive
SOCS1	AL137186.	0.51451	1.15E-26	postive
PLIN4	AL139260.	0.67986	4.74E-52	postive
ZNF419	AL139287.	0.51427	1.23E-26	postive
DUOX1	AL139288.	0.56458	7.20E-33	postive
ALOX12	AL139349.	0.55751	6.28E-32	postive
ATM	AL157392.	0.51111	2.80E-26	postive

SETD1B	AL157392.	0.56098	2.18E-32	postive
SP1	AL157392.	0.60322	1.96E-38	postive
YY1AP1	AL157392.	0.5252	6.66E-28	postive
ZNF419	AL157392.	0.51417	1.26E-26	postive
VLDLR	AL157394.	0.57297	5.14E-34	postive
PCK2	AL161668.	0.60476	1.14E-38	postive
SCP2	AL161668.	0.53755	2.16E-29	postive

EGLN2	AL161729.	0.53983	1.13E-29	postive
PRKAA2	AL163953.	0.51591	7.99E-27	postive
IREB2	AL353804.	0.50498	1.35E-25	postive
PIK3CA	AL353804.	0.51192	2.27E-26	postive
SIRT1	AL353804.	0.54839	9.50E-31	postive
SP1	AL353804.	0.55333	2.21E-31	postive

IREB2	AL354733.	0.51057	3.22E-26	postive
SETD1B	AL354733.	0.50103	3.66E-25	postive
SIRT1	AL354733.	0.51847	4.06E-27	postive
ABCC1	AL354836.	0.537	2.53E-29	postive
PROM2	AL354836.	0.51755	5.17E-27	postive
FANCD2	AL355488.	0.54533	2.32E-30	postive

HELLS	AL355488.	0.50658	8.97E-26	postive
HRAS	AL357079.	0.51068	3.13E-26	postive
VLDLR	AL359076.	0.52205	1.56E-27	postive
HNF4A	AL359915.	0.51869	3.83E-27	postive
ALOX12	AL360181.	0.51835	4.19E-27	postive
SETD1B	AL360181.	0.5533	2.22E-31	postive
SIRT1	AL360181.	0.5208	2.18E-27	postive
SP1	AL360181.	0.50124	3.47E-25	postive

KRAS	AL365226.	0.56975	1.43E-33	postive
ATM	AL365361.	0.62345	1.16E-41	postive
PROM2	AL390719.	0.53339	6.98E-29	postive
HSPB1	AL391056.	0.55074	4.77E-31	postive
RPL8	AL391056.	0.57612	1.87E-34	postive
GOT1	AL391684.	0.667	1.76E-49	postive
HRAS	AL441992.	0.50164	3.14E-25	postive

IREB2	AL450326.	0.51805	4.54E-27	postive
SNX4	AL450326.	0.51134	2.64E-26	postive
TXNRD1	AL512353.	0.51782	4.82E-27	postive
NOX1	AL591686.	0.81151	8.05E-89	postive
DRD4	AL596223.	0.61098	1.21E-39	postive
SLC2A6	AL596223.	0.50683	8.42E-26	postive
VLDLR	AL596244.	0.50889	4.96E-26	postive

HBA1	AL596442.	0.59361	5.59E-37	postive
PLIN4	AL596442.	0.63258	3.38E-43	postive
FANCD2	AL606489.	0.57292	5.23E-34	postive
SP1	AL606489.	0.52591	5.48E-28	postive
STMN1	AL606489.	0.50753	7.04E-26	postive
YY1AP1	AL606489.	0.57534	2.40E-34	postive
ABCC1	AL607028.	0.52984	1.87E-28	postive

PROM2	AL607028.	0.52004	2.67E-27	postive
ATG4D	AL645608.	0.51192	2.27E-26	postive
PROM2	AL645608.	0.52328	1.12E-27	postive
GABPB1	AL662844.	0.51268	1.86E-26	postive
ATF4	AL671710.	0.55811	5.23E-32	postive
MUC1	AL691482.	0.53746	2.22E-29	postive
PTGS2	AL691482.	0.65631	1.93E-47	postive

IREB2	AL731577.	0.55861	4.50E-32	postive
KLHL24	AL731577.	0.50118	3.52E-25	postive
SIRT1	AL731577.	0.53459	4.98E-29	postive
SNX4	AL731577.	0.52183	1.65E-27	postive
ATM	ANKRD10-	0.58012	5.12E-35	postive
SETD1B	ANKRD10-	0.52637	4.84E-28	postive

SP1	ANKRD10-	0.57892	7.56E-35	postive
ATG4D	AP000757.	0.51478	1.08E-26	postive
CS	AP000757.	0.57505	2.64E-34	postive
ABCC1	AP000759.	0.5103	3.46E-26	postive
OTUB1	AP000873.	0.51101	2.87E-26	postive
EGLN2	AP000892.	0.57234	6.28E-34	postive
RPL8	AP000892.	0.57461	3.04E-34	postive

EPAS1	AP001189.	0.54923	7.43E-31	postive
ZEB1	AP001189.	0.5421	5.92E-30	postive
PLIN4	AP001437.	0.5639	8.89E-33	postive
ABCC1	AP001453.	0.53496	4.49E-29	postive
OTUB1	AP001453.	0.50137	3.36E-25	postive
PROM2	AP001453.	0.5174	5.38E-27	postive
SLC38A1	AP001453.	0.5311	1.32E-28	postive

EGLN2	AP001505.	0.58212	2.65E-35	postive
HRAS	AP001505.	0.56066	2.41E-32	postive
VLDLR	AP002336.	0.53055	1.54E-28	postive
EGLN2	AP002360.	0.51069	3.12E-26	postive
HRAS	AP002360.	0.60222	2.80E-38	postive
HSPB1	AP002360.	0.50733	7.42E-26	postive
CHMP6	AP002748.	0.50674	8.62E-26	postive

CYBB	AP002954.	0.74975	1.07E-68	postive
IFNG	AP002954.	0.53851	1.65E-29	postive
HRAS	AP003068.	0.59766	1.38E-37	postive
HSPB1	AP003068.	0.64727	8.84E-46	postive
RPL8	AP003068.	0.5349	4.57E-29	postive
TXNRD1	AP003119.	0.51974	2.89E-27	postive
DDIT3	AP003171.	0.52404	9.11E-28	postive
RPL8	AP003352.	0.53311	7.55E-29	postive

ATM	AP003392.	0.59867	9.70E-38	postive
DUOX2	AP003392.	0.52863	2.60E-28	postive
PIK3CA	AP003392.	0.54102	8.06E-30	postive
SETD1B	AP003392.	0.54495	2.60E-30	postive
SP1	AP003392.	0.54367	3.76E-30	postive
HRAS	AP003419.	0.50422	1.64E-25	postive

EGLN2	AP004609.	0.56943	1.58E-33	postive
SP1	AP005899.	0.56932	1.63E-33	postive
ACVR1B	AP006621.	0.50088	3.80E-25	postive
DUOX2	AP006621.	0.61094	1.23E-39	postive
MUC1	AP006621.	0.5195	3.09E-27	postive
HRAS	ARF4-AS1	0.55678	7.83E-32	postive

HSPB1	ARF4-AS1	0.58123	3.56E-35	postive
RPL8	ARF4-AS1	0.53719	2.40E-29	postive
OTUB1	ARRDC1-A	0.51728	5.56E-27	postive
NRAS	ATP1A1-A	0.55147	3.83E-31	postive
PLIN4	ATP6V0E2-	0.50227	2.68E-25	postive
NF2	BACE1-AS	0.54105	7.99E-30	postive
OTUB1	BACE1-AS	0.54512	2.47E-30	postive
HELLS	C1orf220	0.56767	2.74E-33	postive
ATG16L1	C2orf49-D	0.5005	4.18E-25	postive

ATG16L1	CAPN10-D	0.50171	3.08E-25	postive
SOCS1	CCR5AS	0.59525	3.18E-37	postive
ABCC1	CD27-AS1	0.55177	3.51E-31	postive
CS	CD27-AS1	0.50685	8.38E-26	postive
ISCU	CD27-AS1	0.50063	4.05E-25	postive
HRAS	CH17-340	0.57157	8.02E-34	postive
PML	CHROMR	0.53763	2.12E-29	postive
ATM	CR936218.	0.62354	1.12E-41	postive
IREB2	CR936218.	0.50667	8.77E-26	postive
MAPK1	CR936218.	0.51702	5.96E-27	postive

PIK3CA	CR936218.	0.52779	3.28E-28	postive
PRKAA1	CR936218.	0.5092	4.59E-26	postive
SETD1B	CR936218.	0.59726	1.59E-37	postive
SP1	CR936218.	0.59394	4.99E-37	postive
ISCU	CRIM1-DT	0.53047	1.57E-28	postive
CS	CTBP1-DT	0.51658	6.70E-27	postive
MAPK1	CTBP1-DT	0.51962	2.99E-27	postive

SP1	CTBP1-DT	0.55536	1.20E-31	postive
HRAS	CYTOR	0.58667	5.86E-36	postive
HSPB1	CYTOR	0.54505	2.52E-30	postive
SCP2	DHRS4-AS	0.55299	2.44E-31	postive
FANCD2	DLEU2	0.52661	4.53E-28	postive
HELLS	DLEU2	0.53175	1.10E-28	postive
HMGB1	DLEU2	0.50118	3.52E-25	postive
EGLN2	DM1-AS	0.51006	3.67E-26	postive

OTUB1	DNAJC9-A	0.51232	2.05E-26	postive
ANO6	EBLN3P	0.51562	8.61E-27	postive
ATM	EBLN3P	0.64393	3.51E-45	postive
CHMP5	EBLN3P	0.67211	1.74E-50	postive
IREB2	EBLN3P	0.63019	8.63E-43	postive
KLHL24	EBLN3P	0.56992	1.35E-33	postive
MAPK1	EBLN3P	0.5837	1.58E-35	postive

MAPK8	EBLN3P	0.51698	6.02E-27	postive
NFE2L2	EBLN3P	0.50633	9.57E-26	postive
OXSR1	EBLN3P	0.50379	1.83E-25	postive
PIK3CA	EBLN3P	0.67965	5.24E-52	postive
PRKAA1	EBLN3P	0.56095	2.20E-32	postive
SETD1B	EBLN3P	0.57128	8.79E-34	postive
SIRT1	EBLN3P	0.53831	1.74E-29	postive
SNX4	EBLN3P	0.54295	4.63E-30	postive

SP1	EBLN3P	0.65117	1.72E-46	postive
ZEB1	EBLN3P	0.60002	6.06E-38	postive
CS	EIF3J-DT	0.5167	6.48E-27	postive
GABPB1	EIF3J-DT	0.52384	9.61E-28	postive
SP1	EIF3J-DT	0.52179	1.67E-27	postive
HSPB1	ELFN1-AS1	0.55903	3.96E-32	postive

CAV1	EPB41L4A-	0.51088	2.97E-26	postive
ABCC1	FAM111A-	0.62821	1.87E-42	postive
ATM	FAM111A-	0.53933	1.31E-29	postive
PIK3CA	FAM111A-	0.50623	9.83E-26	postive
SLC38A1	FAM111A-	0.54619	1.81E-30	postive
SP1	FAM111A-	0.60054	5.05E-38	postive
ATG4D	FAM201A	0.51	3.73E-26	postive
CS	FAM201A	0.50019	4.52E-25	postive

SLC38A1	FAM201A	0.52419	8.75E-28	postive
ACVR1B	FBXL19-AS	0.50543	1.21E-25	postive
CS	FBXL19-AS	0.53973	1.16E-29	postive
DUOX2	FBXL19-AS	0.58129	3.48E-35	postive
SLC38A1	FBXL19-AS	0.51189	2.29E-26	postive
SP1	FBXL19-AS	0.55316	2.32E-31	postive
ANO6	FGD5-AS1	0.5624	1.41E-32	postive
ATG16L1	FGD5-AS1	0.51595	7.89E-27	postive

ATM	FGD5-AS1	0.56831	2.24E-33	postive
BACH1	FGD5-AS1	0.5211	2.01E-27	postive
BECN1	FGD5-AS1	0.59774	1.34E-37	postive
IREB2	FGD5-AS1	0.69201	1.33E-54	postive
KLHL24	FGD5-AS1	0.56365	9.61E-33	postive
MAPK1	FGD5-AS1	0.68848	7.58E-54	postive

MAPK8	FGD5-AS1	0.59089	1.41E-36	postive
NFE2L2	FGD5-AS1	0.50081	3.87E-25	postive
NRAS	FGD5-AS1	0.56367	9.54E-33	postive
OXSR1	FGD5-AS1	0.68783	1.04E-53	postive
PIK3CA	FGD5-AS1	0.68572	2.89E-53	postive
SETD1B	FGD5-AS1	0.58202	2.74E-35	postive
SIRT1	FGD5-AS1	0.55719	6.91E-32	postive
SNX4	FGD5-AS1	0.65211	1.16E-46	postive

SP1	FGD5-AS1	0.69317	7.50E-55	postive
ZEB1	FGD5-AS1	0.51916	3.37E-27	postive
HBA1	FLJ20021	0.54736	1.29E-30	postive
PLIN4	FLJ20021	0.62355	1.12E-41	postive
GABPB1	FLJ37453	0.50599	1.04E-25	postive
RPL8	FOXP4-AS	0.64815	6.12E-46	postive

ATF4	GAS5	0.54888	8.23E-31	postive
RPL8	GAS5	0.65518	3.13E-47	postive
DPP4	GCC2-AS1	0.56593	4.73E-33	postive
PANX1	GCC2-AS1	0.61078	1.30E-39	postive
STMN1	GIHCG	0.51619	7.42E-27	postive
OTUB1	GPRC5D-A	0.52574	5.74E-28	postive
AKR1C3	GSEC	0.54309	4.45E-30	postive
G6PD	GSEC	0.5685	2.12E-33	postive
MAFG	GSEC	0.50099	3.70E-25	postive
NQO1	GSEC	0.50175	3.06E-25	postive
PGD	GSEC	0.5261	5.20E-28	postive
PTGS2	HCG11	0.7622	3.00E-72	postive

ATG16L1	HCG18	0.52016	2.59E-27	postive
CS	HCG18	0.54543	2.26E-30	postive
MAPK1	HCG18	0.50291	2.28E-25	postive
MAPK14	HCG18	0.59009	1.85E-36	postive
SP1	HCG18	0.5813	3.47E-35	postive
IFNG	HLA-DQB1	0.53349	6.78E-29	postive
HSPB1	HMGA1P4	0.54023	1.01E-29	postive
ABCC1	HMGN3-A	0.5457	2.09E-30	postive
HNF4A	HNF4A-AS	0.55234	2.96E-31	postive
PCK2	HNF4A-AS	0.52821	2.92E-28	postive
SCP2	HNF4A-AS	0.52108	2.02E-27	postive

CAV1	HOTAIRM1	0.50019	4.51E-25	postive
HBA1	HOTAIRM1	0.58428	1.30E-35	postive
HIC1	HOTAIRM1	0.68291	1.12E-52	postive
PLIN4	HOTAIRM1	0.73764	1.97E-65	postive
HBA1	HOXB-AS1	0.56275	1.27E-32	postive
HIC1	HOXB-AS1	0.53069	1.48E-28	postive
PLIN4	HOXB-AS1	0.80339	9.01E-86	postive
ATM	INE1	0.51662	6.61E-27	postive
SETD1B	INE1	0.50162	3.15E-25	postive

CA9	ITGB1-DT	0.63783	4.18E-44	postive
CS	ITGB1-DT	0.5011	3.59E-25	postive
CYBB	ITGB2-AS1	0.6172	1.22E-40	postive
IFNG	ITGB2-AS1	0.56076	2.33E-32	postive
FANCD2	KDM4A-AS	0.54118	7.70E-30	postive
HSPB1	KMT2E-AS	0.51904	3.48E-27	postive
PROM2	KRT7-AS	0.51783	4.81E-27	postive
HNF4A	LBX2-AS1	0.5183	4.24E-27	postive
ATM	LENG8-AS	0.50688	8.32E-26	postive

SP1	LENG8-AS	0.51207	2.18E-26	postive
ZNF419	LENG8-AS	0.51886	3.66E-27	postive
FANCD2	LINC00205	0.5072	7.67E-26	postive
STMN1	LINC00205	0.52673	4.39E-28	postive
ZNF419	LINC00205	0.50339	2.02E-25	postive
ATM	LINC00265	0.61233	7.37E-40	postive
PML	LINC00265	0.53101	1.35E-28	postive
PTGS2	LINC00265	0.51123	2.71E-26	postive
SETD1B	LINC00265	0.5117	2.40E-26	postive
SLC38A1	LINC00265	0.5538	1.91E-31	postive

SP1	LINC00265	0.5287	2.56E-28	postive
ABCC1	LINC00342	0.55132	4.01E-31	postive
PROM2	LINC00342	0.58716	4.96E-36	postive
PLIN4	LINC00622	0.57578	2.09E-34	postive
CAV1	LINC00839	0.50276	2.37E-25	postive
HIC1	LINC00839	0.53574	3.61E-29	postive
PML	LINC00839	0.52862	2.61E-28	postive
SLC1A5	LINC00839	0.51713	5.78E-27	postive
ATM	LINC00909	0.50485	1.39E-25	postive
SP1	LINC00909	0.55547	1.16E-31	postive

EPAS1	LINC00924	0.50131	3.41E-25	postive
ATM	LINC00926	0.5719	7.24E-34	postive
NQO1	LINC00942	0.58249	2.35E-35	postive
TXNRD1	LINC00942	0.53215	9.84E-29	postive
ATG4D	LINC00992	0.52842	2.76E-28	postive
CS	LINC00992	0.50129	3.43E-25	postive
ABCC1	LINC01011	0.52271	1.31E-27	postive
SCP2	LINC01018	0.67689	1.92E-51	postive
GPX4	LINC01023	0.50047	4.21E-25	postive
CD44	LINC01116	0.51926	3.29E-27	postive
SLC1A5	LINC01116	0.64248	6.36E-45	postive
VLDLR	LINC01116	0.62674	3.28E-42	postive
DPP4	LINC01124	0.58827	3.43E-36	postive
PANX1	LINC01124	0.57684	1.48E-34	postive
STMN1	LINC01194	0.50449	1.53E-25	postive
FANCD2	LINC01224	0.5259	5.49E-28	postive

HELLS	LINC01224	0.5034	2.02E-25	postive
STMN1	LINC01224	0.54562	2.14E-30	postive
SLC40A1	LINC01269	0.53856	1.63E-29	postive
PIK3CA	LINC01278	0.53227	9.53E-29	postive
SP1	LINC01278	0.50422	1.64E-25	postive
WIPI2	LINC01474	0.53408	5.76E-29	postive
SOCS1	LINC01503	0.50702	8.03E-26	postive
ALOX12	LINC01521	0.52474	7.53E-28	postive
BECN1	LINC01521	0.52305	1.19E-27	postive
CS	LINC01521	0.54215	5.82E-30	postive
IREB2	LINC01521	0.52672	4.39E-28	postive
MAPK1	LINC01521	0.55352	2.08E-31	postive
PIK3CA	LINC01521	0.52383	9.65E-28	postive
SP1	LINC01521	0.54168	6.67E-30	postive
CA9	LINC01559	0.55454	1.54E-31	postive
ATM	LINC01560	0.5162	7.39E-27	postive
GABPB1	LINC01560	0.50661	8.90E-26	postive
IREB2	LINC01560	0.5055	1.18E-25	postive
PIK3CA	LINC01560	0.55847	4.69E-32	postive
SP1	LINC01560	0.57347	4.39E-34	postive
GPX2	LINC01770	0.50342	2.00E-25	postive
SLC38A1	LINC01836	0.50926	4.51E-26	postive
ATM	LINC01857	0.50357	1.93E-25	postive

CYBB	LINC01857	0.59434	4.35E-37	postive
IFNG	LINC01871	0.67077	3.21E-50	postive
CYBB	LINC01943	0.59131	1.22E-36	postive
IFNG	LINC01943	0.63881	2.82E-44	postive
PCK2	LINC02028	0.52735	3.70E-28	postive
ABCC1	LINC02035	0.65529	2.99E-47	postive
ALOX12	LINC02035	0.53361	6.56E-29	postive
CAV1	LINC02035	0.51557	8.74E-27	postive
PIK3CA	LINC02035	0.51947	3.11E-27	postive
PROM2	LINC02035	0.5654	5.59E-33	postive
SP1	LINC02035	0.52747	3.58E-28	postive
DUOX2	LINC02041	0.57802	1.01E-34	postive
CYBB	LINC02084	0.61538	2.40E-40	postive
IFNG	LINC02084	0.69479	3.35E-55	postive
PML	LINC02084	0.50129	3.43E-25	postive
HSPB1	LINC02313	0.55244	2.87E-31	postive
ABCC1	LINC02331	0.52915	2.26E-28	postive
DUOX2	LINC02331	0.50748	7.14E-26	postive
IFNG	LINC02446	0.81165	7.13E-89	postive
TXNRD1	LINC02561	0.53995	1.09E-29	postive
DPP4	LINC02637	0.51208	2.18E-26	postive
IL33	LINC02889	0.58057	4.42E-35	postive
DRD4	LMNTD2-A	0.81493	3.79E-90	postive
HBA1	LNCTAM34	0.67346	9.35E-51	postive

PLIN4	LNCTAM34	0.80053	9.85E-85	postive
AKR1C1	LUCAT1	0.66671	2.00E-49	postive
AKR1C2	LUCAT1	0.50528	1.25E-25	postive
AKR1C3	LUCAT1	0.54599	1.92E-30	postive
PGD	LUCAT1	0.57395	3.76E-34	postive
SQSTM1	LUCAT1	0.52552	6.10E-28	postive
SRXN1	LUCAT1	0.62259	1.61E-41	postive
TXNRD1	LUCAT1	0.65766	1.08E-47	postive
SLC1A5	MACORIS	0.54774	1.15E-30	postive
MT3	MAFA-AS1	0.53835	1.73E-29	postive
ATF4	MAPKAPK5	0.50364	1.90E-25	postive
DDIT3	MAPKAPK5	0.51031	3.44E-26	postive
EGLN2	MAPKAPK5	0.52669	4.43E-28	postive
HRAS	MAPKAPK5	0.68353	8.31E-53	postive
HSPB1	MAPKAPK5	0.56127	2.00E-32	postive
OTUB1	MAPKAPK5	0.60309	2.06E-38	postive
ALOX12	MCCC1-AS	0.50128	3.44E-25	postive
RPL8	MHENCR	0.51933	3.23E-27	postive
HRAS	MINCR	0.52961	1.99E-28	postive
HSPB1	MINCR	0.60829	3.20E-39	postive
RPL8	MINCR	0.67127	2.55E-50	postive
CYBB	MIR155HG	0.76251	2.43E-72	postive
IFNG	MIR155HG	0.74837	2.58E-68	postive
SLC1A5	MIR181A2H	0.52084	2.15E-27	postive

ZNF419	MIR181A2H	0.5072	7.67E-26	postive
DRD4	MIR200CH	0.6143	3.58E-40	postive
VEGFA	MIR210HG	0.53235	9.31E-29	postive
TP53	MIR222HG	0.52032	2.48E-27	postive
ABCC1	MIR23AHG	0.53494	4.52E-29	postive
SLC40A1	MIR325HG	0.50971	4.03E-26	postive
HRAS	MIR4435-2	0.53874	1.54E-29	postive
HSPB1	MIR4435-2	0.52804	3.07E-28	postive
ATM	MIR4453H	0.55977	3.16E-32	postive
FBXW7	MIR4453H	0.53528	4.11E-29	postive
GABPB1	MIR4453H	0.5064	9.41E-26	postive
HBA1	MIR497HG	0.58495	1.04E-35	postive
PLIN4	MIR497HG	0.7492	1.53E-68	postive
PLIN4	MIR503HG	0.58158	3.16E-35	postive
SOCS1	MIR583HG	0.50417	1.66E-25	postive
PLIN4	MIR99AHG	0.5059	1.07E-25	postive
BECN1	MKLN1-AS	0.50978	3.95E-26	postive
MAFG	MKLN1-AS	0.61987	4.50E-41	postive
TXNRD1	MKLN1-AS	0.50954	4.21E-26	postive
TXNRD1	MSC-AS1	0.52373	9.92E-28	postive
HSPB1	MUC12-AS	0.57684	1.48E-34	postive
EGLN2	MYLK-AS1	0.5189	3.62E-27	postive
SIRT1	NADK2-AS	0.50055	4.13E-25	postive
ATG3	NCK1-DT	0.50092	3.76E-25	postive

ATG7	NCK1-DT	0.51288	1.77E-26	postive
FANCD2	NCK1-DT	0.50968	4.05E-26	postive
ALOX12	NFYC-AS1	0.52862	2.61E-28	postive
ATM	NFYC-AS1	0.51569	8.47E-27	postive
IREB2	NFYC-AS1	0.50505	1.33E-25	postive
PIK3CA	NFYC-AS1	0.50223	2.71E-25	postive
SP1	NFYC-AS1	0.51914	3.40E-27	postive
GABPB1	NIFK-AS1	0.52962	1.98E-28	postive
SP1	NNT-AS1	0.51128	2.68E-26	postive
ATM	NORAD	0.53718	2.40E-29	postive
IREB2	NORAD	0.55479	1.43E-31	postive
KLHL24	NORAD	0.50906	4.76E-26	postive
MAPK1	NORAD	0.5795	6.25E-35	postive
PIK3CA	NORAD	0.53585	3.50E-29	postive
SETD1B	NORAD	0.56021	2.76E-32	postive
SP1	NORAD	0.63463	1.50E-43	postive
ABCC1	NRAV	0.65101	1.85E-46	postive
CS	NRAV	0.56824	2.30E-33	postive
OTUB1	NRAV	0.51162	2.45E-26	postive
SLC38A1	NRAV	0.60528	9.43E-39	postive
SP1	NRAV	0.512	2.22E-26	postive
ABCC1	NRSN2-AS	0.54926	7.38E-31	postive
CS	NRSN2-AS	0.53325	7.25E-29	postive
SLC38A1	NRSN2-AS	0.50657	9.00E-26	postive

VDAC2	NRSN2-AS	0.52981	1.88E-28	postive
VDAC2	NUTM2A-A	0.5157	8.43E-27	postive
VDAC2	NUTM2B-A	0.52337	1.09E-27	postive
ANO6	OIP5-AS1	0.50501	1.34E-25	postive
EIF2AK4	OIP5-AS1	0.54577	2.04E-30	postive
IREB2	OIP5-AS1	0.67617	2.67E-51	postive
KLHL24	OIP5-AS1	0.50084	3.84E-25	postive
MAPK1	OIP5-AS1	0.52375	9.84E-28	postive
PIK3CA	OIP5-AS1	0.52488	7.25E-28	postive
SIRT1	OIP5-AS1	0.52712	3.94E-28	postive
SP1	OIP5-AS1	0.57946	6.33E-35	postive
EMC2	OTUD6B-A	0.66746	1.43E-49	postive
HSF1	OTUD6B-A	0.53045	1.58E-28	postive
MTDH	OTUD6B-A	0.58402	1.42E-35	postive
ANO6	PAXIP1-AS	0.57254	5.91E-34	postive
IREB2	PAXIP1-AS	0.55457	1.52E-31	postive
PIK3CA	PAXIP1-AS	0.55548	1.16E-31	postive
CYBB	PCED1B-A	0.70044	1.90E-56	postive
IFNG	PCED1B-A	0.63838	3.35E-44	postive
HBA1	PDCD4-AS	0.66079	2.75E-48	postive
PLIN4	PDCD4-AS	0.81226	4.13E-89	postive
CAPG	PELATON	0.5349	4.57E-29	postive
CYBB	PELATON	0.52969	1.95E-28	postive
YWHAE	PITPNA-AS	0.55602	9.84E-32	postive

HRAS	PPP1R14B-	0.52676	4.34E-28	postive
HSPB1	PPP1R35-A	0.50175	3.06E-25	postive
HSPB1	PRKAR1B-	0.50096	3.73E-25	postive
ABCC1	PRKAR1B-	0.52184	1.65E-27	postive
CS	PRKAR1B-	0.50548	1.19E-25	postive
BAP1	PRKAR2A-	0.56425	7.97E-33	postive
HRAS	PRR34-AS1	0.55238	2.93E-31	postive
HSPB1	PRR34-AS1	0.50989	3.84E-26	postive
RPL8	PRRT3-AS1	0.5424	5.43E-30	postive
SP1	PSMA3-AS	0.56271	1.28E-32	postive
IFNG	PSMB8-AS	0.51275	1.83E-26	postive
FANCD2	PTOV1-AS	0.5183	4.25E-27	postive
STMN1	PTOV1-AS	0.51994	2.74E-27	postive
ZNF419	PTOV1-AS	0.60782	3.79E-39	postive
HELLS	PTOV1-AS	0.5197	2.93E-27	postive
ZNF419	PTOV1-AS	0.50949	4.26E-26	postive
CAPG	PTPRN2-A	0.50846	5.55E-26	postive
CYBB	PTPRN2-A	0.68676	1.75E-53	postive
CHMP6	PXN-AS1	0.52256	1.36E-27	postive
HRAS	PXN-AS1	0.58493	1.05E-35	postive
HSPB1	PXN-AS1	0.52222	1.49E-27	postive
OTUB1	PXN-AS1	0.50341	2.01E-25	postive
RPL8	PXN-AS1	0.55393	1.84E-31	postive
ATM	RAD51-AS	0.51345	1.52E-26	postive

GABPB1	RAD51-AS	0.52256	1.36E-27	postive
SP1	RAD51-AS	0.53623	3.14E-29	postive
HRAS	RASSF1-AS	0.52285	1.26E-27	postive
HSPB1	RASSF1-AS	0.5434	4.07E-30	postive
KRAS	RASSF8-AS	0.70526	1.57E-57	postive
CA9	RBPMS-AS	0.52204	1.56E-27	postive
MAPK1	REPIN1-AS	0.53673	2.73E-29	postive
HBA1	RFX5-AS1	0.61135	1.05E-39	postive
PLIN4	RFX5-AS1	0.77859	2.79E-77	postive
HSF1	RHPN1-AS	0.52024	2.53E-27	postive
CS	SBF2-AS1	0.51159	2.47E-26	postive
FANCD2	SCAT2	0.51211	2.16E-26	postive
HELLS	SCAT2	0.50109	3.61E-25	postive
HBA1	SCGB1B2P	0.58409	1.38E-35	postive
PLIN4	SCGB1B2P	0.62405	9.22E-42	postive
DPP4	SIAH2-AS1	0.52879	2.49E-28	postive
HRAS	SLC12A9-A	0.50531	1.24E-25	postive
HSPB1	SLC12A9-A	0.58461	1.16E-35	postive
RPL8	SLC12A9-A	0.68361	7.98E-53	postive
HSPB1	SLCO4A1-	0.54471	2.79E-30	postive
ATF4	SNHG1	0.52674	4.37E-28	postive
OTUB1	SNHG1	0.60537	9.13E-39	postive
OTUB1	SNHG12	0.51552	8.84E-27	postive
ATF4	SNHG17	0.53507	4.36E-29	postive

RPL8	SNHG17	0.59625	2.25E-37	postive
HRAS	SNHG19	0.52338	1.09E-27	postive
HSPB1	SNHG19	0.55456	1.53E-31	postive
RPL8	SNHG19	0.61356	4.70E-40	postive
ATF4	SNHG20	0.50936	4.40E-26	postive
EGLN2	SNHG25	0.66311	9.94E-49	postive
HRAS	SNHG25	0.51302	1.70E-26	postive
TP53	SNHG29	0.5074	7.29E-26	postive
ABCC1	SNHG4	0.54767	1.18E-30	postive
RPL8	SNHG5	0.60841	3.07E-39	postive
HRAS	SNHG6	0.60401	1.48E-38	postive
HSF1	SNHG6	0.5523	3.00E-31	postive
HSPB1	SNHG6	0.61251	6.90E-40	postive
RPL8	SNHG6	0.8395	1.39E-100	postive
OTUB1	SNHG7	0.51792	4.69E-27	postive
RPL8	SNHG7	0.6048	1.12E-38	postive
RPL8	SNHG8	0.59841	1.06E-37	postive
EGLN2	SNHG9	0.55757	6.16E-32	postive
HRAS	SNHG9	0.57555	2.25E-34	postive
HSPB1	SNHG9	0.5345	5.11E-29	postive
ATG4D	SPINT1-AS	0.50867	5.26E-26	postive
PROM2	SPINT1-AS	0.55996	2.98E-32	postive
ATF4	SREBF2-AS	0.5263	4.93E-28	postive
NF2	SREBF2-AS	0.64613	1.42E-45	postive

ATM	STARD4-A	0.51868	3.84E-27	postive
IREB2	STARD4-A	0.53596	3.39E-29	postive
SP1	STARD4-A	0.51861	3.90E-27	postive
ATG13	STARD7-A	0.51171	2.39E-26	postive
SP1	TAPT1-AS1	0.55002	5.89E-31	postive
ABCC1	TGFB2-AS1	0.52476	7.49E-28	postive
PROM2	TGFB2-AS1	0.61954	5.09E-41	postive
ABCC1	THAP9-AS	0.50511	1.31E-25	postive
ALOX12	THAP9-AS	0.50381	1.81E-25	postive
FANCD2	THUMPD3	0.53838	1.71E-29	postive
G6PD	TMCC1-AS	0.50179	3.02E-25	postive
FANCD2	TMPO-AS1	0.56102	2.16E-32	postive
HELLS	TMPO-AS1	0.55127	4.07E-31	postive
STMN1	TMPO-AS1	0.6356	1.02E-43	postive
GABPB1	TOLLIP-AS	0.52828	2.87E-28	postive
EGLN2	TP53TG1	0.50535	1.23E-25	postive
DPP4	TPRG1-AS	0.61422	3.68E-40	postive
HNF4A	TPRG1-AS	0.53519	4.21E-29	postive
PANX1	TPRG1-AS	0.59286	7.23E-37	postive
GCLC	TRAM2-AS	0.51827	4.28E-27	postive
MUC1	TRAPPC12	0.52393	9.39E-28	postive
SP1	TRAPPC12	0.56921	1.69E-33	postive
EGLN2	TRIM52-AS	0.5054	1.21E-25	postive
HRAS	TRIM52-AS	0.54199	6.11E-30	postive

HSPB1	TRIM52-AS	0.51341	1.54E-26	postive
RPL8	TRIM52-AS	0.5562	9.33E-32	postive
MAPK14	U91328.1	0.54626	1.78E-30	postive
RIPK1	U91328.1	0.60338	1.85E-38	postive
ABCC1	UBA6-AS1	0.55801	5.40E-32	postive
IREB2	UBL7-AS1	0.54106	7.97E-30	postive
EMC2	UBR5-AS1	0.58285	2.08E-35	postive
ABCC1	VIM-AS1	0.6124	7.18E-40	postive
PROM2	VIM-AS1	0.59652	2.05E-37	postive
HSF1	VPS13B-D	0.53675	2.72E-29	postive
RPL8	VPS13B-D	0.54044	9.52E-30	postive
CS	WAC-AS1	0.53176	1.10E-28	postive
ABCC1	WARS2-AS	0.57118	9.09E-34	postive
ALOX12	WARS2-AS	0.51247	1.97E-26	postive
NRAS	WARS2-AS	0.50848	5.52E-26	postive
SLC38A1	WARS2-AS	0.54176	6.52E-30	postive
SP1	WARS2-AS	0.58093	3.92E-35	postive
GABPB1	WASL-DT	0.50528	1.25E-25	postive
RPL8	YTHDF3-A	0.59615	2.33E-37	postive
HRAS	Z69706.1	0.50294	2.26E-25	postive
ATM	Z83843.1	0.5128	1.81E-26	postive
SETD1B	Z83843.1	0.50884	5.04E-26	postive
GABPB1	Z95115.1	0.50396	1.75E-25	postive
SOCS1	Z98257.1	0.56906	1.78E-33	postive

CHMP5	ZEB1-AS1	0.5269	4.19E-28	postive
SP1	ZEB1-AS1	0.50276	2.37E-25	postive
HSF1	ZFAS1	0.52011	2.62E-27	postive
OTUB1	ZFAS1	0.58845	3.22E-36	postive
RPL8	ZFAS1	0.68349	8.45E-53	postive
G6PD	ZFPM2-AS	0.54714	1.37E-30	postive
PGD	ZFPM2-AS	0.53444	5.19E-29	postive
SQSTM1	ZFPM2-AS	0.55663	8.19E-32	postive
PHKG2	ZNF213-A	0.50493	1.37E-25	postive
HRAS	ZNF232-A	0.55125	4.10E-31	postive
HSPB1	ZNF232-A	0.51617	7.46E-27	postive
ATM	ZNF32-AS	0.56405	8.49E-33	postive
HELLS	ZNF32-AS	0.50424	1.63E-25	postive
MAPK8	ZNF32-AS	0.54283	4.80E-30	postive
PIK3CA	ZNF32-AS	0.51687	6.19E-27	postive
SETD1B	ZNF32-AS	0.53767	2.09E-29	postive
SP1	ZNF32-AS	0.59495	3.53E-37	postive
HBA1	ZNF426-D	0.65738	1.22E-47	postive
PLIN4	ZNF426-D	0.7923	7.87E-82	postive
ZNF419	ZNF528-A	0.59872	9.54E-38	postive
EGLN2	ZNF529-A	0.5456	2.15E-30	postive
OTUB1	ZNF529-A	0.51156	2.49E-26	postive
ZNF419	ZNF529-A	0.52098	2.08E-27	postive
ZNF419	ZNF582-A	0.5406	9.09E-30	postive

ZNF419	ZNF667-A	0.53386	6.11E-29	postive
ZNF419	ZNF790-A	0.59622	2.27E-37	postive
HSF1	ZNNT1	0.51715	5.75E-27	postive
EGLN2	ZSCAN16-	0.50795	6.32E-26	postive

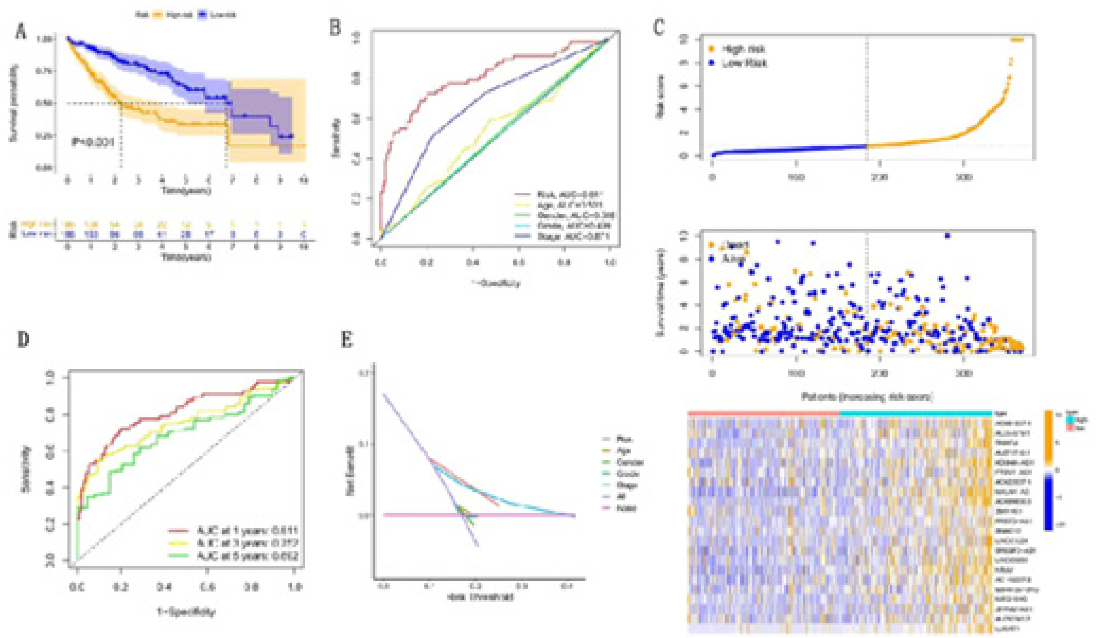


Figure 3: Based on FRlncRNAs signature:

a) Kaplan-Meier curve results.

b) AUC values of risk factors.

c) risk survival status plot.

d) AUC for predicting 1-, 3-, and 5-year survival of HCC.

e) DCA of risk factors.

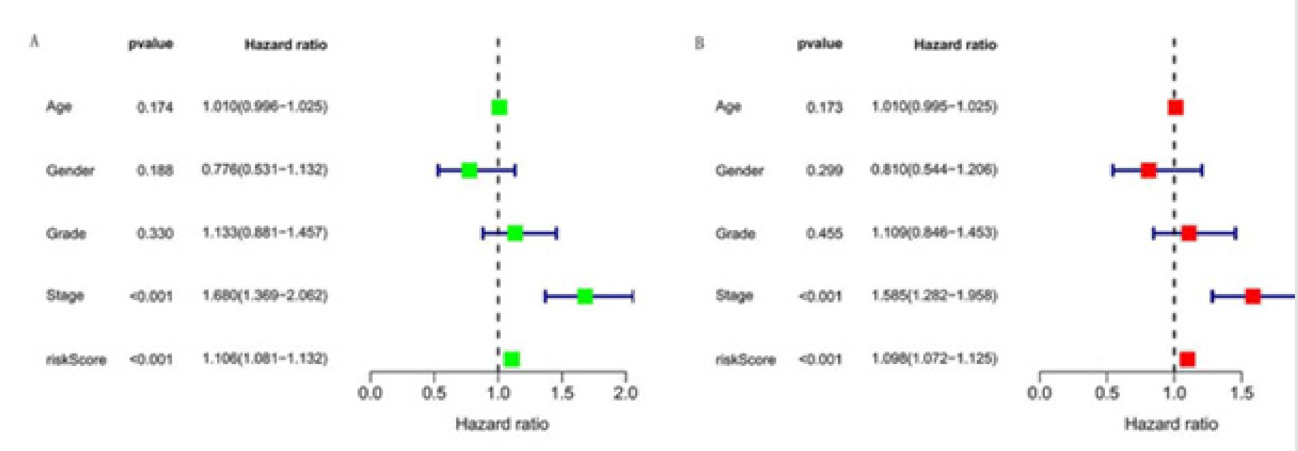


Figure 4:

a) Univariate and

b) multifactorial COX analysis of FRlncRNA expression.

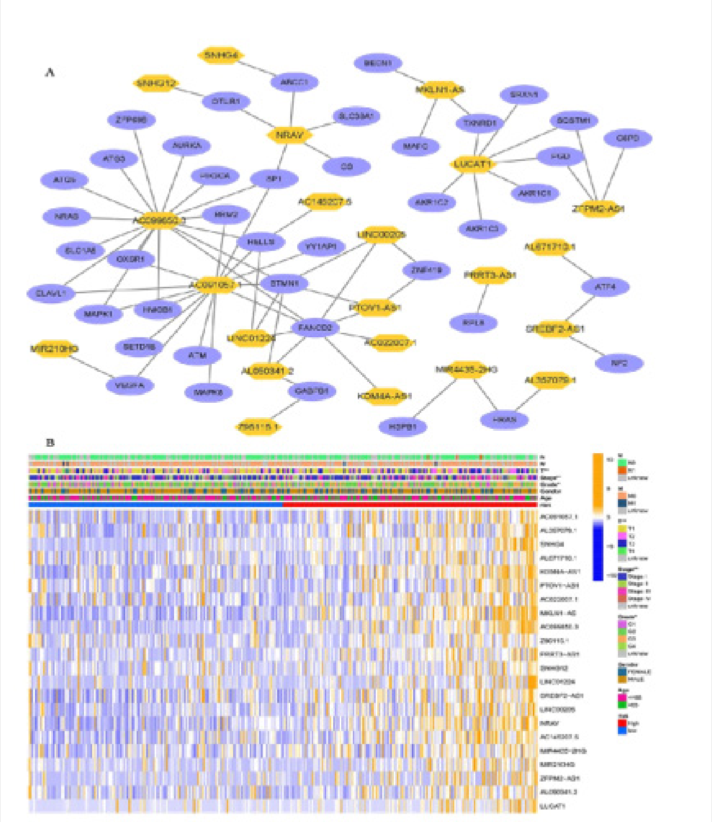


Figure 5:

a) Relationship between characteristic lncRNA and mRNA expressions (yellow - lncRNA, purple - mRNA).

b) A heat map of prognostic models and clinicopathological manifestations characterized by FRlncRNAs. *p < 0.05, **p < 0.01, ***p< 0.001.

GSEA Enrichment Analysis of Risk Scores

The majority of prognostic features of lncRNAs associated with ferroptosis regulate immune and tumor-related pathways, including ubiquitin-mediated proteolysis, homologous recombination, RIG-1-like receptor signaling pathway, colorectal cancer, FC gamma R-mediated phagocytosis, TGF-β signaling pathway, notch signaling pathway, T cell receptor signaling pathway, regulation of autophagy, toll receptor signaling pathway, Aminoacyl tRNA biosynthesis, and RNA degradation (Supplementary Figure 2, 7).

Immunoassay and Gene Expression

To determine whether the model is associated with tumor immunity, we compared the HCC risk score derived from the TIMER, CIBERSORT, CIBERSORT-ASS, QUANTISEQ, MCPCOUNTER, XCELL, and EPIC algorithms with an immunoreactive heatmap of tumor-infiltrating immune cells. The heatmap indicated that B cells, T cells, neutrophils granulocytes, macrophages, and medullary dendritic cells, including regulatory T cells, memory T cells, M0 macrophages, M2 macrophages, CD8+ T cells, lymphocytes, and CD4+ Th2 cells were significantly different between the high- and low-risk groups (Supplementary Figure 3). A correlation analysis of immune cell subpopulations and related functions in ssGSEA using the TCGA-LIHC database revealed that immune cells, including B cells, cytolytic macrophages, MHC-class-I, mast cells, neutrophils, NK cells, helper T cells, Type-I-IFN, and Type-II-IFN differed significantly between high- and low-risk groups (Supplementary Figure 4a). Considering the importance of immune checkpoint blockade based therapeutic strategies in HCC, we further investigated the differences in immune checkpoint expression between the high-and low-risk groups and found significant differences in the expressions of TNFSF18, IDO2, CD276, NRP1, and TNFSF4 between the two groups of patients (Supplementary Figure 4b). The comparison of m6A-related mRNA expressions between those two groups exhibited that RBM15, HNRNPC, YTHDC1, YTHDF1, WTAP, METTL3, ALKBH5, YTHDF2, and FTO were significant (Supplementary Figure 4c).

Expression of FRlncRNAs in HCC

The expression of ferroptosis-related lncRNAs in hepatocellular carcinoma was validated by a series of bioinformatic analyses of 22 lncRNAs in patients with hepatocellular carcinoma and a predictive model constructed from prognosis-related differential ferroptosis genes. Based on this result, further experimental validation of these 22 genes was conducted. Before experimental validation, these 22 genes were independently researched in literature databases using the terms gene names and cancer. However, MIR4435-2HG, SNHG4, PRRT3-AS1, and PTOV1-AS1 were studied less in HCC. Consequently, in the subsequent experimental validation, these lncRNAs were logically chosen as gene targets for additional experimental proof of their relevance in HCC. HCC cell lines and hepatic stellate cell lines were used to validate the expression level of this lncRNA to investigate the expression of MIR4435-2HG, SNHG4, PRRT2-AS1, and PTOV1-AS1. The results of quantitative real-time PCR (qRT-PCR) analysis revealed that these lncRNAs were «upregulated» in HCC cell lines relative to hepatic stellate cell lines (Figure 6). In addition, these results indicated that these lncRNAs might play a crucial role in HCC.

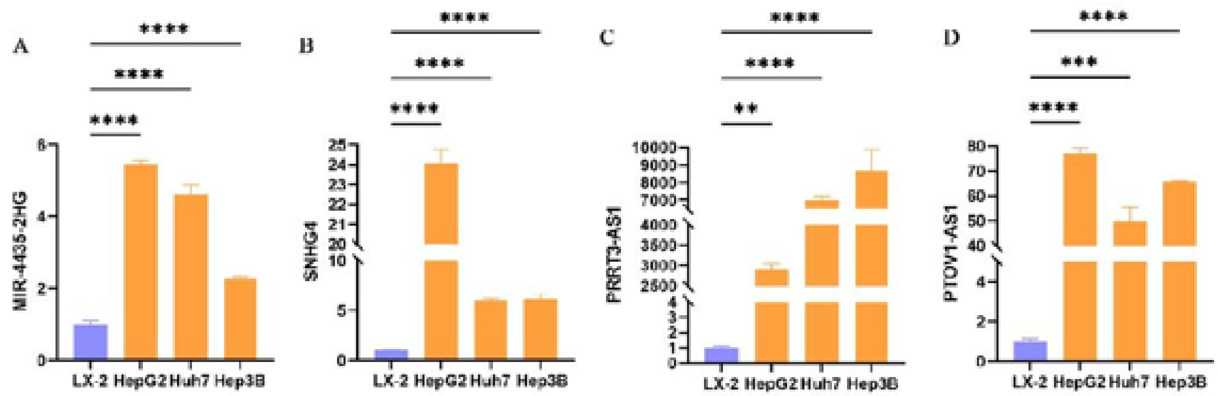


Figure 6: Expressions of MIR4435-2HG, SNHG4, PRRT3-AS1, and PTOVI-AS1 in LX-2, HepG2, Huh7, and Hep3B. *p< 0.05, **p< 0.01, *** p < 0.001, **** p < 0.0001.

Discussion

In many cancers, such as gastric cancer [25] and head and neck squamous cell carcinoma, models of lncRNAs for predicting prognosis have been validated in previous studies. Ferroptosis can overcome the chemotherapy resistance of malignant cells and promote elimination of defective cells. Therefore, it may be a novel method for treating tumors. Based on the TCGA dataset, this study identified a novel model of prognostic lncRNAs associated with ferroptosis. The role of immune infiltrating cells in the tumor microenvironment and immune checkpoint inhibitors in the prognosis of HCC was subsequently investigated. Finally, this study identified potential biomarkers and therapeutic targets in the ferroptosis pathway. Our analysis revealed a total of 84 DEGs associated with ferroptosis. KEGG analysis revealed that these genes are primarily involved in neurodegeneration—multiple disease pathways, chemical carcinogenesis-reactive oxygen species, microRNAs in cancer, lipid and atherosclerosis, central carbon metabolism in cancer, serotonergic synapse, fluid shear stress and atherosclerosis, and ferroptosis. A recent study found that SREBP1/SCD1-mediated lipid formation protects cancer cells from oxidative stress and ferroptosis when PI3K-AKT-mTOR signaling mutations are activated [26]. Fin56 is an inducer of type 3 ferroptosis, and Torin2 is a potent mTOR inhibitor used to activate autophagy, which has synergistic effects on the cytotoxicity of bladder cancer cells, as reported by Sun, et al. [27]. Recent research [28] discovered that ischemia-reperfusion (I/R)-induced upregulation of miR182-5p and miR378a-3p led to ferroptosis activation in kidney injury by downregulating GPX4 and SLC7A11. Metformin was found to induce ferroptosis in a mouse breast cancer xenograft model by upregulating miR324-3p [29]. In addition to isoglochidonine-induced ferroptosis, the miR122-5p/TP53/SLC7A11 pathway prevents brain hemorrhage-induced ferroptosis in neuronal cells [30]. In brief, our study identified 22 differentially expressed lncRNAs as independent HCC prognostic factors. KDM4A-AS1 protects AR and AR splice variants (AR/AR-Vs) from MDM2-mediated degradation of ubiquitin protectors, according to recent research. In addition, KDM4A-AS1 enhanced enzalutamide resistance in desmoplastic prostate cancer by inhibiting AR/AR-V degradation, and antisense oligonucleotide drugs targeting KDM4A-AS1 significantly reduced the growth of enzalutamide-resistant tumors [31]. A novel transcriptional gene, Yin Yang-1 (YY1), LINC00205, can accelerate HCC cell proliferation by sponging miR26a-5p to promote CDK6 expression [32]. LIN01224 absorbs miR193a-5p in gastric cancer and targets the upregulation of CDK8 to hasten the malignant transformation of gastric cancer [33]. LUCAT1 promoted TSCC cell proliferation, cell cycle, and migration by targeting miR375 [34]. Knockdown of LUCAT1 increased miR375 expression in tongue squamous cell carcinoma (TSCC) cells, and low miR374 expression was associated with a poor prognosis in TSCC. Overexpression of CACNA2D2 significantly inhibits non-small-cell lung cancer cell proliferation [35]. MIR210HG recruits DNA methyltransferase 1, which promotes methylation of the CACNA2D2 promoter region. In gastric cancer cells, LncRNA MIR44435-2HG binds to and inhibits the decapentaplegic protein (DSP), activating WNT/β-catenin signaling and triggering epithelial-mesenchymal transition [36]. Overexpression of the LncRNA muskelin1 antisense RNA (MKLN1-AS) increases the stability of Yes-associated transcriptional regulator 1 (YAP1) and promotes the proliferation, metastasis, and invasion of hepatocellular carcinoma cells [37]. LncRNA NRAV stimulates the production of the respiratory syncytial virus by sponging the miR-509-3p profile [38]. Silencing LncRNA PRRT3-AS1 activates peroxisome proliferator-activated receptor γ (PPARγ), inhibiting the mTOR signaling pathway to promote apoptosis and autophagy and inhibit prostate cancer cell proliferation [39]. By promoting LPS-induced inflammation in human lung fibroblasts and mouse lung tissue in vitro and in vivo, LncRNA SNHG4 suppresses METTL-3-mediated transcriptional activator 2 (SATA2) mRNA at m6A levels [40]. Through regulation of the miR-15a/PDK4 axis [41], SNHG12 promotes colon carcinogenesis and progression. STAT1-inducible lncRNA ZFPM2 antisense RNA1 (ZFPM2-AS1) promotes colon cancer development by regulating the target of miR-653, the gene GOLM1, to reverse the inhibitory effect of miR-653 on the proliferation and metastasis of HCC cells [42]. However, few studies have examined the role of FRlncRNAs in HCC prognosis. The outcomes of our study may provide valuable insights for future cancer prevention efforts.

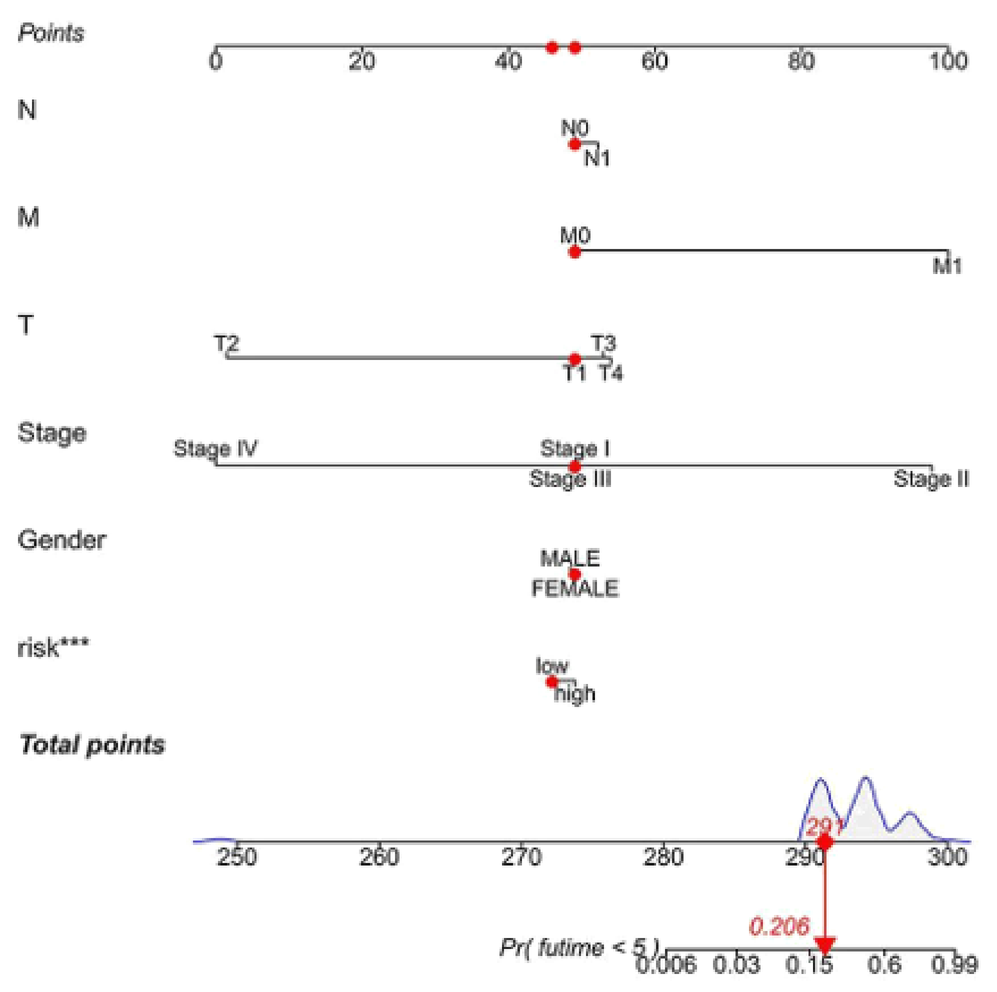
This study investigated ferroptosis biomarkers that aid in predicting the prognosis of HCC, which could serve as a reliable treatment guide for the disease. However, our model, primarily based on bioinformatics research, lacks experimental validation of these indicators. Therefore, additional validation employing distinct cohorts is required. Furthermore, given that our findings have not been validated using clinical samples, we cannot fully guarantee the dependability of our findings. In addition, the model's established prognostic indicators require further validation [43].

Conclusion

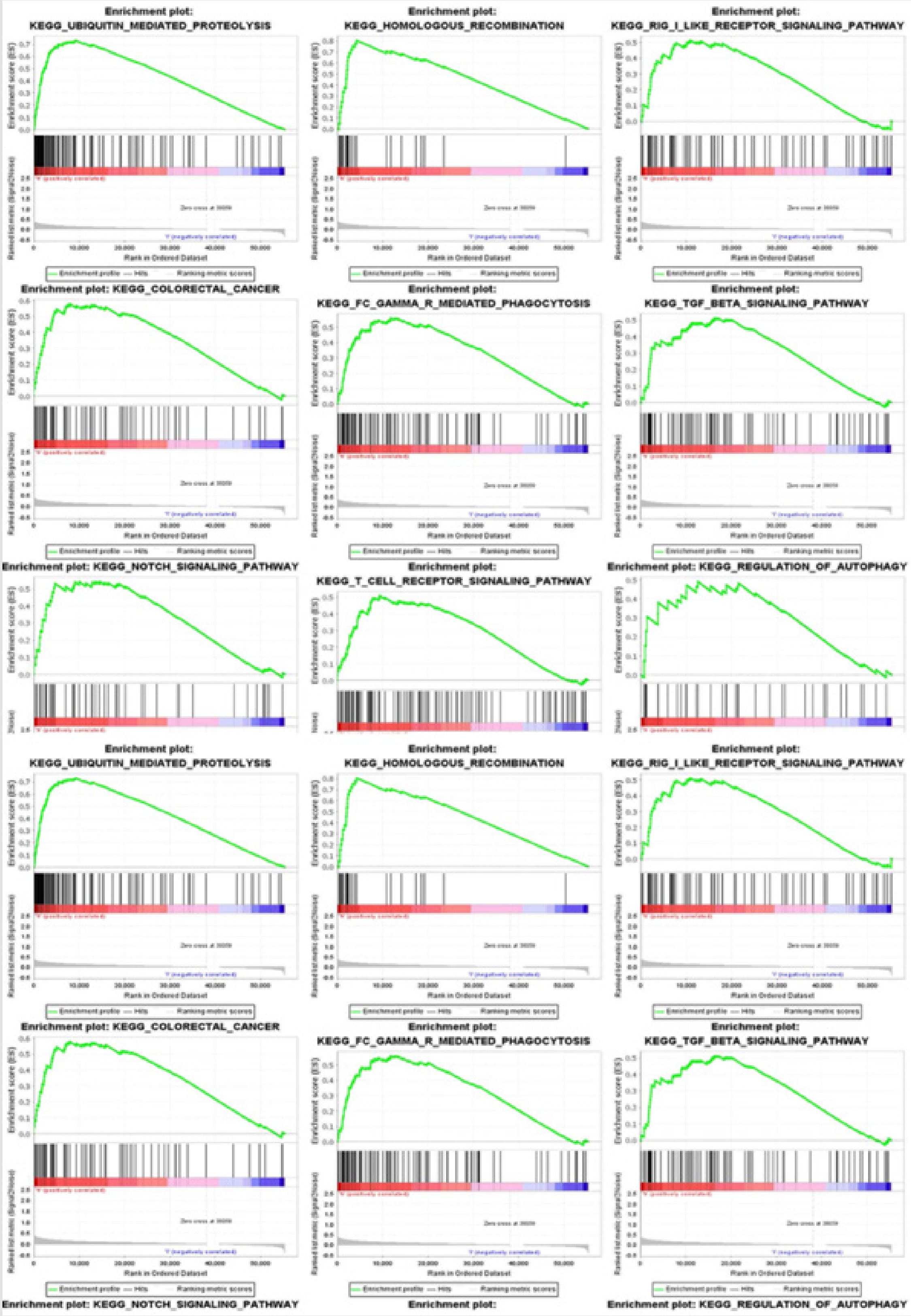
In conclusion, we developed a model of FRlncRNAs for predicting prognosis and immune response in HCC patients, which was strongly correlated with a risk score, survival time, and clinical data on cancer. Consequently, the results suggest that our model of FRlncRNAs provides a personalized, predictive instrument for prognosis and immune response in HCC patients.

Supplementary description:

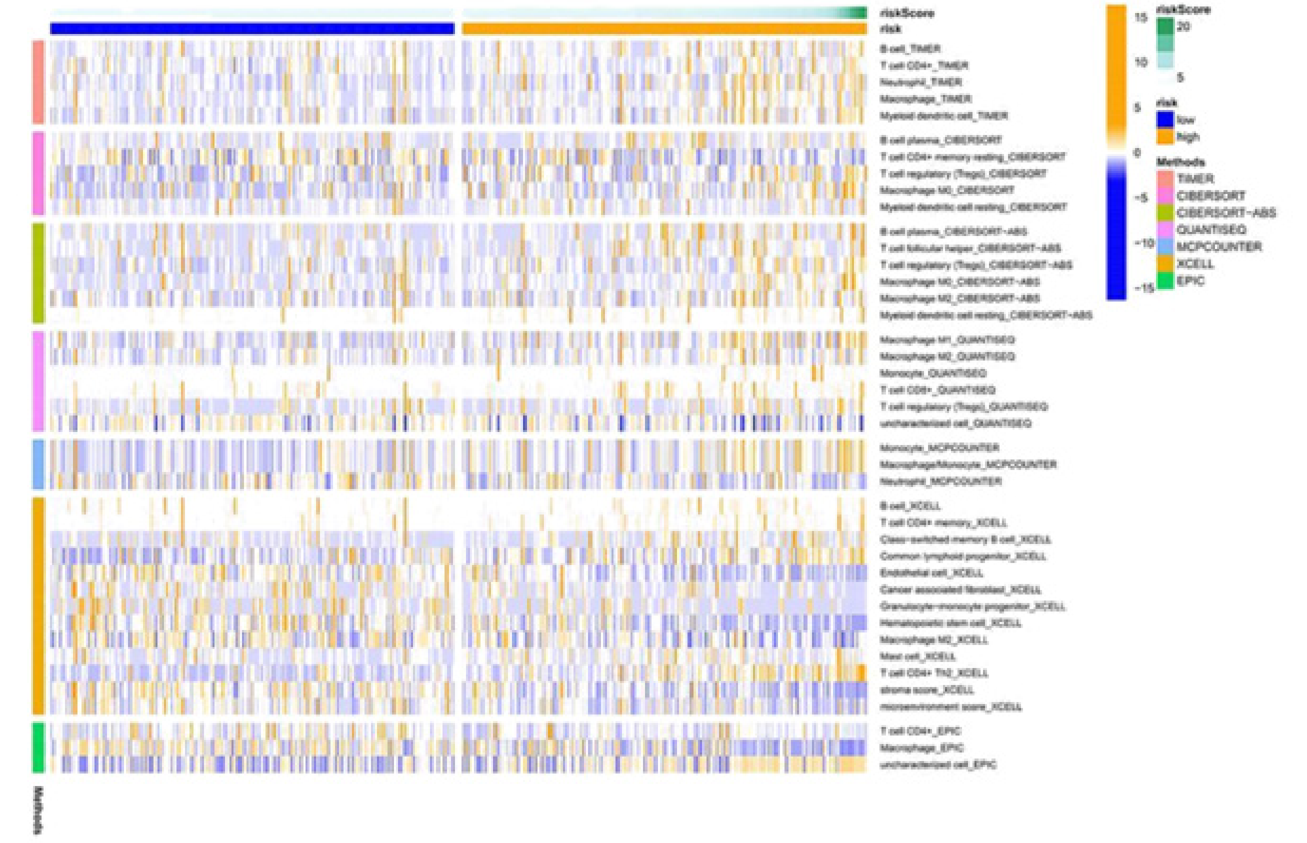
(Supplementary Tables 1-8), (Supplementary Figures 1-4)



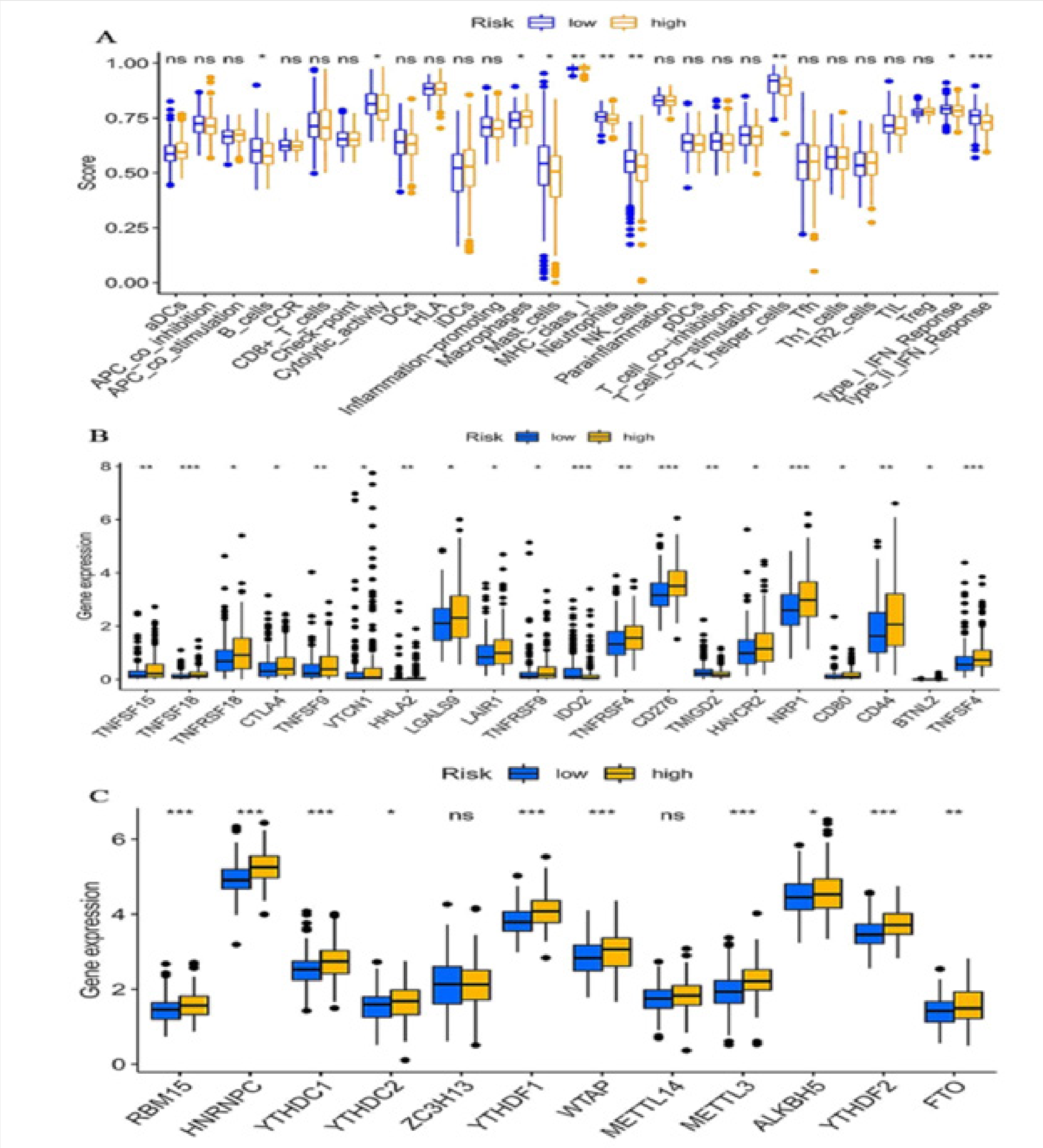
Supplementary Figure 1: A Nomogram of FRlncRNAs for clinicopathological factors and prognosis.



Supplementary Figure 2: Gene set enrichment analysis of FRlncRNAs based on TCGA.



Supplementary Figure 3: A heat map of immune responses in high- and low-risk groups based on TIMER, CIBERSORT, CIBERSORT-ASS, QUANTISEQ, MCPCOUNTER, XCELL, and EPIC algorithms. *p< 0.05, **p< 0.01, ***p<0.001.



Supplementary Figure 4:

a) Association of immune cell subpopulations with related functions of ssGSEA.

b) Expression of immune checkpoints in the high- and low-risk groups for HCC.

c) Expression of m6A-related genes between the high and low-risk groups for HCC. $^{*}p< 0.05$, $^{**}p< 0.01$, $^{***}p < 0.001$.

Declarations

This manuscript was submitted as a pre-print with the link https://www.researchsquare.com/article/rs-1166940/v1.

Acknowledgments

We acknowledge the TCGA and FerrDb databases for providing their platforms and the contributors for uploading their valuable datasets.

Funding

This study was supported by grants from the Commission of China-Hebei Provincial Health Commission (No. 20211094).

Authors contributions

Congyue Zhang conducted a literature review, gathered data, and designed and wrote the manuscript. Zhankai Hu aided in data collection. Huifang Zhou and Chaoqun Zhang reviewed the paper's draft and suggested revisions. Finally, Sun Dianxing revised the manuscript critically. All authors have read and approved the final manuscript.

Availability of data and material

The raw data for this study were obtained from the TCGA database (https://portal.gdc.cancer.gov/), the specific sample is TCGA-LIHC, and the accession number is listed in the Supplementary file, which is a publicly accessible database.

Ethics approval and consent to participate: Both TCGA and FerrDb are public databases. Patients participating in the database have received ethical approval. Users can download relevant data for free and publish relevant articles for research purposes. Since our study is based on open-source data, there are no ethical or other conflicts of interest. We confirm that all procedures were executed following applicable rules and regulations. This study was conducted following the World Medical Association Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests, and all authors attest to its accuracy.

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ISSN: 2574-1241

DOI: 10.26717/BJSTR.2023.48.007604

Shreya Seth. Biomed J Sci & Tech Res