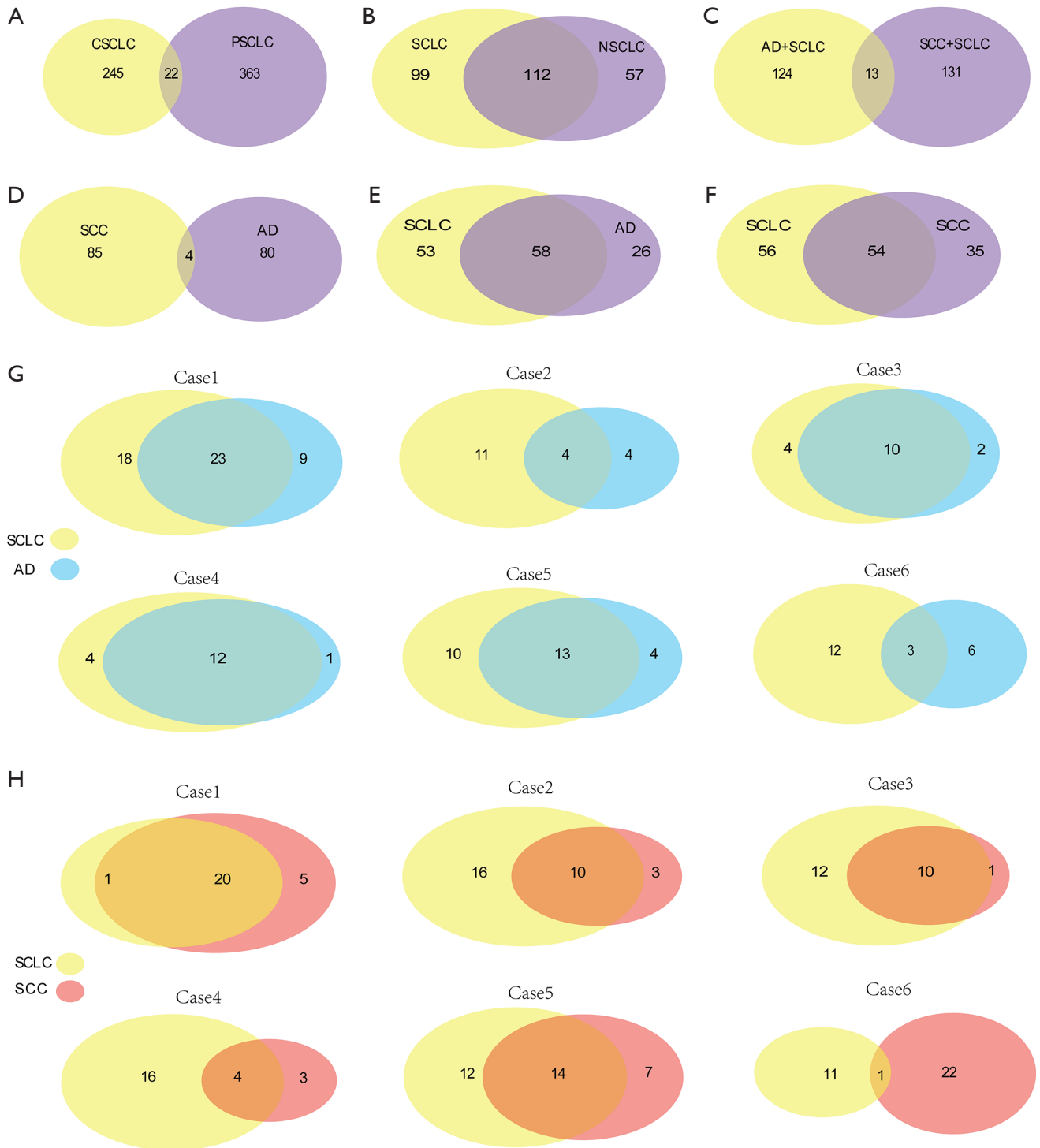

Figure S1 The number of common and unique mutations in different components. (A) The number of common and unique mutations in combined small cell lung cancer (CSCLC) and pure small cell lung cancer (SCLC). (B) The number of common and unique mutations in the non-small cell lung cancer (NSCLC) and SCLC components of CSCLC. (C) The number of common and unique mutations in CSCLC expressing adenocarcinoma (AD), and SCLC and CSCLC expressing squamous cell carcinoma (SCC) and SCLC. (D) The number of common and unique mutations in the SCC and AD components. (E,G) The number of common and unique mutations in the SCLC and AD components of CSCLC. (F,H) The number of common and unique mutations in SCLC and SCC components of CSCLC.

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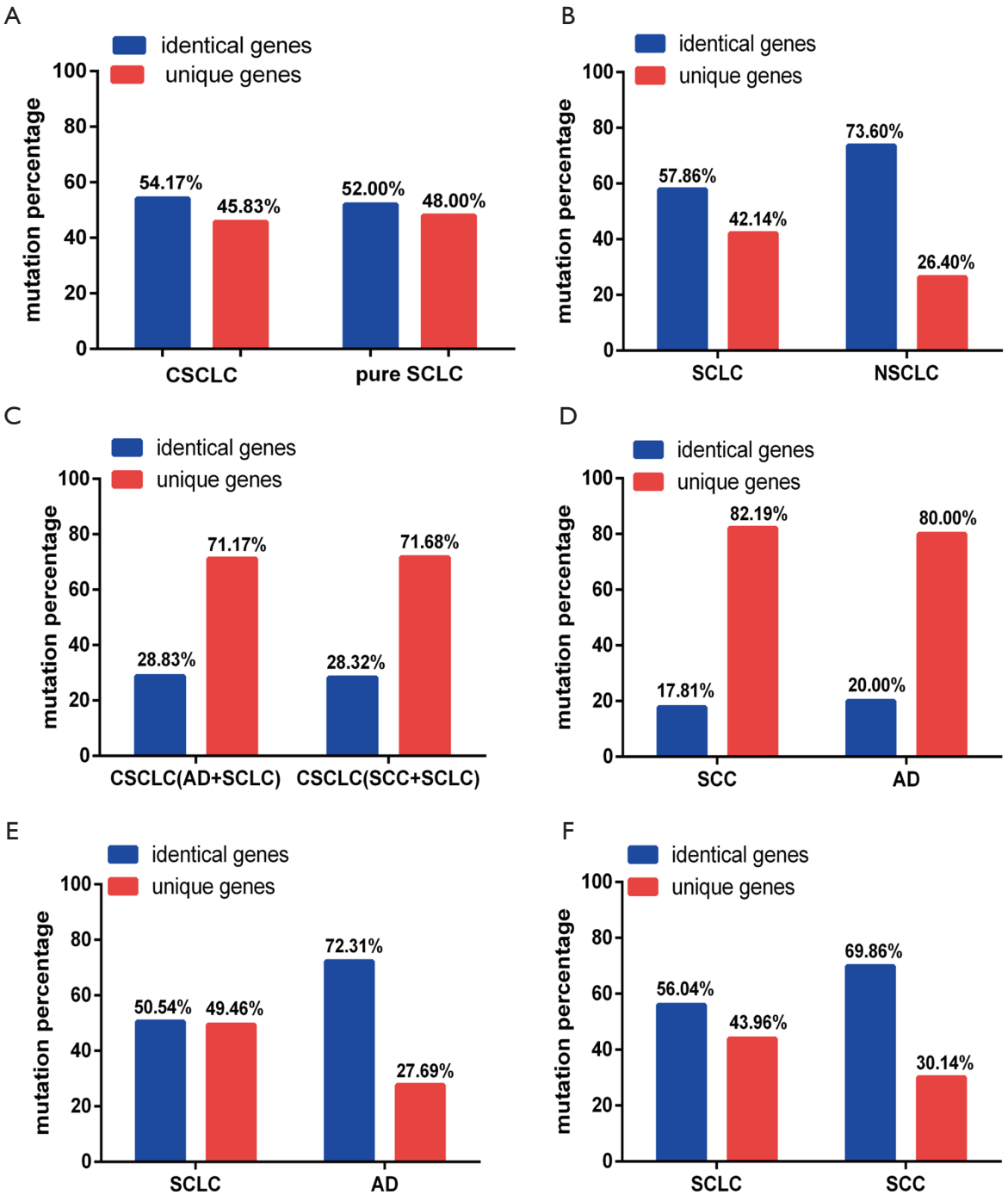

Figure S2 The rate of identical and unique genes with mutations in different components. (A) The percentage of identical and unique genes with mutations in combined small cell lung cancer (CSCLC) and pure small cell lung cancer (SCLC). (B) The rate of identical and unique genes with mutations in the non-small cell lung cancer (NSCLC) and SCLC components of CSCLC. (C) The rate of identical and unique genes with mutations in CSCLC expressing adenocarcinoma (AD) and SCLC, and CSCLC expressing squamous cell carcinoma (SCC) and SCLC. (D) The rate of identical and unique genes with mutations in the SCC and AD components. € The rate of identical and unique genes with mutations in the SCLC and AD components of CSCLC. (F) The rate of identical and unique genes with mutations in the SCLC and SCC components of CSCLC.

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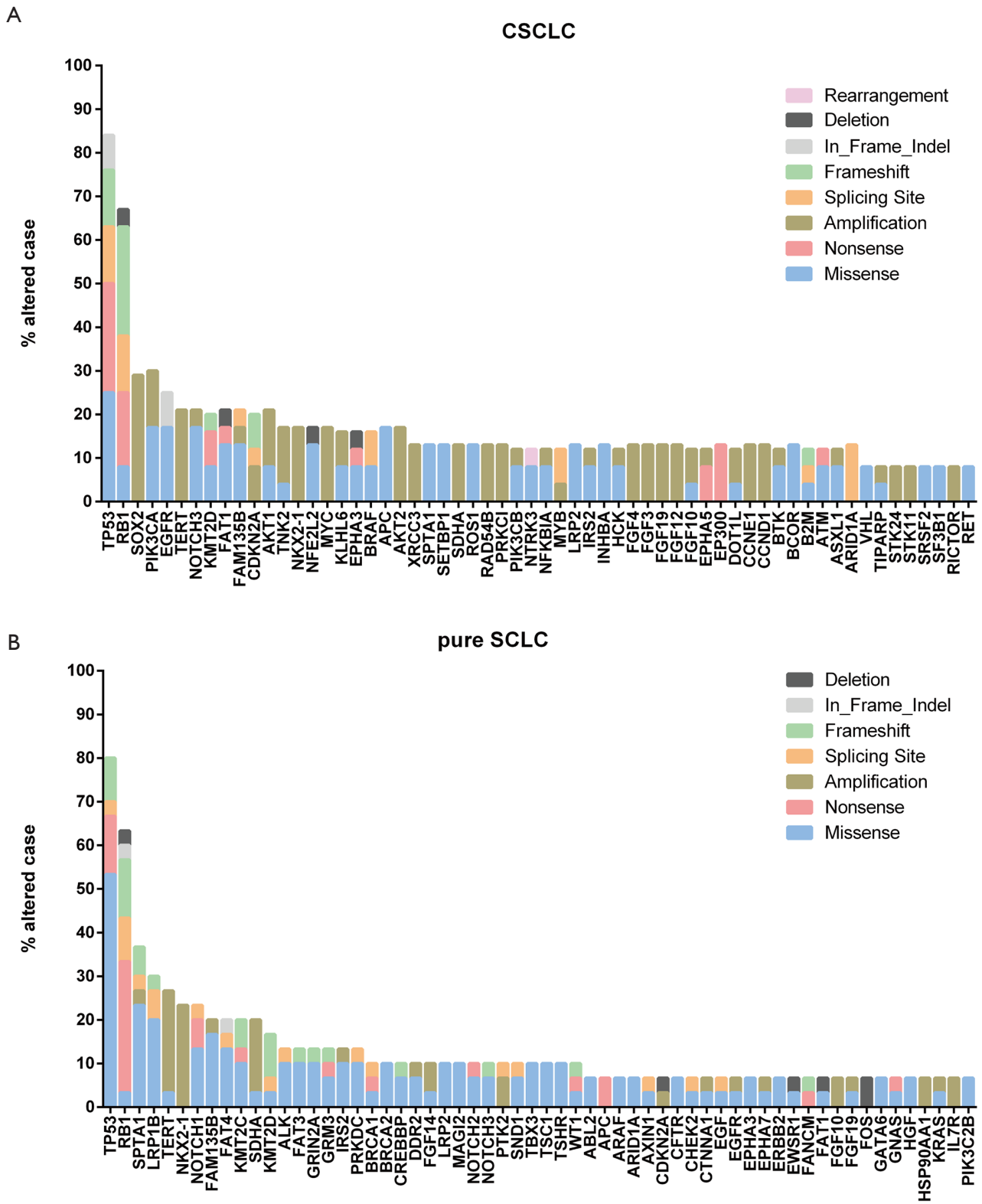

Figure S3 The frequency of the top 60 genomic alterations in the 12 combined small cell lung cancer (CSCLC) cases and 30 pure small cell lung cancer (SCLC) cases. (A) The frequency of genes with diverse mutations in CSCLC. (B) The frequency of genes with diverse mutations in pure SCLC.

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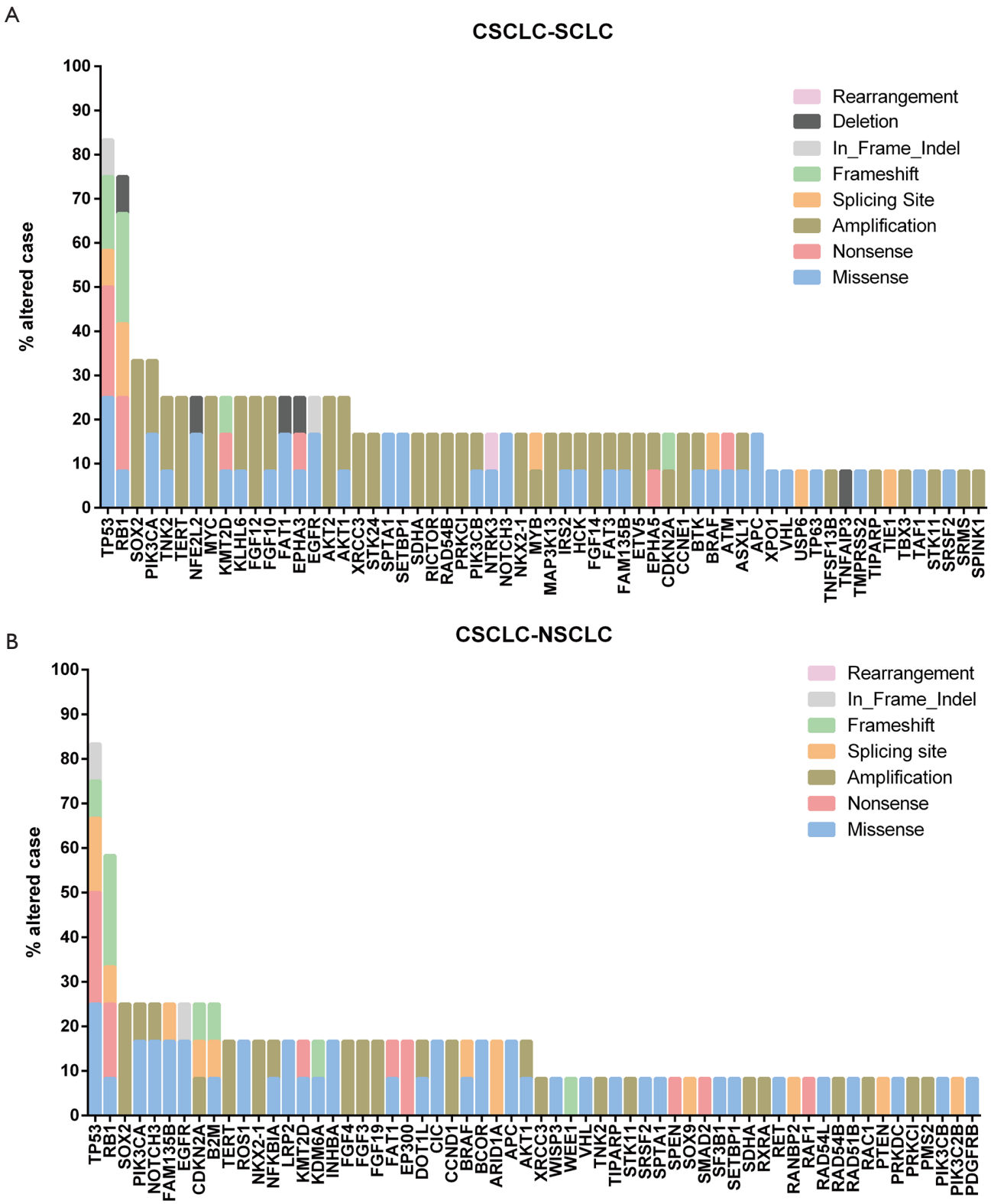

Figure S4 The frequency of the top 60 genomic alterations in the small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) components of combined small cell lung cancer (CSCLC). (A) The frequency of genes with diverse mutations in the SCLC component of CSCLC. (B) The frequency of genes with diverse mutations in the NSCLC component of CSCLC.

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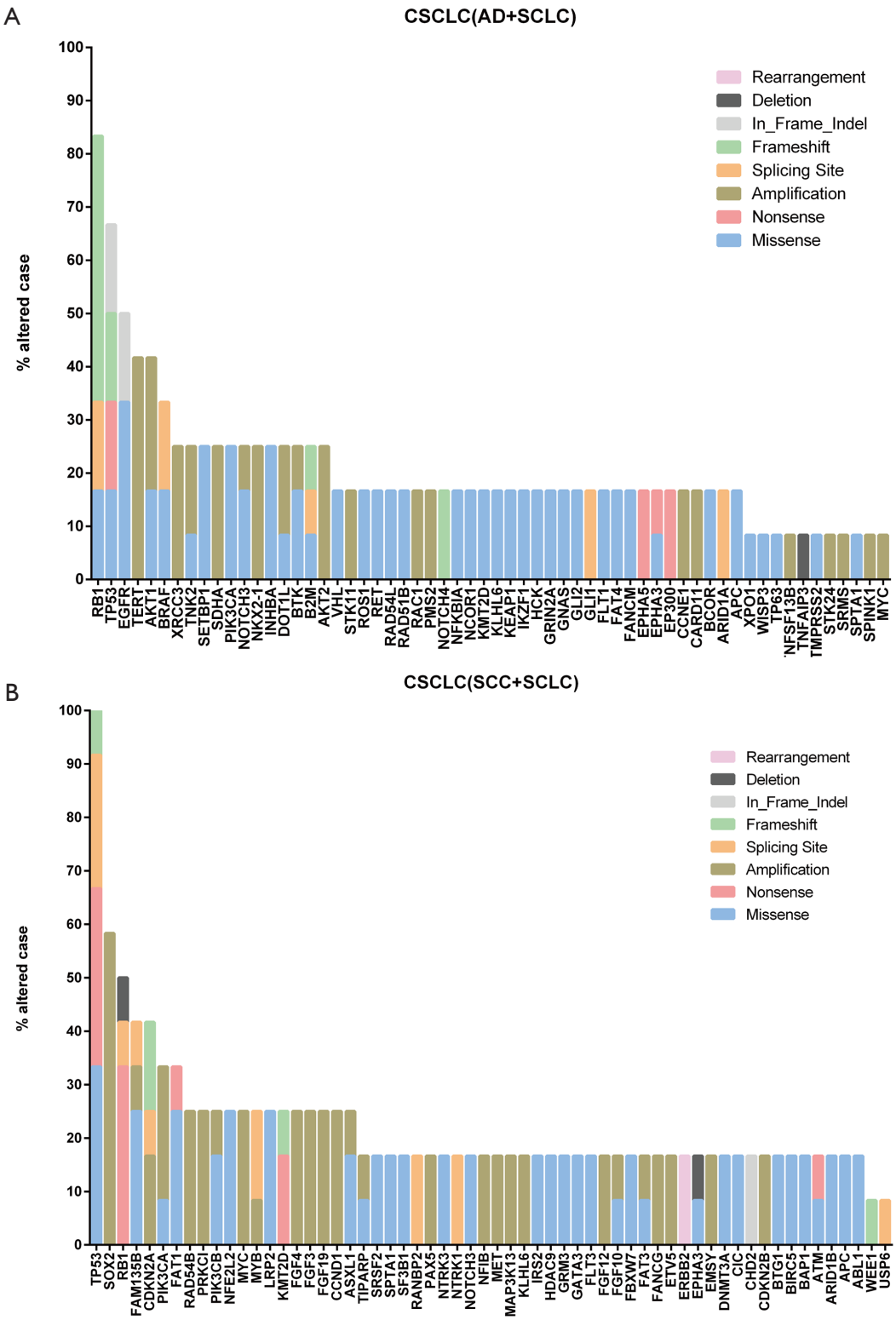

Figure S5 The frequency of the top 60 genomic alterations in the combined small cell lung cancer (CSCLC) cases expressing adenocarcinoma (AD) and small cell lung cancer (SCLC), and 6 cases of CSCLC with squamous cell carcinoma (SCC) and SCLC. (A) The frequency of genes with diverse mutations in the CSCLC cases with AD and SCLC. (B) The frequency of genes with diverse mutations in CSCLC with SCC and SCLC.

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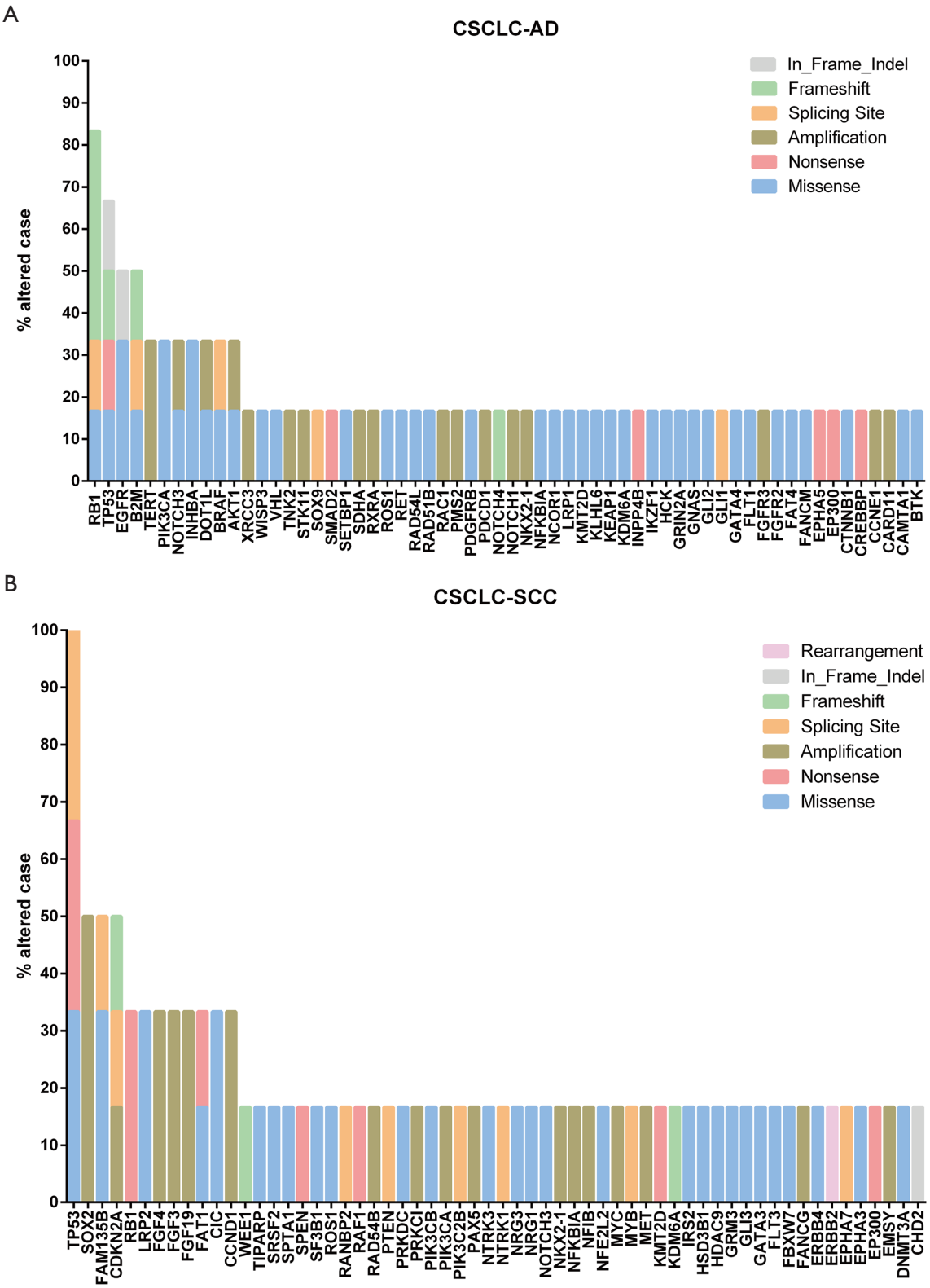

Figure S6 The frequency of the top 60 genomic alterations in the adenocarcinoma (AD) and squamous cell carcinoma (SCC) components. (A) The frequency of genes with diverse mutations in the AD component. (B) The frequency of genes with diverse mutations in the SCC component.

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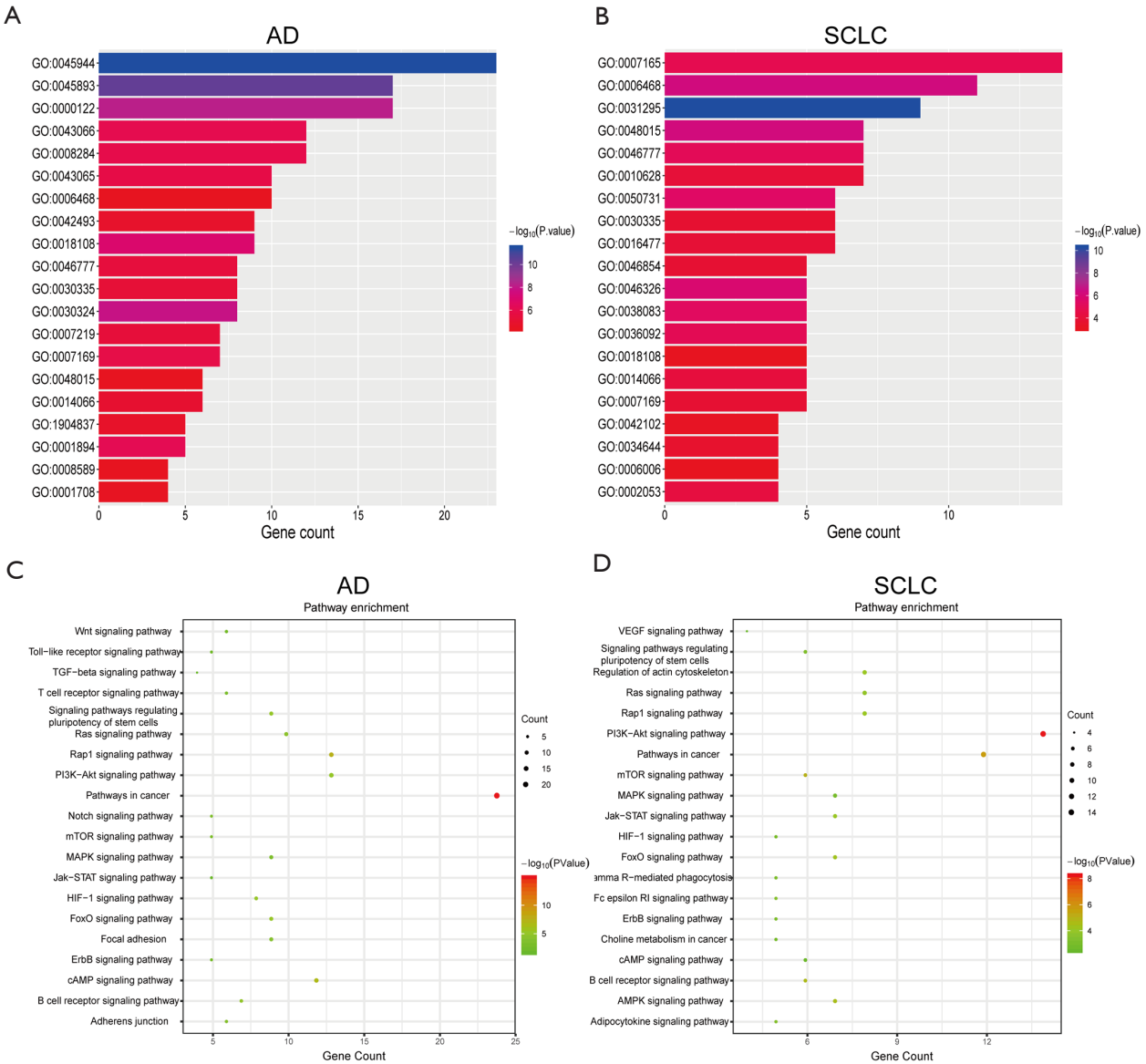

Figure S7 The biological processes and pathways of Kyoto Encyclopedia of Genes and Genomes (KEGG) of mutated genes in the different components predicted by the Database for Annotation, Visualization and Integrated Discovery (DAVID). (A,B) Images of the biological processes of the mutated genes in adenocarcinoma (AD) and the small cell lung cancer (SCLC) component of combined small cell lung cancer (CSCLC). (C,D) Images of signaling pathways of the mutated genes in the AD and SCLC components of CSCLC.

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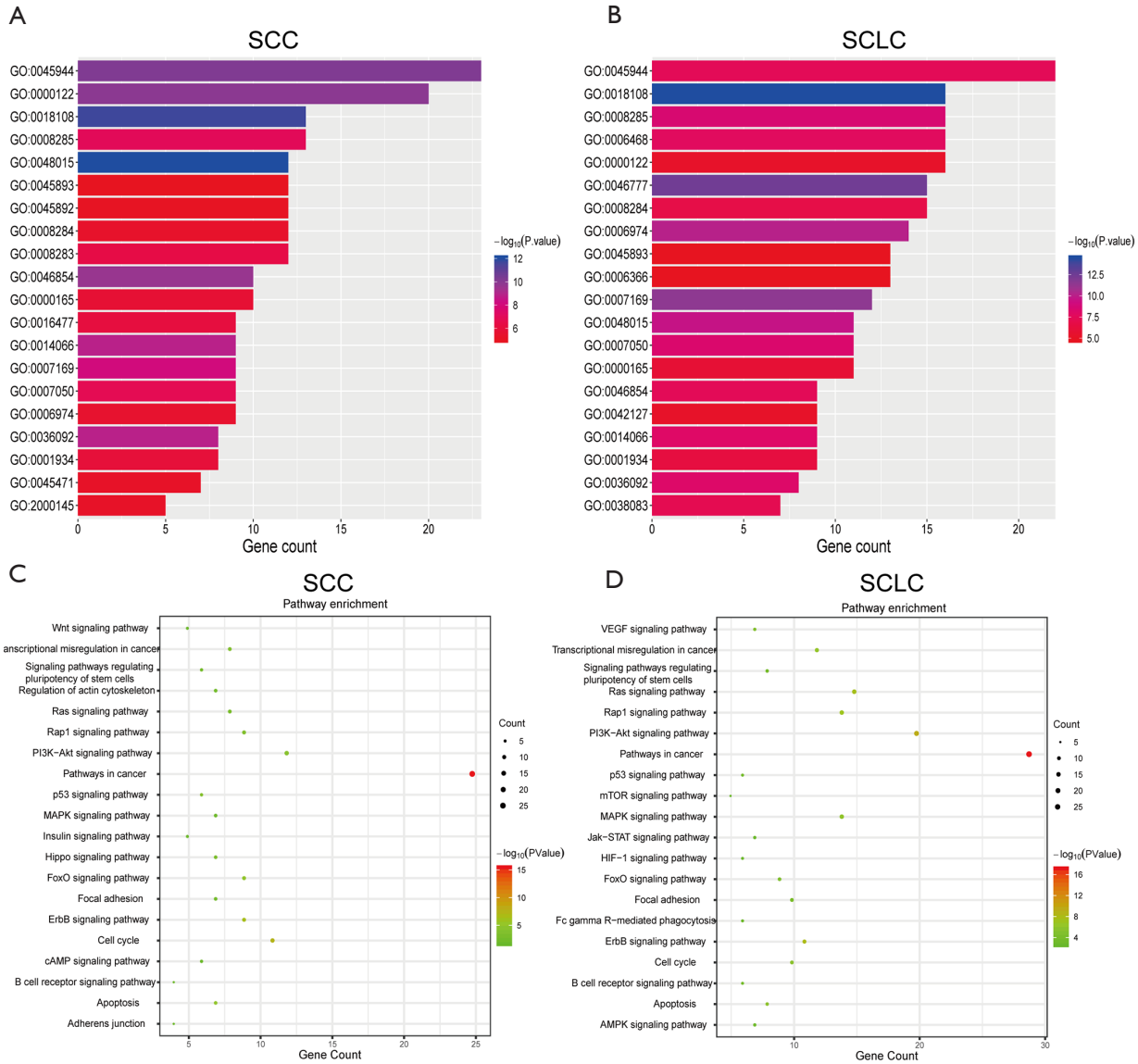

Figure S8 The biological processes and pathways of Kyoto Encyclopedia of Genes and Genomes (KEGG) of mutated genes in the different components predicted by the Database for Annotation, Visualization and Integrated Discovery (DAVID). (A,B) Images of biological process of mutated genes in squamous cell carcinoma (SCC) and small cell lung cancer (SCLC) components of combined small cell lung cancer (CSCLC). (C,D) Images of the signaling pathways of the mutated genes in the SCC and SCLC components of CSCLC.

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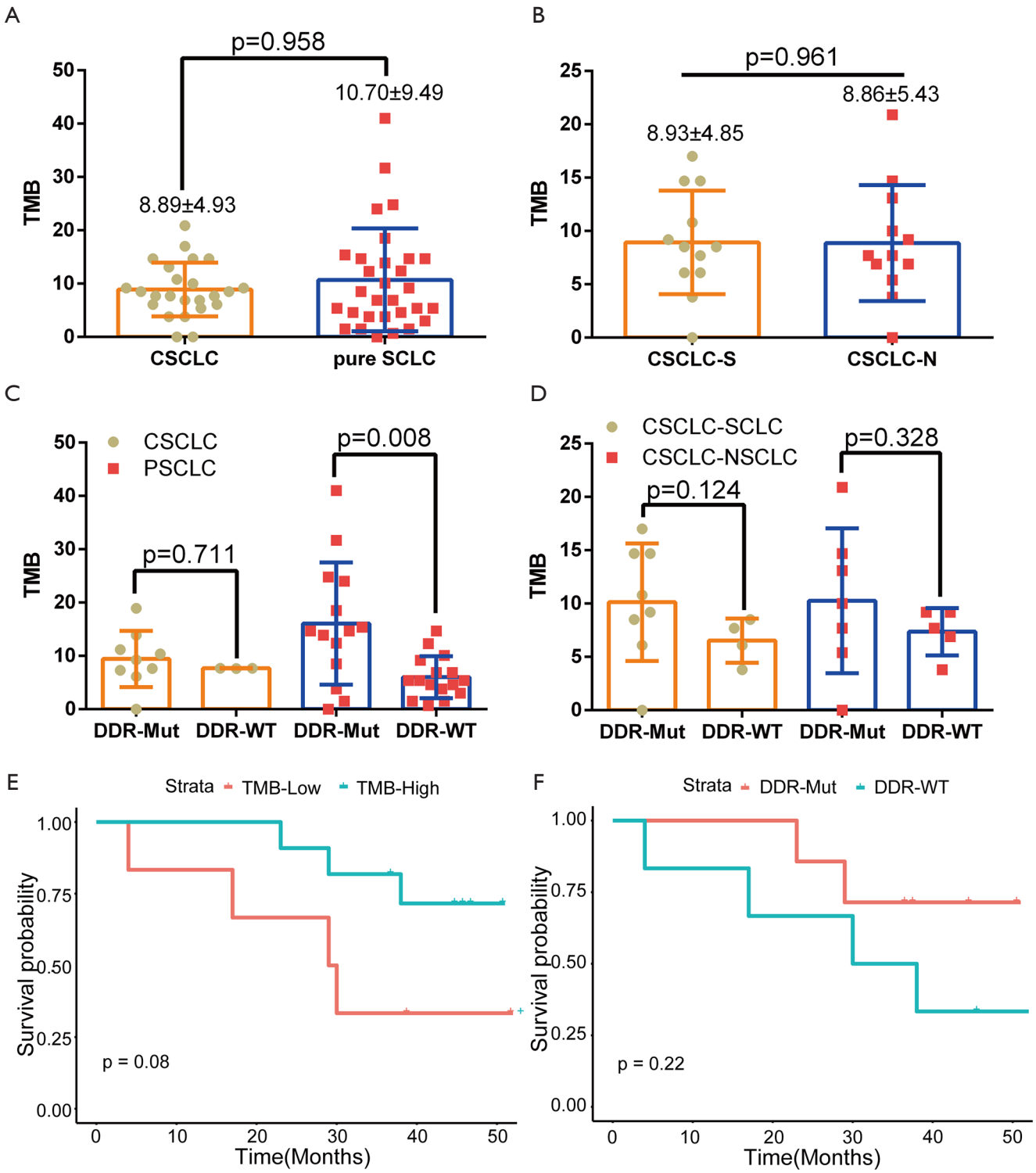

Figure S9 The level and role of tumor mutation burden (TMB) in different components. (A) The TMB of pure small cell lung cancer (SCLC) was higher than that of combined small cell lung cancer (CSCLC) without significance (P>0.05). (B) The TMBs in the SCLC and non-small cell lung cancer (NSCLC) component of CSCLC were similar without significance (P>0.05). (C,D) No significance was observed in the level of TMB between DNA damage response (DDR)mutation (DDR-Mut) and DDR wild-type (DDR-WT) groups (P>0.05). (E,F) No significance was observed in the prognosis of pure SCLC between TMB high and TMB low groups, and between DDR-Mut and DDR-WT groups (P>0.05).

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Table S1 Clinicopathologic characteristics of combined small cell lung cancer (CSCLC)

Case	Gender	Age	Smoking	Surgery type	Location	Pathologic component	Size(cm)	pStage	Chemotherapy	Radiotherapy
1	M	73	Yes	Lobectomy	LLL	SCLC, SCC	2	IIB	Unknown	Unknown
2	M	76	Yes	Segmentectomy	LUL	SCLC, AD	2	IA2	No	Yes
3	M	66	Yes	Lobectomy	RUL	SCLC, AD	3.5	IB	Unknown	Unknown
4	M	65	Yes	Lobectomy	LUL	SCLC, SCC	5	IIA	Yes	Yes
5	M	63	Yes	Lobectomy	RLL	SCLC, SCC	7.5	IIIB	Yes	Unknown
6	M	66	No	Lobectomy	RUL	SCLC, SCC	3.5	IB	Yes	Yes
7	M	57	Yes	Lobectomy	LUL	SCLC, AD	6.5	IIIB	Yes	Unknown
8	M	60	Yes	Lobectomy	RLL	SCLC, SCC	3.1	IB	Yes	Unknown
9	F	78	Yes	Segmentectomy	RUL	SCLC, AD	1.8	IIIA	Yes	Yes
10	F	59	No	Lobectomy	LUL	SCLC, AD	3.5	IIIA	Yes	Unknown
11	M	77	Yes	Lobectomy	LLL	SCLC, SCC	5.5	IIIA	Yes	Yes
12	M	74	Yes	Lobectomy	RUL	SCLC, AD	3.5	IIB	Yes	Unknown

M, male; F, female; LUL, left upper lobe; LLL, left lower lobe; RUL, right upper lobe; RLL, right lower lobe.

Table S2 Clinicopathologic characteristics of pure small cell lung cancer (SCLC)

Case	Gender	Age	Smoking	Surgery type	Location	Pathological diagnosis	Size (cm)	pStage	Chemotherapy	Radiotherapy
1	M	63	Yes	Lobectomy	LUL	SCLC	7.5	IIIA	Yes	Yes
2	M	59	Yes	Lobectomy	LLL	SCLC	7	IIIA	Yes	Unknown
3	F	63	No	Lobectomy	LUL	SCLC	3.5	IB	Unknown	Unknown
4	M	40	Yes	Lobectomy	LUL	SCLC	3.2	IB	Yes	Yes
5	M	42	Yes	Lobectomy	RUL	SCLC	3.7	IIB	Unknown	Unknown
6	M	58	Yes	Lobectomy	LLL	SCLC	4	IIB	Yes	Unknown
7	M	54	Yes	Pneumonectomy	LUL	SCLC	3.7	IIIA	Yes	Unknown
8	F	76	No	Lobectomy	RUL	SCLC	2.5	IA3	Unknown	Unknown
9	F	64	Yes	Lobectomy	LLL	SCLC	6	IIIB	Unknown	Unknown
10	F	56	No	Lobectomy	LUL	SCLC	4	IIIA	Unknown	Unknown
11	M	62	Yes	Lobectomy	RUL	SCLC	5	IIA	Unknown	Unknown
12	M	76	Yes	Lobectomy	RLL	SCLC	5	IIA	Unknown	Unknown
13	M	71	Yes	Lobectomy	RUL	SCLC	3	IA3	Unknown	Unknown
14	M	65	Yes	Lobectomy	RUL	SCLC	4.5	IIB	Unknown	Unknown
15	M	62	Yes	Lobectomy	LUL	SCLC	3.5	IB	Yes	Unknown
16	M	69	Yes	Lobectomy	LUL	SCLC	2	IB	Yes	Unknown
17	M	55	No	Lobectomy	LUL	SCLC	1.8	IIIA	Unknown	Unknown
18	M	62	Yes	Pneumonectomy	LLL	SCLC	7	IIB	Yes	Unknown
19	F	39	Yes	Pneumonectomy	LLL	SCLC	5.5	IIB	Yes	Unknown
20	M	54	No	Lobectomy	RUL	SCLC	1.5	IIIA	Yes	Unknown
21	M	80	Yes	Lobectomy	RUL	SCLC	2.5	IA3	No	No
22	M	56	Yes	Lobectomy	LUL	SCLC	1.7	IIIA	Yes	Unknown
23	M	76	Yes	Lobectomy	LUL	SCLC	5	IIIA	Yes	Yes
24	M	62	No	Lobectomy	RLL	SCLC	2.8	IIIA	Yes	Unknown
25	F	67	No	Lobectomy	LUL	SCLC	5	IIA	Yes	Unknown
26	F	68	Yes	Lobectomy	LUL	SCLC	2	IA2	Yes	Yes
27	M	64	Yes	Lobectomy	RML	SCLC	1.2	IA2	Yes	Unknown
28	M	73	Yes	Lobectomy	LLL	SCLC	2.5	IB	Yes	Unknown
29	M	55	No	Lobectomy	LUL	SCLC	3.2	IIIA	Yes	Yes
30	M	66	Yes	Lobectomy	LUL	SCLC	4	IIB	Yes	Unknown

M, male; F, female; LUL, left upper lobe; LLL, left lower lobe; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe.

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Table S3 Immunohistochemistry for different component of combined small cell lung cancer (CSCLC)

Case	Component	CD56	CgA	Syn	TTF1	Napsin A	P40	CK5/6
1	SCLC	+	+	+	+	–	–	–
	Squamous	–	–	–	–	–	+	+
2	SCLC	+	–	+	+	–	–	–
	Adenocarcinoma	–	–	–	+	+	–	–
3	SCLC	+	–	+	+	–	–	–
	Adenocarcinoma	–	–	–	+	+	–	–
4	SCLC	+	–	+	–	NA	+	+
	Squamous	–	–	–	–	NA	+	+
5	SCLC	+	+	+	–	NA	–	–
	Squamous	–	–	–	–	NA	+	+
6	SCLC	+	–	–	–	–	–	–
	Squamous	–	–	–	–	–	+	+
7	SCLC	+	+	+	+	–	–	–
	Adenocarcinoma	–	–	–	–	–	–	–
8	SCLC	–	–	+	–	NA	–	–
	Squamous	–	–	–	–	NA	+	+
9	SCLC	+	+	+	+	–	–	NA
	Adenocarcinoma	–	–	–	+	+	–	NA
10	SCLC	+	+	+	+	–	–	NA
	Adenocarcinoma	–	–	–	+	–	–	NA
11	SCLC	–	–	–	–	–	–	–
	Squamous	–	–	–	–	–	–	+
12	SCLC	+	–	+	+	–	–	NA
	Adenocarcinoma	–	–	–	+	–	–	NA

CgA, chromogranin A; Syn, synaptophysin; TTF-1, thyroid transcription factor 1; CK5/6, cytokeratin 5/6; NA: not available; SCLC, small cell lung cancer.

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Table S4 Common mutations in small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) components of combined small cell lung cancer (CSCLC)

Genes	Common mutation	SCLC [12], frequency	NSCLC [12], frequency
TP53	10	10	10
RB1	7	7	7
PIK3CA	3	4	3
EGFR	2	3	3
AKT1	2	2	1
AKT2	1	3	1
MYC	1	3	1
NKX2-1	1	2	2
SOX2	1	4	3
TERT	1	3	2

Table S5 Common mutations in small cell lung cancer (SCLC) and adenocarcinoma (AD) components of combined small cell lung cancer (CSCLC)

Genes	Common mutation	SCLC [6], frequency	AD [6], frequency
RB1	5	5	5
TP53	5	4	4
AKT1	2	2	1
EGFR	2	3	3
BRAF	2	1	1
AKT2	1	2	1
NKX2-1	1	2	1
SDHA	1	2	1
TERT	1	3	2
XRCC3	1	2	1

Table S6 Common mutations in small cell lung cancer (SCLC) and squamous cell carcinoma (SCC) components of combined small cell lung cancer (CSCLC)

Genes	Common mutation	SCLC [6], frequency	SCC [6], frequency
TP53	5	5	5
RB1	2	2	2
SOX2	1	4	3
CDKN2A	2	2	2
FGF19	1	1	2
FGF3	1	1	2
FGF4	1	1	2
MYC	1	2	1
PIK3CA	1	2	1
PRKCI	1	2	1

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