Figure S1

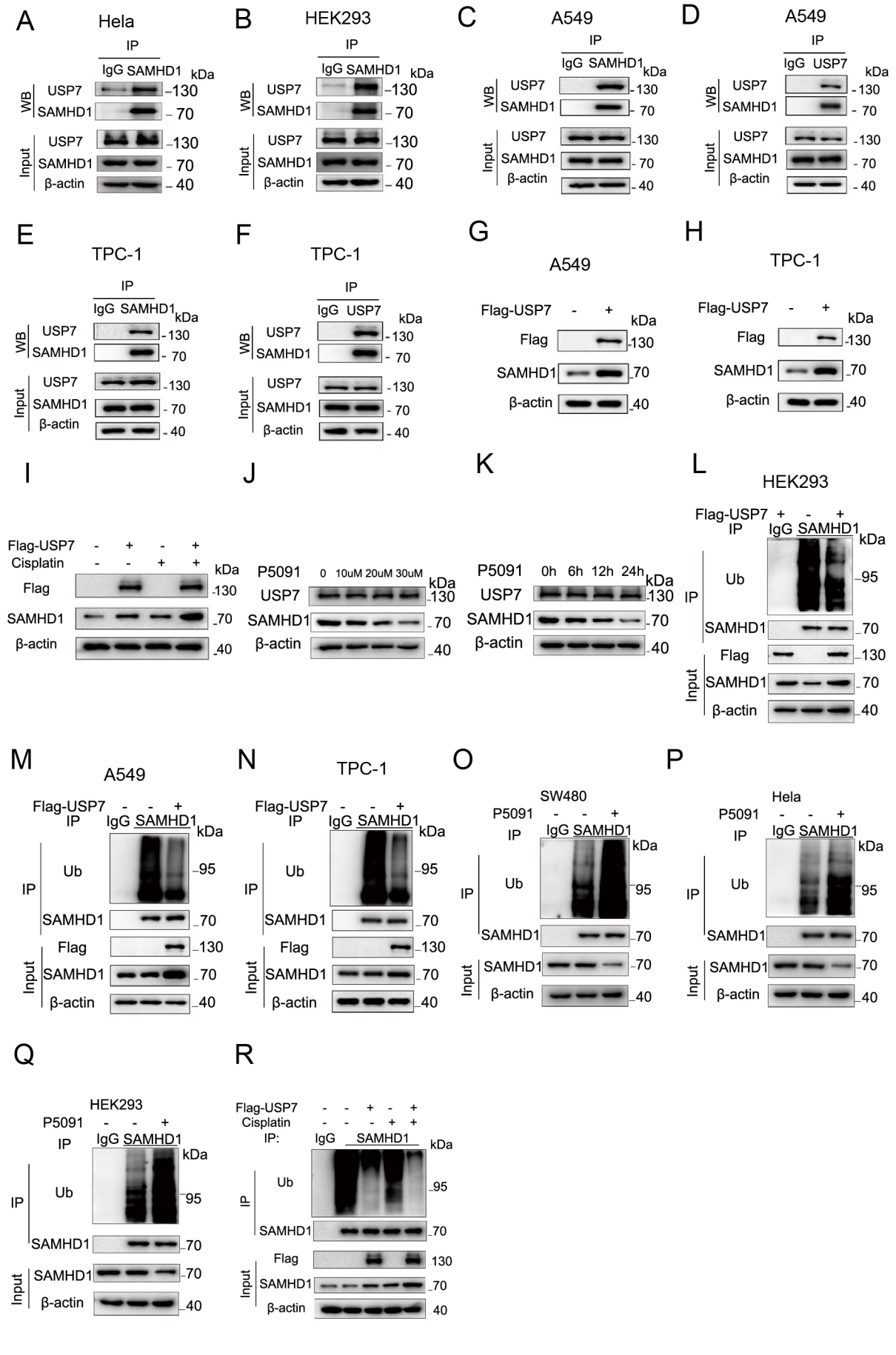

A
Hela
IP
IgG SAMHD1
kDa
WB
USP7
SAMHD1
130
70
Input
USP7
SAMHD1
β-actin
130
70
40
B
HEK293
IP
IgG SAMHD1
kDa
WB
USP7
SAMHD1
130
70
Input
USP7
SAMHD1
β-actin
130
70
40
C
A549
IP
IgG SAMHD1
kDa
WB
USP7
SAMHD1
130
70
Input
USP7
SAMHD1
β-actin
130
70
40
D
A549
IP
IgG USP7
kDa
WB
USP7
SAMHD1
130
70
Input
USP7
SAMHD1
β-actin
130
70
40
E
TPC-1
IP
IgG SAMHD1
kDa
WB
USP7
SAMHD1
130
70
Input
USP7
SAMHD1
β-actin
130
70
40
F
TPC-1
IP
IgG USP7
kDa
WB
USP7
SAMHD1
130
70
Input
USP7
SAMHD1
β-actin
130
70
40
G
A549
Flag-USP7 - +
kDa
Flag
SAMHD1
β-actin
130
70
40
H
TPC-1
Flag-USP7 - +
kDa
Flag
SAMHD1
β-actin
130
70
40
I
Flag-USP7 - + - +
Cisplatin - - + +
kDa
Flag
SAMHD1
β-actin
130
70
40
J
P5091 0 10uM 20uM 30uM
kDa
USP7
SAMHD1
β-actin
130
70
40
K
P5091 0h 6h 12h 24h
kDa
USP7
SAMHD1
β-actin
130
70
40
L
HEK293
Flag-USP7 + - +
IP
IgG SAMHD1
kDa
IP
Ub
SAMHD1
95
70
Input
Flag
SAMHD1
β-actin
130
70
40
M
A549
Flag-USP7 - - +
IP
IgG SAMHD1
kDa
IP
Ub
SAMHD1
95
70
Input
Flag
SAMHD1
β-actin
130
70
40
N
TPC-1
Flag-USP7 - - +
IP
IgG SAMHD1
kDa
IP
Ub
SAMHD1
95
70
Input
Flag
SAMHD1
β-actin
130
70
40
O
SW480
P5091 - - +
IP
IgG SAMHD1
kDa
IP
Ub
SAMHD1
95
70
Input
SAMHD1
β-actin
70
40
P
Hela
P5091 - - +
IP
IgG SAMHD1
kDa
IP
Ub
SAMHD1
95
70
Input
SAMHD1
β-actin
70
40
Q
HEK293
P5091 - - +
IP
IgG SAMHD1
kDa
IP
Ub
SAMHD1
95
70
Input
SAMHD1
β-actin
70
40
R
Flag-USP7 - - + - +
Cisplatin - - - + +
IP:
IgG SAMHD1
kDa
IP
Ub
SAMHD1
95
70
Input
Flag
SAMHD1
β-actin
130
70
40

Figure S2

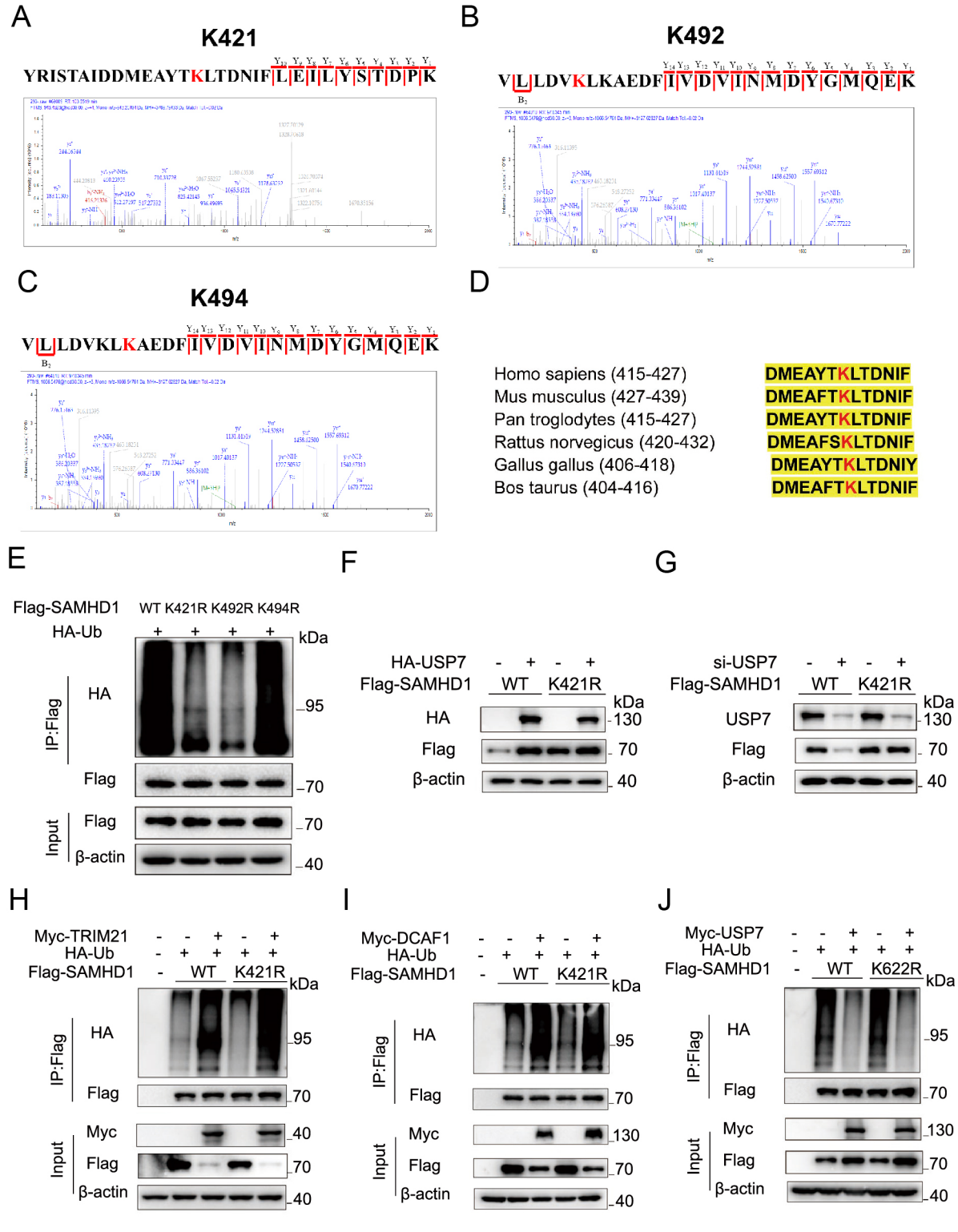

A
K421
YRISTAIDDMEAYTKLTDNIF
B
K492
VLLDVKLKAEDFIVDVINMDYGMQEK
C
K494
VLLDVKLKAEDFIVDVINMDYGMQEK
D
Homo sapiens (415-427) DMEAYTKLTDNIF
Mus musculus (427-439) DMEAFTKLTDNIF
Pan troglodytes (415-427) DMEAYTKLTDNIF
Rattus norvegicus (420-432) DMEAFSKLTDNIF
Gallus gallus (406-418) DMEAYTKLTDNIY
Bos taurus (404-416) DMEAFTKLTDNIF
E
Flag-SAMHD1 WT K421R K492R K494R
HA-Ub
IP:Flag
HA
Flag
Input
Flag
β-actin
kDa
95
70
40
F
HA-USP7
Flag-SAMHD1
WT
K421R
HA
Flag
β-actin
130
70
40
G
si-USP7
Flag-SAMHD1
WT
K421R
USP7
Flag
β-actin
130
70
40
H
Myc-TRIM21
HA-Ub
Flag-SAMHD1
WT
K421R
IP:Flag
HA
Flag
Input
Myc
Flag
β-actin
95
70
40
I
Myc-DCAF1
HA-Ub
Flag-SAMHD1
WT
K421R
IP:Flag
HA
Flag
Input
Myc
Flag
β-actin
95
70
130
70
40
J
Myc-USP7
HA-Ub
Flag-SAMHD1
WT
K622R
IP:Flag
HA
Flag
Input
Myc
Flag
β-actin
95
70
130
70
40

Figure S3

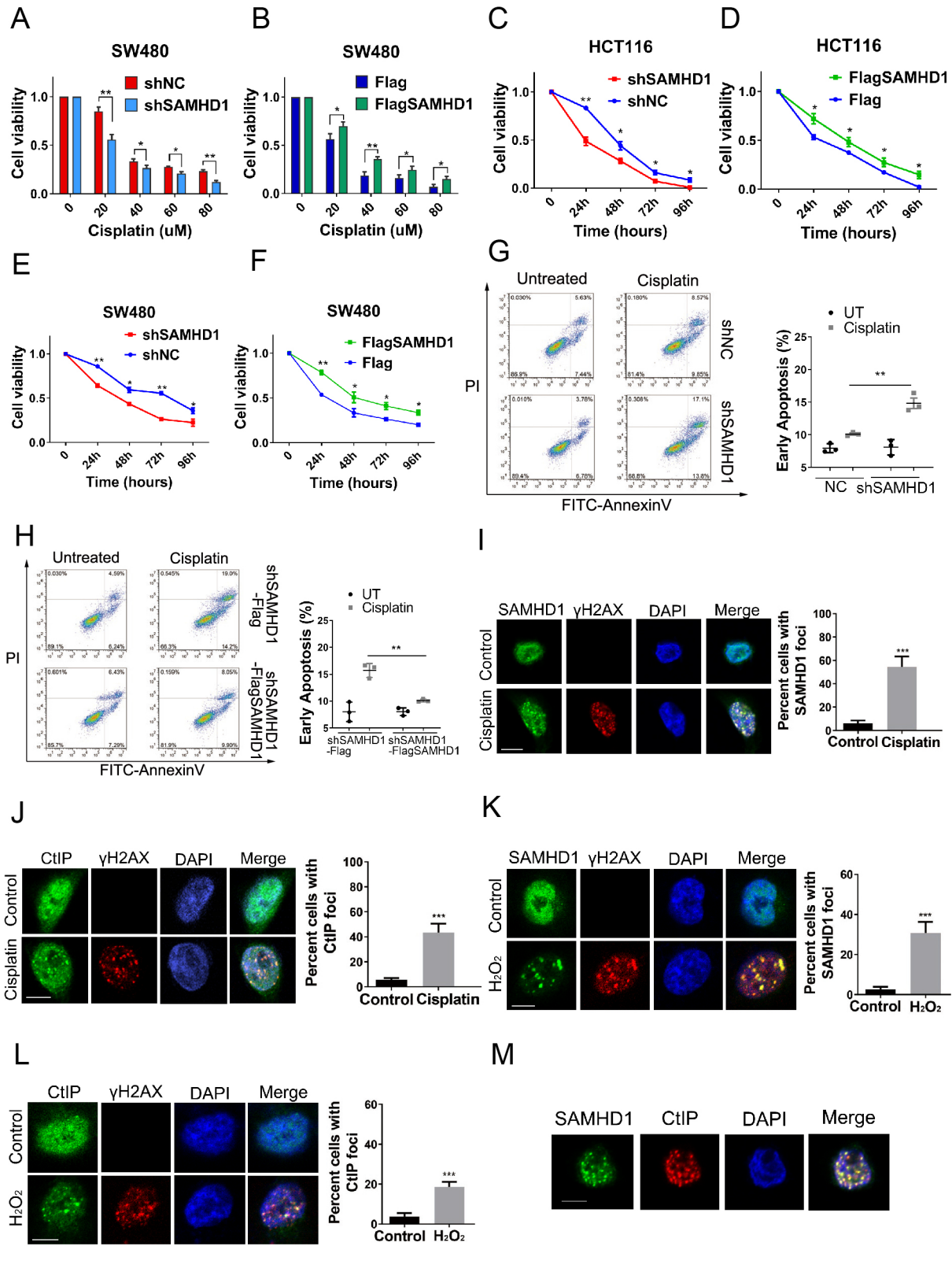

A
SW480
shNC
shSAMHD1
Cell viability
Cisplatin (uM)
B
SW480
Flag
FlagSAMHD1
Cell viability
Cisplatin (uM)
C
HCT116
shSAMHD1
shNC
Cell viability
Time (hours)
D
HCT116
FlagSAMHD1
Flag
Cell viability
Time (hours)
E
SW480
shSAMHD1
shNC
Cell viability
Time (hours)
F
SW480
FlagSAMHD1
Flag
Cell viability
Time (hours)
G
Untreated
Cisplatin
shNC
shSAMHD1
PI
FITC-AnnexinV
UT
Cisplatin
Early Apoptosis (%)
NC
shSAMHD1
H
Untreated
Cisplatin
shSAMHD1 -Flag
shSAMHD1 -FlagSAMHD1
PI
FITC-AnnexinV
UT
Cisplatin
Early Apoptosis (%)
shSAMHD1 -Flag
shSAMHD1 -FlagSAMHD1
I
SAMHD1
γH2AX
DAPI
Merge
Control
Cisplatin
Percent cells with SAMHD1 foci
Control
Cisplatin
J
CtIP
γH2AX
DAPI
Merge
Control
Cisplatin
Percent cells with CtIP foci
Control
Cisplatin
K
SAMHD1
γH2AX
DAPI
Merge
Control
H2O2
Percent cells with SAMHD1 foci
Control
H2O2
L
CtIP
γH2AX
DAPI
Merge
Control
H2O2
Percent cells with CtIP foci
Control
H2O2
M
SAMHD1
CtIP
DAPI
Merge

Figure S4

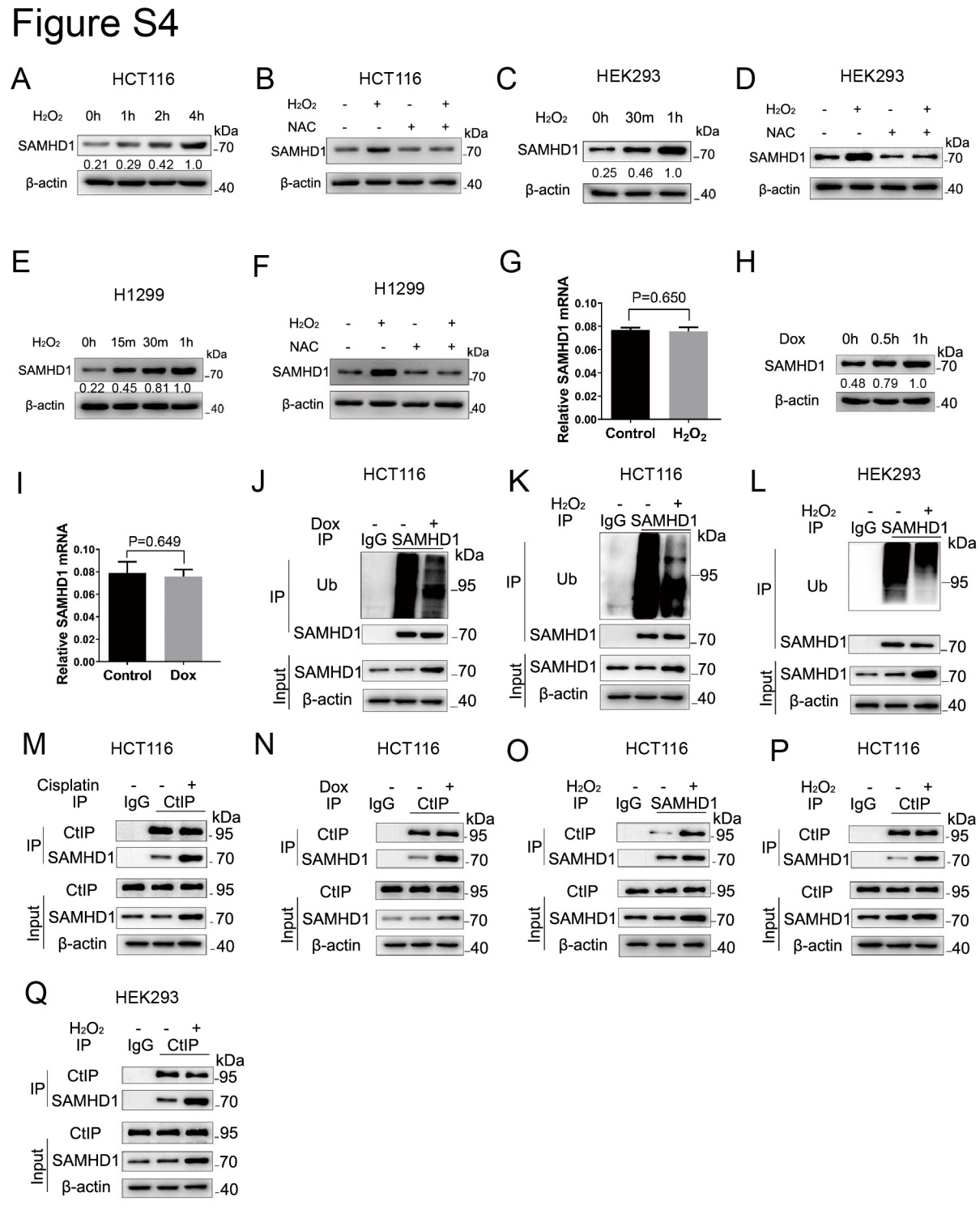

A
HCT116
H2O2 0h 1h 2h 4h
kDa
SAMHD1 70
0.21 0.29 0.42 1.0
β-actin 40
B
HCT116
H2O2 - + - +
NAC - - + +
kDa
SAMHD1 70
β-actin 40
C
HEK293
H2O2 0h 30m 1h
kDa
SAMHD1 70
0.25 0.46 1.0
β-actin 40
D
HEK293
H2O2 - + - +
NAC - - + +
kDa
SAMHD1 70
β-actin 40
E
H1299
H2O2 0h 15m 30m 1h
kDa
SAMHD1 70
0.22 0.45 0.81 1.0
β-actin 40
F
H1299
H2O2 - + - +
NAC - - + +
kDa
SAMHD1 70
β-actin 40
G
Relative SAMHD1 mRNA
P=0.650
0.10
0.08
0.06
0.04
0.02
0.00
Control
H2O2
H
Dox 0h 0.5h 1h
kDa
SAMHD1 70
0.48 0.79 1.0
β-actin 40
I
Relative SAMHD1 mRNA
P=0.649
0.10
0.08
0.06
0.04
0.02
0.00
Control
Dox
J
HCT116
Dox - - +
IP IgG SAMHD1
kDa
IP
Ub 95
SAMHD1 70
Input
SAMHD1 70
β-actin 40
K
HCT116
H2O2 - - +
IP IgG SAMHD1
kDa
IP
Ub 95
SAMHD1 70
Input
SAMHD1 70
β-actin 40
L
HEK293
H2O2 - - +
IP IgG SAMHD1
kDa
IP
Ub 95
SAMHD1 70
Input
SAMHD1 70
β-actin 40
M
HCT116
Cisplatin - - +
IP IgG CtIP
kDa
IP
CtIP 95
SAMHD1 70
Input
CtIP 95
SAMHD1 70
β-actin 40
N
HCT116
Dox - - +
IP IgG CtIP
kDa
IP
CtIP 95
SAMHD1 70
Input
CtIP 95
SAMHD1 70
β-actin 40
O
HCT116
H2O2 - - +
IP IgG SAMHD1
kDa
IP
CtIP 95
SAMHD1 70
Input
CtIP 95
SAMHD1 70
β-actin 40
P
HCT116
H2O2 - - +
IP IgG CtIP
kDa
IP
CtIP 95
SAMHD1 70
Input
CtIP 95
SAMHD1 70
β-actin 40
Q
HEK293
H2O2 - - +
IP IgG CtIP
kDa
IP
CtIP 95
SAMHD1 70
Input
CtIP 95
SAMHD1 70
β-actin 40

Figure S5

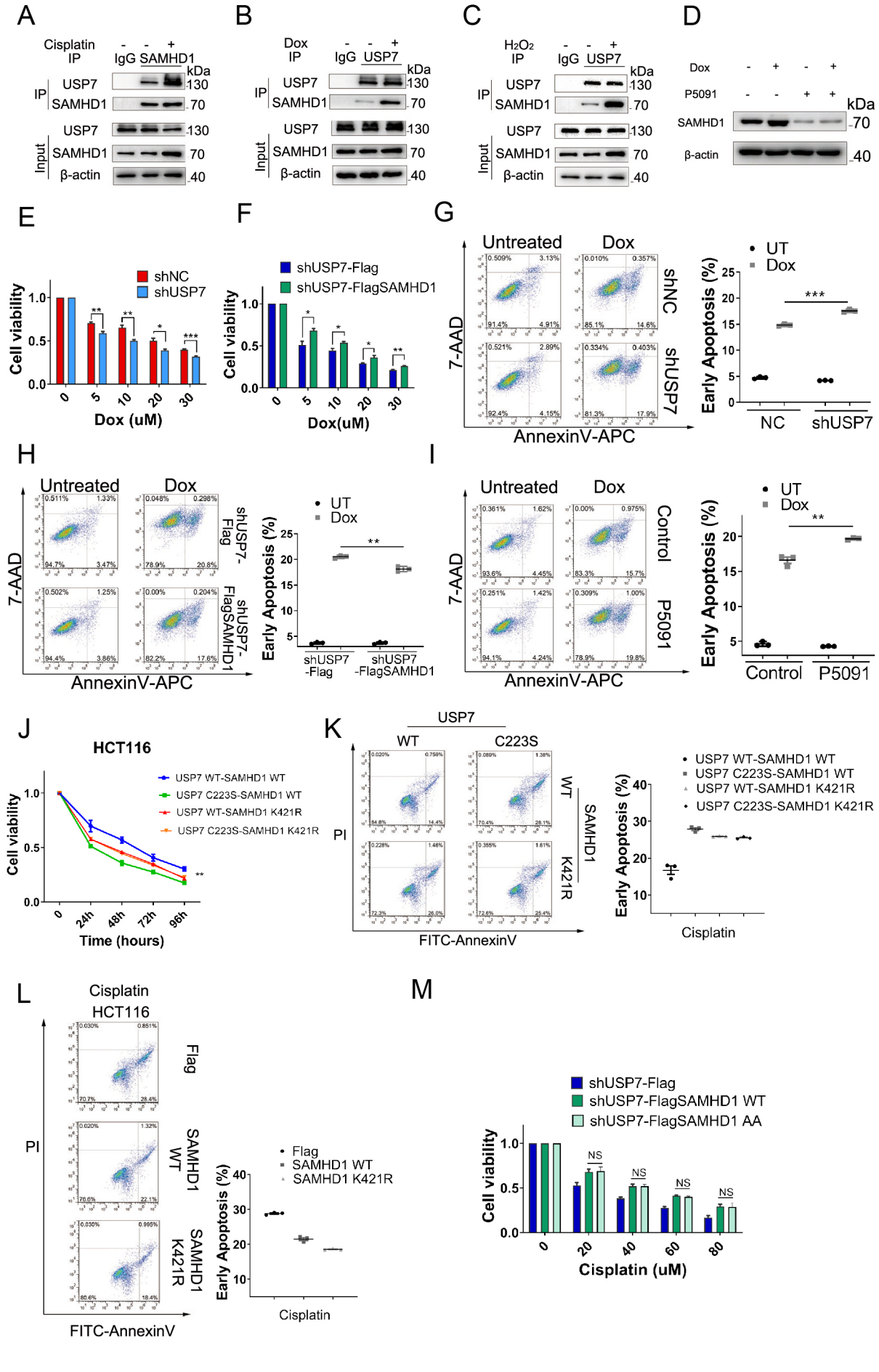

A
Cisplatin
IP
IgG
SAMHD1
kDa
IP
USP7
SAMHD1
Input
USP7
SAMHD1
β-actin
130
70
40
B
Dox
IP
IgG
USP7
C
H2O2
D
Dox
P5091
E
shNC
shUSP7
Cell viability
Dox (uM)
F
shUSP7-Flag
shUSP7-FlagSAMHD1
Dox(uM)
G
Untreated
Dox
shNC
shUSP7
7-AAD
AnnexinV-APC
UT
Dox
Early Apoptosis (%)
NC
shUSP7
H
shUSP7-Flag
shUSP7-FlagSAMHD1
I
Control
P5091
J
HCT116
USP7 WT-SAMHD1 WT
USP7 C223S-SAMHD1 WT
USP7 WT-SAMHD1 K421R
USP7 C223S-SAMHD1 K421R
Time (hours)
K
USP7
WT
C223S
PI
FITC-AnnexinV
Cisplatin
L
Cisplatin
HCT116
Flag
SAMHD1 WT
SAMHD1 K421R
M
shUSP7-Flag
shUSP7-FlagSAMHD1 WT
shUSP7-FlagSAMHD1 AA
NS
Cisplatin (uM)

Figure S6

A

Colon adenocarcinoma	SAMHD1 expression				
	Low	Medium	High	n	P
Tumor	4	15	11	30	<0.001
Peritumor	25	4	1	30	

B

Lung adenocarcinoma	SAMHD1 expression				
	Low	Medium	High	n	P
Tumor	8	25	15	48	<0.001
Peritumor	33	12	3	48	

C

Thyroid carcinoma	SAMHD1 expression				
	Low	Medium	High	n	P
Tumor	13	23	22	58	<0.001
Peritumor	49	9	0	58	

D

Colon adenocarcinoma	USP7 expression				
	Low	Medium	High	n	P
Tumor	10	11	9	30	<0.001
Peritumor	28	1	1	30	

E

Lung adenocarcinoma	USP7 expression				
	Low	Medium	High	n	P
Tumor	11	29	8	48	<0.001
Peritumor	34	12	2	48	

F

Thyroid carcinoma	USP7 expression				
	Low	Medium	High	n	P
Tumor	2	25	31	58	<0.001
Peritumor	38	19	1	58	

Figure S7

A

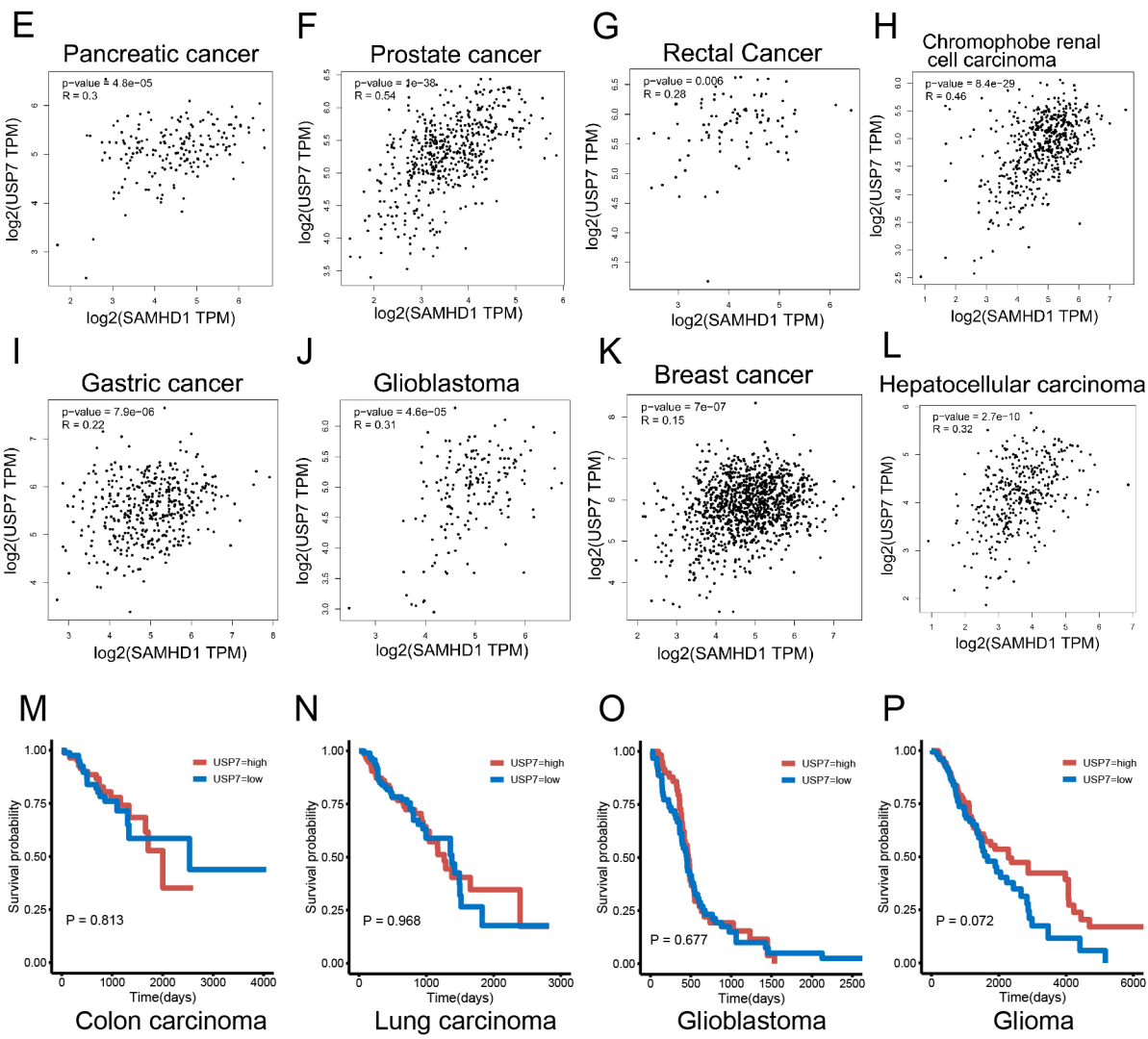
Colon adenocarcinoma	SAMHD1 expression Low	High	n	HR	95%CI	P
Live	78	45	123	2.15	1.07-4.32	0.020
Death	15	19	34			

B

Lung adenocarcinoma	SAMHD1 expression Low	High	n	HR	95%CI	P
Live	22	86	108	3.34	1.65-6.74	0.030
Death	3	62	65			

C

Glioblastoma	SAMHD1 expression Low	High	n	HR	95%CI	P
Live	4	23	27	1.99	1.17-3.38	0.034
Death	9	87	96			

D

Glioma	SAMHD1 expression Low	High	n	HR	95%CI	P
Live	142	39	181	1.56	1.00-2.43	0.026
Death	76	35	111