

## Supporting Information

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EBF2 Links KMT2D-Mediated H3K4me1 to Suppress Pancreatic Cancer Progression via Upregulating KLLN

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**1. Table S1. List of proteins identified by Mass Spectrometry**

No.	Protein names	Score	Intensity H3	Intensity H3K4me1	No.	Protein names	Score	Intensity H3	Intensity H3K4me1
1	HTATSF1	323.31	0	7896300000	267	SRPRB	6.2092	0	6369800
2	ACIN1	323.31	0	4538700000	268	KNOP1	6.0187	0	11633000
3	AP3B1	323.31	0	7022400000	269	VAR5	5.9202	0	23386000
4	SRRM2	311.46	0	4108200000	270	USP15	5.8594	0	189950000
5	MARS	294.58	0	1815900000	271	NPM3	5.7768	0	130200000
6	YBX1	289.03	0	982660000	272	AKAP8L	5.6751	0	12950000
7	RARS	285.78	0	3337800000	273	RBM28	5.6321	0	93962000
8	UBR4	277.05	0	2466900000	274	SRCAP	5.4613	0	84452000
9	EIF3C	249.44	0	8652500000	275	PGAM5	5.2471	0	177960000
10	HNRNPUL1	246.43	0	9168800000	276	CEBPZ	5.1627	0	96981000
11	EIF3L	237.02	0	1299900000	277	MRPS34	4.9979	0	171250000
12	SSBP1	232.46	0	1380200000	278	SKIV2L2	4.9587	0	10405000
13	EIF3A	231.93	0	3973000000	279	SEC63	4.9458	0	68709000
14	<b>EBF2</b>	228.34	0	1117500000	280	MRS2	4.944	0	43330000
15	SQSTM1	201.95	0	93569000	281	KDM5B	4.9246	0	54916000
16	DDX21	191.54	0	1351800000	282	MRPL46	4.9129	0	38520000
17	MRPL44	187.09	0	482350000	283	PCNA	4.8947	0	132910000
18	ZC3H18	177.01	0	2525800000	284	SRPK2	4.8922	0	215950000
19	PNN	176.74	0	6795000000	285	RECQL	4.8399	0	158410000
20	CTR9	176.34	0	3612700000	286	NUP160	4.6445	0	32284000
21	UBR5	173.91	0	1156600000	287	HP1BP3	4.6364	0	116600000
22	ANP32B	170.49	0	7289400000	288	GPATCH8	4.6311	0	97992000
23	UBTF	167.27	0	3916500000	289	EIF6	4.6221	0	9906100
24	SUPT16H	165.02	0	6535100000	290	XPC	4.599	0	15627000
25	ZC3HAV1	162.87	0	666660000	291	BCLAF1	4.4624	0	264370000
26	CSNK2A1	161.86	0	2541600000	292	RNPS1	4.4449	0	109410000
27	RPA1	159.91	0	1151900000	293	TGFBR3	4.4394	0	60024000
28	SART3	156.04	0	9491300000	294	RPL18	4.427	0	1134900000
29	PELP1	144.49	0	1705500000	295	CHD8	4.4223	0	220130000
30	VPRBP	142.38	0	2635900000	296	MRPL40	4.3467	0	9106800
31	CHD1	140.57	0	4252600000	297	ETF1	4.3146	0	161510000
32	SUPT5H	139.75	0	575100000	298	FXR2	4.3006	0	10034000
33	YTHDC2	137.06	0	1013900000	299	VDAC3	4.2833	0	148810000
34	TCOF1	136.86	0	1.3374E+10	300	POLR2H	4.2578	0	30638000
35	ANP32E	135.75	0	601580000	301	GADD45G	4.2353	0	154270000
36	SRP19	134.87	0	1279700000	302	CCNT1	4.2337	0	8169600
37	POP1	134.51	0	1630400000	303	EIF3H	4.1855	0	65074000
38	MRPL21	126.13	0	952400000	304	SFXN1	4.15	0	11507000
39	ADNP	121.54	0	560900000	305	PSMC5	4.1154	0	27908000
40	NOLC1	120.13	0	5982000000	306	FBL	4.0944	0	135770000
41	MRPS9	118.37	0	1088900000	307	SDC4	4.0302	0	399050000
42	OSBPL3	118.29	0	600260000	308	RANBP2	4.0103	0	47693000
43	MRPS35	114.54	0	318450000	309	GNL3	3.9746	0	38386000
44	SRP72	112.5	0	777370000	310	PRPF4B	3.9183	0	34627000
45	MRPL49	111.58	0	387310000	311	POLR2A	3.8829	0	40259000
46	UPF1	104.58	0	792370000	312	SAP18	3.8462	0	1718400000
47	MYBBP1A	104.45	0	444120000	313	FAM120A	3.8346	0	11234000

48	HNRNPA3	103.28	0	1934600000	314	MRPS22	3.8162	0	92141000
49	MOV10	102.95	0	533520000	315	RPL27A	3.8007	0	667330000
50	ZFR	101.51	0	240470000	316	ABCF2	3.7097	0	84742000
51	ILF2	100.63	0	1817800000	317	DDX24	3.6927	0	96521000
52	YTHDC1	100.62	0	1189900000	318	RALY	3.6885	0	165630000
53	KANK1	100.29	0	204870000	319	NOP56	3.6663	0	48512000
54	SSRP1	100.06	0	3678500000	320	SNRNP70	3.6617	0	48567000
55	RPL7A	97.91	0	4769100000	321	RRP1	3.6333	0	47194000
56	MRPS7	97.44	0	781560000	322	NARS2	3.5733	0	202130000
57	SRP14	96.11	0	806630000	323	RCC2	3.5239	0	107540000
58	RPL3;rp13	95.599	0	794780000	324	HSDL2	3.4933	0	11551000
59	RPL6	94.284	0	8141500000	325	PURB	3.4897	0	29084000
60	SDC1	92.562	0	339690000	326	MKI67	3.4549	0	6825700
61	MRPS31	91.975	0	400000000	327	EIF3G	3.447	0	7627500
62	GEMIN5	89.707	0	449550000	328	TRIP12	3.429	0	27239000
63	BMS1	88.833	0	882430000	329	SNRPE	3.411	0	190350000
64	CHD4	87.379	0	1057900000	330	CMTR1	3.3932	0	67189000
65	CSNK2B	81.872	0	1079400000	331	SRSF1	3.3601	0	79616000
66	MRPL9	80.942	0	987370000	332	GARS	3.3145	0	87683000
67	LYAR	78.947	0	317120000	333	CYFIP1	3.2795	0	10915000
68	MRPL32	78.456	0	113670000	334	GNL1	3.2446	0	37484000
69	DAP3	76.701	0	1093900000	335	KAT7	3.2375	0	41303000
70	LARP1	75.466	0	2459900000	336	CYR61	3.1639	0	77535000
71	ALYREF	75.302	0	123690000	337	MRPL27	3.1597	0	405530000
72	CSNK2A2	74.896	0	686270000	338	CWC22	3.1341	0	219580000
73	TOP1	73.12	0	1988000000	339	NOC3L	3.113	0	16120000
74	EIF3D	73.023	0	136400000	340	RUVBL2	3.1087	0	23569000
75	IPO9	72.8	0	285170000	341	TARS	3.108	0	34473000
76	YBX3	71.661	0	91788000	342	DDX27	3.0674	0	47628000
77	XRCC6	70.34	0	1788800000	343	FGF2	3.0607	0	95695000
78	MTDH	69.724	0	107060000	344	MRPL30	3.0043	0	82321000
79	SRSF4	69.634	0	1304800000	345	ARID4B	2.9889	0	19855000
80	MEPCE	68.283	0	1310500000	346	SRSF6	2.9869	0	231750000
81	SNRPA1	67.446	0	1831000000	347	SMC4	2.9812	0	12317000
82	RPL17	67.111	0	707290000	348	MRPL24	2.9591	0	375890000
83	PAF1	66.293	0	1257300000	349	MRPS5	2.8542	0	45555000
84	MRPL37	65.128	0	1266000000	350	STT3A	2.8342	0	18287000
85	AIMP2	60.102	0	1394100000	351	AGO2	2.8341	0	42849000
86	HUWE1	59.885	0	241240000	352	HARS2	2.7924	0	24467000
87	SIN3A	59.318	0	147780000	353	XRN1	2.7891	0	21950000
88	DDB1	58.246	0	391740000	354	MCM3	2.7687	0	55361000
89	RPL9	57.67	0	292860000	355	PUF60	2.7179	0	27475000
90	HBS1L	57.319	0	119680000	356	SMARCA1	2.7146	0	42301000
91	SNRPD1	56.654	0	662720000	357	THOC2	2.6787	0	26731000
92	C1QBP	56.644	0	1897700000	358	DDB2	2.6122	0	76330000
93	CHAF1A	56.542	0	149660000	359	AFF4	2.5955	0	65078000
94	MRPS10	54.7	0	151040000	360	HNRNPDL	2.5913	0	155110000
95	MRPL23	54.582	0	306380000	361	CENPV	2.5591	0	47536000
96	KPNA1	53.375	0	74055000	362	EIF2B5	2.5085	0	124100000
97	DARS	52.994	0	3628000000	363	MTA2	2.4967	0	42633000
98	NKTR	52.312	0	240410000	364	HSD17B10	2.4804	0	21611000

99	ATRX	51.138	0	427210000	365	POP7	2.4757	0	74688000
100	U2AF1	50.675	0	124020000	366	RPL36A	2.4734	0	354030000
101	LARP7	50.621	0	732800000	367	KPNA3	2.4682	0	53524000
102	MRPL13	50.194	0	625830000	368	TSR1	2.4667	0	46266000
103	EIF5B	49.981	0	1982500000	369	WDR77	2.4553	0	29751000
104	UBE2O	48.515	0	669500000	370	MRPS2	2.446	0	54458000
105	HNRNPUL2	47.353	0	81489000	371	OSTC	2.4153	0	27290000
106	MRPS30	47.289	0	335170000	372	ANKRD17	2.4108	0	72376000
107	RTF1	46.344	0	631090000	373	IPO5	2.3681	0	15613000
108	LUC7L3	45.969	0	30206000	374	SON	2.3402	0	44968000
109	HNRNPH3	45.779	0	159490000	375	DIEXF	2.339	0	35418000
110	SLC25A11	44.991	0	38404000	376	DYNLL1	2.3234	0	53565000
111	RRP1B	44.756	0	30244000	377	MRPS24	2.3206	0	108190000
112	TRIM26	44.574	0	1025200000	378	EIF2AK2	2.3187	0	25113000
113	CHD9	43.543	0	229820000	379	MYO1B	2.315	0	30724000
114	MRPL38	42.445	0	1050300000	380	POLR2B	2.3092	0	20610000
115	ILF3	41.931	0	1355400000	381	PRPF8	2.2781	0	30614000
116	MRPL1	41.059	0	247210000	382	ANKRD28	2.2702	0	9595400
117	MRPL4	39.04	0	520120000	383	SART1	2.2564	0	29376000
118	CHD2	38.685	0	58144000	384	KDM5A	2.2454	0	37390000
119	NAT10	38.676	0	284330000	385	SUPT6H	2.2369	0	19793000
120	MYO10	38.367	0	29476000	386	MRPL17	2.2165	0	205110000
121	NRD1	37.853	0	650390000	387	CDC27	2.1971	0	53137000
122	EHMT2	36.75	0	524760000	388	MRPL48	2.19	0	27915000
123	RPP30	36.684	0	101650000	389	SNRPB	2.1489	0	442710000
124	DDX20	36.006	0	107100000	390	CD44	2.1317	0	61177000
125	CHCHD2	35.844	0	414570000	391	DIS3L2	2.0858	0	14929000
126	U2AF2	35.188	0	223580000	392	IGF2BP3	2.0529	0	16730000
127	THUMPD1	35.08	0	89588000	393	FARSA	2.0453	0	21695000
128	AIMP1	34.59	0	1619300000	394	RBMS2	2.045	0	28918000
129	RBMX	34.409	0	974150000	395	DRG1	2.0273	0	21009000
130	GTF3C5	33.651	0	17588000	396	RPA2	2.0053	0	37721000
131	MRPL39	33.504	0	718740000	397	BPTF	1.9867	0	38418000
132	RPL32	33.467	0	22700000	398	CSE1L	1.9861	0	19616000
133	MRPS27	33.15	0	284230000	399	ELAVL1	1.9392	0	63875000
134	PSMD3	32.721	0	252570000	400	HIST1H1D	1.9357	0	50220000
135	HIST1H1C	32.678	0	7668100000	401	LUC7L2	1.9329	0	42209000
136	MCM4	32.474	0	128500000	402	ZRANB2	1.8425	0	24065000
137	PPP6R3	32.027	0	85889000	403	EFTUD2	1.84	0	42951000
138	CHORDC1	31.483	0	53583000	404	COPB1	1.797	0	5685900
139	PCM1	31.006	0	356880000	405	SURF4	1.7851	0	43379000
140	NCBP1	29.141	0	761070000	406	SRRT	1.7831	0	35492000
141	HLTF	29.004	0	158150000	407	ZNF622	1.7801	0	33485000
142	TPR	28.744	0	79484000	408	XPOT	1.7611	0	20769000
143	PELO	28.597	0	69560000	409	AHCYL2	1.7609	0	10464000
144	RAB5C	27.421	0	76752000	410	STK26	1.7518	0	7960300
145	UHRF1	27.349	0	193760000	411	RGPD3	1.7044	0	19086000
146	LARS	26.795	0	447230000	412	HNRNPL	1.7008	0	42192000
147	RSL1D1	26.481	0	308140000	413	KHDRBS1	1.6877	0	97730000
148	CDK9	26.264	0	42480000	414	RBBP6	1.6833	0	9479400
149	LSM2	26.011	0	57902000	415	VKORC1	1.6714	0	14044000

150	BRIX1	24.804	0	268860000	416	ACTR2	1.6711	0	18076000
151	XRN2	24.146	0	325110000	417	WDR3	1.6503	0	23264000
152	CDK11B	23.995	0	2544800000	418	U2SURP	1.6422	0	28839000
153	EBNA1BP2	23.307	0	406210000	419	MRPL37	1.6013	0	11499000
154	AHSA1	23.025	0	42713000	420	ATP5J2	1.5952	0	12636000
155	EIF3I	22.974	0	830570000	421	EWSR1	1.5843	0	15510000
156	RPL23A	22.934	0	4062200000	422	SBDS	1.5319	0	15834000
157	RPL28	21.871	0	692380000	423	DCAF8	1.5234	0	16023000
158	DHX36	21.532	0	38176000	424	PWP1	1.4951	0	20134000
159	MRPL45	21.144	0	325410000	425	RPL29	1.481	0	158670000
160	THRAP3	21.033	0	131920000	426	MRPL50	1.4798	0	31933000
161	MRPL43	20.593	0	375610000	427	HDAC1	1.4541	0	147130000
162	MRPL2	20.395	0	462460000	428	LSM6	1.4444	0	39537000
163	DKC1	20.321	0	370350000	429	PKN2	1.4279	0	7552600
164	MYO1C	20.132	0	124860000	430	RPS15	1.4235	0	247630000
165	H2AFY	20.078	0	53080000	431	EMG1	1.4163	0	45913000
166	RPL35A	19.183	0	1649700000	432	ZUBR1	1.4071	0	51455000
167	HDGFRP2	19.048	0	124480000	433	PYGB	1.3982	0	30335000
168	PTCD3	19.041	0	778300000	434	VAPA	1.393	0	53288000
169	EIF2A	18.664	0	333350000	435	SLC16A3	1.3902	0	19643000
170	LEO1	18.282	0	881610000	436	MRPL47	1.385	0	177910000
171	MYO1E	18.018	0	205930000	437	PHRF1	1.3832	0	62224000
172	TCOF1	17.804	0	68357000	438	JMJD6	1.3644	0	8421700
173	EMD	17.688	0	110550000	439	SF3B2	1.3634	0	25601000
174	TRA2B	17.333	0	461930000	440	RTCB	1.3582	0	39156000
175	MRT04	17.317	0	162270000	441	TRA2A	1.3254	0	57130000
176	TSPYL2	17.132	0	193250000	442	MGST1	1.3221	0	12387000
177	TRMT6	17.132	0	41169000	443	RAB6A	1.3148	0	10271000
178	G3BP1	17.054	0	282100000	444	TBC1D31	1.2893	0	168040000
179	ATAD2	16.99	0	161340000	445	PDS5B	1.2628	0	13142000
180	PPP2R2A	16.902	0	67883000	446	TGS1	1.2489	0	11437000
181	GATAD2B	16.87	0	75360000	447	PDCD11	1.2489	0	6719800
182	PDCD6IP	16.367	0	84939000	448	CDC5L	1.2378	0	49167000
183	SDC2	16.269	0	704170000	449	SLC16A1	1.2159	0	35473000
184	KIAA1429	16.13	0	82081000	450	MRPL52	1.2064	0	49872000
185	WDR5	16.093	0	905550000	451	RAB14	1.196	0	18492000
186	USP39	15.99	0	98228000	452	APEX1	1.1939	0	13543000
187	SRSF10	15.93	0	91394000	453	RB1CC1	1.1806	0	85266000
188	RPS26	15.527	0	1552200000	454	RAC1	1.178	0	29761000
189	SETD1B	15.384	0	50299000	455	ANAPC7	1.1767	0	13942000
190	MRPL19	14.915	0	1268800000	456	SNRPA	1.1711	0	115620000
191	SETD1A	14.258	0	65851000	457	ANP32A	1.1646	0	449110000
192	C7orf50	14.241	0	28687000	458	SAP30BP	1.1623	0	16914000
193	RFC1	14.132	0	72707000	459	RPP40	1.1601	0	18098000
194	EIF3E	13.873	0	566310000	460	EPB41L1	1.1431	0	10636000
195	SMARCA5	13.66	0	339880000	461	CDK2	1.1372	0	24090000
196	NHP2L1	13.494	0	44145000	462	STRAP	1.1281	0	38476000
197	MRPL15	13.437	0	793950000	463	SLC25A13	1.1231	0	8883900
198	TRIM44	12.751	0	20472000	464	DDX47	1.102	0	25140000
199	NKRF	12.731	0	372750000	465	DDX50	1.0847	0	13237000
200	CFAP20	12.709	0	247120000	466	TRIM25	1.0296	0	26349000

201	GEMIN4	12.592	0	206330000	467	RBBP5	1.029	0	56774000
202	NOP2	12.503	0	182870000	468	SUDS3	1.0202	0	18576000
203	IWS1	12.449	0	1924500000	469	APLP2	1.0095	0	20417000
204	AP3D1	12.246	0	285840000	470	FLII	1.0044	0	54608000
205	MRPS18B	12.141	0	106150000	471	ZZEF1	0.99944	0	7008900
206	COPA	11.884	0	91198000	472	YARS	0.99138	0	10924000
207	MORF4L2	11.817	0	87947000	473	RPS10	0.98946	0	16148000
208	RRP9	11.775	0	249040000	474	DROSHA	0.9851	0	23753000
209	MSH6	11.611	0	90444000	475	PHF8	0.96102	0	8176600
210	EIF3G	11.514	0	440120000	476	BRD2	0.94978	0	14359000
211	RBM39	11.339	0	50703000	477	FTSJ3	0.93238	0	133180000
212	BUB3	11.134	0	105580000	478	ABCF3	0.92995	0	5264900
213	RPL27	10.83	0	403110000	479	DDX19A	0.91998	0	22568000
214	KPNA4	10.714	0	375760000	480	ATP5L	0.91901	0	22361000
215	RPS24	10.695	0	181830000	481	OLA1	0.91591	0	77902000
216	HIST1H1B	10.668	0	1130900000	482	TLN2	0.91357	0	157200000
217	TROVE2	10.663	0	193260000	483	USP7	0.91171	0	23650000
218	HIST1H1A	10.064	0	69507000	484	MRPS17	0.91035	0	20804000
219	USP34	10.027	0	134710000	485	H1FO	0.90818	0	176040000
220	PRMT5	9.8984	0	82474000	486	CCPG1	0.90635	0	27975000
221	PABPN1	9.8053	0	45860000	487	CHERP	0.89254	0	18251000
222	NOC2L	9.7955	0	955940000	488	RPP25L	0.89134	0	10917000
223	MRPL3	9.6545	0	388970000	489	NAA10	0.89128	0	12172000
224	EEF1E1	9.5625	0	500340000	490	PSMD5	0.89026	0	6231200
225	PPP1R12A	9.4533	0	232110000	491	SNRPF	0.8777	0	50340000
226	NIFK	9.2011	0	194060000	492	CAPN13	0.87264	0	38295000
227	SRPK1	9.0009	0	165410000	493	LARP4	0.86611	0	6340000
228	ASPH	8.9914	0	42969000	494	METAP2	0.85846	0	44724000
229	NCAPH	8.9325	0	72607000	495	ANK3	0.85588	0	255060000
230	PRPF19	8.7914	0	259950000	496	MRPL34	0.8529	0	43214000
231	PPM1G	8.6643	0	238980000	497	ICT1	0.84966	0	260530000
232	DNTTIP2	8.6196	0	51143000	498	MRPL33	0.84339	0	26026000
233	DHX57	8.5614	0	65578000	499	CAV1	0.84157	0	53113000
234	BCR	8.5399	0	52712000	500	SDE2	0.83853	0	714480000
235	MRPL28	8.4658	0	436970000	501	ATAD3A	0.83604	0	6033900
236	EHMT1	8.313	0	363160000	502	MTCH2	0.82464	0	4415300
237	RAB21	8.2978	0	44536000	503	MLLT1	0.82284	0	21763000
238	ZCCHC10	8.2069	0	74648000	504	HERC2	0.82023	0	8769200
239	GPC1	8.1677	0	281460000	505	CIRBP	0.80148	0	20086000
240	PRPS1	8.1305	0	86873000	506	RBM3	0.79563	0	21237000
241	TRMT61A	8.1067	0	247350000	507	DDX23	0.76751	0	9385600
242	LBR	7.9991	0	34970000	508	ESYT1	0.766	0	8163200
243	WIZ	7.9716	0	60601000	509	MRPS18A	0.76232	0	187570000
244	SNRPD2	7.964	0	1367000000	510	GTPBP4	0.76128	0	31063000
245	CENPB	7.9572	0	302150000	511	MORC3	0.75093	0	10826000
246	MRPL20	7.8099	0	673180000	512	BIRC2	0.746	0	10420000
247	NCBP2	7.8038	0	178110000	513	SDAD1	0.73938	0	10724000
248	MRPS25	7.7768	0	55992000	514	KANK2	0.72957	0	23980000
249	POP4	7.7508	0	23946000	515	MAP2K3	0.72537	0	12829000
250	RANGAP1	7.6909	0	32277000	516	RPP25	0.7242	0	57526000
251	CTDP1	7.6488	0	9107100	517	CDK18	0.70898	0	283270000

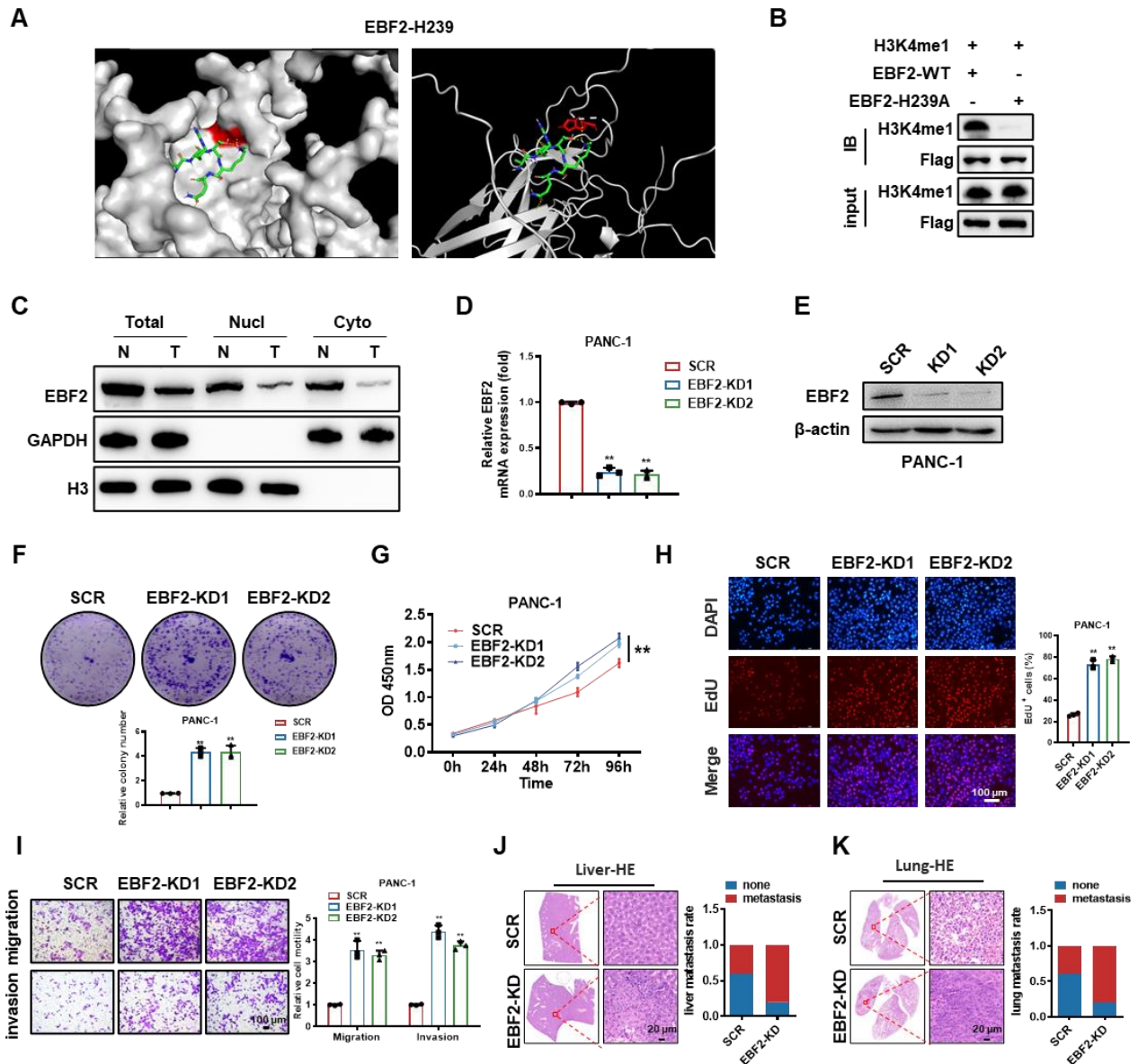
252	CHD3	7.5987	0	167930000	518	MAP2K2	0.70599	0	7107200
253	PICALM	7.5079	0	5716300	519	CSNK1A1	0.69604	0	100810000
254	TMEM33	7.3898	0	48582000	520	MRPS23	0.69348	0	22728000
255	CMAS	7.3057	0	72763000	521	RPL36	0.68738	0	61609000
256	ESF1	7.1547	0	105780000	522	ADAR	0.68158	0	6643300
257	NOP58	7.1129	0	93309000	523	DST	0.68073	0	11345000
258	DDX18	7.0385	0	67938000	524	ARL2	0.66001	0	7923500
259	EIF3K	7.037	0	66541000	525	SSR3	0.65757	0	28405000
260	IGF2BP1	6.8127	0	71858000	526	CDC23	0.65467	0	21910000
261	DHFR	6.6955	0	45311000	527	DYNC1H1	0.65256	0	5615700
262	SRSF7	6.6158	0	349980000	528	GATAD2A	0.6523	0	9298600
263	H1FX	6.5894	0	461120000	529	CARD18	0.64474	0	14770000
264	MAP4	6.5123	0	152000000	530	ARHGEF10	0.63716	0	12303000
265	MRPL22	6.4563	0	395150000	531	MRPL35	0.62419	0	18545000
266	PURA	6.2532	0	37329000					

**2. Table S2. Clinicopathologic characteristics of EBF2 and KMT2D expression in PCa patients**

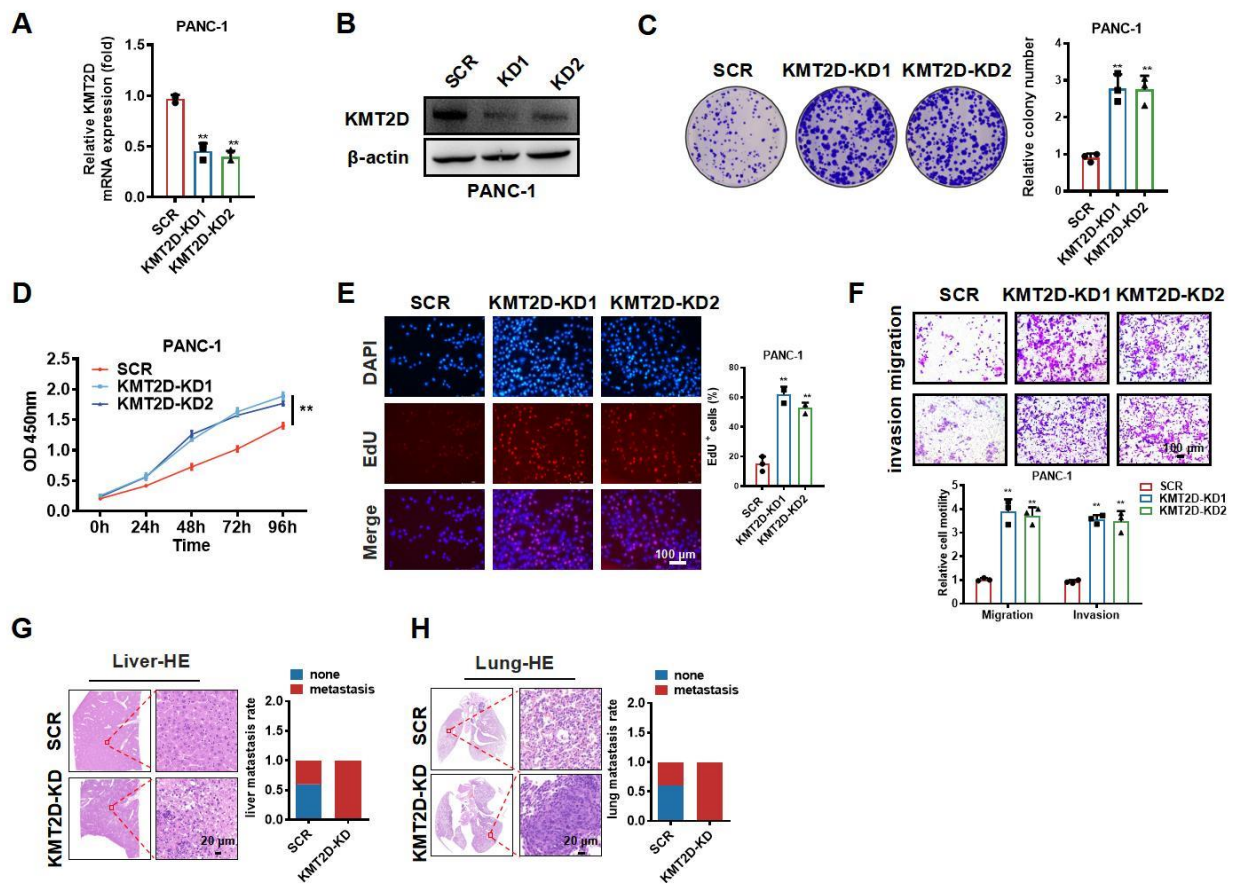
Characteristics	Cases	IHC score of EBF2		IHC score of KMT2D	
		Mean±s.d.	P value <sup>a</sup>	Mean±s.d.	P value <sup>a</sup>
<b>Age</b>					
> 50	73	90.89 ± 6.556	0.4413	81.16 ± 5.558	0.6513
≤50	17	102.9 ± 15.88		87.06 ± 12.51	
<b>Grade</b>					
<i>I-II</i>	53	111.7 ± 7.903	0.0002	100.3 ± 8.1	0.0135
<i>III-III</i>	37	66.62 ± 7.752		147.6 ± 12.2	
<b>Tumor Size</b>					
<i>T1- T2</i>	44	117.6 ± 9.506	<0.0001	105.6 ± 7.561	<0.0001
<i>T3-T4</i>	45	69.56 ± 6.111		59.56 ± 5.032	
<b>Lymph node status</b>					
<i>N0</i>	32	116.1 ± 12.03	0.0017	100.2 ± 9.206	0.0018
<i>N1-2</i>	56	77.5 ± 5.800		69.11 ± 5.073	
<b>Metastasis</b>					
<i>M0</i>	66	103.3 ± 7.437	0.0050	88.48 ± 6.344	0.0414
<i>M1</i>	24	65.21 ± 7.805		65.21 ± 6.486	
<b>Survival</b>					
<i>Yes</i>	7	224.3 ± 18.50	<0.0001	180.7 ± 14.24	<0.0001
<i>No</i>	83	82.11 ± 4.720		73.98 ± 4.257	

<sup>a</sup> P values were derived using Student's *t*-test to compare values for the two parameters in each category.

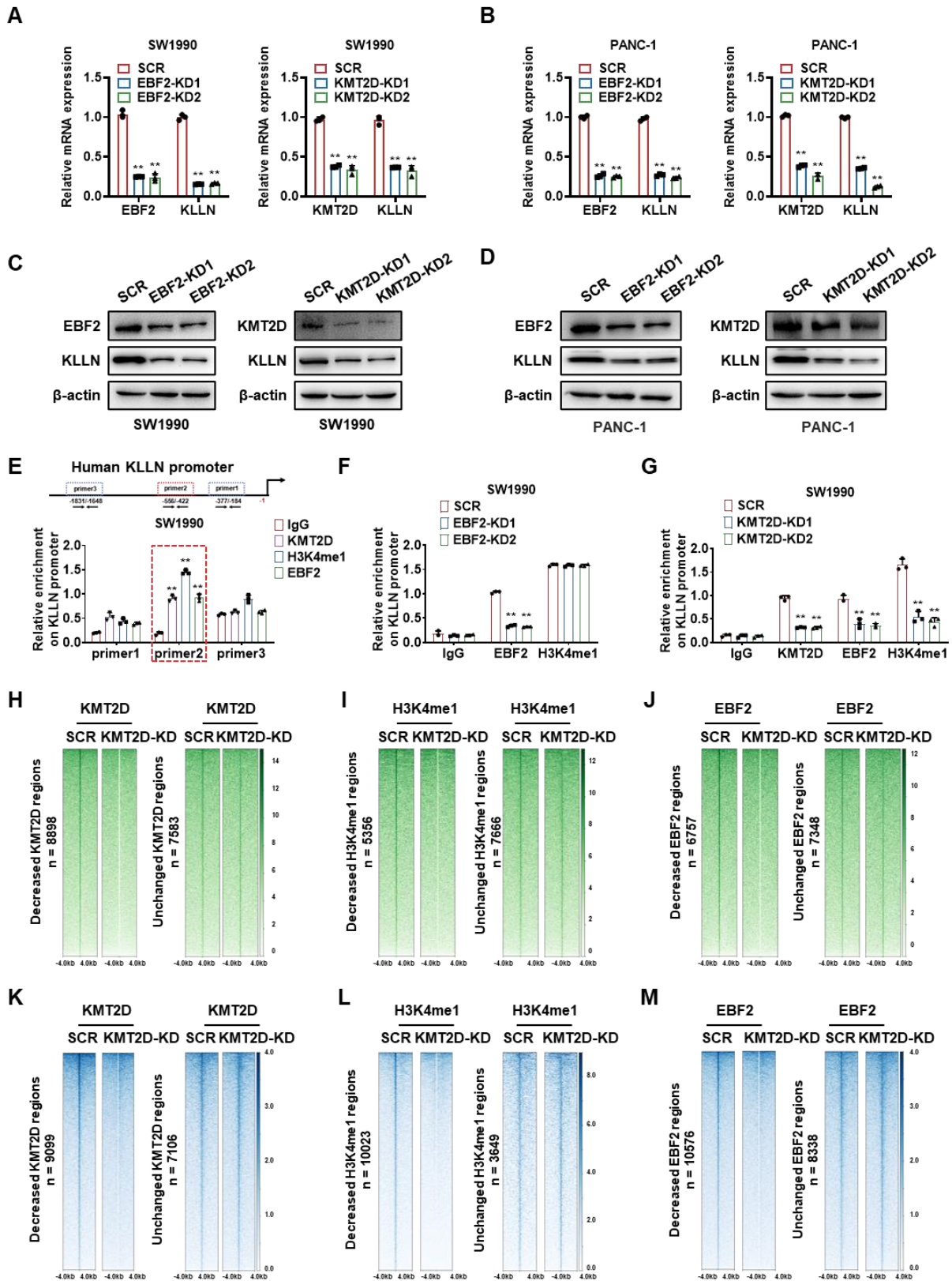




**3. Figure S1. EBF2 inhibits PADC cell proliferation and metastasis *in vitro* and *in vivo*.** A) Overall structure of the EBF2-H3K4me1 complex. Gray, EBF2; red, His239 (H239) of EBF2; green, a H3K4me1-containing histone H3 tail peptide. B) Co-IP assay to determine the interactions between Flag-tagged EBF2-WT or EBF2-H239A and H3K4me1 in SW1990 cells. C) Cellular distribution of EBF2 in normal pancreatic and PC tissue. D-E) The mRNA (D) and protein expression (E) of EBF2 in EBF2-depleted PANC-1 cells verified by qPCR and Western blot assays. Data in D are presented as mean  $\pm$  SEM, \*\* $P$ <0.01 by one-way ANOVA test. F-I) Colony-formation (F), CCK-8 (G), EdU incorporation (H) and Transwell assays (I) assessed the effects of EBF2 knockdown on proliferation, migration and invasion of PANC-1 cells *in vitro*. Data in F-I are presented as mean  $\pm$  SEM, \*\* $P$ <0.01 by two-way ANOVA test (G) and one-way ANOVA test (F, H and I). J-K) H&E staining showed that both liver (J) and lung metastasis rates (K) were increased in mice injected with EBF2-KD SW1990-luc cells. Scale bar, 20 $\mu$ m.

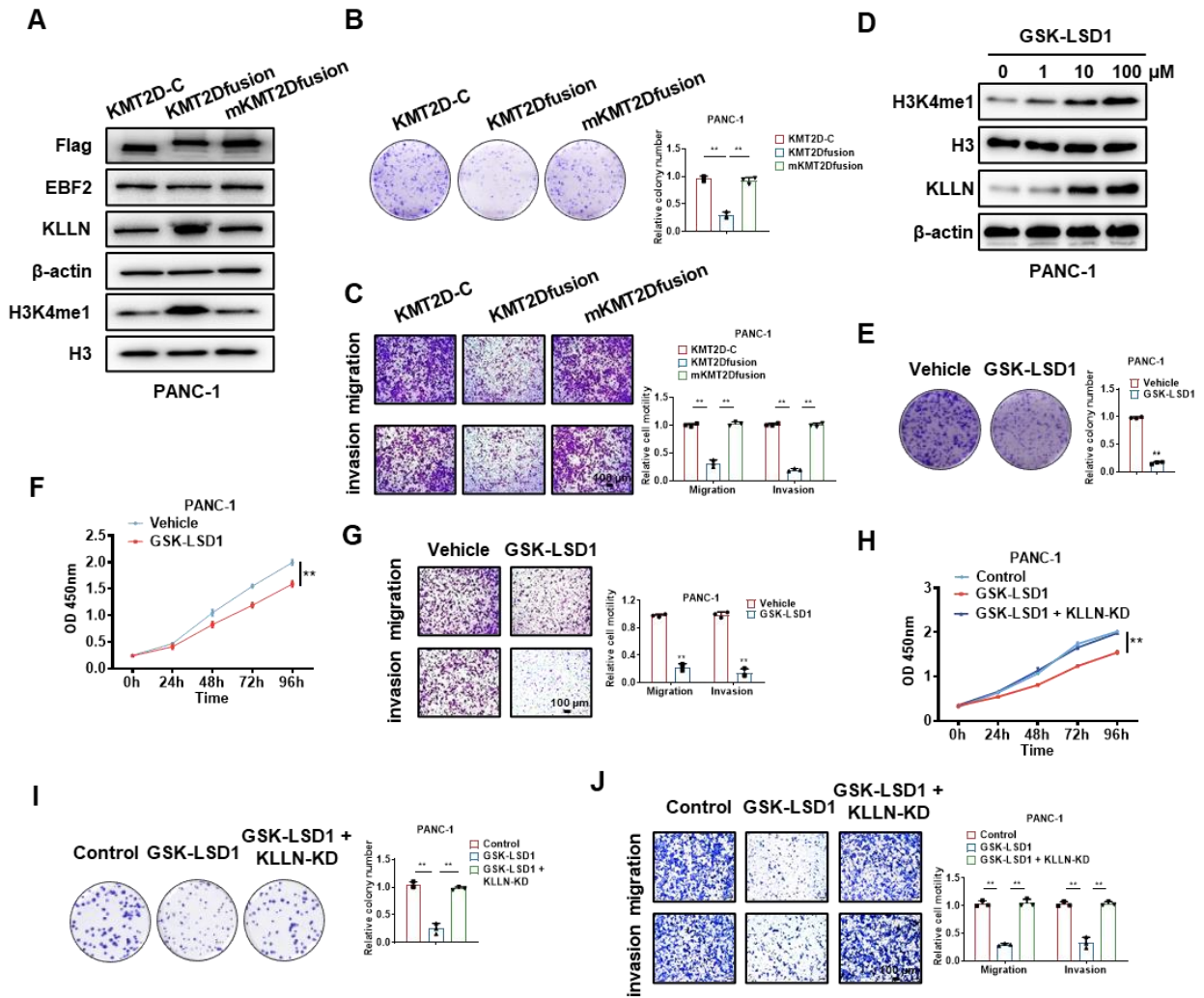


**4. Figure S2. KMT2D inhibits cell proliferation and metastasis *in vitro* and *in vivo*.** A-B) The mRNA (A) and protein (B) levels of KMT2D in KMT2D-depleted PANC-1 cells verified by qPCR and Western blot assays. Data in A are presented as mean  $\pm$  SEM, \*\* $P < 0.01$  by one-way ANOVA test. C-F) Colony-formation (C), CCK-8 (D), EdU incorporation (E) and Transwell (F) assays assessed the effects of KMT2D knockdown on proliferation, migration and invasion of PANC-1 cells *in vitro*. Data in C-F are presented as mean  $\pm$  SEM, \*\* $P < 0.01$  by two-way ANOVA test (D) and one-way ANOVA test (C, E and F). G-H) H&E staining showed that both liver (G) and lung (H) metastasis rates increased in mice injected with KMT2D-KD SW1990-luc cells. Scale bar, 20 $\mu$ m.

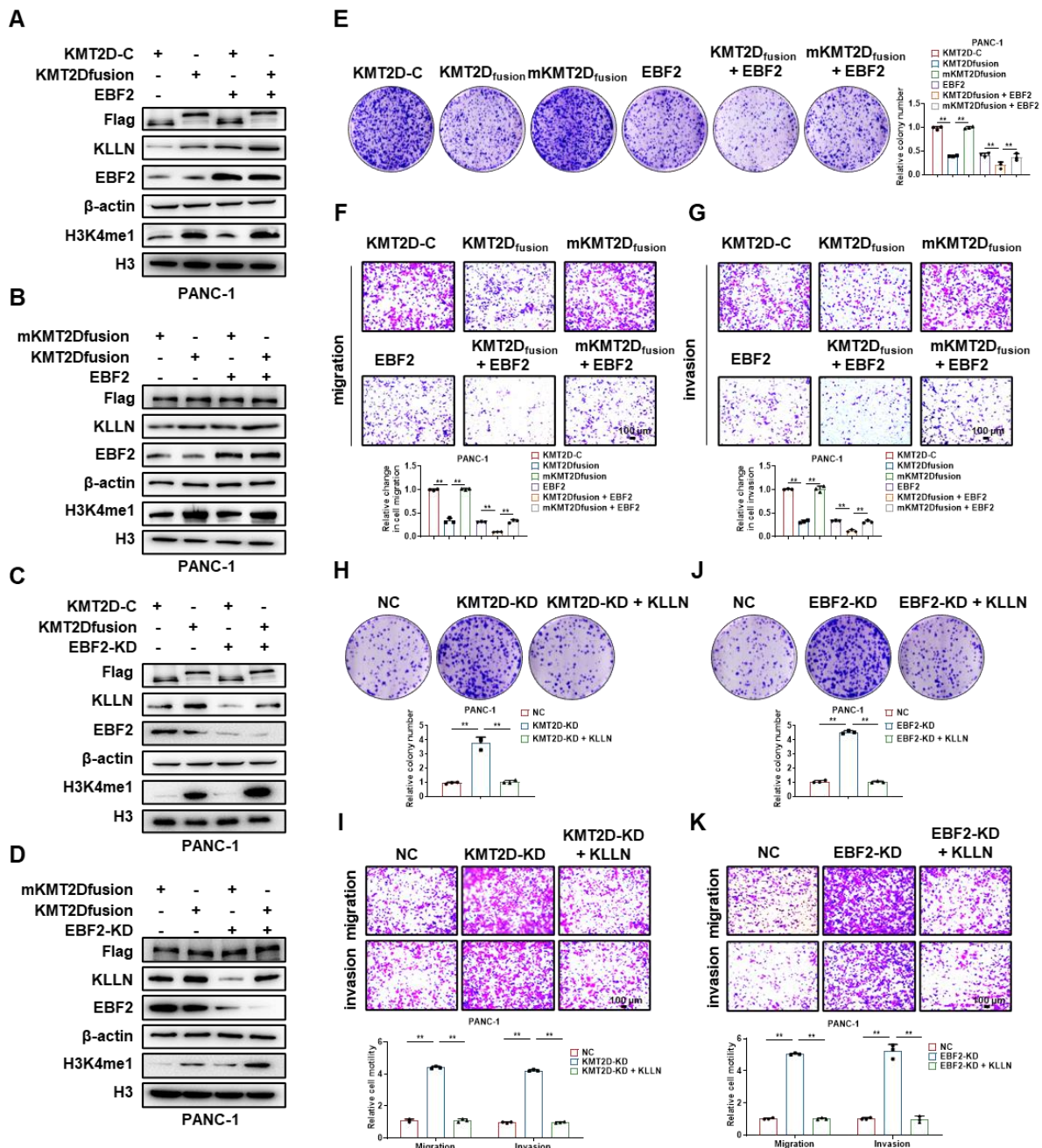


**5. Figure S3. KLLN is a common transcriptional target of KMT2D and EBF2 in PDAC cells.** A-B) qRT-PCR analysis of KLLN mRNA level in EBF2 or KMT2D-depleted SW1990 (A) and PANC-1 (B) cells. Data in A-B are presented as mean  $\pm$  SEM,  $**P < 0.01$  by one-way ANOVA test. C-D) Western blot analysis of KLLN

protein level in EBF2 or KMT2D-depleted SW1990 (C) and PANC-1 (D) cells. E) ChIP analysis of KMT2D, H3K4me1 and EBF2 binding to the promoter region of KLLN gene in SW1990 cells. F) ChIP-qPCR analysis of EBF2 and H3K4me1 bindings to the TSS and promoter regions of KLLN in SCR, EBF2-KD1 and EBF2-KD2 SW1990 cells. G) ChIP-qPCR analysis of KMT2D, EBF2 and H3K4me1 bindings to the TSS and promoter regions of KLLN in SCR, KMT2D-KD1 and KMT2D-KD2 SW1990 cells. Data in E-G are presented as mean  $\pm$  SEM,  $**P < 0.01$  by Student's *t*-test (E) and one-way ANOVA test (F and G). H) Heatmap of input normalized KMT2D ChIP signal in control (SCR), KMT2D-KD over 8898 distal KMT2D regions with decreased signals in KMT2D-KD and 7583 distal KMT2D regions with invariable signals, with regions sorted by strength of KMT2D signal. I) Heatmap of input normalized H3K4me1 ChIP signal in SCR and KMT2D-KD over 5356 distal H3K4me1 regions with decreased signals in KMT2D-KD and 7666 distal H3K4me1 regions with invariable signals, with regions sorted by strength of H3K4me1 signal. J) Heatmap of input normalized EBF2 ChIP signal in SCR and KMT2D-KD over 6757 distal EBF2 regions with decreased signals in KMT2D-KD and 7348 distal EBF2 regions with invariable signals, with regions sorted by strength of EBF2 signal. K) Heatmap of KMT2D CUT&Tag signal in SCR and KMT2D-KD with regions sorted by strength of KMT2D signal. L) Heatmap of H3K4me1 CUT&Tag signals in SCR and KMT2D-KD with regions sorted by strength of H3K4me1 signal. M) Heatmap of EBF2 CUT&Tag signals in SCR and KMT2D-KD with regions sorted by strength of EBF2 signal.

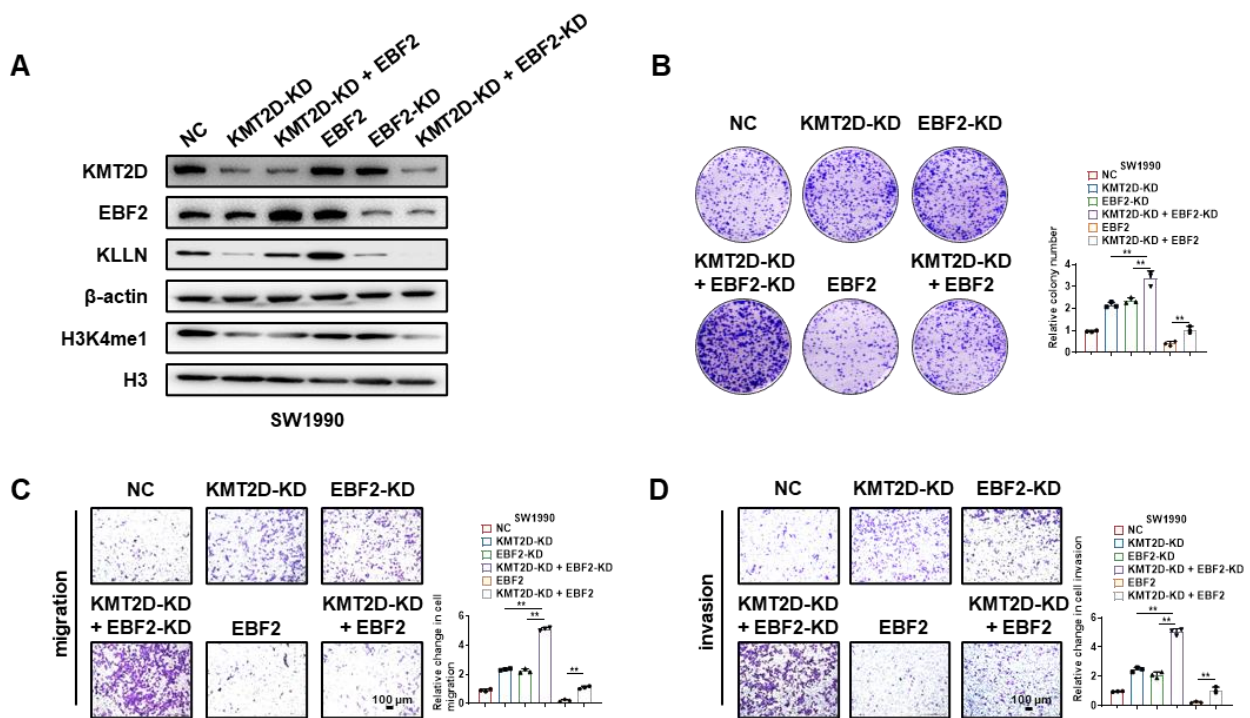


**5. Figure S4. GSK-LSD1 inhibits the proliferation, migration and invasion of PDAC cells.** A) Western blot analysis of KLLN and H3K4me1 levels in PANC-1 cells transfected with KMT2D-C, KMT2D<sub>fusion</sub> and mKMT2D<sub>fusion</sub>. B-C) Colony-formation (B) and Transwell (C) assays of PANC-1 cells transfected with KMT2D-C, KMT2D<sub>fusion</sub> and mKMT2D<sub>fusion</sub>. Data in B-C are presented as mean ± SEM, \*\**P*<0.01 by one-way ANOVA test. D) Western blot analysis of H3K4me1 and KLLN levels in PANC-1 cells treated with 0, 1, 10 or 100μM GSK-LSD1. E-G) Colony-formation (E), CCK-8 (F) and Transwell (G) assays of PANC-1 cells treated with Vehicle and GSK-LSD1. Data in E-G are presented as mean ± SEM, \*\**P*<0.01 by Student's *t*-test (E and G), two-way ANOVA test (F). H-J) CCK-8 (H), colony-formation (I) and Transwell (J) assays were used to detect the proliferation, migration and invasion of control, GSK-LSD1 and GSK-LSD1 + KLLN PANC-1 cells. Data in H-J are presented as mean ± SEM, \*\**P*<0.01 by two-way ANOVA test (H), one-way ANOVA test (I-J).



**6. Figure S5. KMT2D and EBF2 cooperate to activate the expression of KLLN.** A) Western blot analysis of KLLN and H3K4me1 levels in PANC-1 cells transfected with KMT2D-C, KMT2D<sub>fusion</sub> or EBF2. B) Western blot analysis of KLLN and H3K4me1 levels in PANC-1 cells transfected with mKMT2D<sub>fusion</sub>, KMT2D<sub>fusion</sub> or EBF2. C) Western blot analysis of KLLN and H3K4me1 levels in PANC-1 cells transfected with KMT2D-C, KMT2D<sub>fusion</sub> or EBF2-KD. D) Western blot analysis of KLLN and H3K4me1 levels in PANC-1 cells transfected with mKMT2D<sub>fusion</sub>, KMT2D<sub>fusion</sub> or EBF2-KD. β-actin and H3 were used as protein loading control. E-G) Colony-formation (E), migration (F) and invasion (G) assays of PANC-1 cells treated with KMT2D-C, KMT2D<sub>fusion</sub>, mKMT2D<sub>fusion</sub>, EBF2, KMT2D<sub>fusion</sub> + EBF2, mKMT2D<sub>fusion</sub> + EBF2. H-I) Colony-formation (H), Transwell (I) assays of PANC-1 cells transfected with NC, KMT2D-KD or KMT2D-KD +

KLLN. J-K) Colony-formation (J), Transwell (K) assays of PANC-1 cells transfected with NC, EBF2-KD or EBF2-KD + KLLN. Data in E-K are presented as mean  $\pm$  SEM,  $**P < 0.01$  by one-way ANOVA test.



**7. Figure S6. EBF2 and KMT2D cooperate to inhibit the proliferation, migration and invasion of PDAC cells *in vitro*.** A) Western blot analysis of KLLN and H3K4me1 levels in NC, KMT2D-KD, KMT2D-KD+EBF2, EBF2, EBF2-KD or KMT2D-KD+EBF2-KD SW1990 cells. B-D) Colony-formation (B) and migration (C) and invasion (D) assays of PANC-1 cells with NC, KMT2D-KD, KMT2D-KD + EBF2, EBF2, EBF2-KD or KMT2D-KD+EBF2-KD. Data in B-D are presented as mean  $\pm$  SEM,  $**P < 0.01$  by one-way ANOVA test.