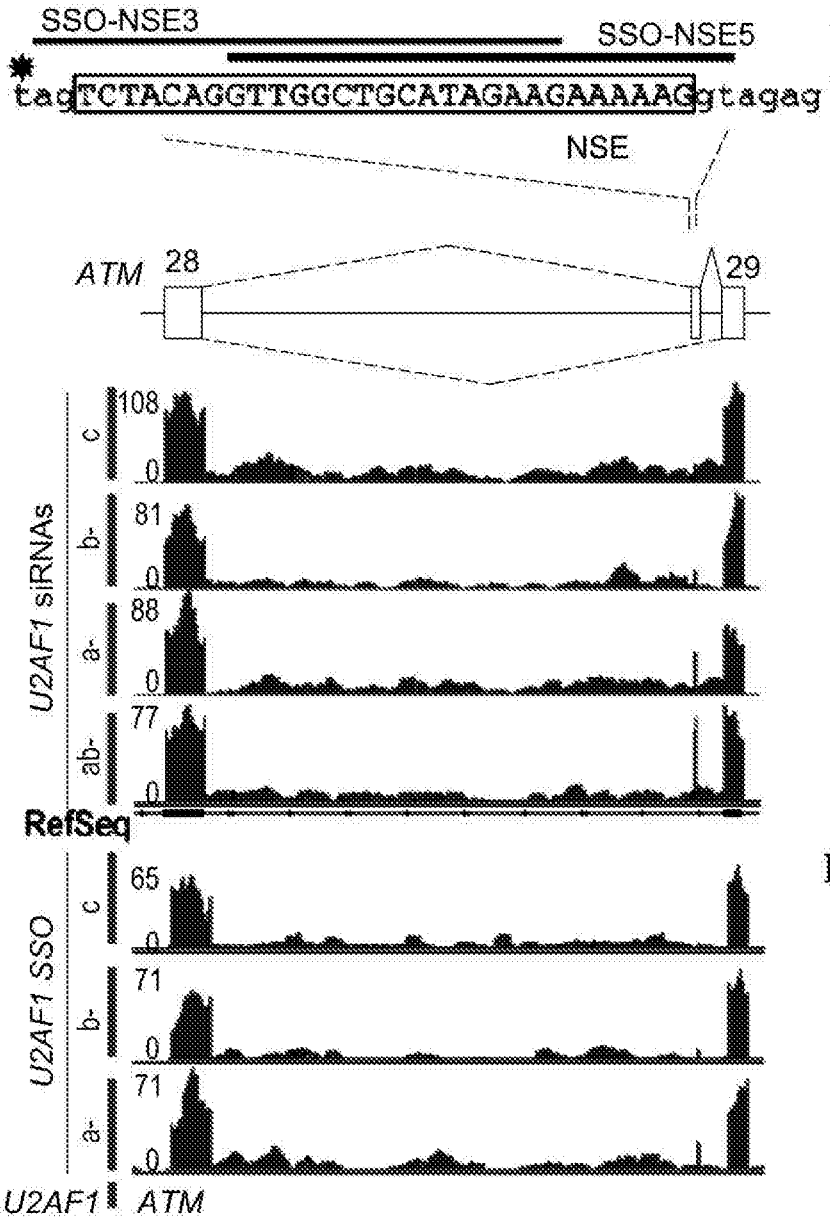


Fig. 1A

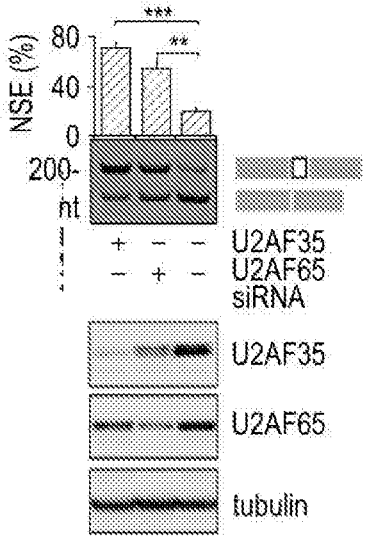


Fig. 1B

Fig.

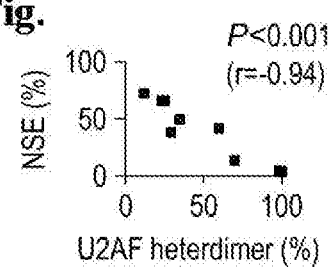


Fig. 1C

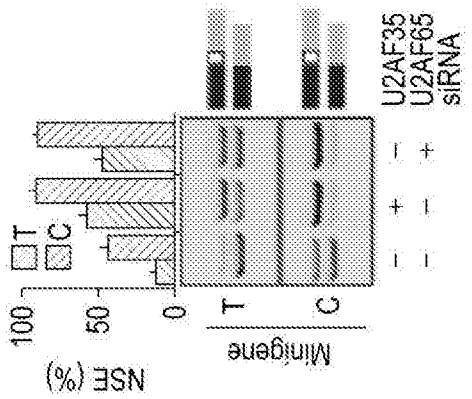


Fig. 2C

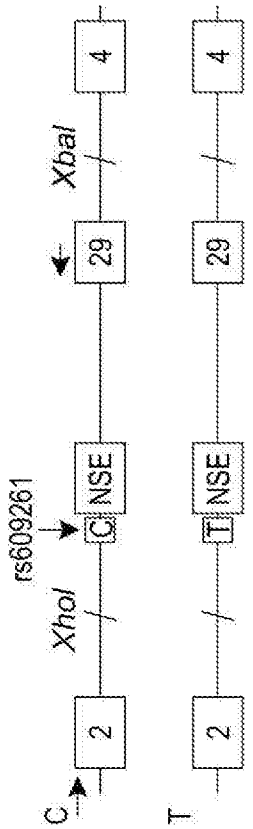


Fig. 2B

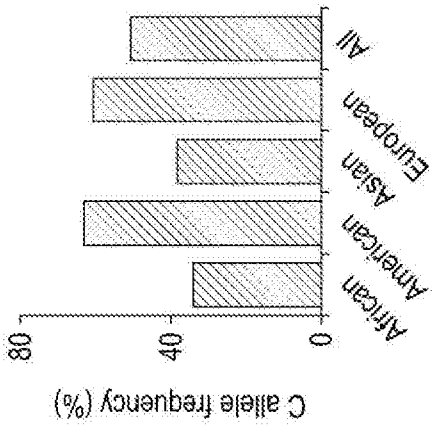


Fig. 2A

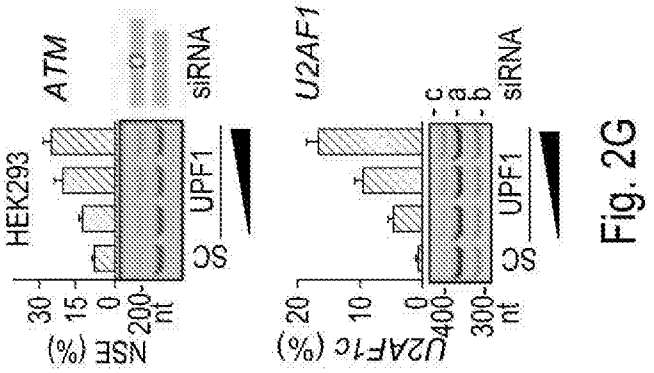


Fig. 2G

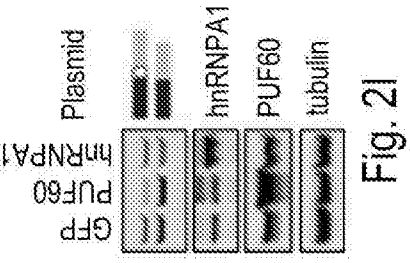


Fig. 2I

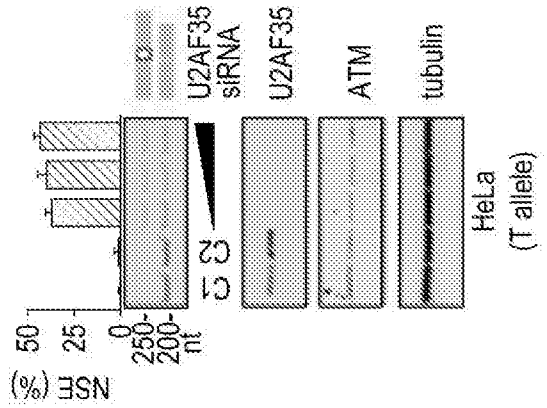


Fig. 2F

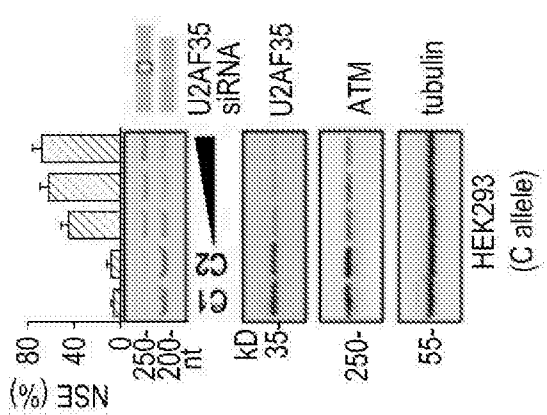


Fig. 2E

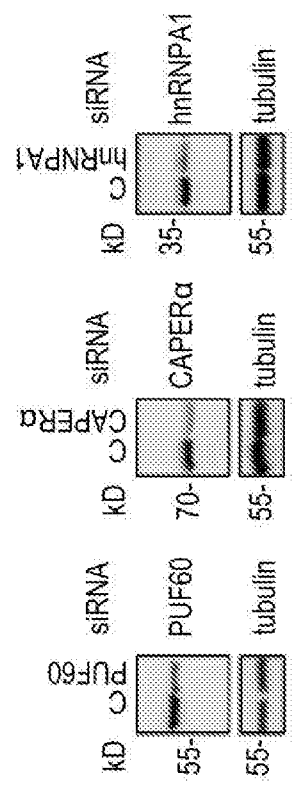


Fig. 2H

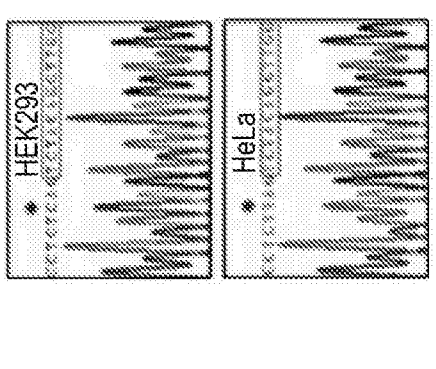
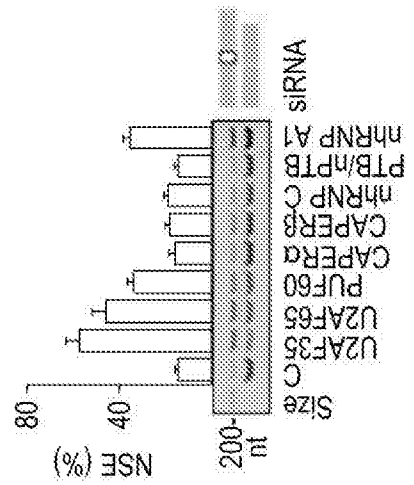


Fig. 2D



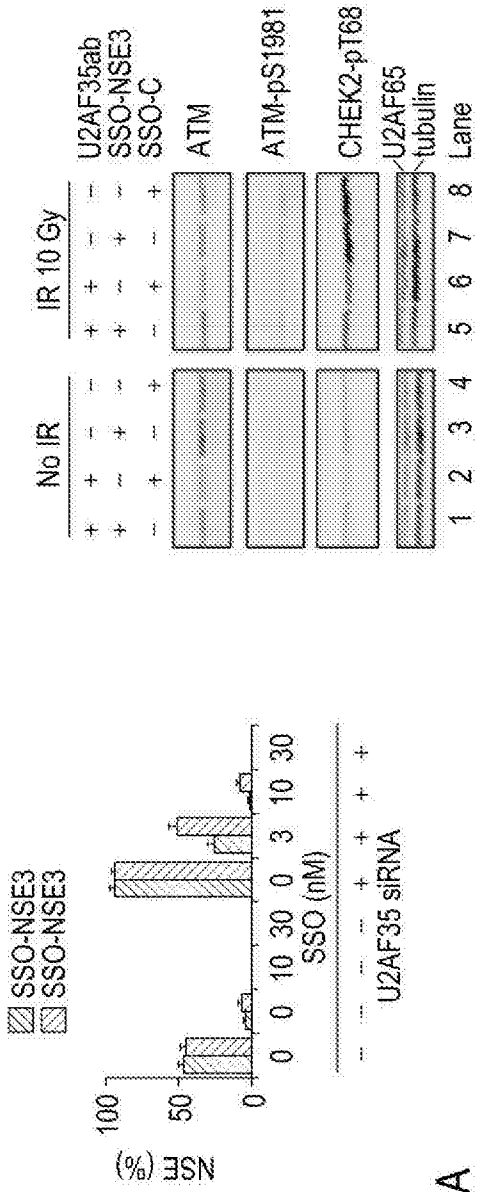


Fig. 3A

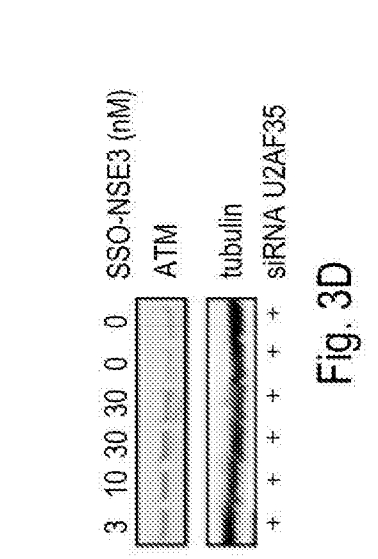


Fig. 3C

Fig. 3D

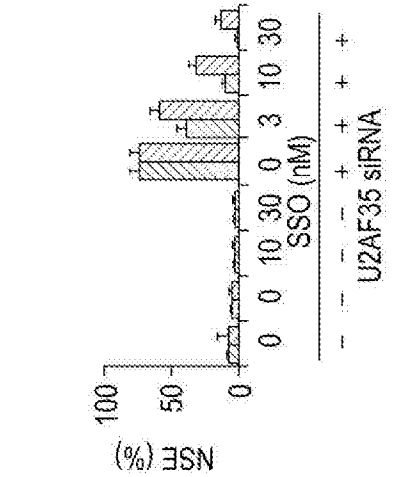


Fig. 3B

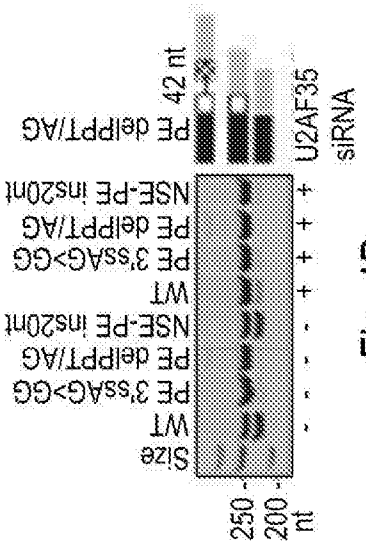

Size
WT
PE 3'ssAG>GG
PE delPPT/AG
NSE-PE ins20nt
WT
PE 3'ssAG>GG
PE delPPT/AG
NSE-PE ins20nt
PE delPPT/AG
42 nt
U2AF35
siRNA
250
200
nt

Fig. 4B

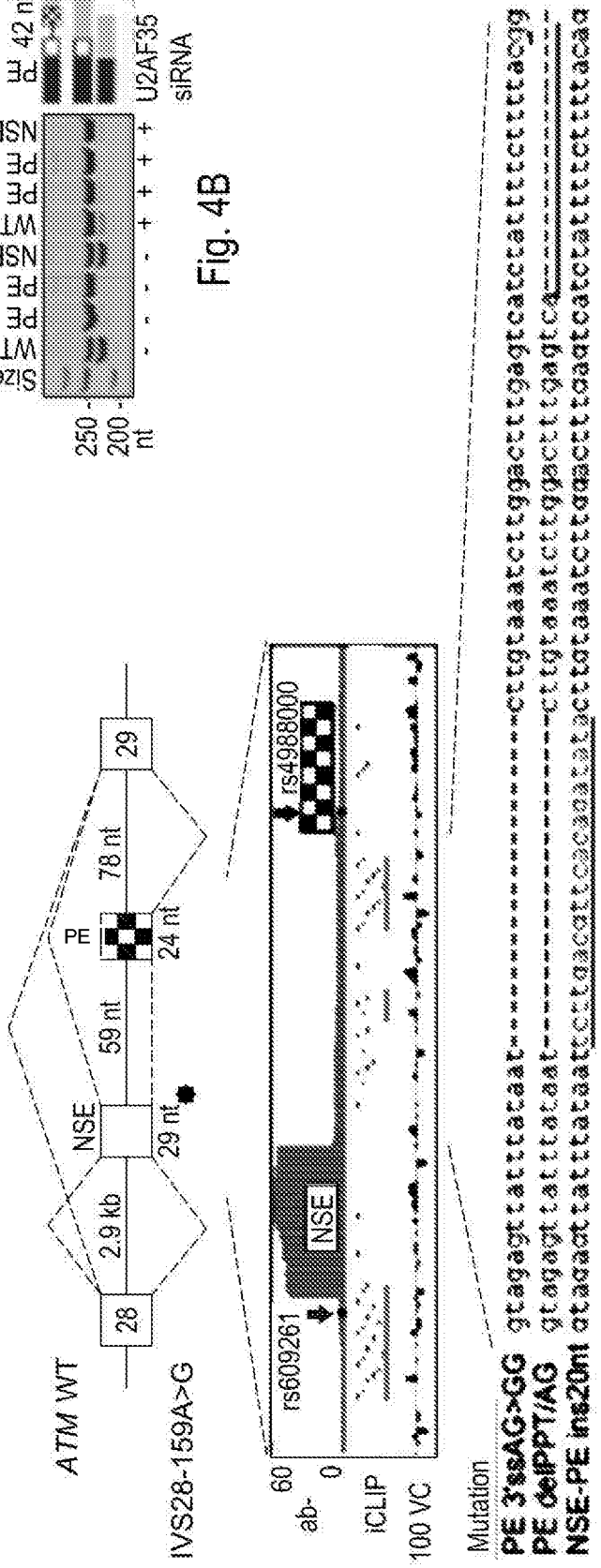

ATM WT
IVS28-159A>G
28
2.9 kb
NSE
29 nt
59 nt
PE
24 nt
78 nt
29
ab-
60
0
iCLIP
100 VC
rs609261
NSE
rs4988000
Mutation
PE 3'ssAG>GG
PE delPPT/AG
NSE-PE ins20nt

Fig. 4A

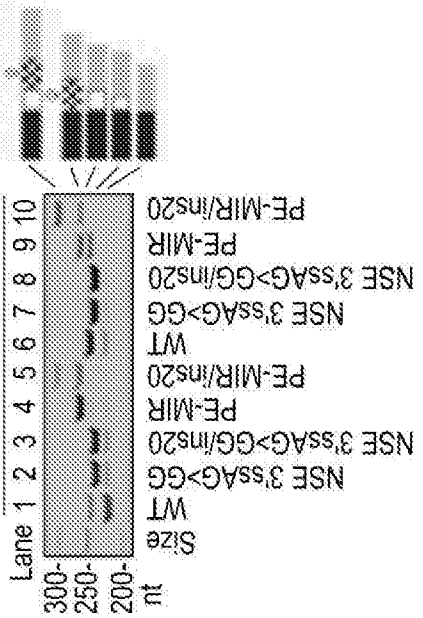


Fig. 4C

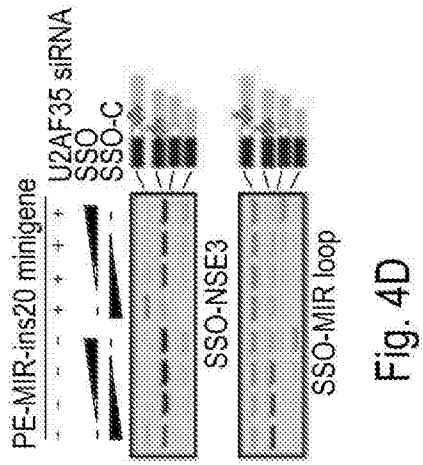


Fig. 4D

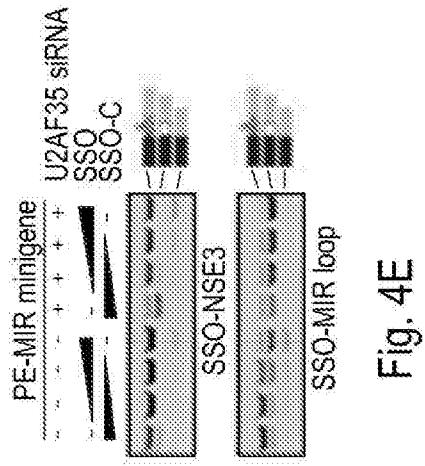


Fig. 4E

Fig. 4F

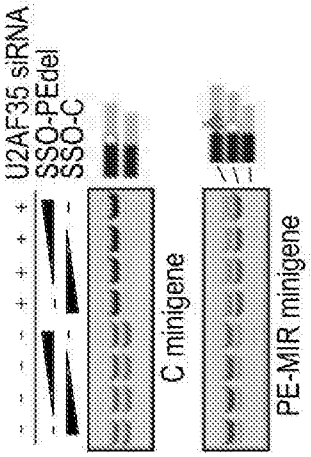


Fig. 4G

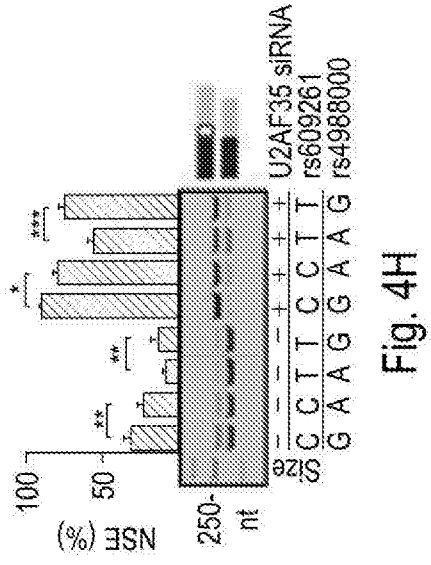


Fig. 4H

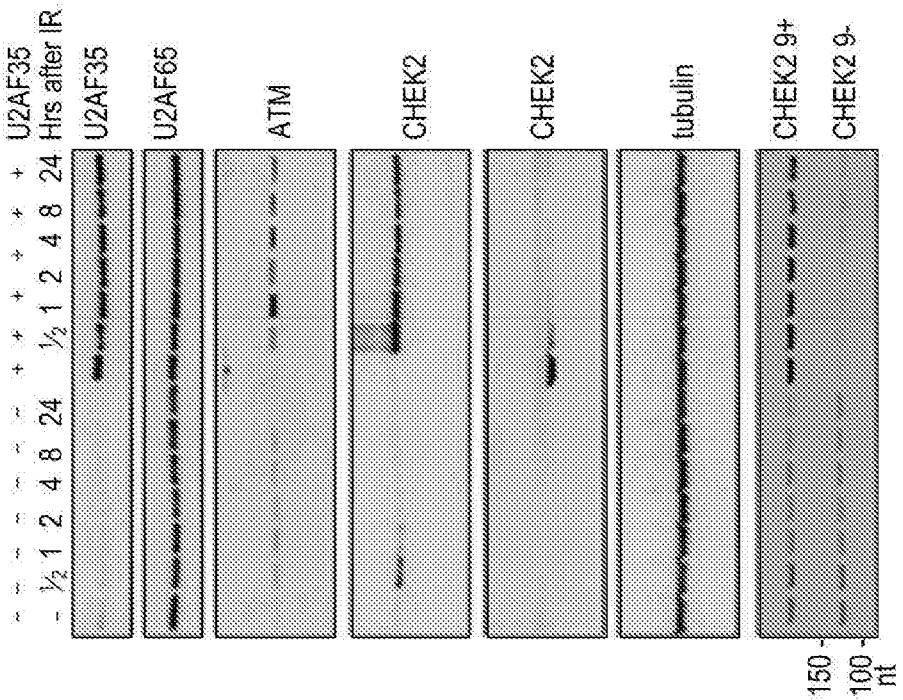

U2AF35
Hrs after IR
- ½ 1 2 4 8 24 - - - - - - + + + + + +
½ 1 2 4 8 24
U2AF35
U2AF65
ATM
CHEK2
CHEK2
tubulin
CHEK2 9+
CHEK2 9-
150
100
nt

Fig. 5B

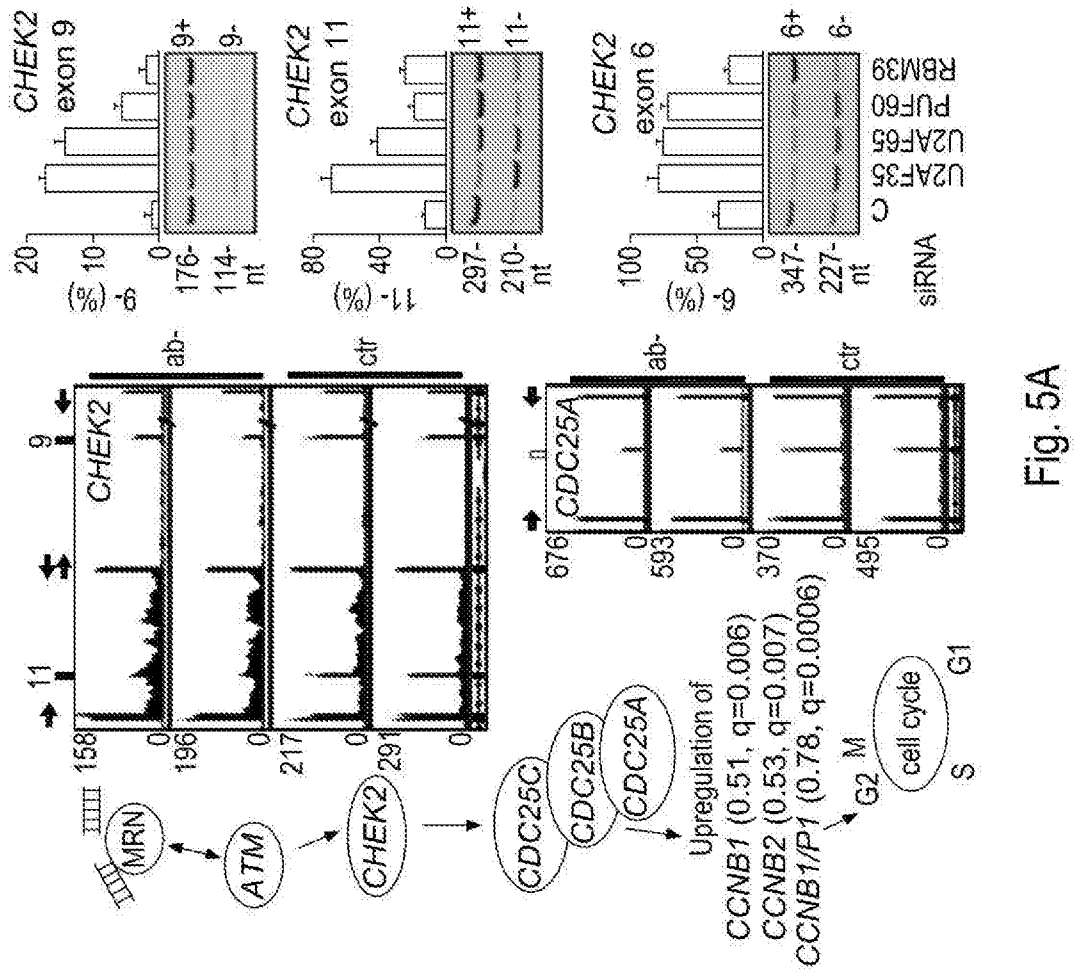

CHEK2 exon 9
CHEK2 exon 11
CHEK2 exon 6
9+
9-
11+
11-
6+
6-
U2AF35
U2AF65
PUF60
RBM39
C
siRNA
ab-
ctr
CHEK2
CDC25A
MRN
ATM
CHEK2
CDC25C
CDC25B
CDC25A
Upregulation of
CCNB1 (0.51, q=0.006)
CCNB2 (0.53, q=0.007)
CCNB1/P1 (0.78, q=0.0006)
cell cycle
G2
M
S
G1

Fig. 5A

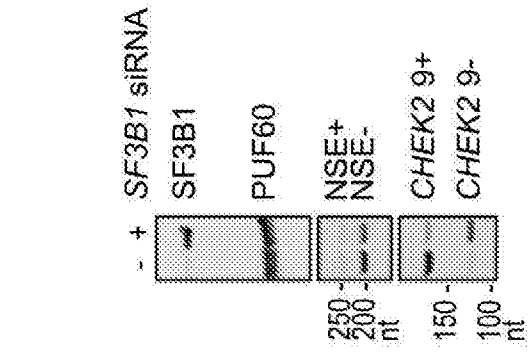


Fig. 5G

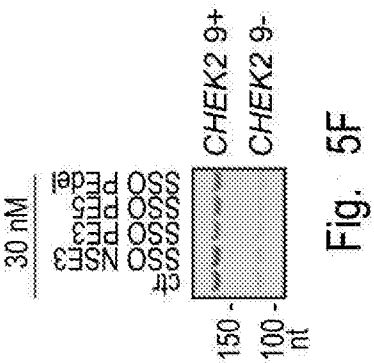


Fig. 5F



Fig. 5E

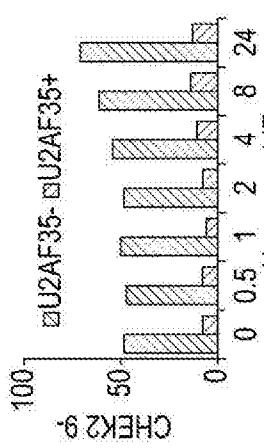


Fig. 5C

Fig. 5D

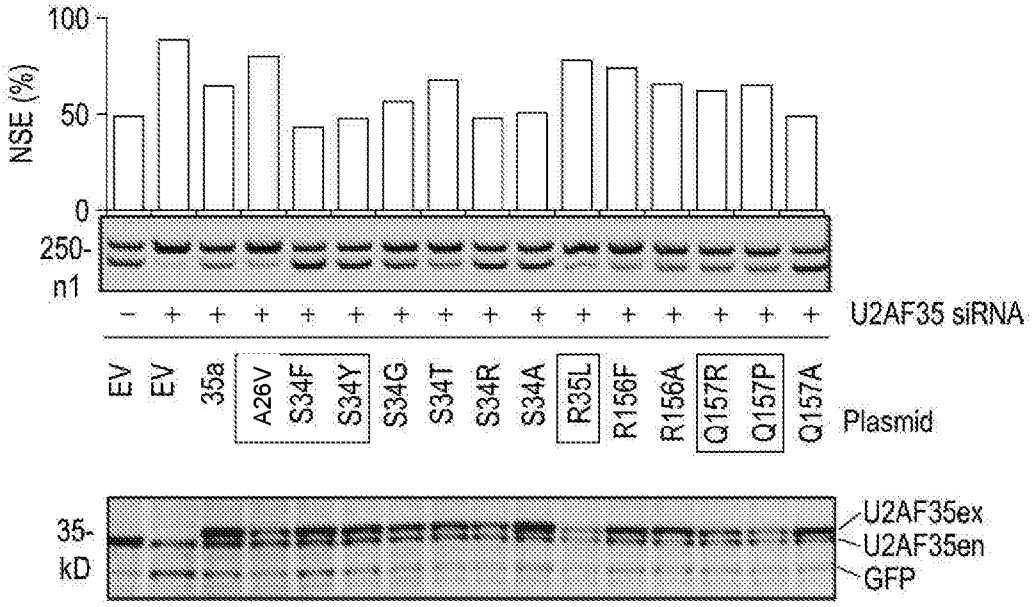

100
50
0
NSE (%)
250-
n1
U2AF35 siRNA
EV
EV
35a
A26V
S34F
S34Y
S34G
S34T
S34R
S34A
R35L
R156F
R156A
Q157R
Q157P
Q157A
Plasmid
35-
kD
U2AF35ex
U2AF35en
GFP

Fig. 6

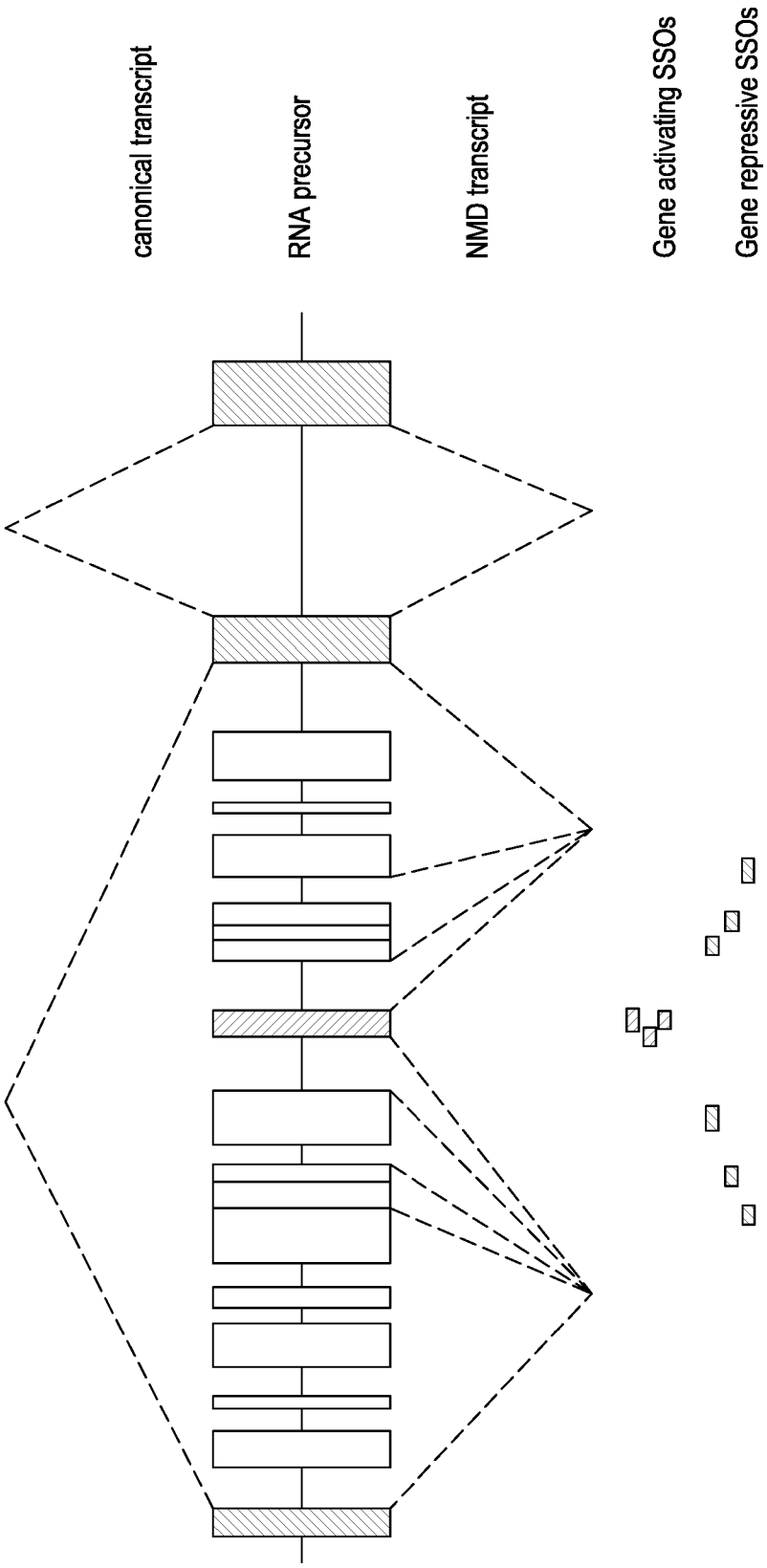

canonical transcript
RNA precursor
NMD transcript
Gene activating SSOs
Gene repressive SSOs

Fig. 7

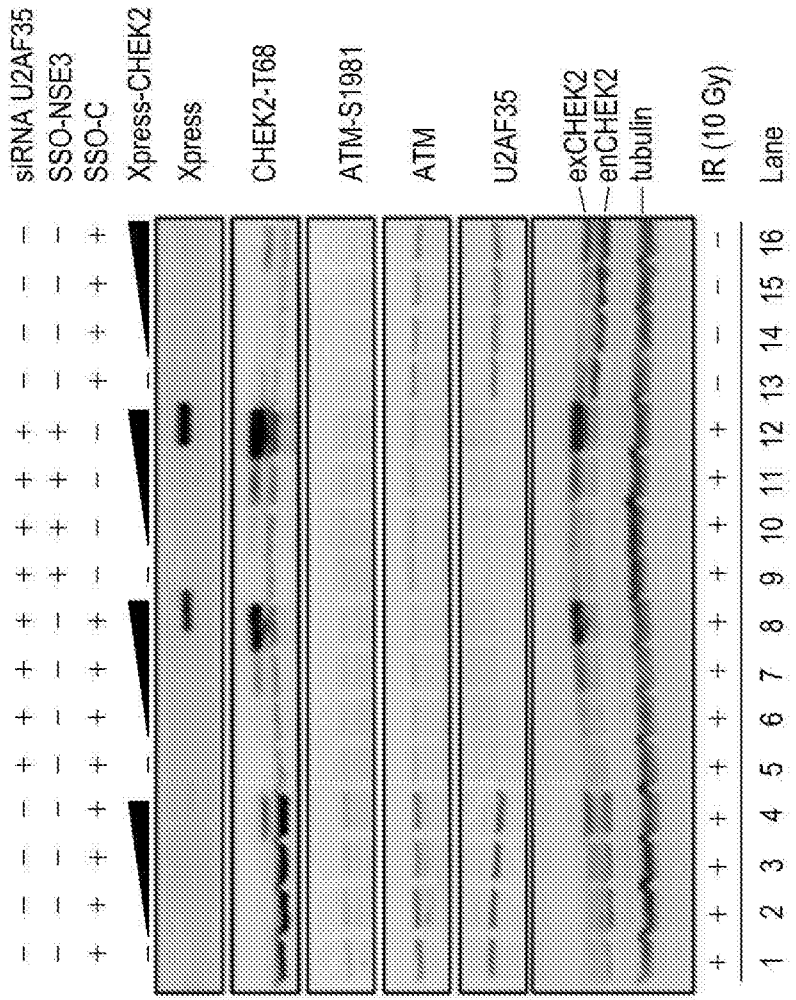


Fig. 8A

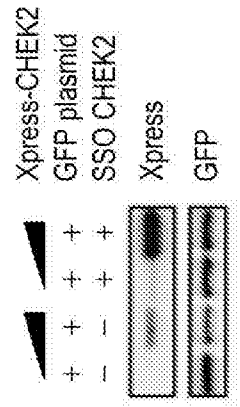


Fig. 8B

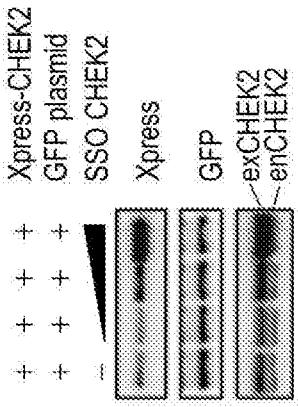


Fig. 8C

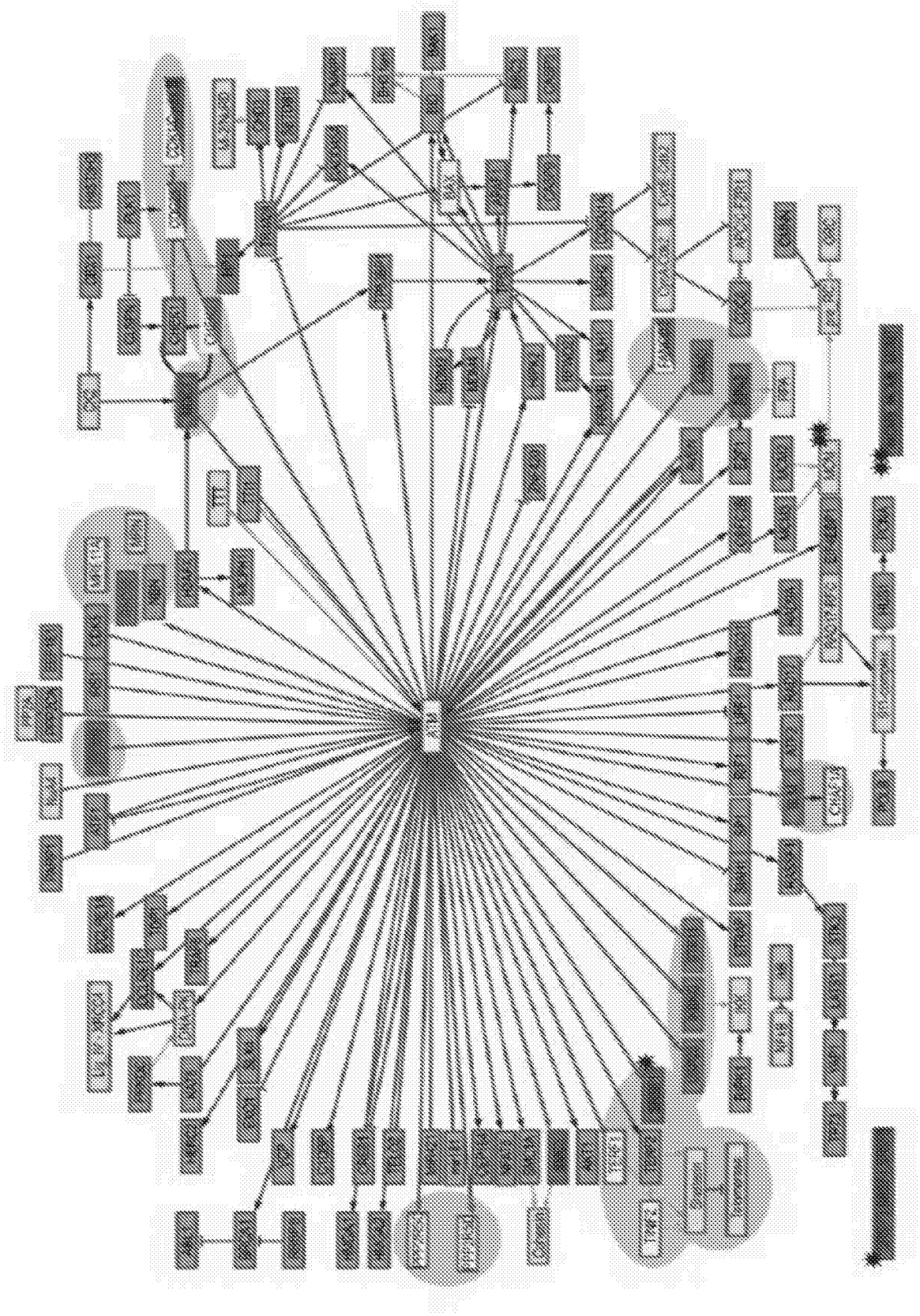


Fig. 9

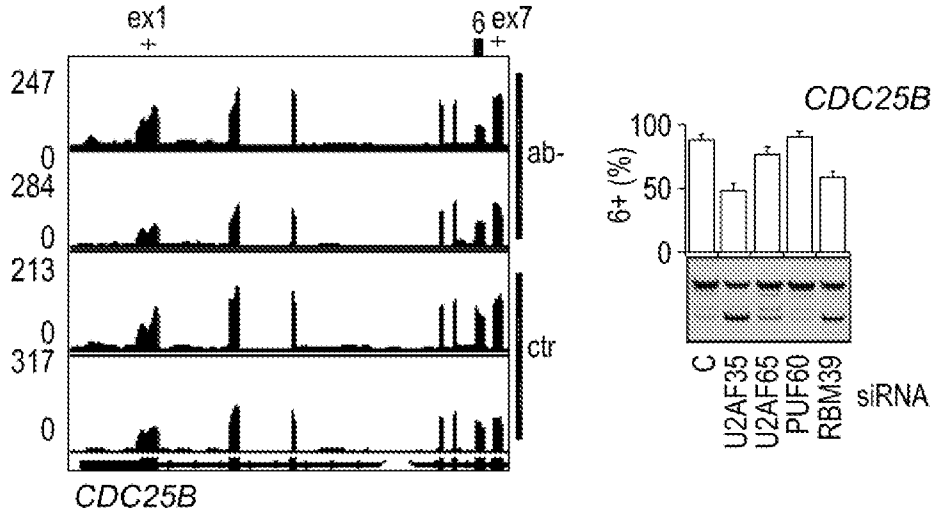


Fig. 10A

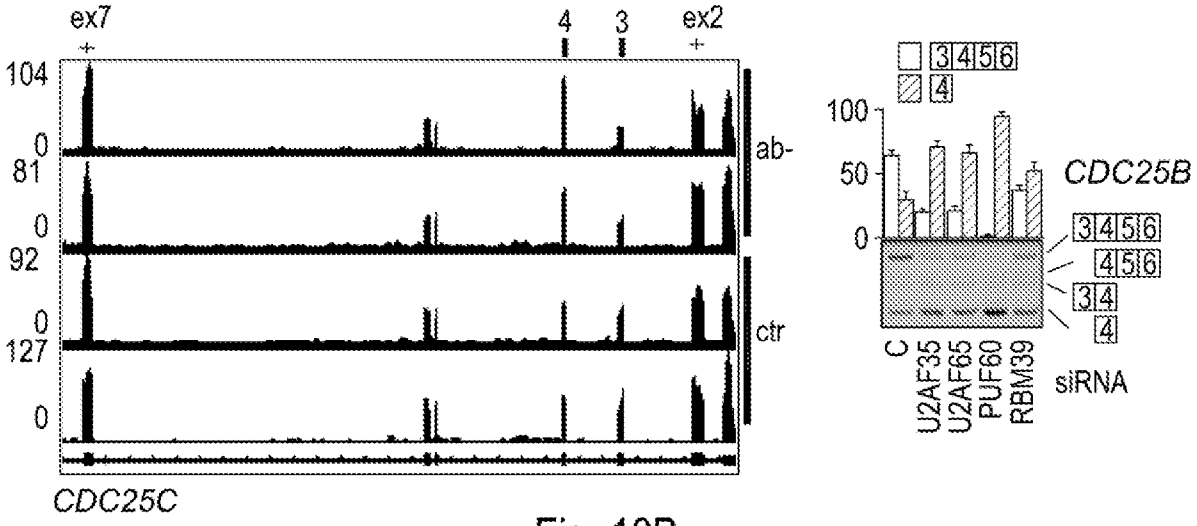


Fig. 10B

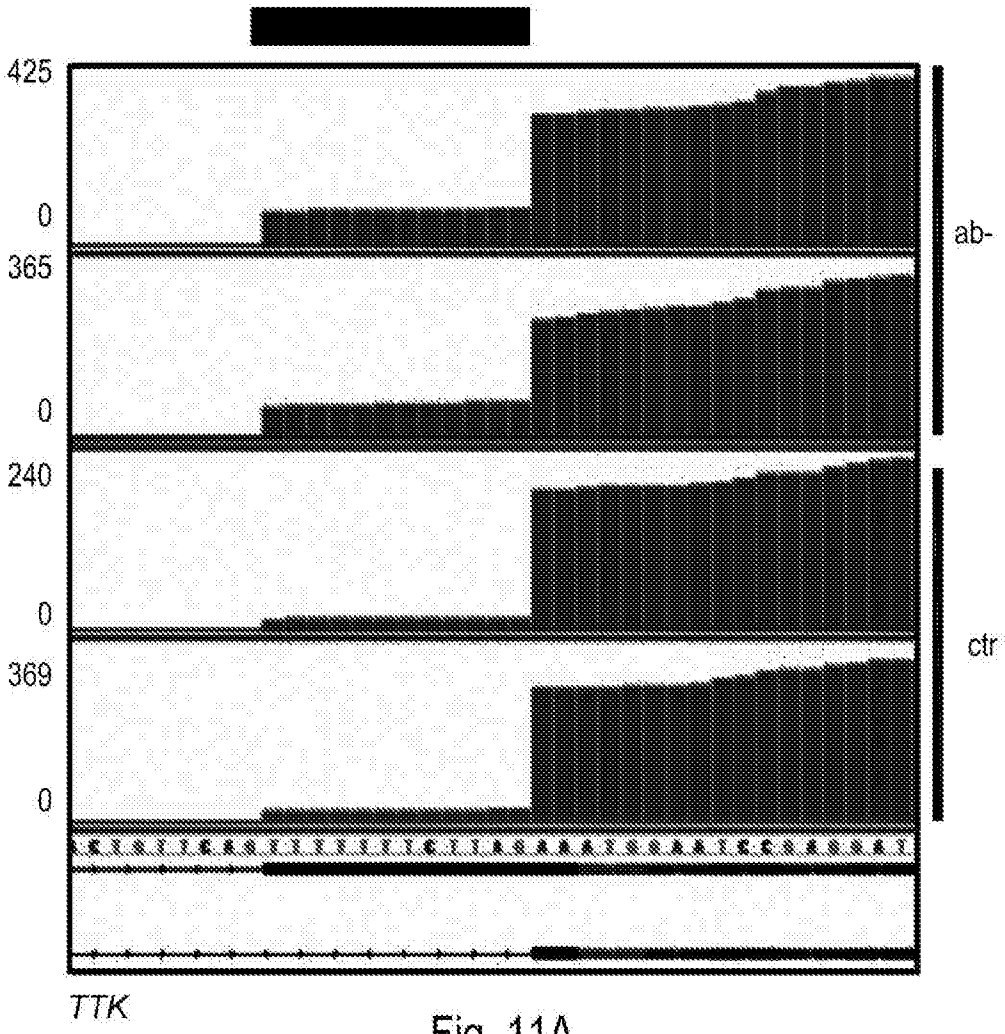


Fig. 11A

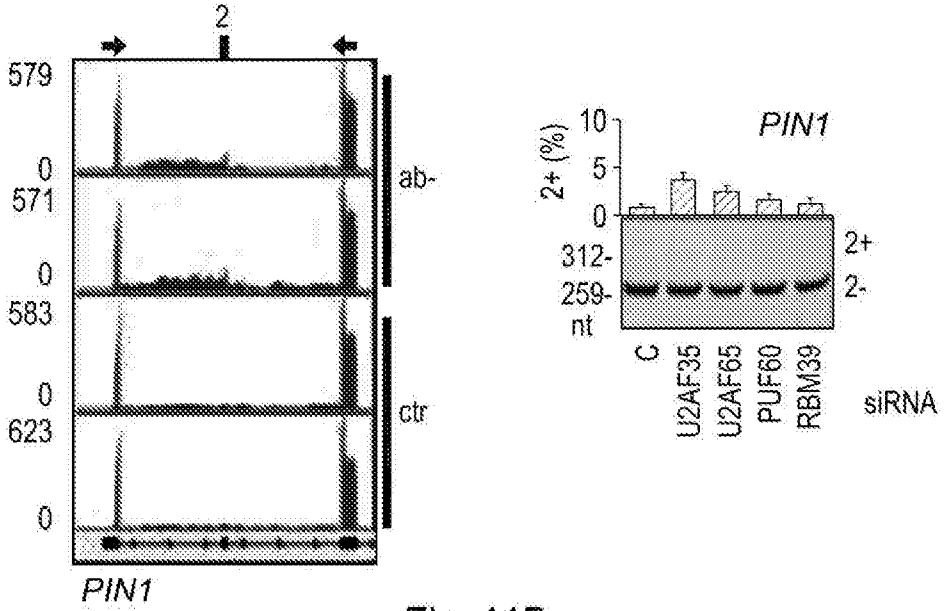


Fig. 11B

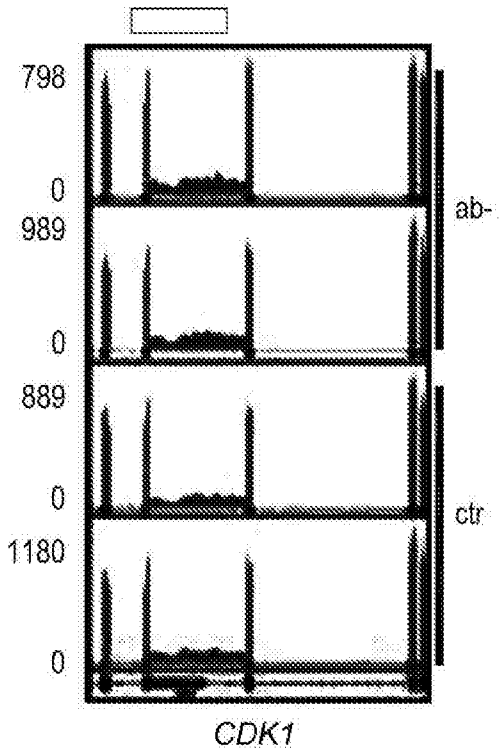
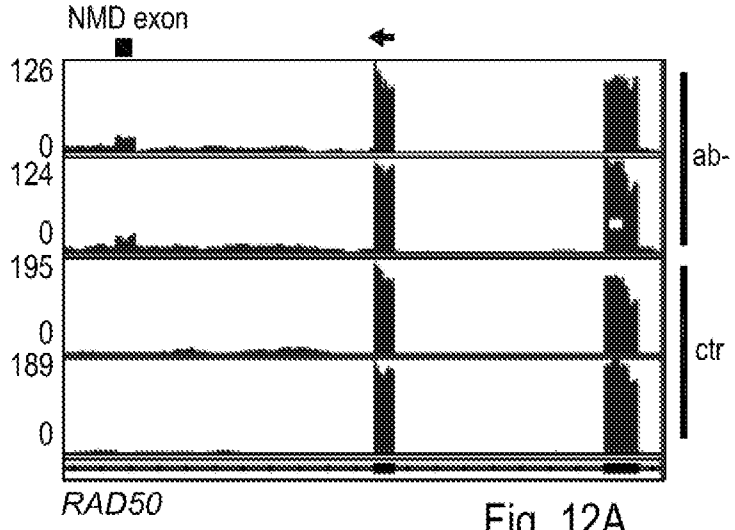


Fig. 11C



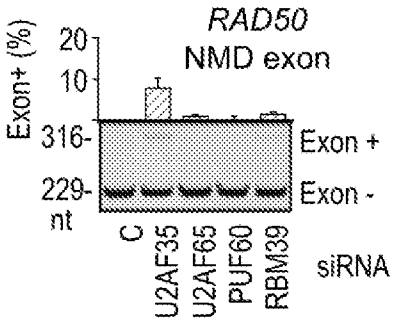
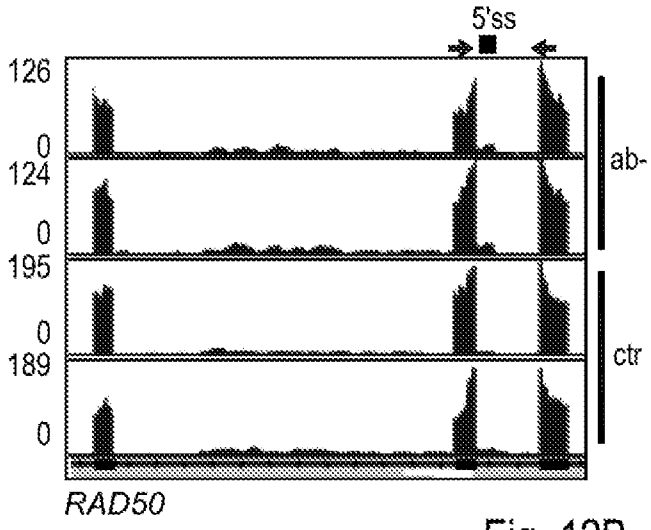


Fig. 12A



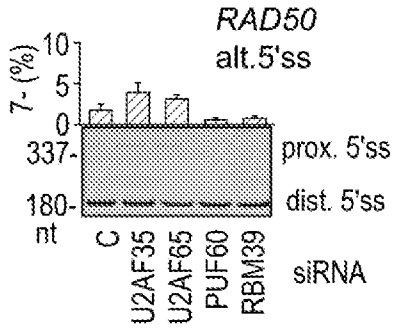


Fig. 12B

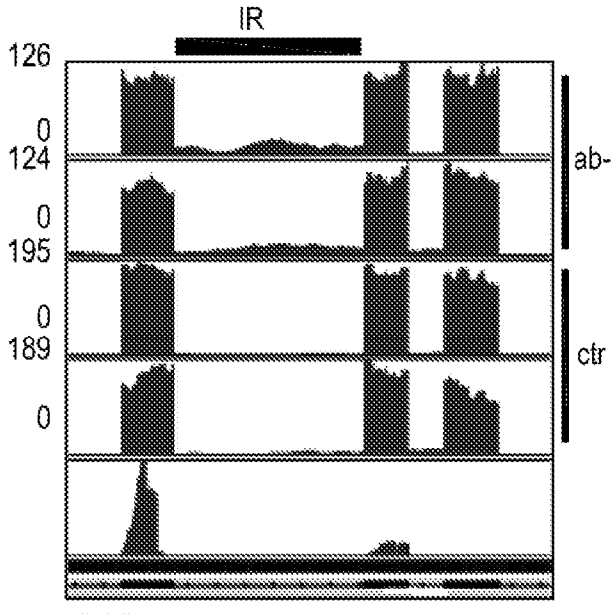


Fig. 12C

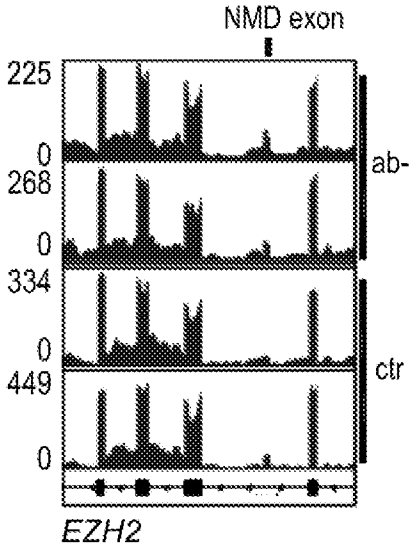


Fig. 12D

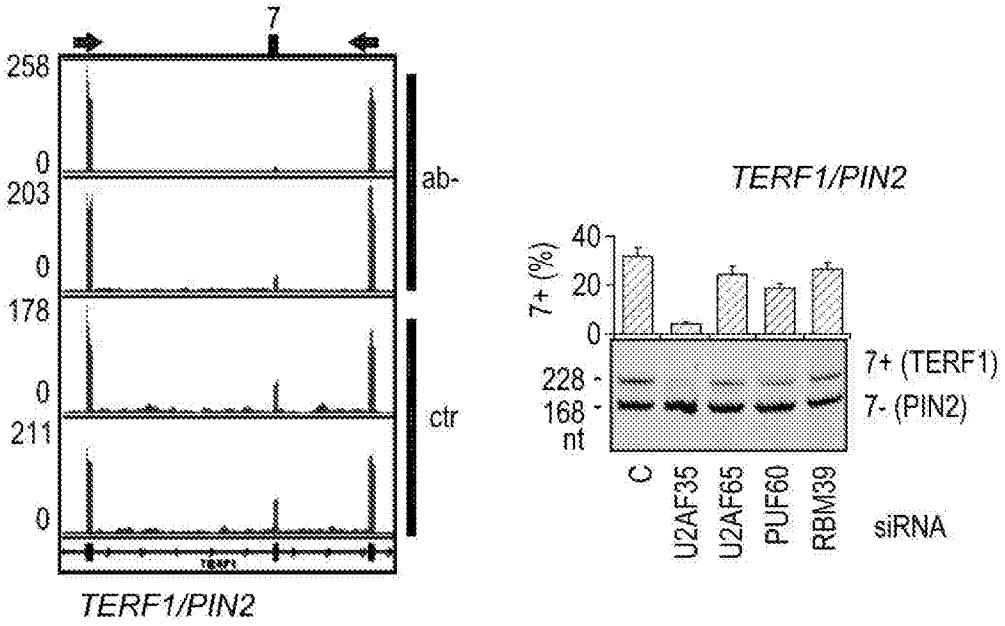


Fig. 13A

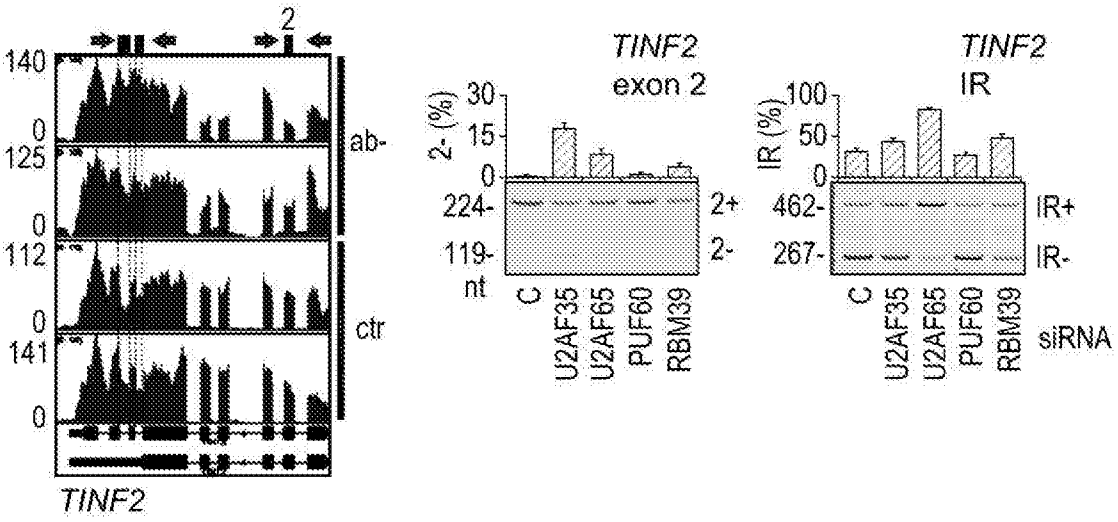


Fig. 13B

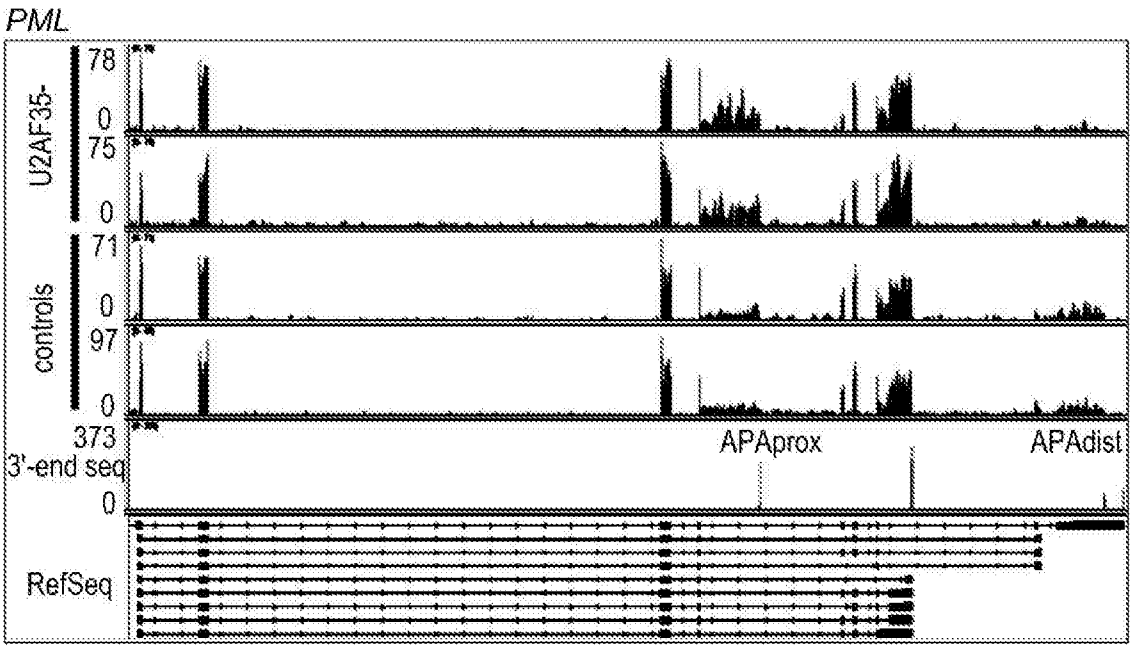


Fig. 14A

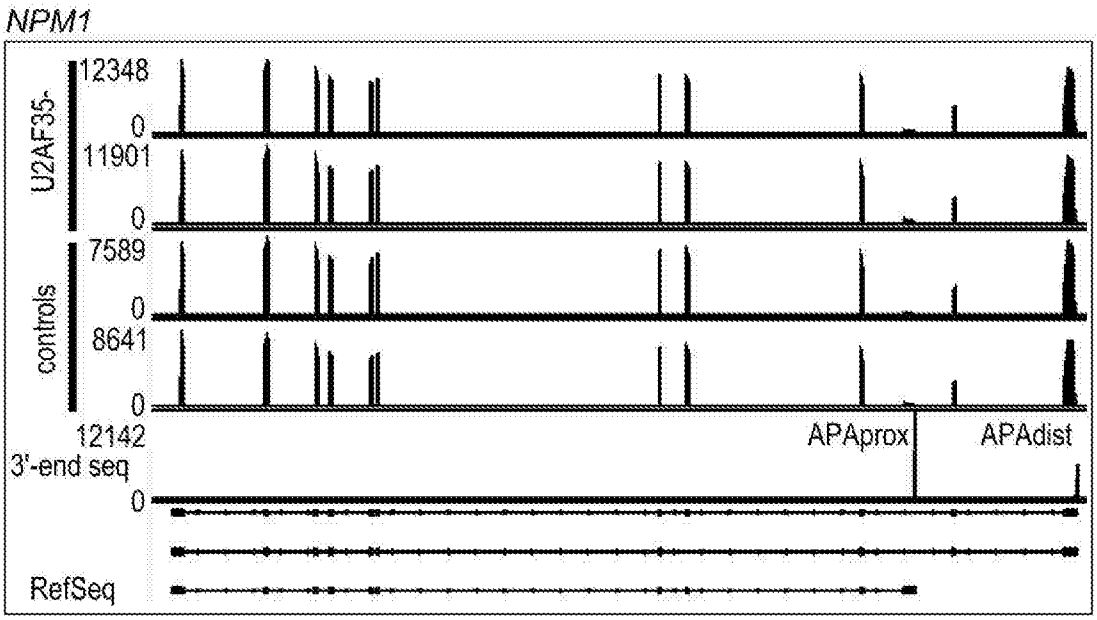


Fig. 14B

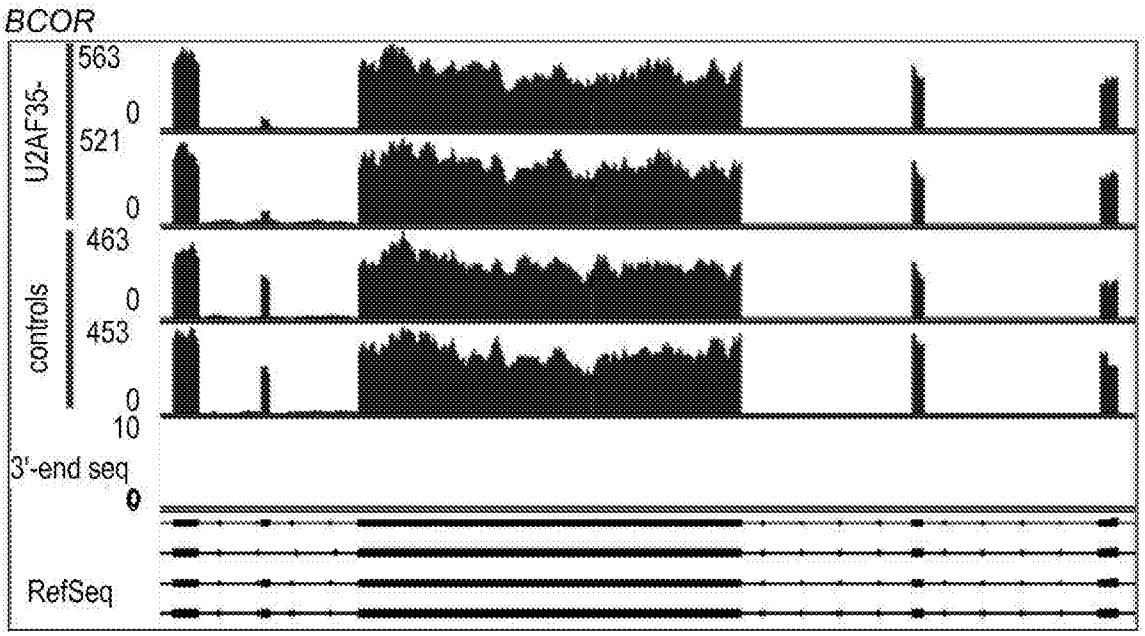


Fig. 14C

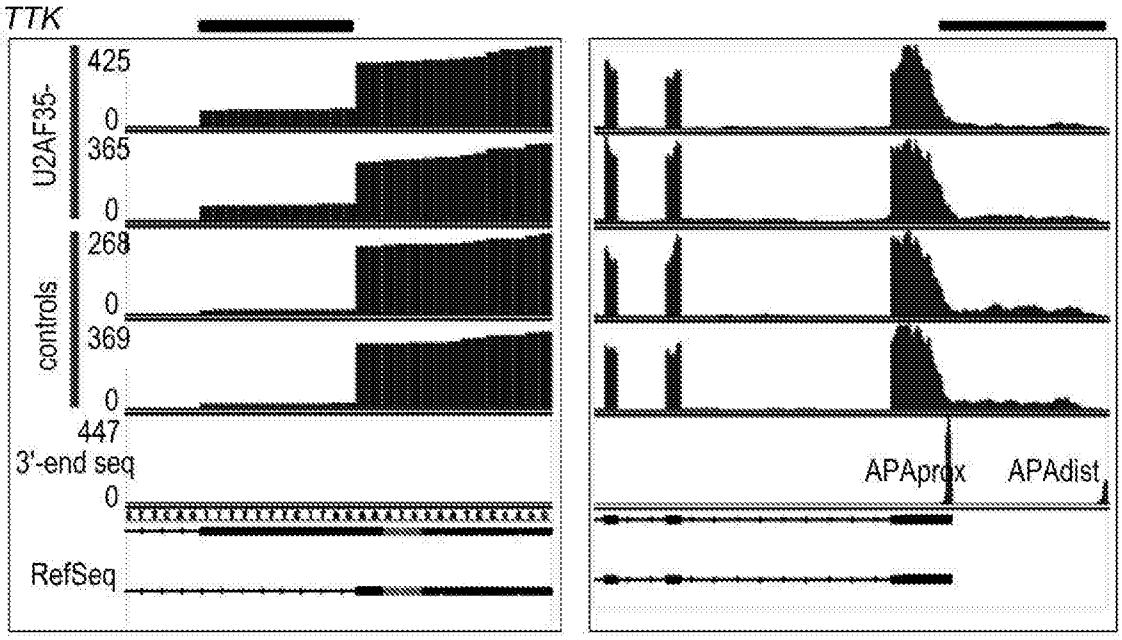


Fig. 14D

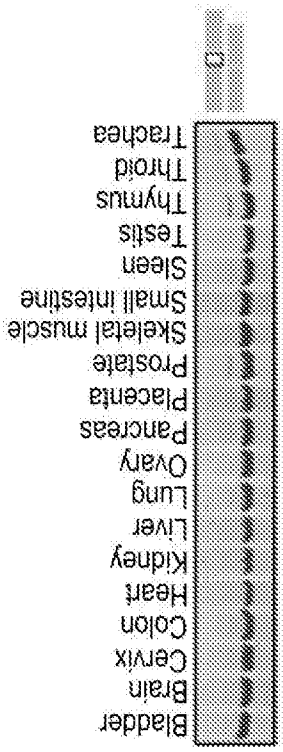


Fig. 15A

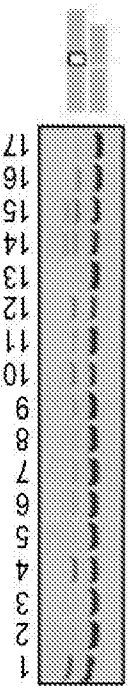


Fig. 15B

Fig. 15D

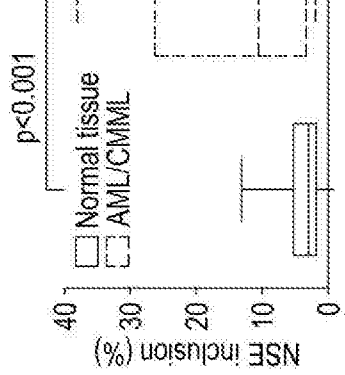


Fig. 15C

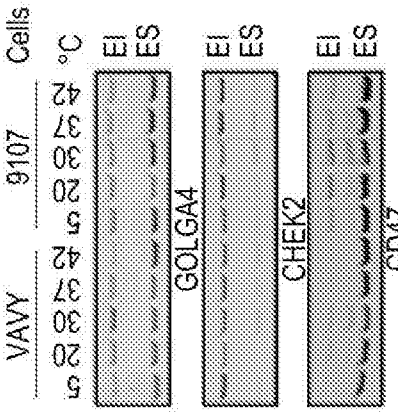


Fig. 15E

ACCESSION NUMBER

Accession number for RNA-Seq data is E-MTAB-2682 (ArrayExpress).

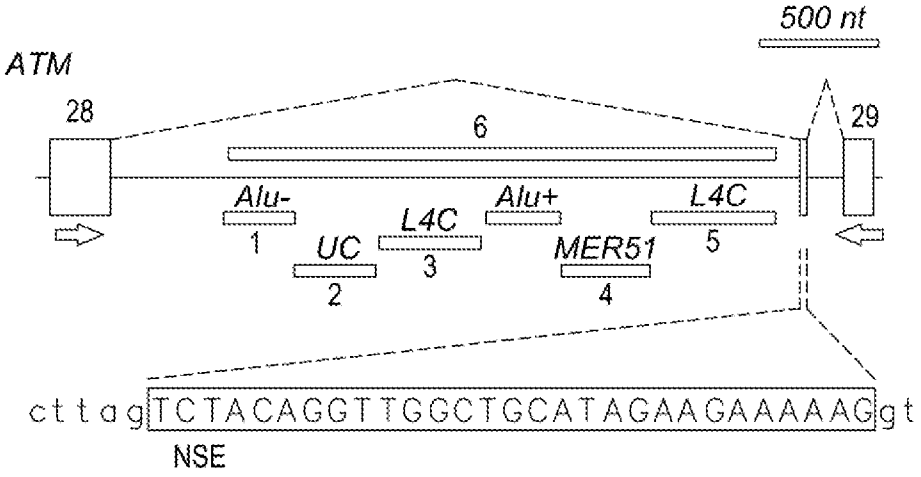


Fig. 16A

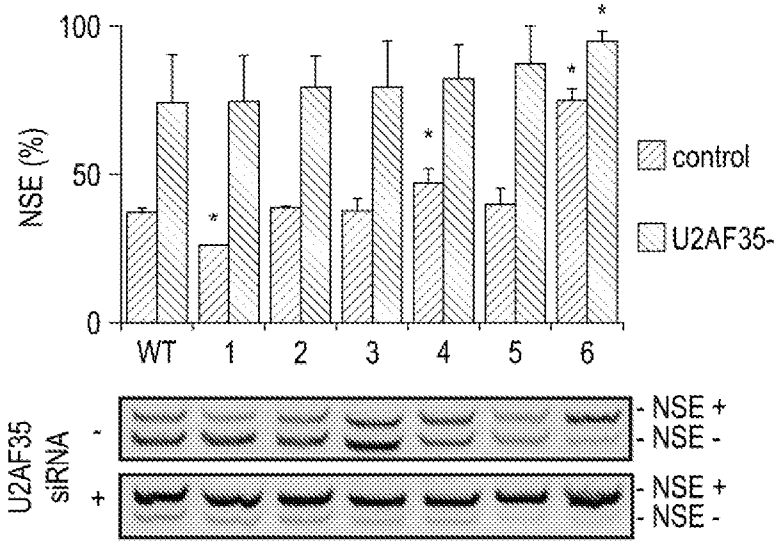


Fig. 16B

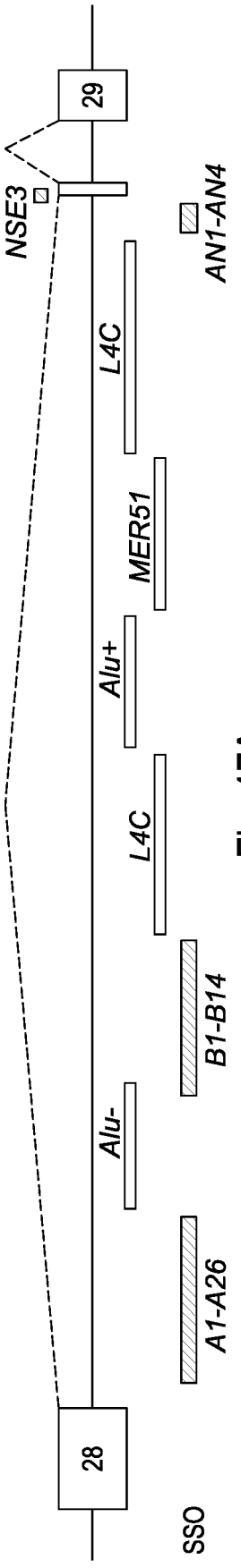


Fig. 17A

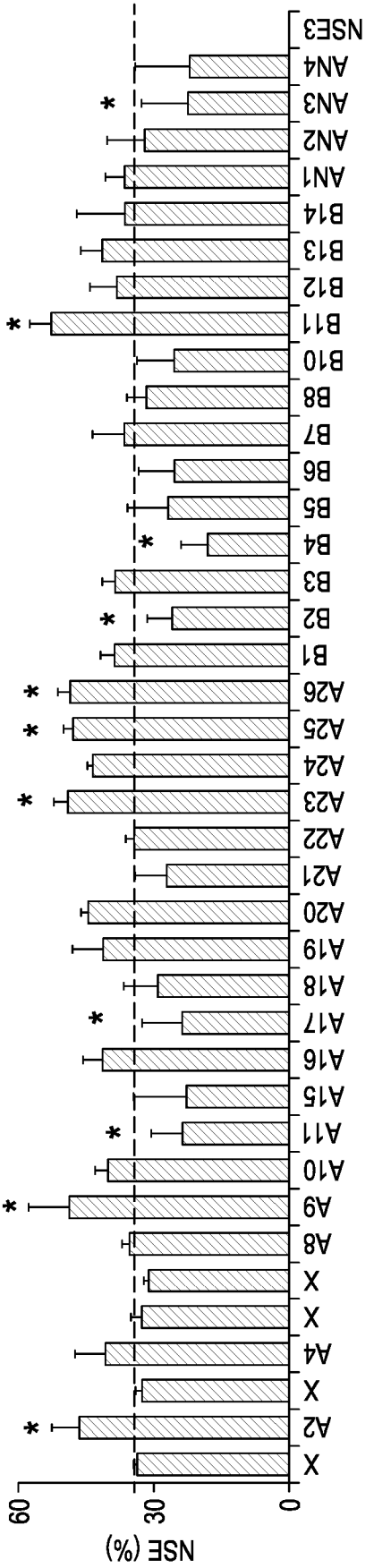


Fig. 17B

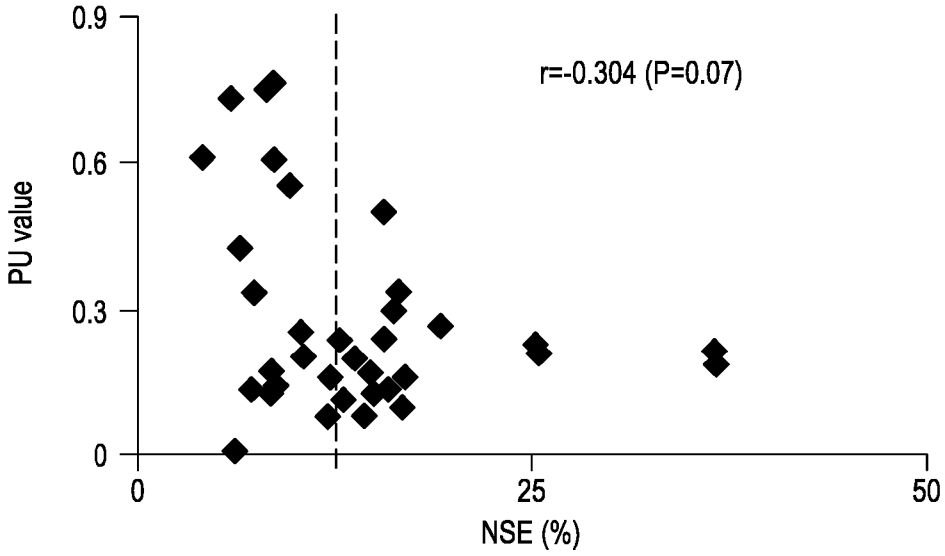


Fig. 17C

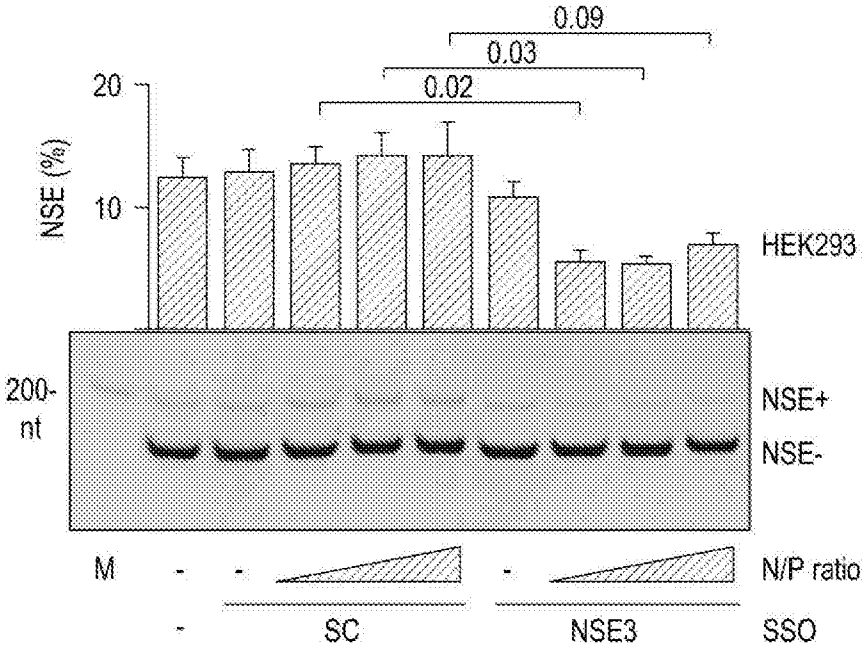


Fig. 18A

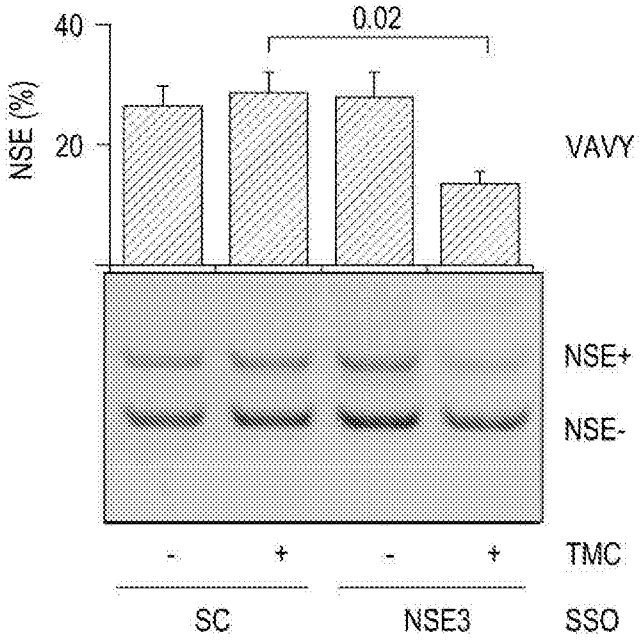


Fig. 18B


ATM intron 28
MER51A§LTR/ER
ATM intron 28
MER51A§LTR/ER
ATM intron 28
MER51A§LTR/ER
ATM intron 28
MER51A§LTR/ER
ATM intron 28
MER51A§LTR/ER
ATM intron 28
MER51A§LTR/ER
ATM intron 28
MER51A§LTR/ER
ATM intron 28
MER51A§LTR/ER
ATM intron 28
MER51A§LTR/ER
ATM intron 28
MER51A§LTR/ER

Fig. 19

RT-PCR primers	Sequence (5'-3')	Reference
ATM-F	GAGGGTACCAGAGACAGTGGGATGGC	This study
ATM-R	GGCTCATGTAACGTCATCAAT	This study
PL3	GGGAGACCCAAGCTGGCTA	[1]
CHEK2-E9-F	AGACCCAGCTCTCAATGTTG	This study
CHEK2-E9-R	TAGCTTCTTTCAGGCGTTTA	This study
CHEK2-E11F1	AGTGGTGGGGAATAAACG	This study
CHEK2-E11R	CAGCAGTCCACAGCACGGT	This study
CDC25B-F	CTCAGTCCAGCAGGCGTGTG	This study
CDC25B-R	GGTCTCTGGGCAAAGGCTTC	This study
CDC25A-F	CAGAAGCTGTTGGGATGTAG	This study
CDC25A-R	TCTCCATCGAGAAGGTCCAC	This study
CDC25C-F	TGGCTCAGGACCCAGTTTTA	[2]
CDC25C-R	TCTTCTGCCTGGTCTTCTCC	[2]
TIN2-F1	CCTGGCTTGGTTCGCTACC	This study
TIN2-R3	TGCTTCACCTGCTGGTAAAA	This study
TIN2-F6	GAAGAACATGCGATATACACA	This study
TIN2-R8	GTCTAAAACCAAGTCCCCTAT	This study
PIN1-F	GAGGGAAGATGGCGGACGAG	This study
PIN1-R	TCCTCCTTGGTCCGGGTGAT	This study
TERF1-F	GCAGCGGCAAAAGTAGTAGA	This study
TERF1-R	GTCTTGTTGCTGGGTTCCA	This study
RAD50-cr5-F	AAAATCATCAAAACAGCGAG	This study
RAD50-cr5-R	TGGAGCAAGTCGCAGTTTAG	This study
RAD50-E-F	GGCGACAGAAAGGTTATGAA	This study
RAD50-E-R	CGCCACAGGTCACGTATAAT	This study
Cloning primers		
ATM-XhoI	ATAGAATTCTCGAGGGGAGGGTTTTATTCTACTA	This study
ATM-XbaI	ATAGGGCCCTCTAGACTGTGGGGAGACTATGGTAA	This study
CHEK2-EcoRI	ATTAGAATTCTCTCGGGAGTCGGATGTTG	This study
CHEK2-NotI	ATTAGCGGCCGCGGTACATTTCTTTCGTGTTCA	This study
Modified antisense oligonucleotides		
SSO-NSE3	CUUCUAUGCAGCCAACCUGUAGACU	This study
SSO-NSE5	ACCUUUUUCUUCUAUGCAGCCAAC	This study
SSO-PE3	AUUUCCAAAAGUAUUCGAUGACUG	This study
SSO-PE5	UAUAUUACCUUAUUUCCAAAAGUA	This study
SSO-PEBP	CUGUAAAAGAAAAUAGAUGACUCAA	This study
SSO-PEdel	CUGUAAAAGAAAAUAGA	This study
SSO-CHEK2-ex9	ACUUACAAUUCCAAAACAAUAUAAU	This study
SSO-C	AGGUGCUCGCGGGUGG	[3]
SSO-MIR loop	AGUUGCUUCAUCU	[4]
siRNA		
U2AF35ab	GGCUGUGAUUGACUUGAAU	[5]
U2AF65	GCAAGUACGGGCUUGUCAA	[6]
RBM39	GGAUCUACUGUCAUUUGUA	[7]
PUF60	GCAGAUGAACUCGGUGAUG	[6]
UPF1	AAGAUGCAGUUCCGCUCCAUU	[8]

Fig. 20

Mutation	Nucleotide sequence[1] (5'-3')
WT	cgtcgtcgtc

Pseudoexon	Allele	FAS-ESS[1]	PES S[1]	PES E[1]	RESCUE-ESE[1]	SF2/ASF ESE[1]	EIE density[1]
NSE	C	3.45	3.45	5	6	9.3	975.4
NSE	T	3.45	3.45	5	6	9.3	975.4
PE	G	4.17	0	0	3	0	403.8
PE	A	4.17	0	0	5	0	334.2
Reference	[9]	[10]	[11]	[11]	[12]	[13]	[14]

Legend: [1]Densities of the indicated enhancers and silencers predicted in NSE and PE were computed as described [15]. Support vector machine scores for the best predicted BPS of NSE and PE [16] were 1.3 and 0.5.

Fig. 22

Transcript	Levels in depleted cells
UPF3A	Down (q=0.002)
UPF3B[1]	Down (q=0.0006), skipping of a 39-nt exon
SMG7	Up (q=0.0002)
SMG8	Up (q=0.001)
DHX34	Up (q=0.002)
CASC3	Up (q=0.004)
RNPS1	Up (q=0.003) through putative intronic alternative polyadenylation site
RBFOX2	Up (q=0.007)

[1]*UPF3B* was implicated as exhibiting a distinct level of exon inclusion in patients with myeloid neopalsms [17].

Fig. 23

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