Mutations in UVSSA cause UV-sensitive syndrome and impair RNA polymerase IIo processing in transcription-coupled nucleotide-excision repair

Article (Unspecified)

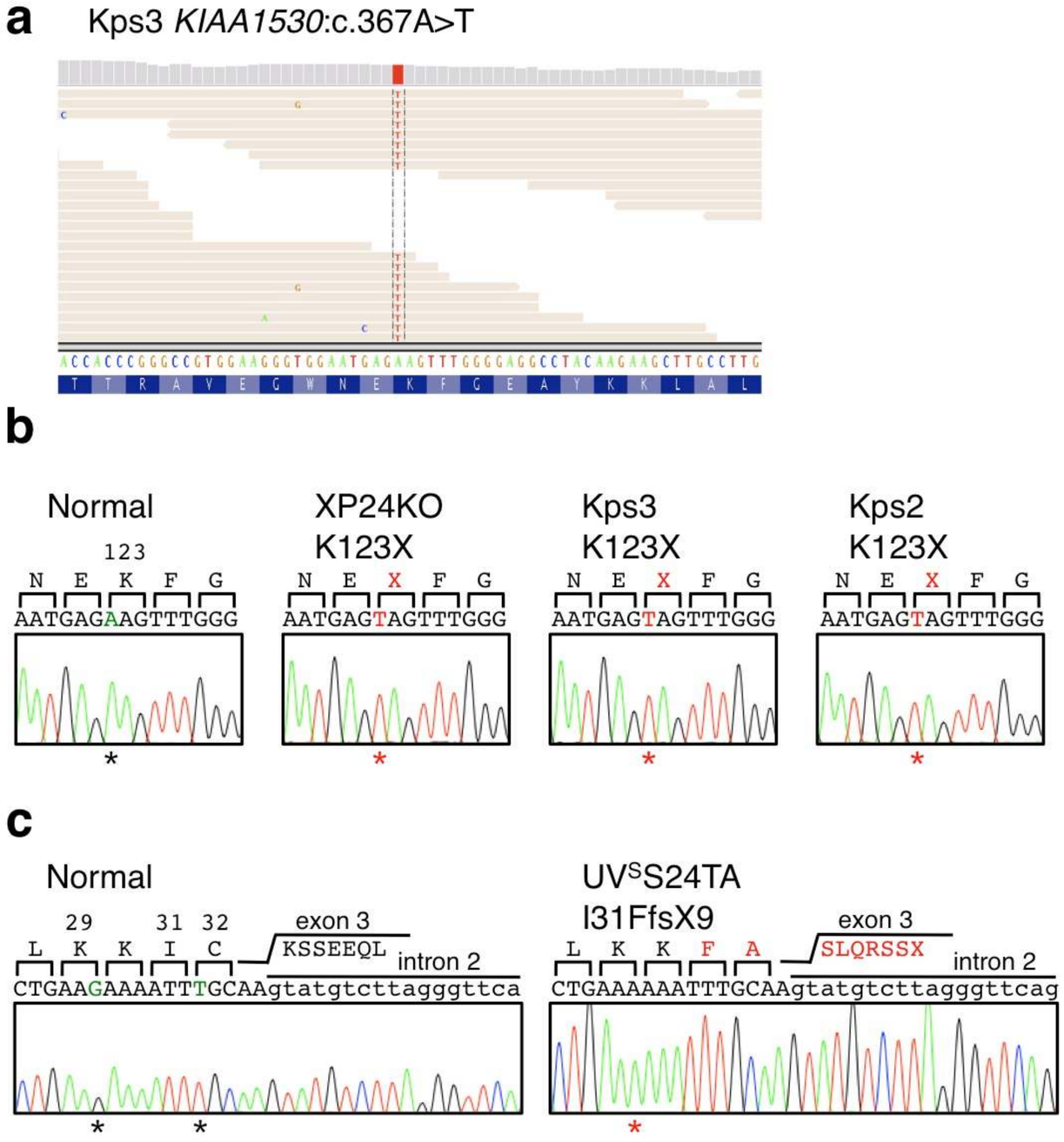
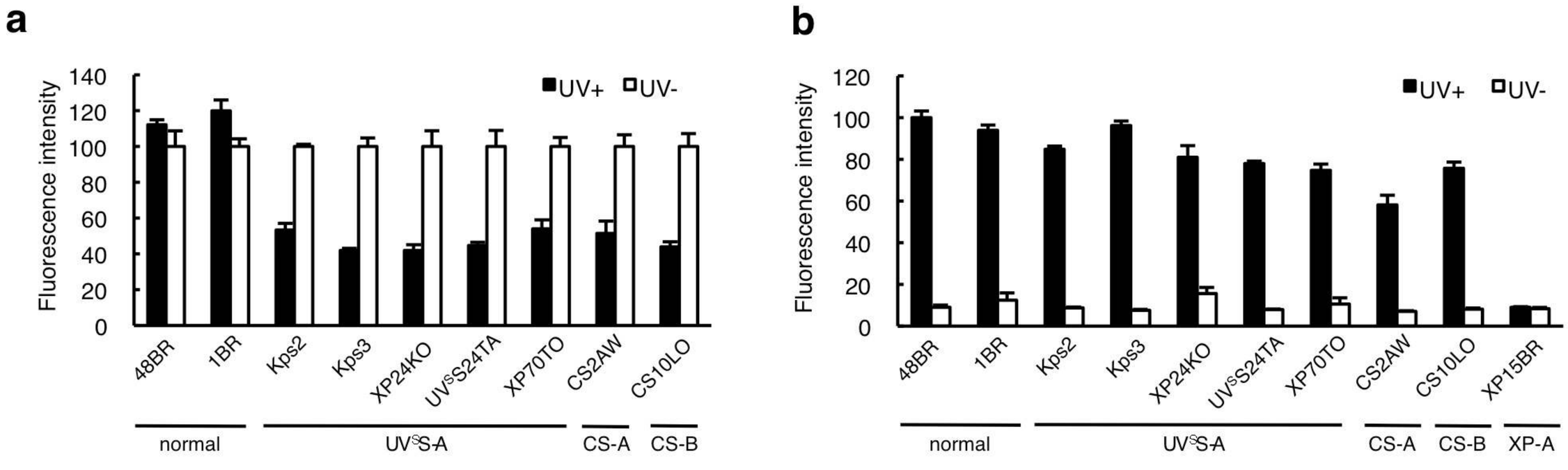
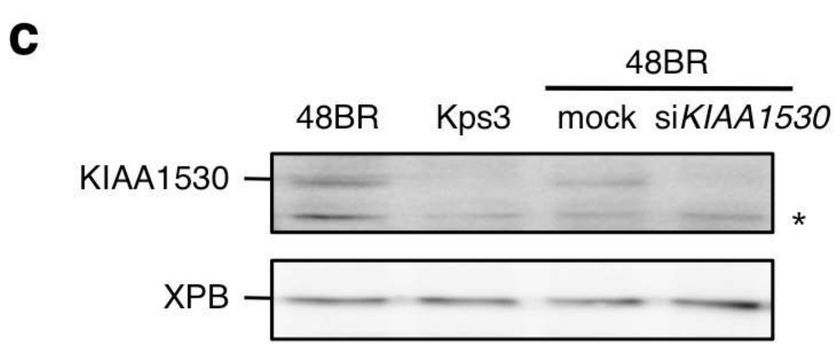
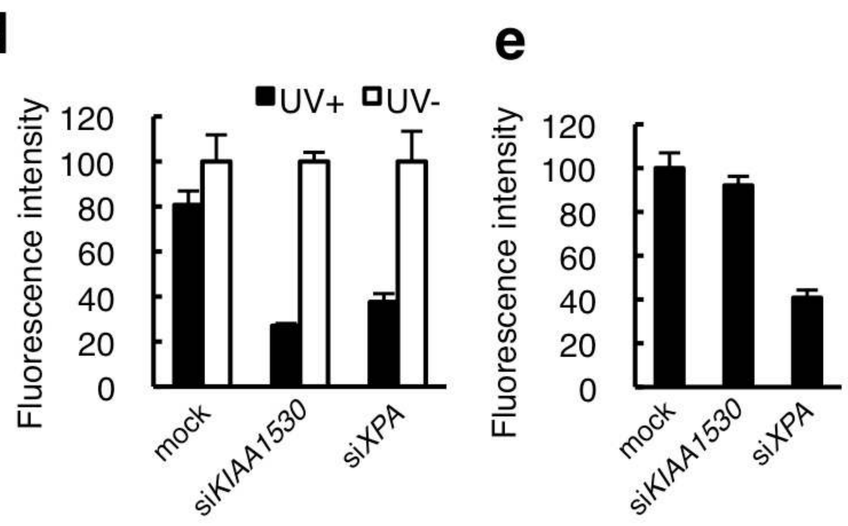

a
Kps3 KIAA1530:c.367A>T
b
Normal
XP24KO
K123X
Kps3
K123X
Kps2
K123X
c
Normal
UVSS24TA
I31FfsX9
XP70TO
C32R
exon 3
intron 2
d
p.I31FfsX9
p.K123X
KIAA1530 (40.7kb)
p.C32R
ORF start
ORF end
e
normal
CS-A
CS-B
UVSS-A
1BR
48BR
CS2AW
CS10LO
KpS2
KpS3
UVSS24TA
XP24KO
KIAA1530
XPB
α-KIAA1530 rabbit
α-XPB mouse
α-KIAA1530 mouse
α-XPB rabbit
f
Chr4
Chr8
Chr12

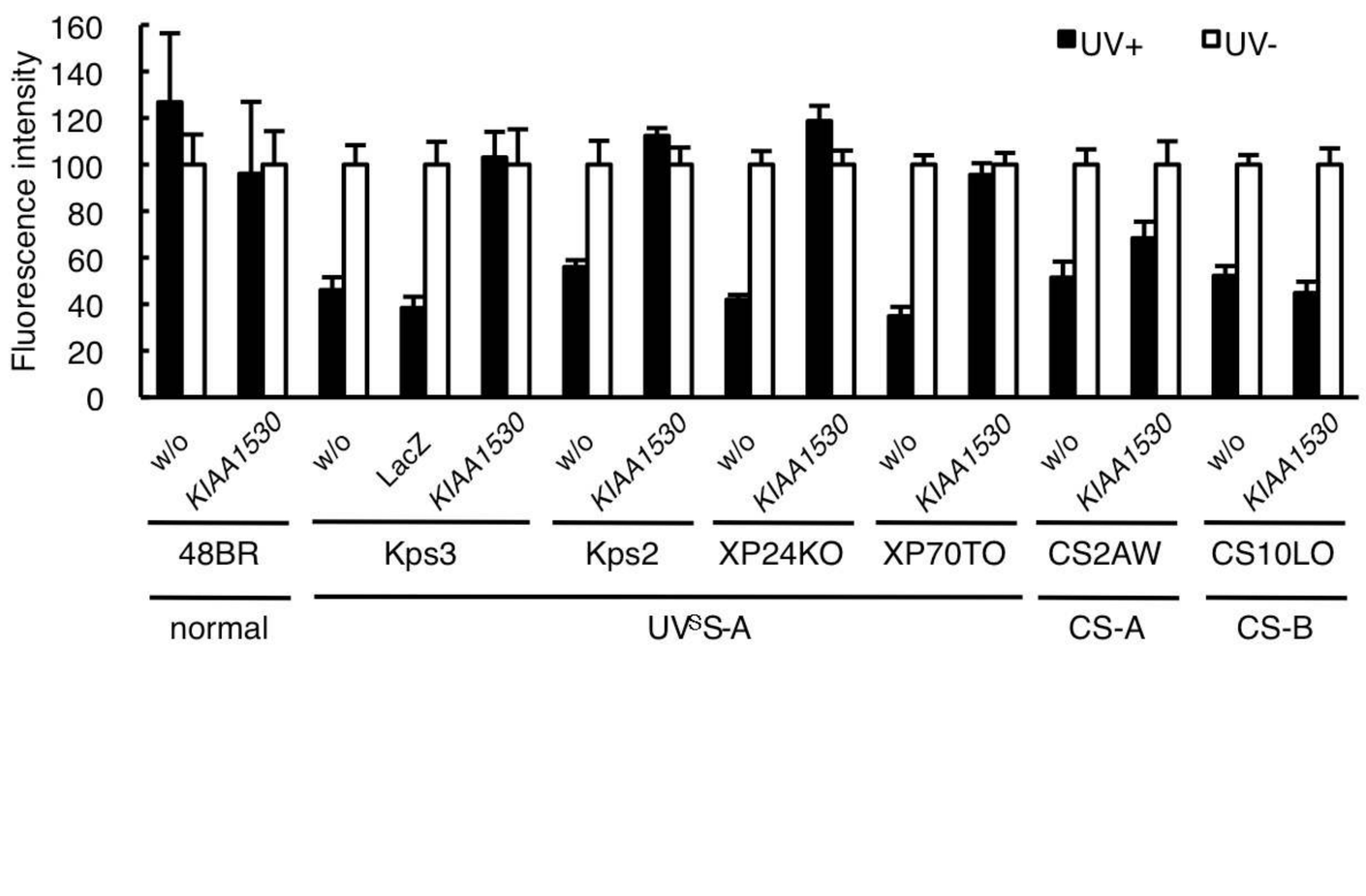
Fig.1


a
Fluorescence intensity
140
120
100
80
60
40
20
0
UV+ UV-
48BR
1BR
Kps2
Kps3
XP24KO
UVˢS24TA
XP70TO
CS2AW
CS10LO
normal
UVˢS-A
CS-A
CS-B
b
Fluorescence intensity
120
100
80
60
40
20
0
UV+ UV-
48BR
1BR
Kps2
Kps3
XP24KO
UVˢS24TA
XP70TO
CS2AW
CS10LO
XP15BR
normal
UVˢS-A
CS-A
CS-B
XP-A


c
48BR
48BR
Kps3
mock
siKIAA1530
KIAA1530
*
XPB


d
Fluorescence intensity
120
100
80
60
40
20
0
UV+ UV-
mock
siKIAA1530
siXPA

e
Fluorescence intensity
120
100
80
60
40
20
0
mock
siKIAA1530
siXPA


f
Fluorescence intensity
160
140
120
100
80
60
40
20
0
UV+ UV-
w/o
KIAA1530
w/o
LacZ
KIAA1530
48BR
Kps3
Kps2
XP24KO
XP70TO
CS2AW
CS10LO
normal
UVˢS-A
CS-A
CS-B

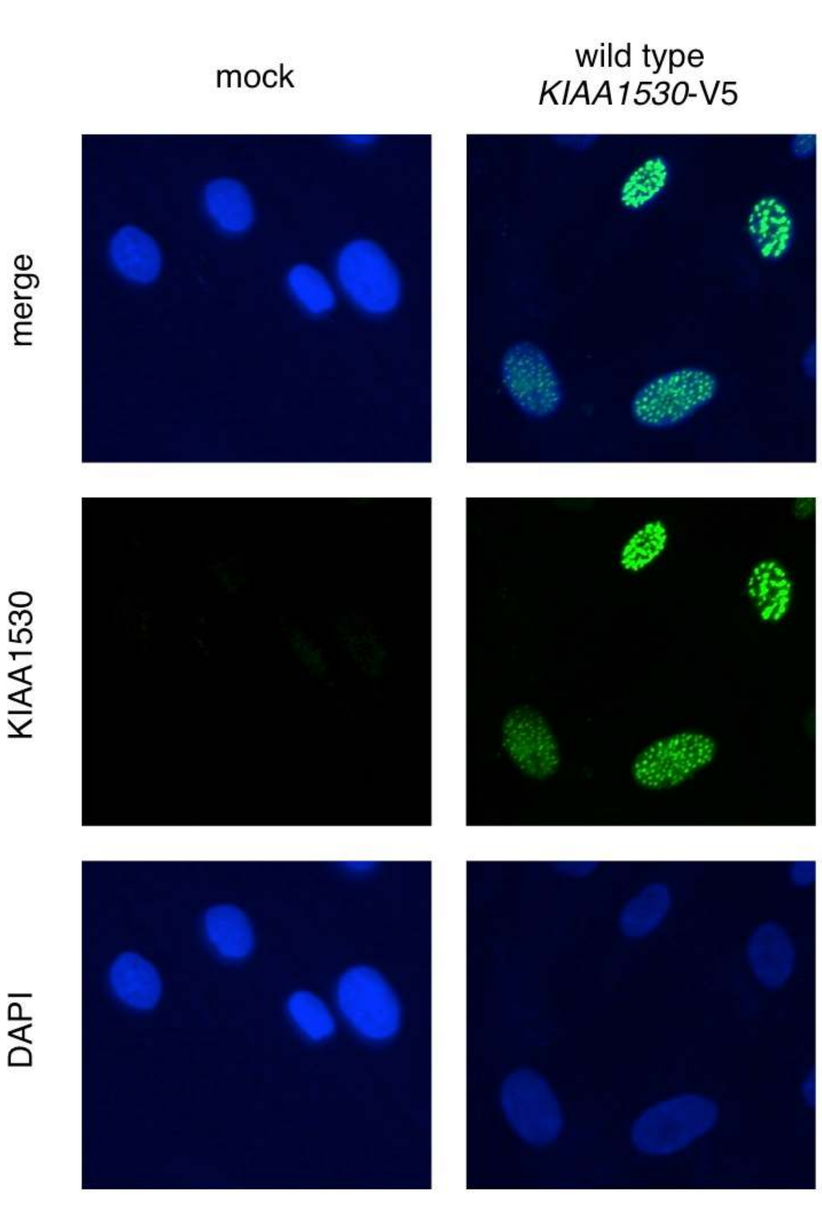
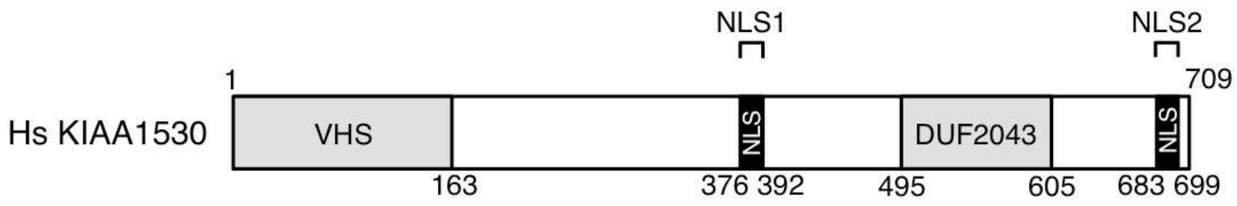
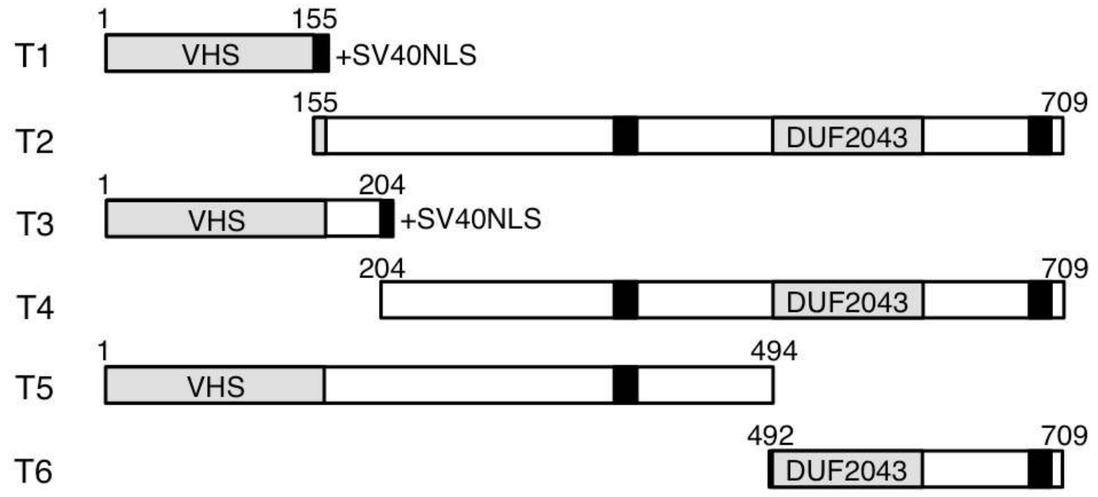

g
mock
wild type
KIAA1530-V5
merge
KIAA1530
DAPI

Fig.2

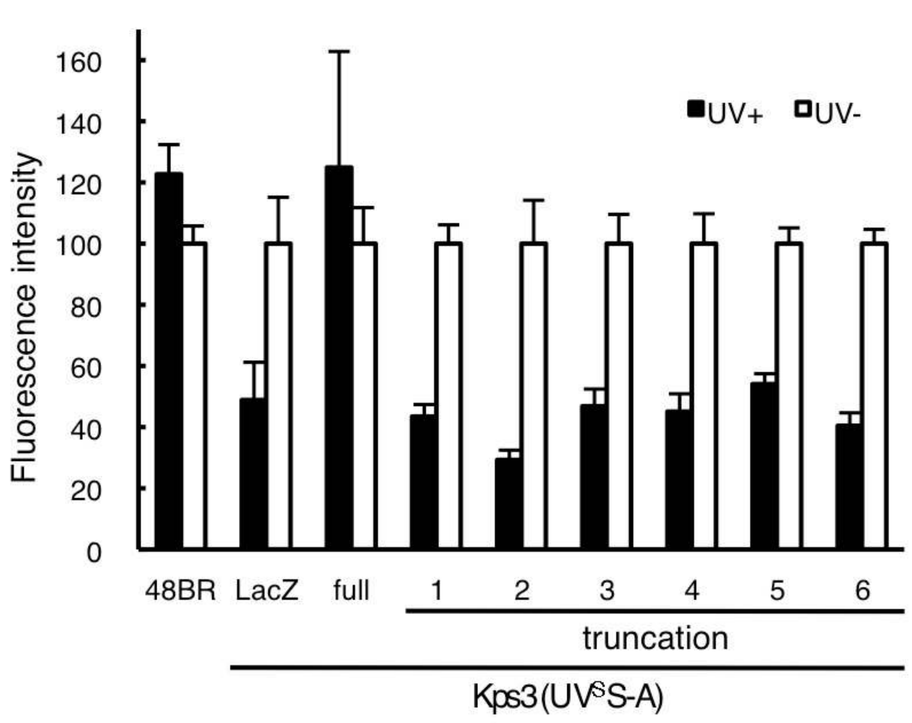
a



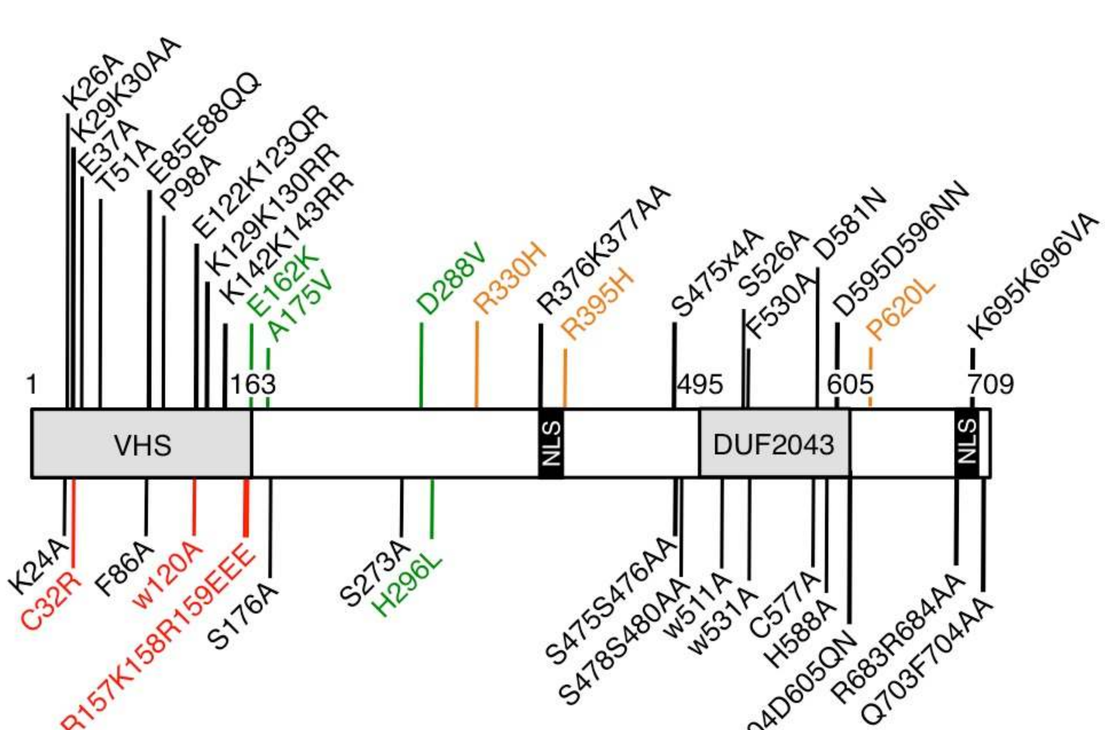
b



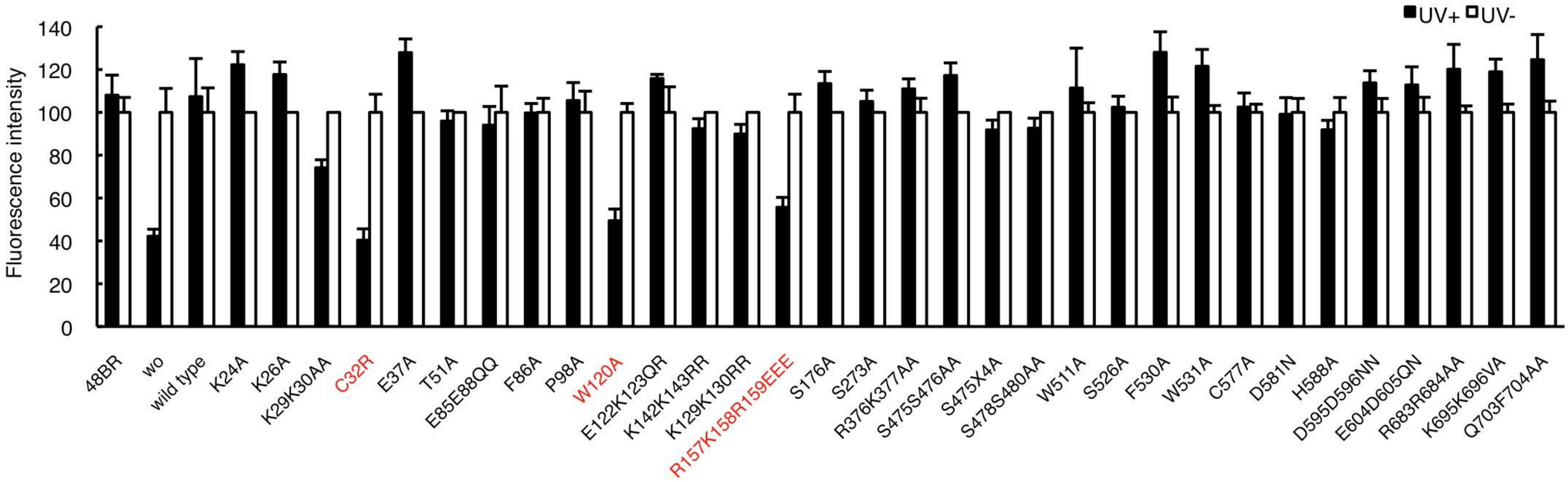
c



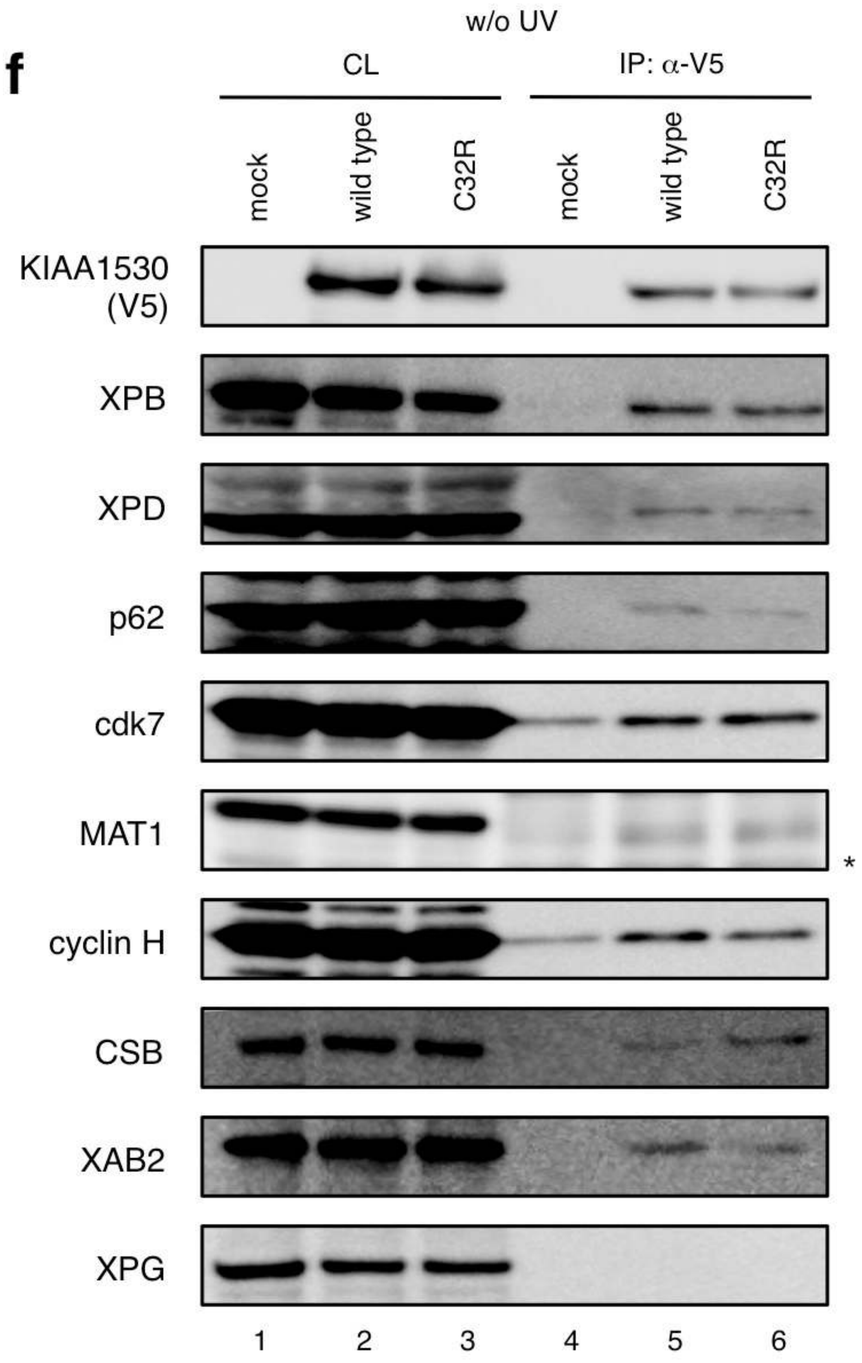
d



e



f



g

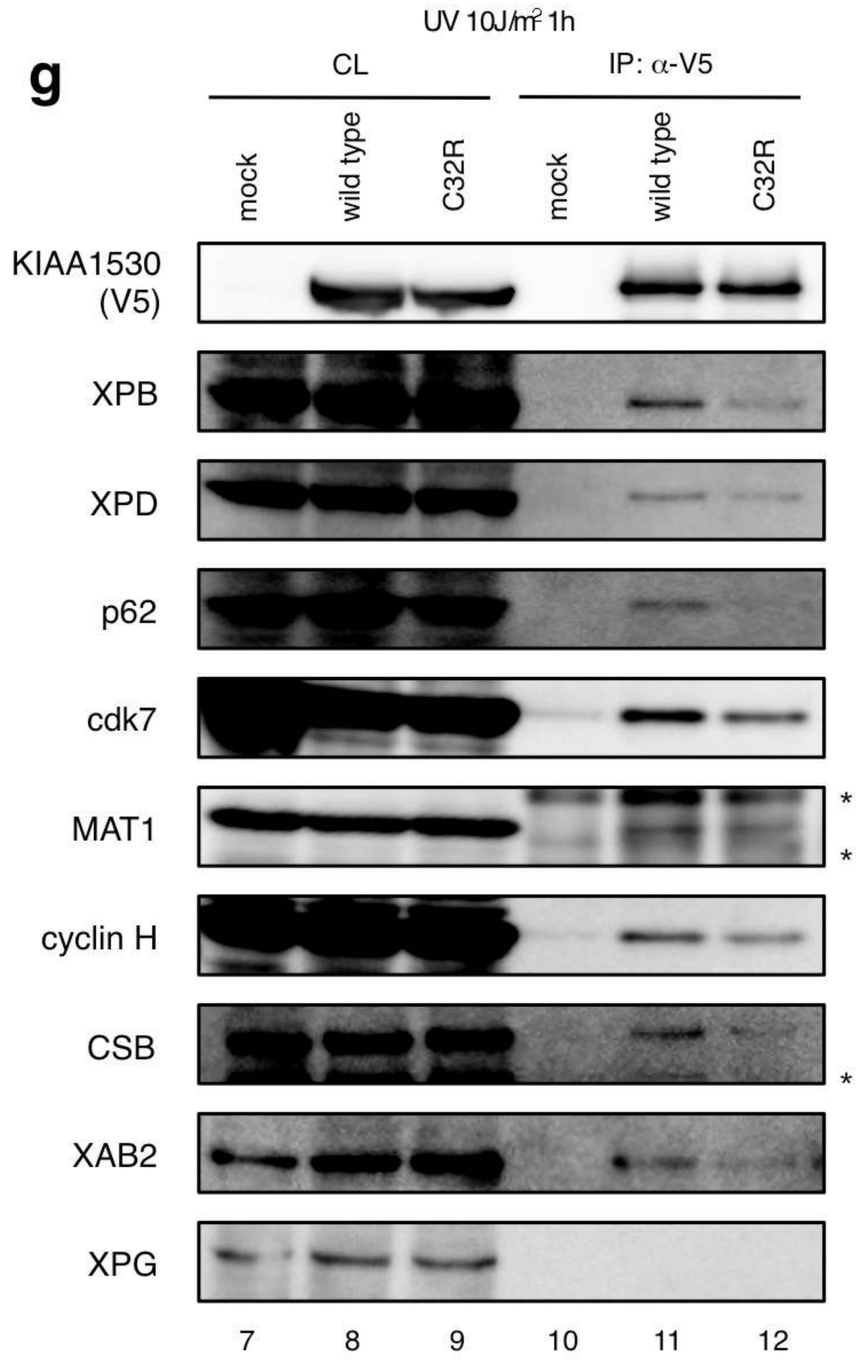
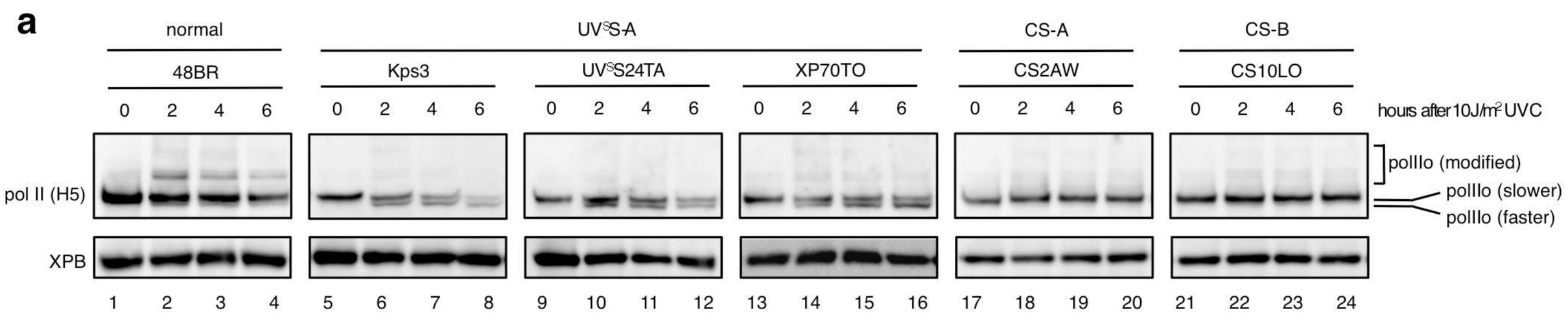
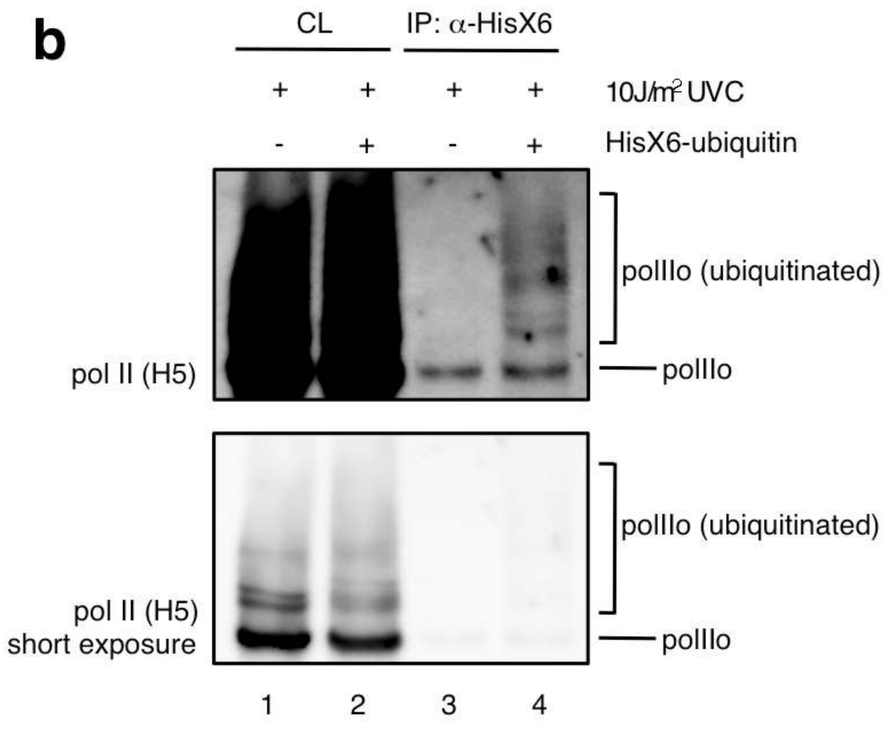
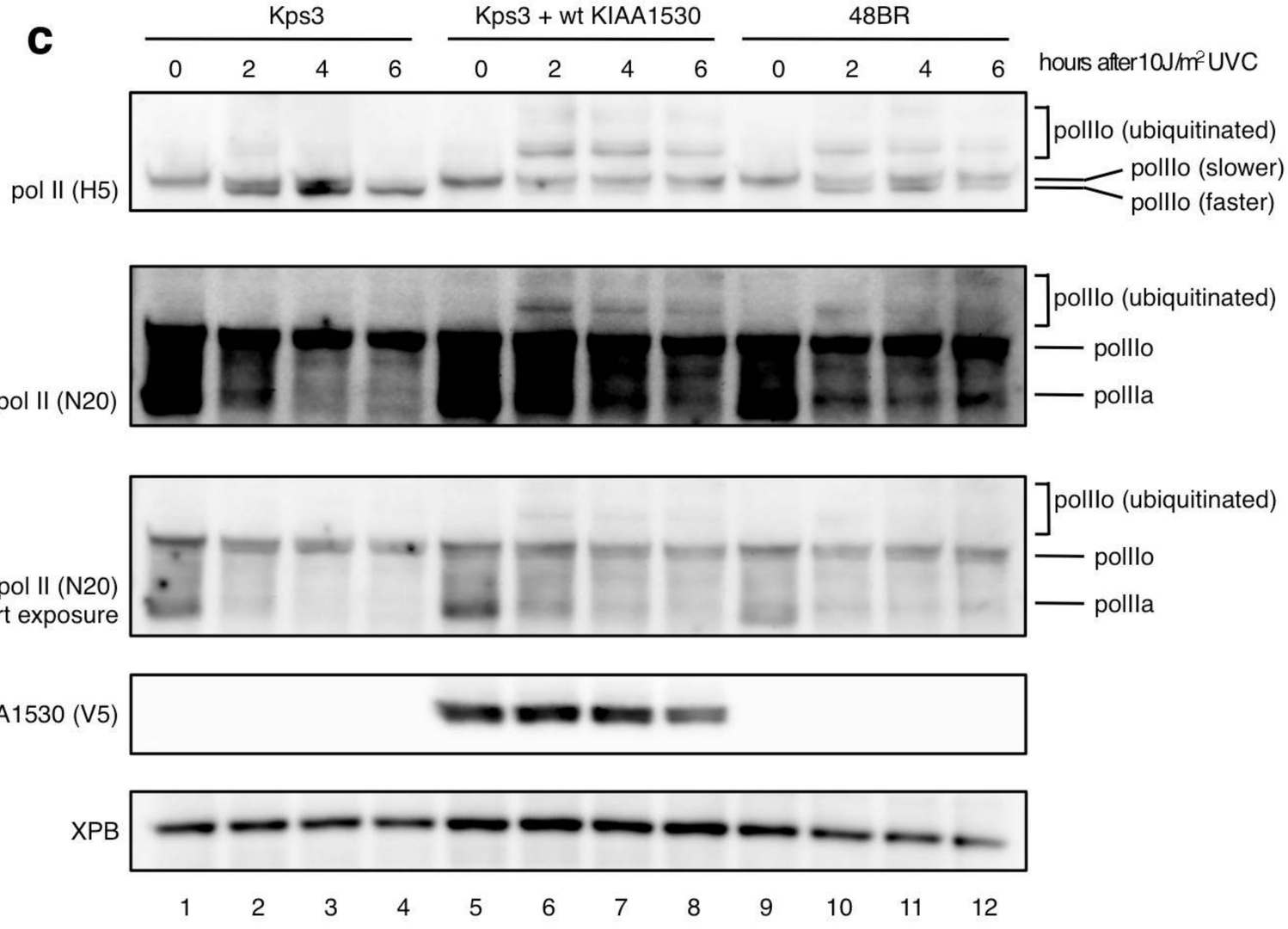
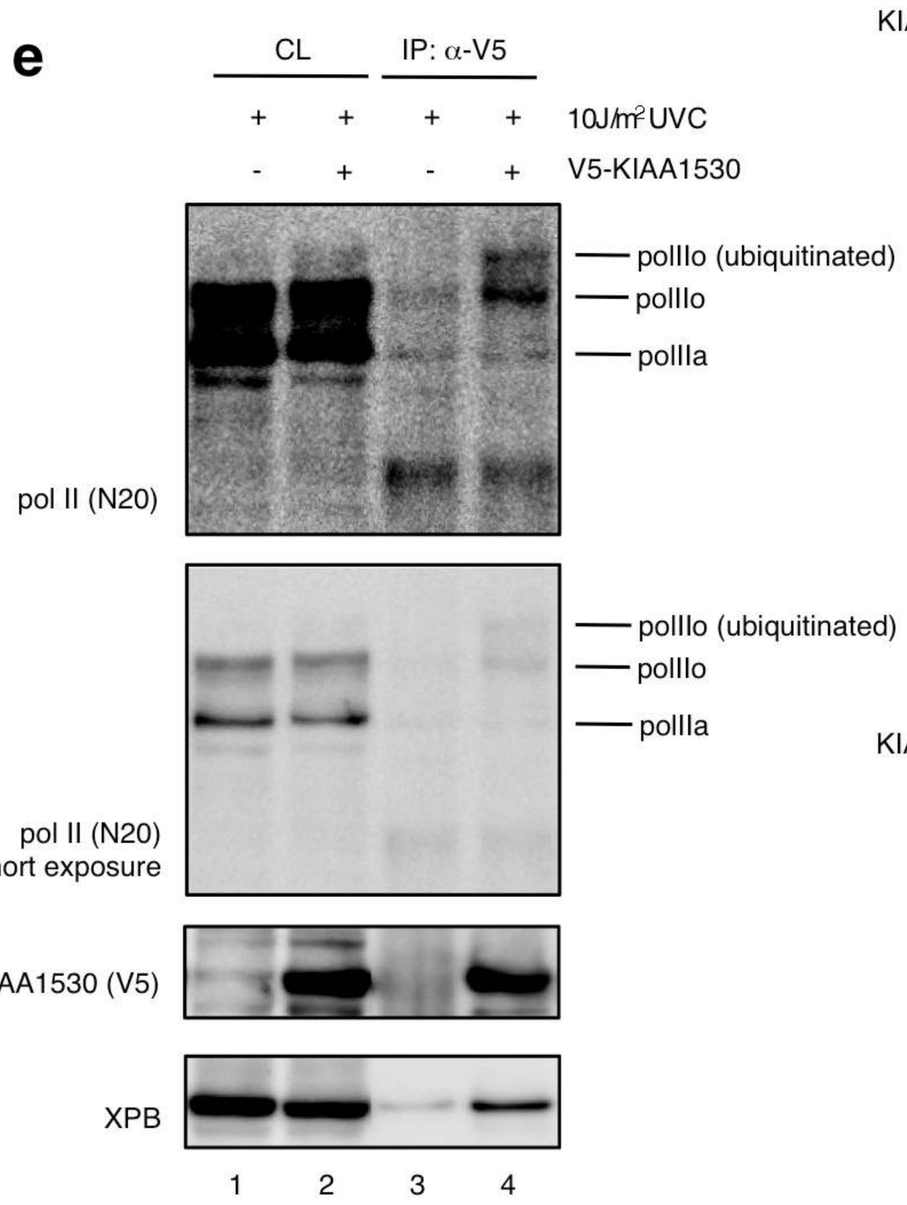


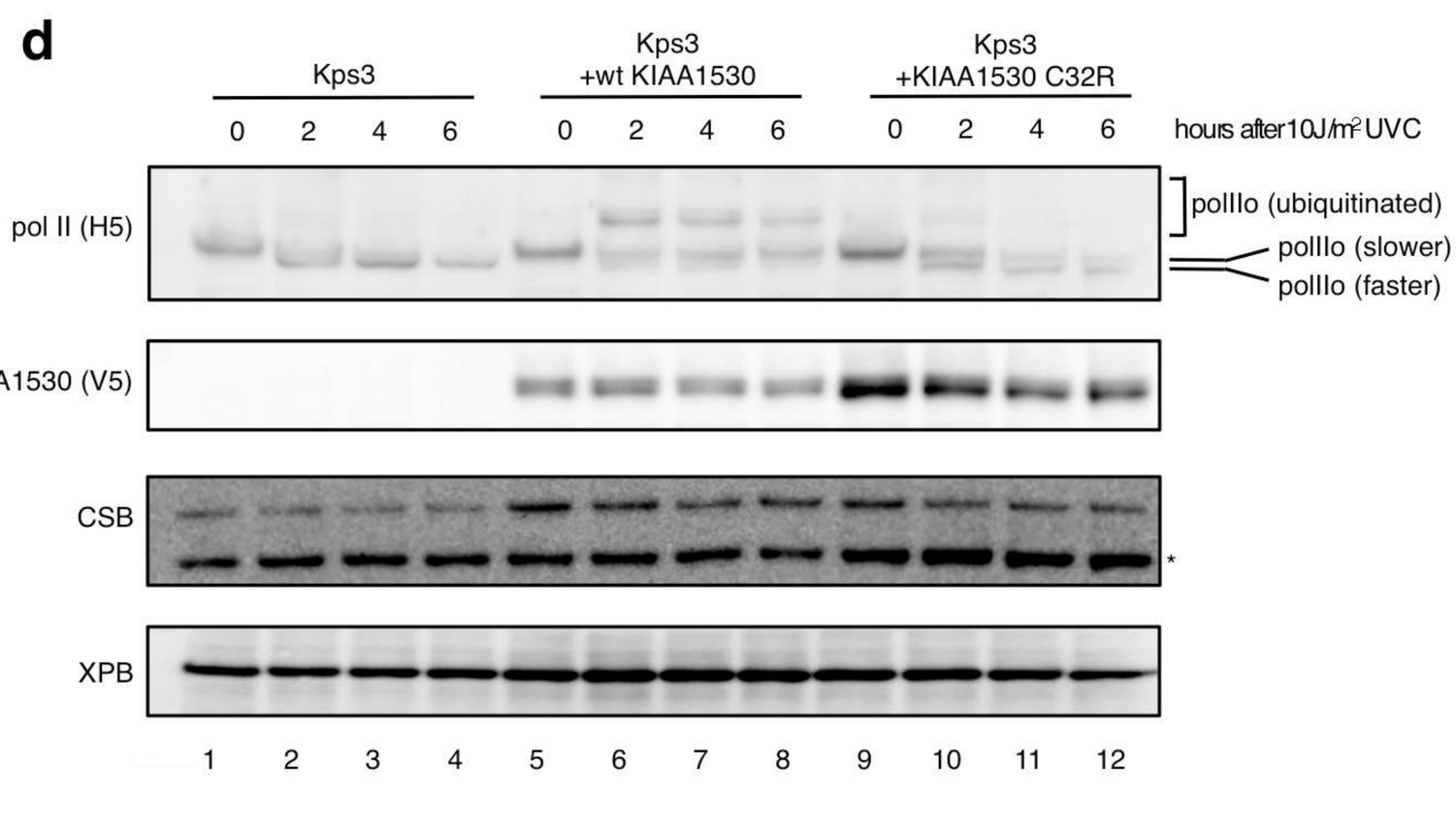
Fig.3


a
normal
UVSS-A
CS-A
CS-B
48BR
Kps3
UVSS24TA
XP70TO
CS2AW
CS10LO
0 2 4 6
hours after 10J/m2 UVC
pol II (H5)
XPB
polIIo (modified)
polIIo (slower)
polIIo (faster)
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24


b
CL
IP: α-HisX6
+ + + + 10J/m2 UVC
- + - + HisX6-ubiquitin
pol II (H5)
polIIo (ubiquitinated)
polIIo
pol II (H5)
short exposure
1 2 3 4


c
Kps3
Kps3 + wt KIAA1530
48BR
0 2 4 6
hours after 10J/m2 UVC
pol II (H5)
polIIo (ubiquitinated)
polIIo (slower)
polIIo (faster)
pol II (N20)
polIIo
polIIa
pol II (N20)
short exposure
KIAA1530 (V5)
XPB
1 2 3 4 5 6 7 8 9 10 11 12


e
CL
IP: α-V5
+ + + + 10J/m2 UVC
- + - + V5-KIAA1530
polIIo (ubiquitinated)
polIIo
polIIa
pol II (N20)
pol II (N20)
short exposure
KIAA1530 (V5)
XPB
1 2 3 4


d
Kps3
Kps3
+wt KIAA1530
Kps3
+KIAA1530 C32R
0 2 4 6
hours after 10J/m2 UVC
pol II (H5)
polIIo (ubiquitinated)
polIIo (slower)
polIIo (faster)
KIAA1530 (V5)
CSB
*
XPB
1 2 3 4 5 6 7 8 9 10 11 12

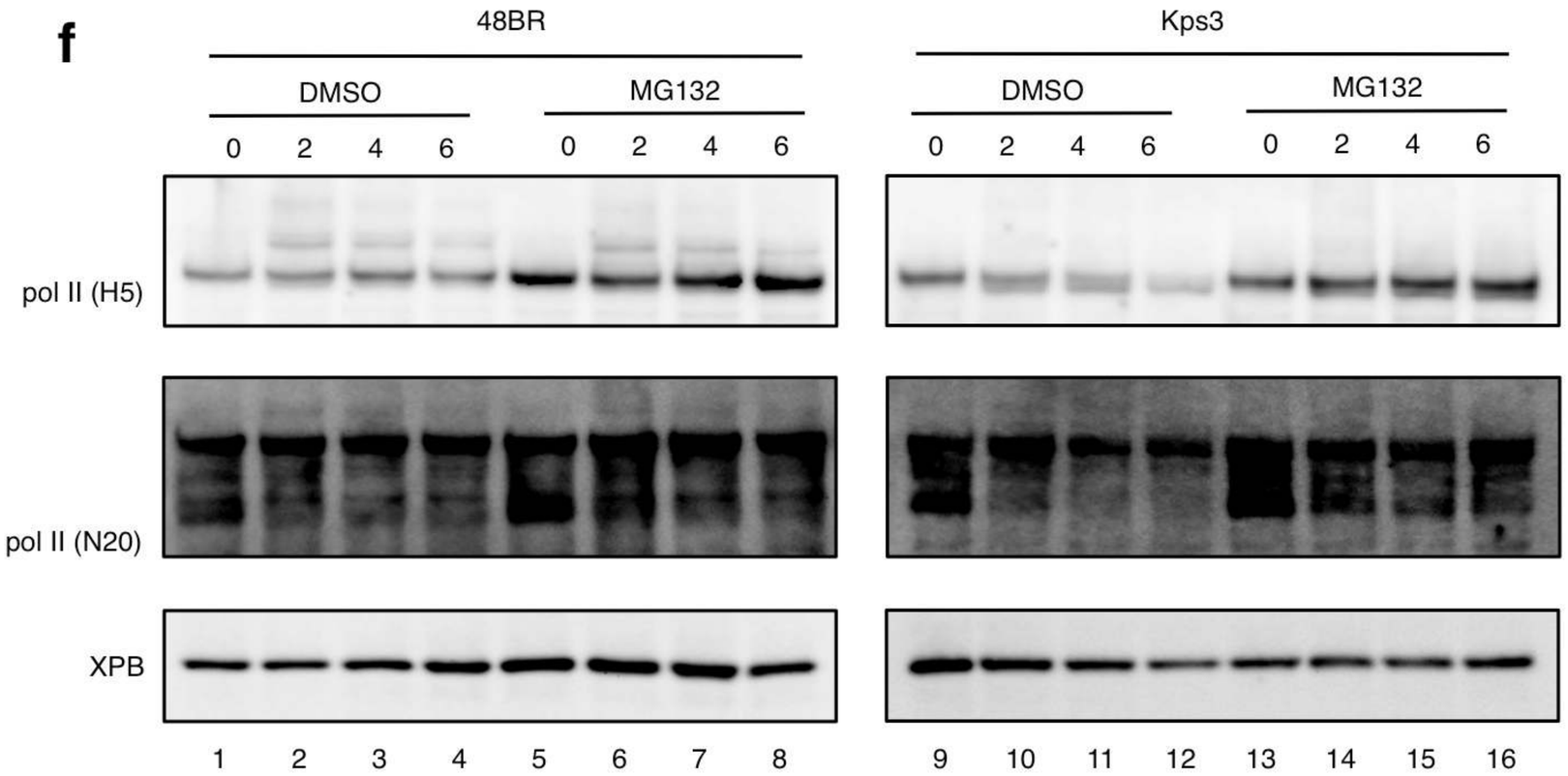
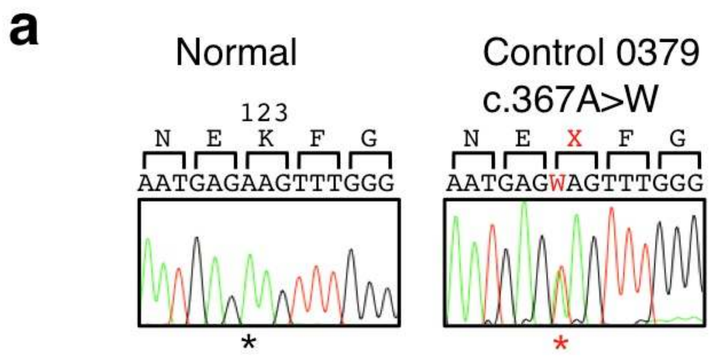
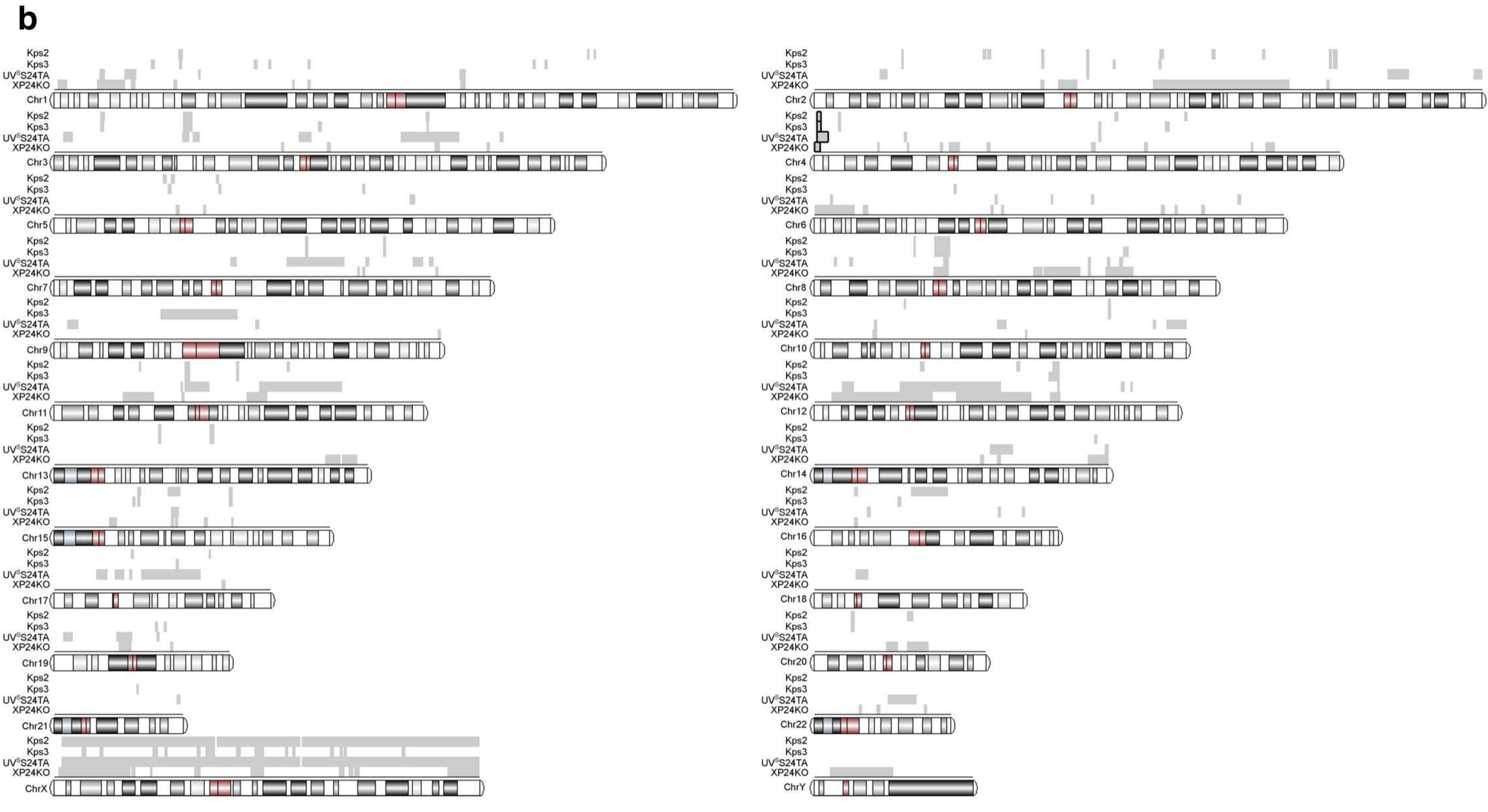
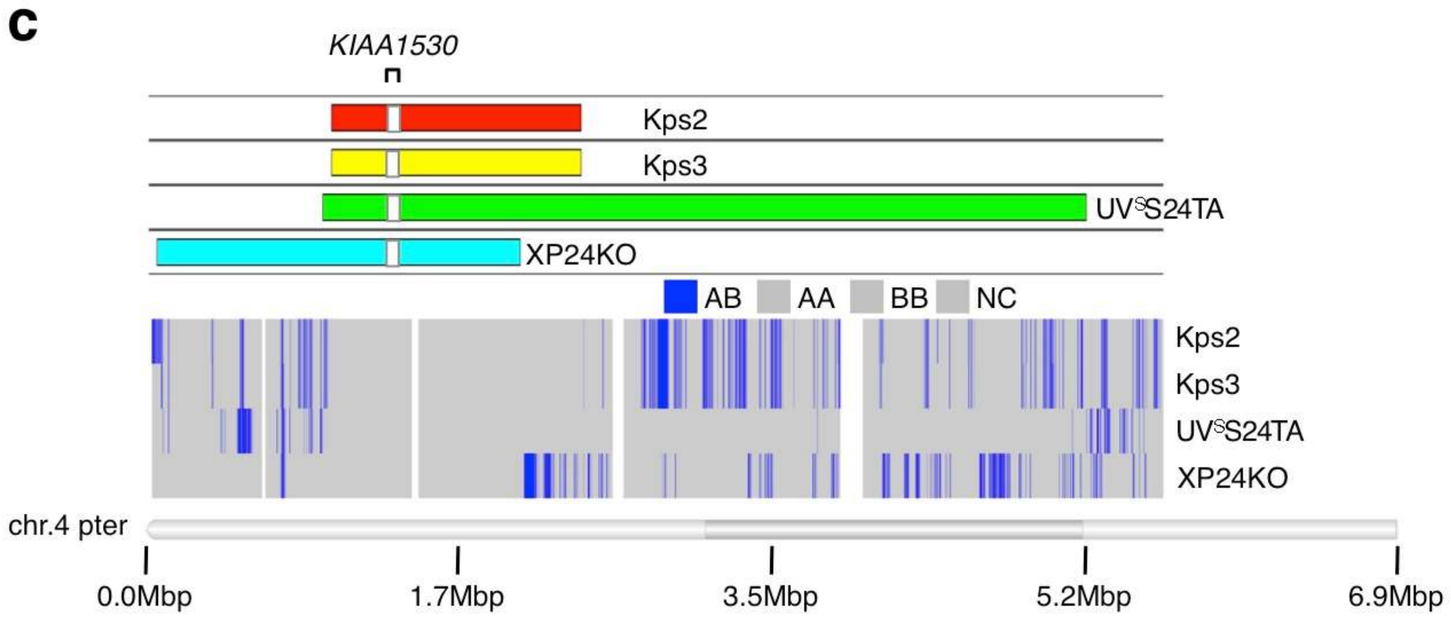

f
48BR
Kps3
DMSO
MG132
DMSO
MG132
0 2 4 6 0 2 4 6 0 2 4 6 0 2 4 6
pol II (H5)
pol II (N20)
XPB
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16

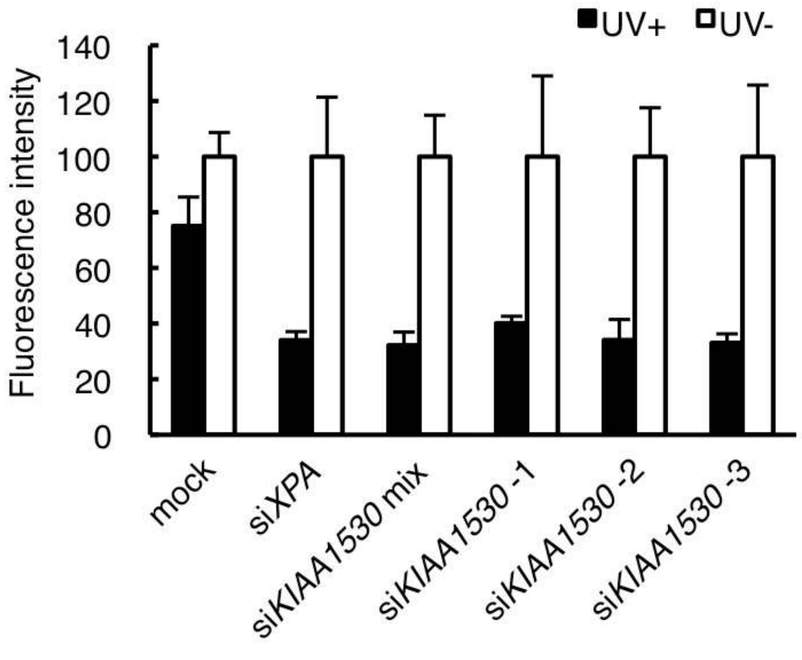
Fig.4



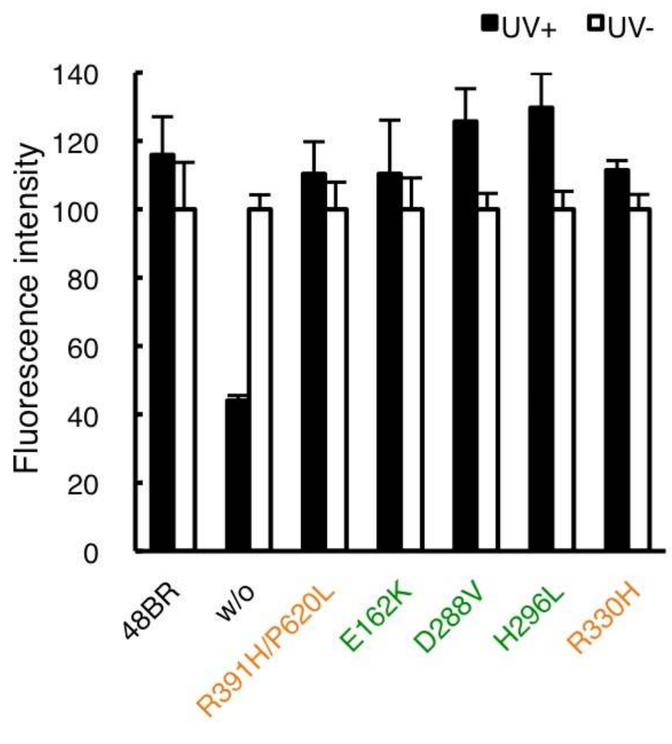




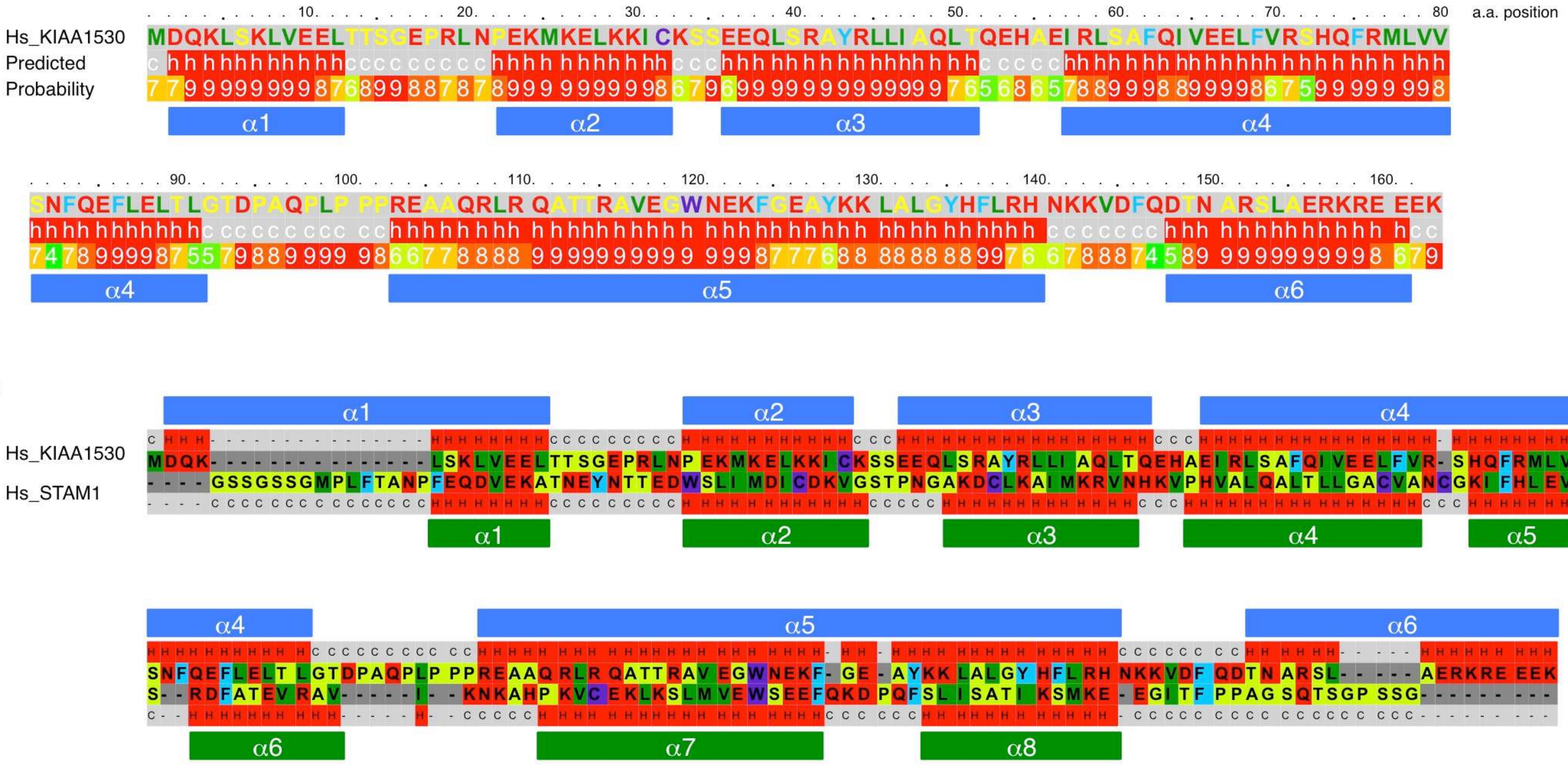
Supplementary figure S2

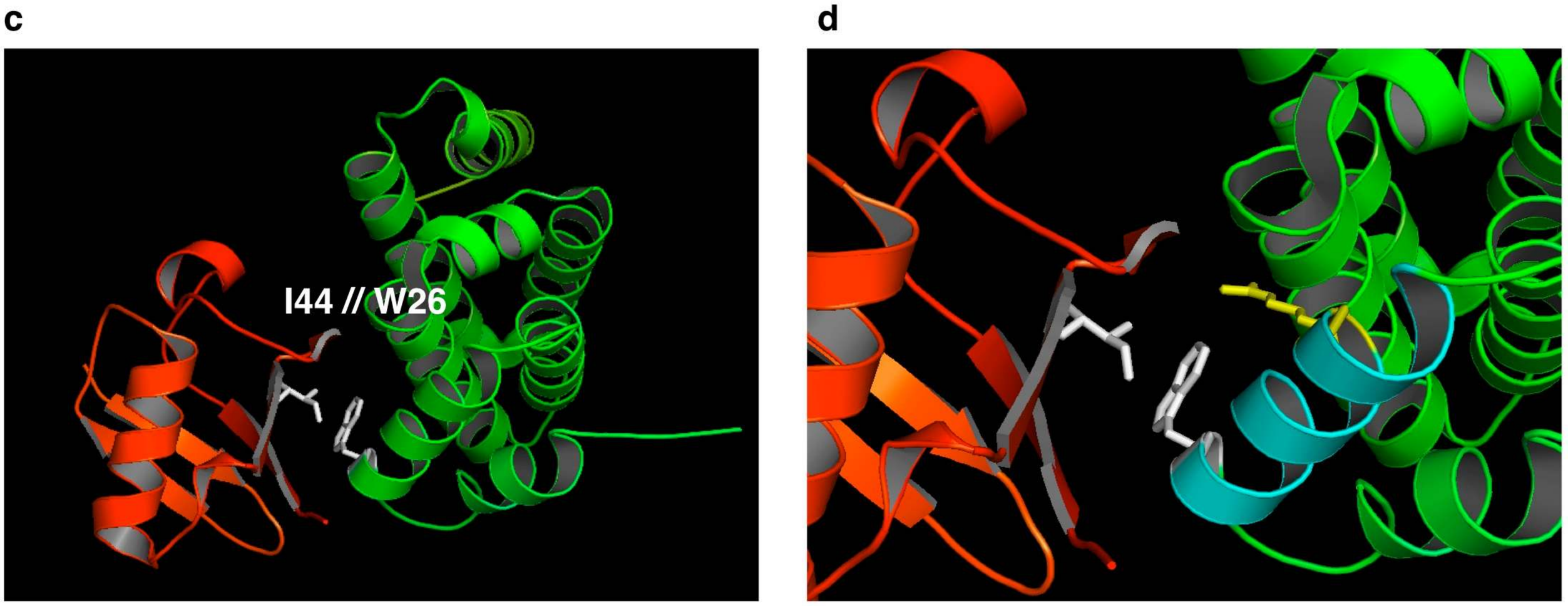


Supplementary figure S3

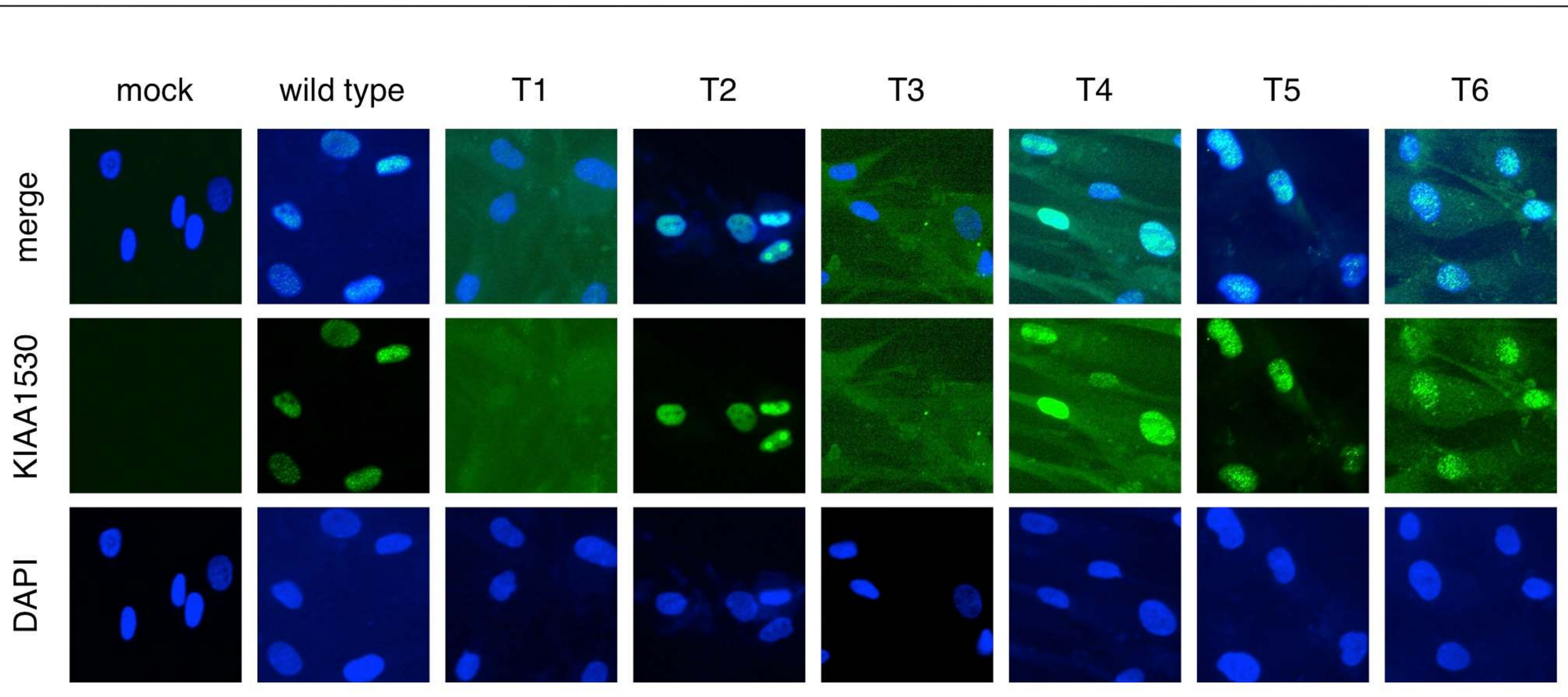


Supplementary figure S4

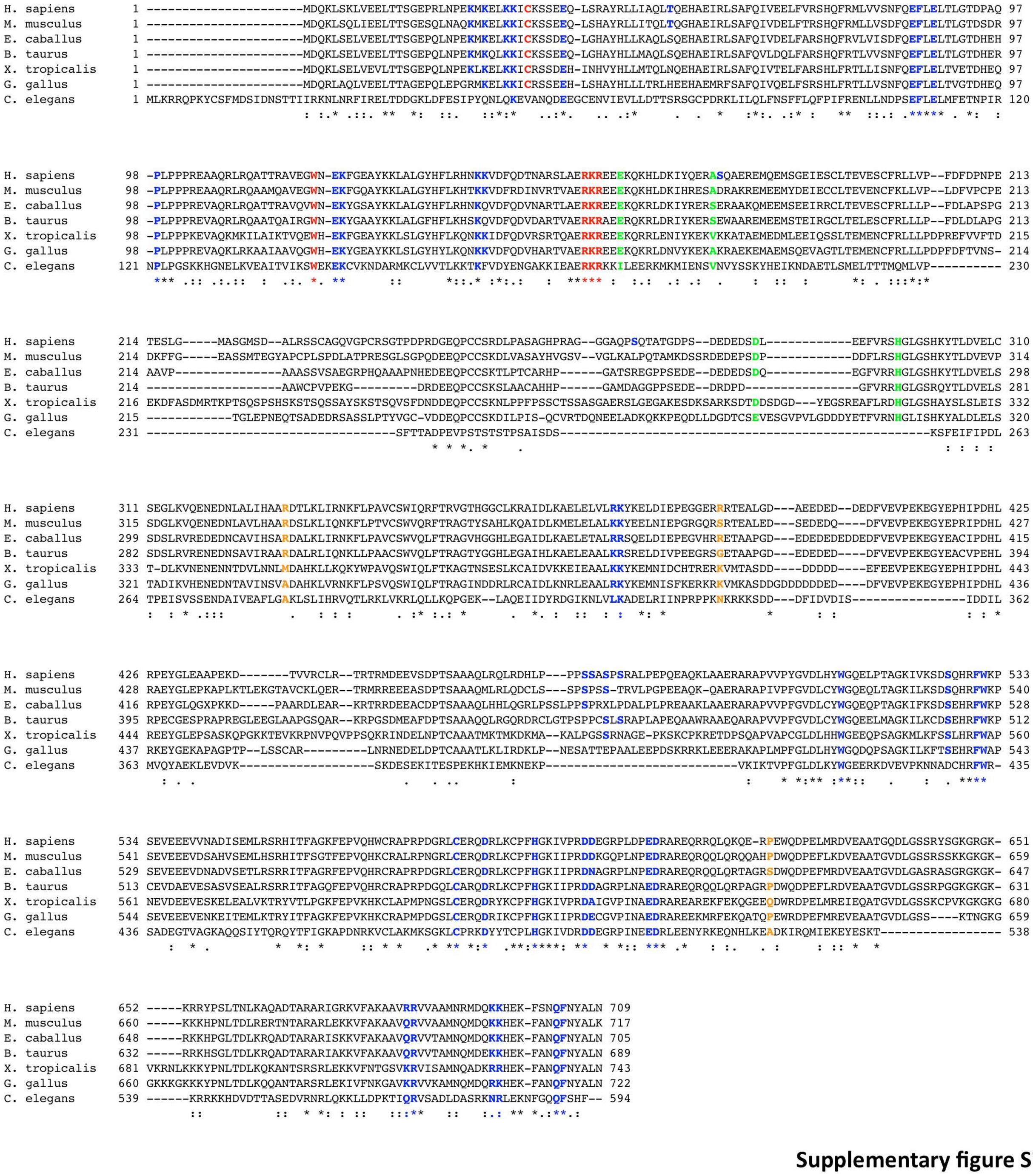




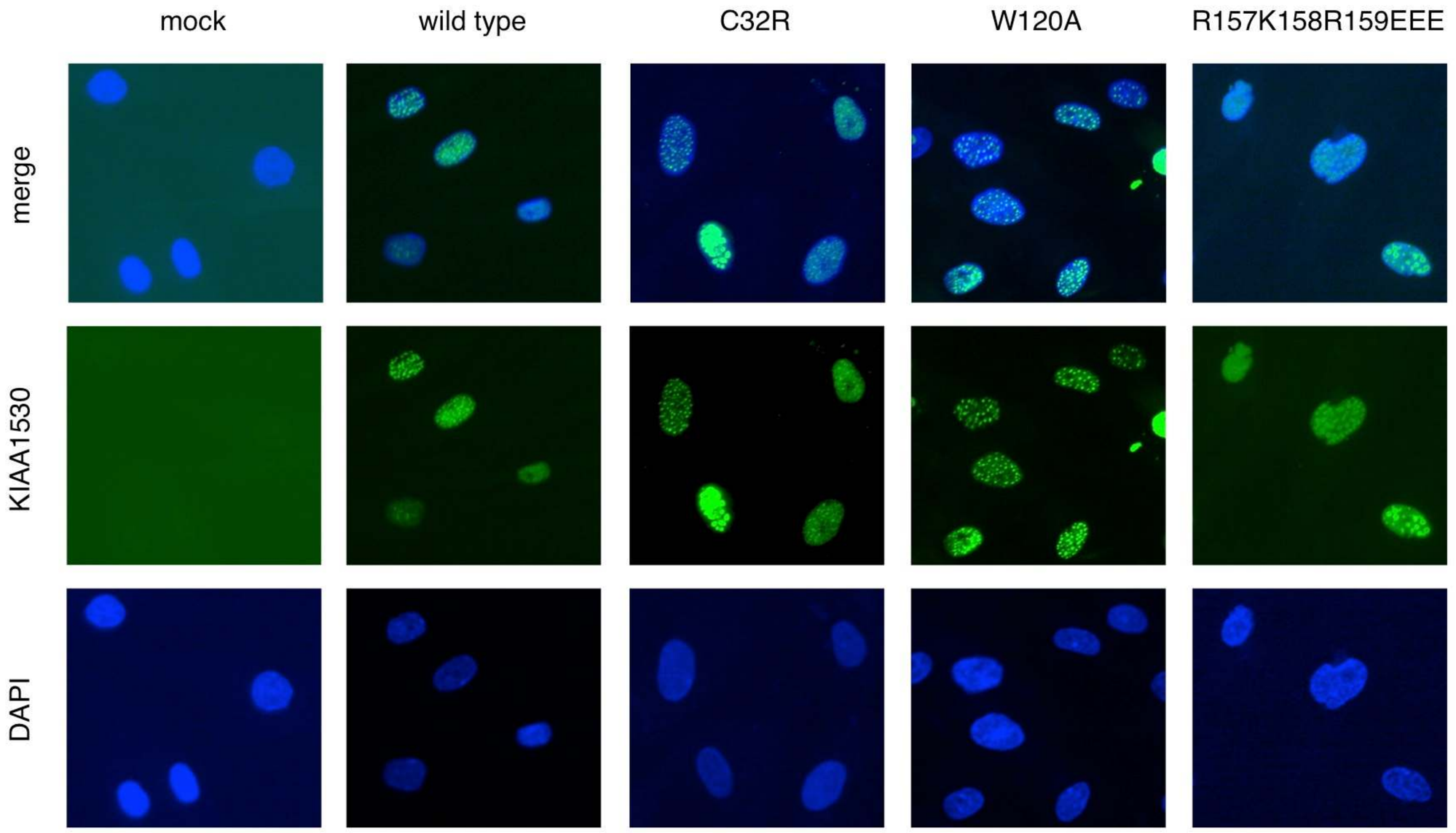
Supplementary figure S5



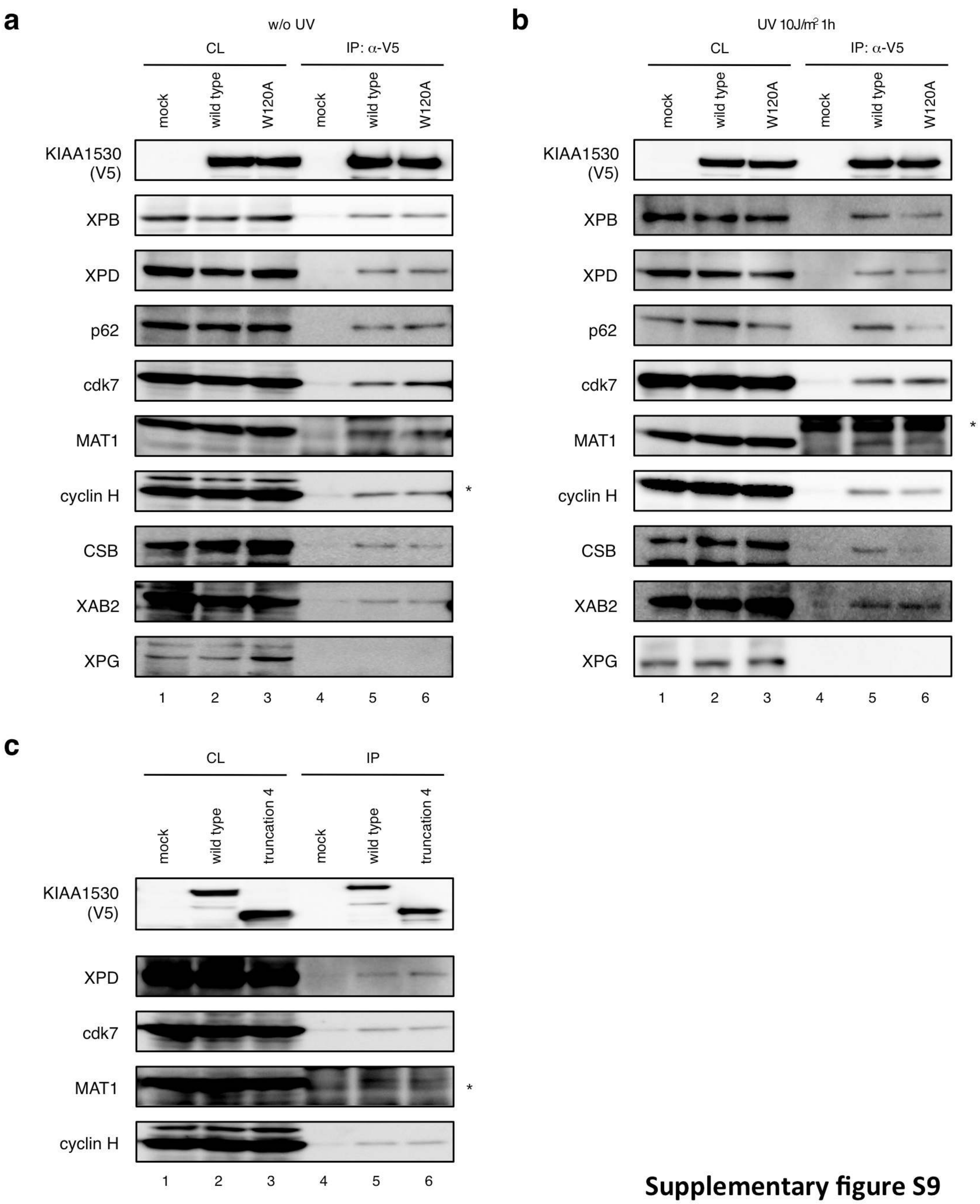
Supplementary figure S6



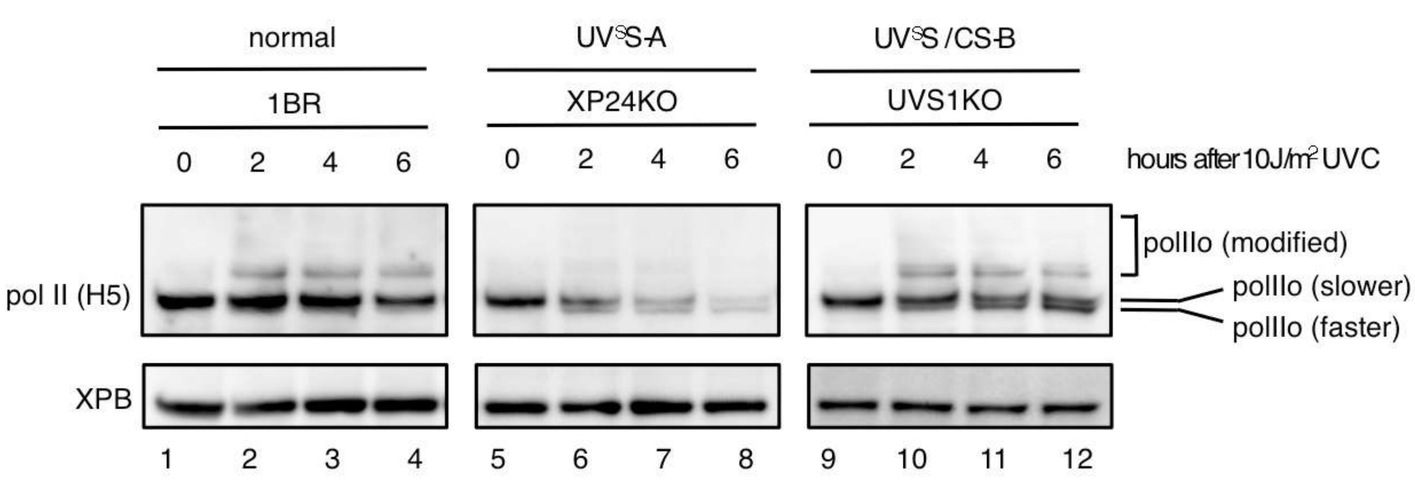
Supplementary figure S7



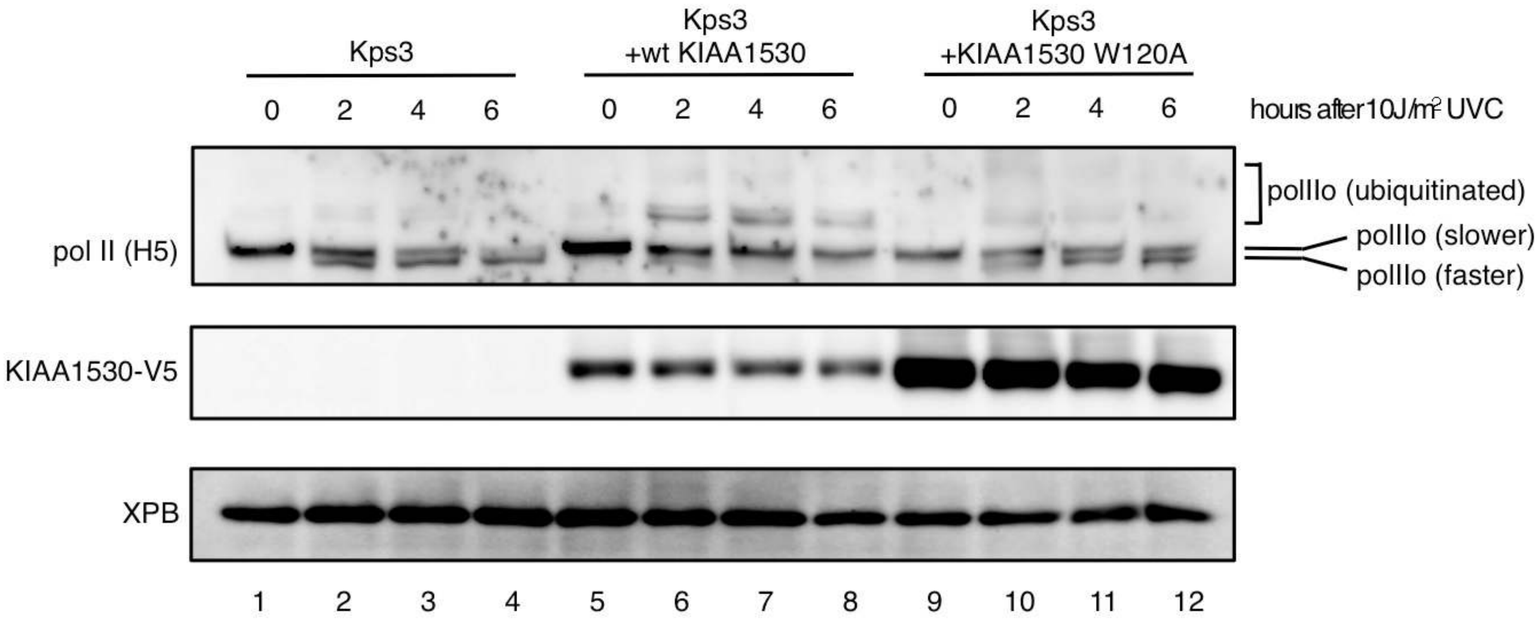
Supplementary figure S8



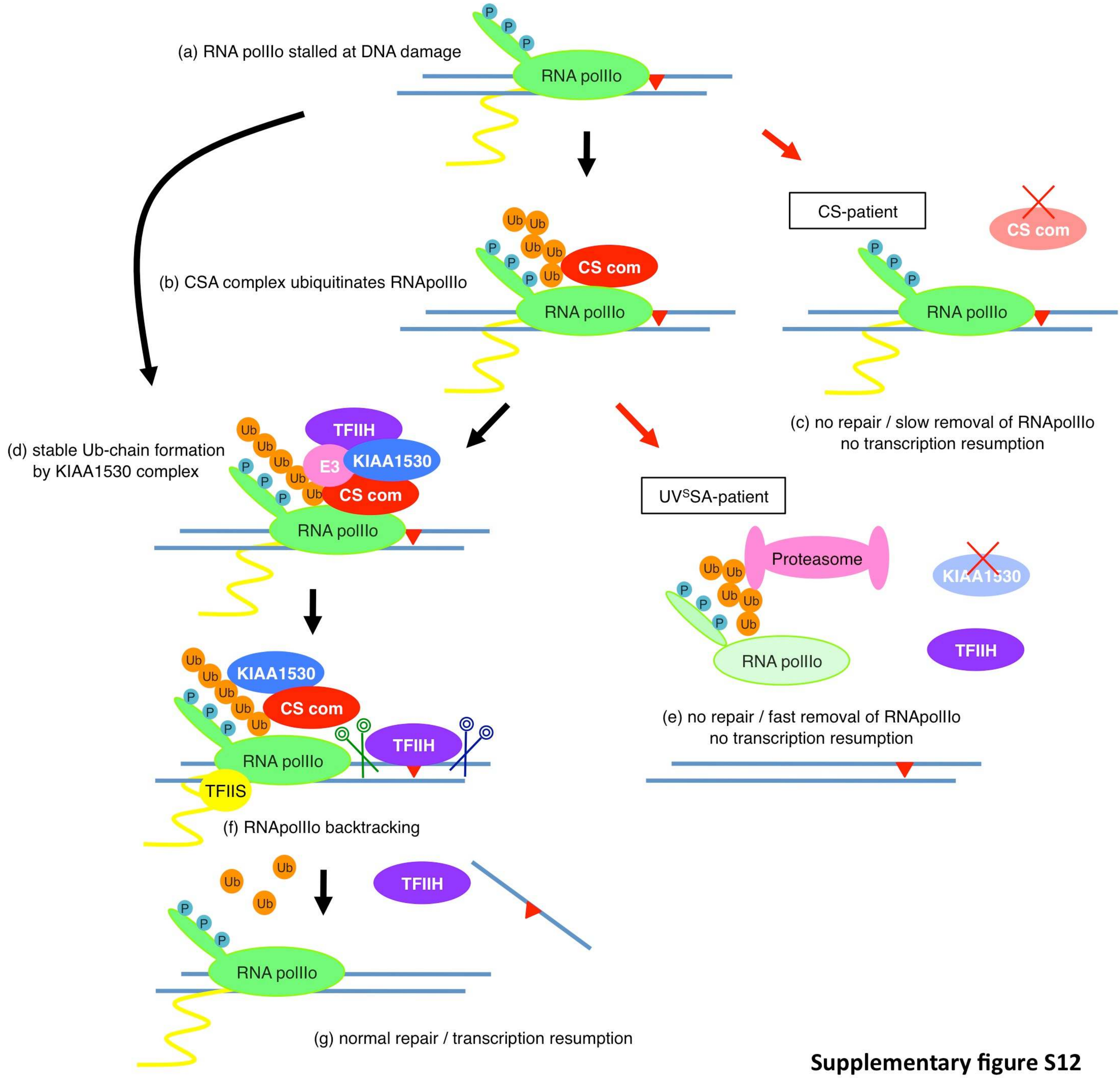
Supplementary figure S9



Supplementary figure S10



Supplementary figure S11



Supplementary figure S12