

Figure S1

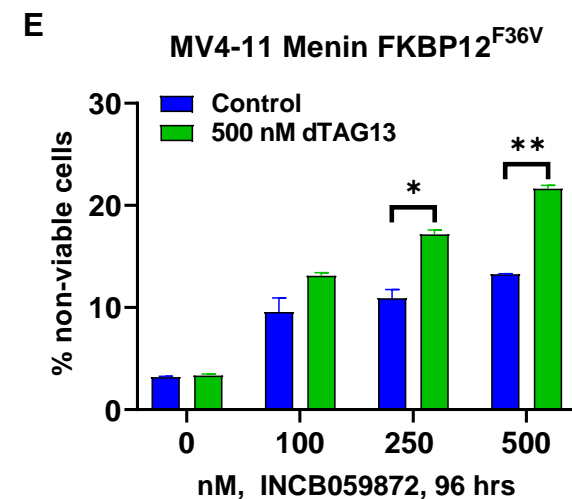
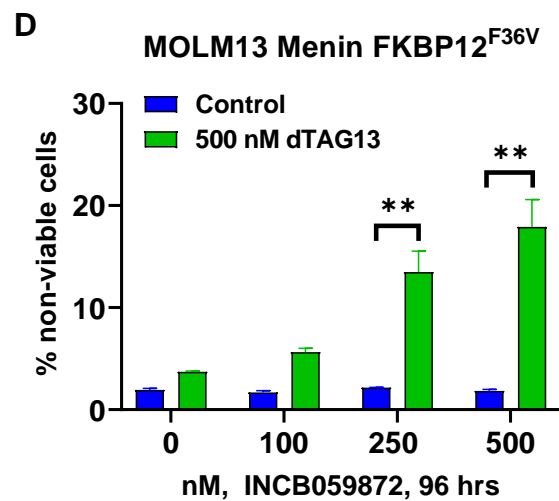
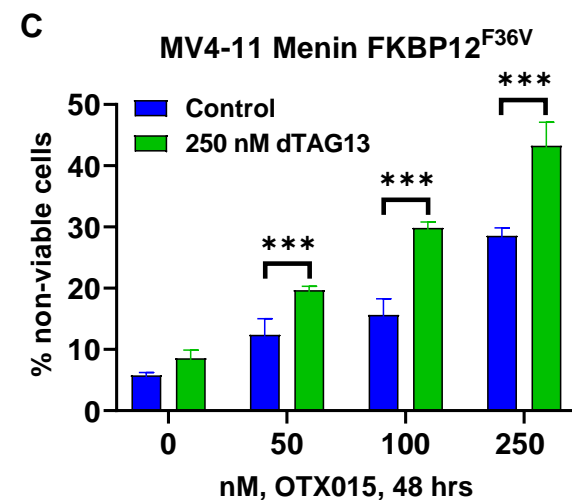
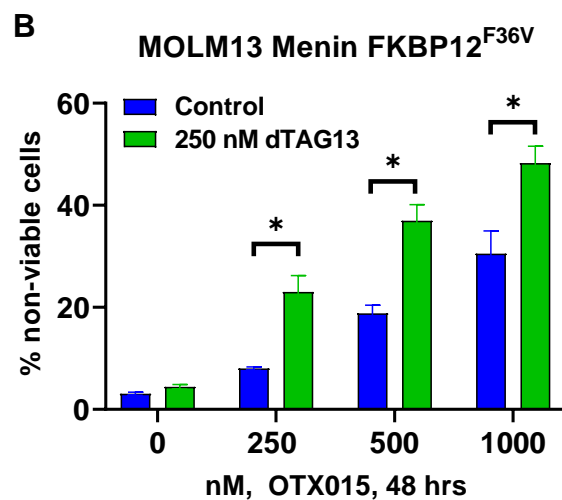
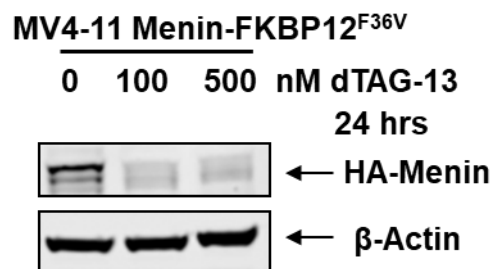
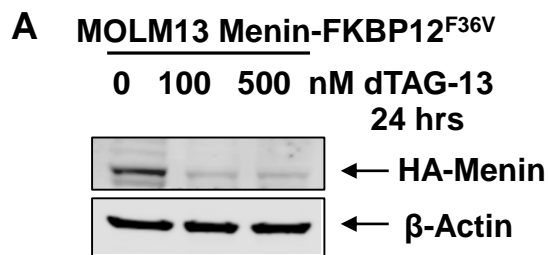
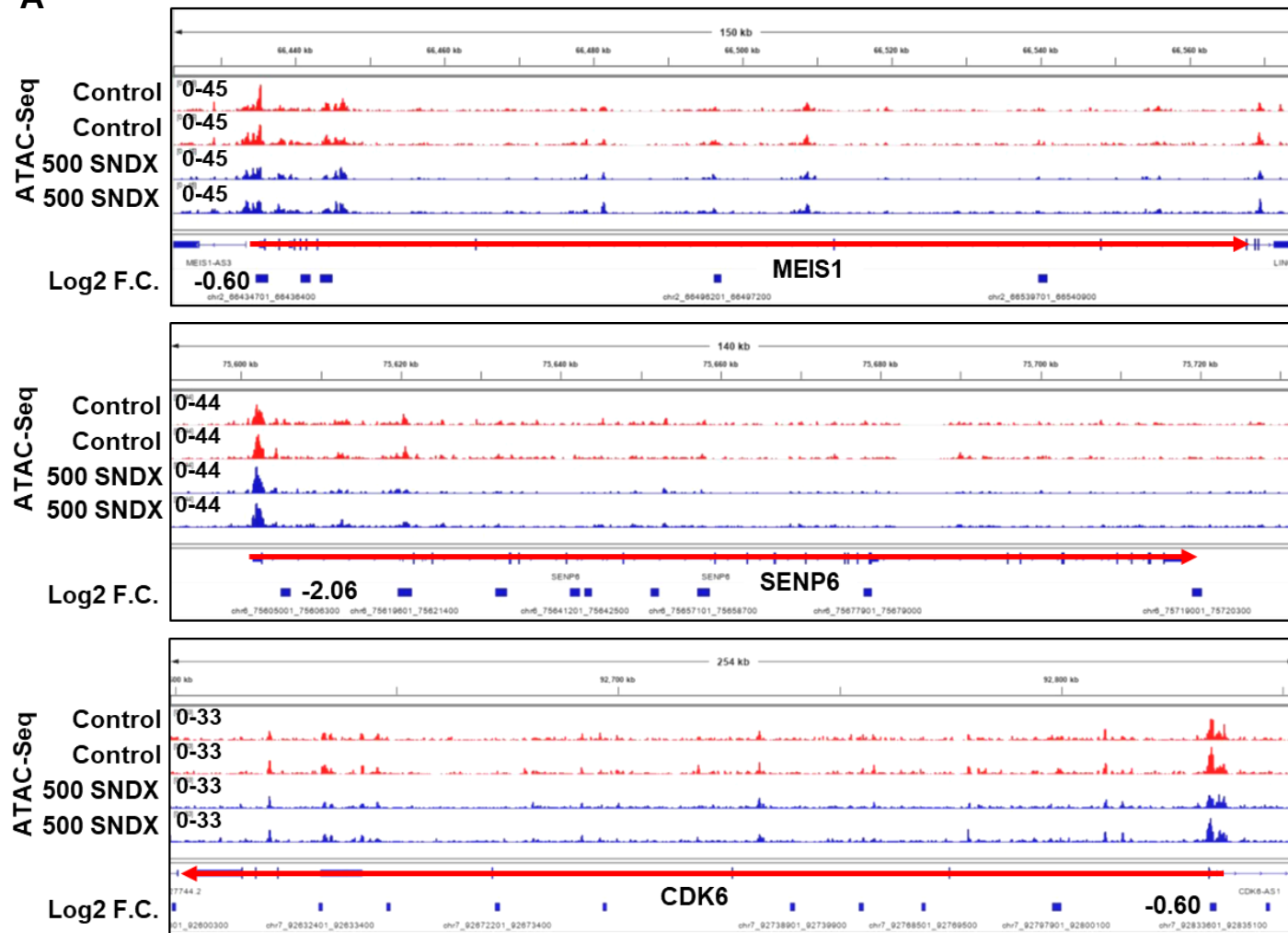


Figure S2

A**MOLM13****Figure S3**

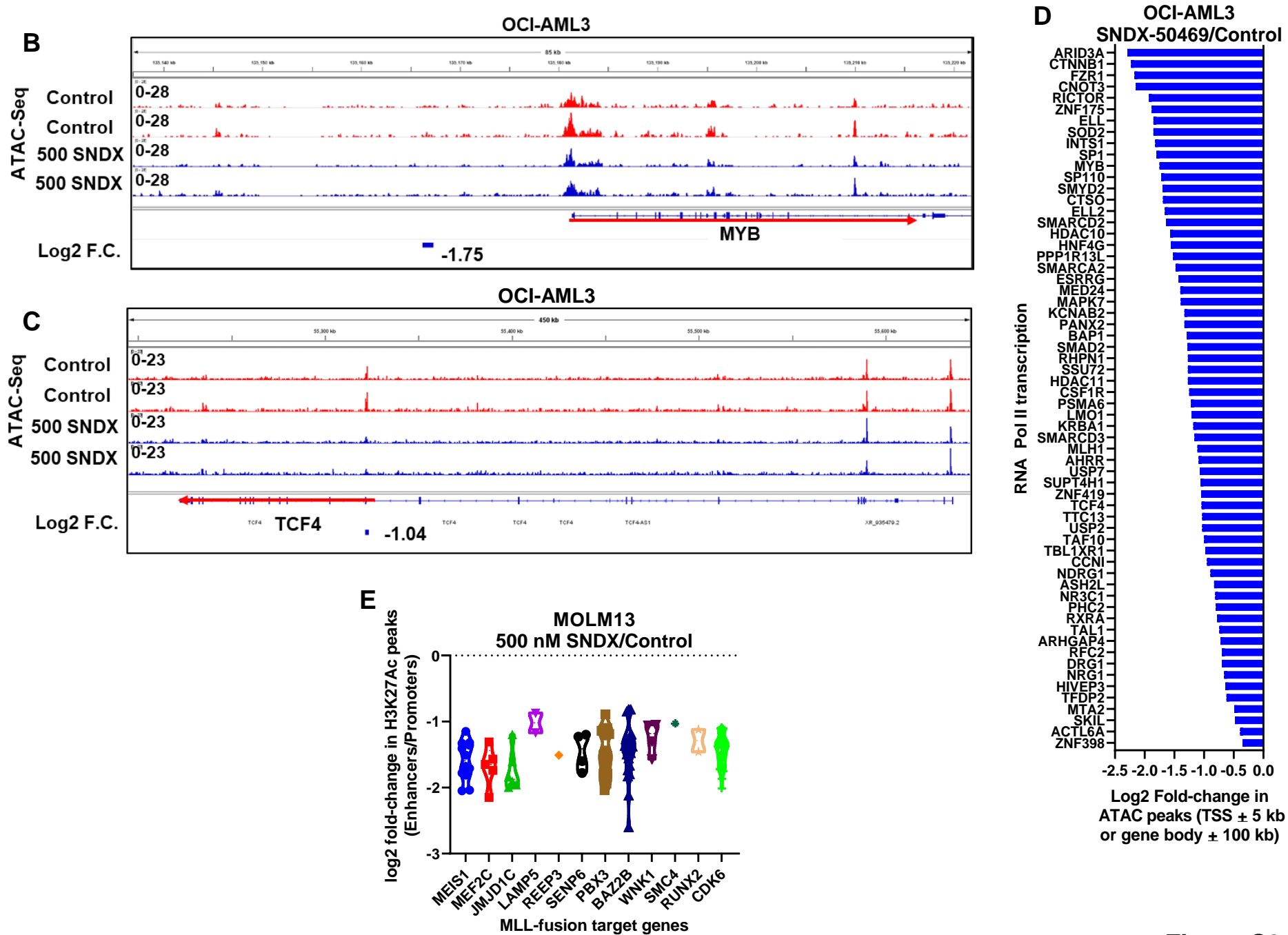


Figure S3

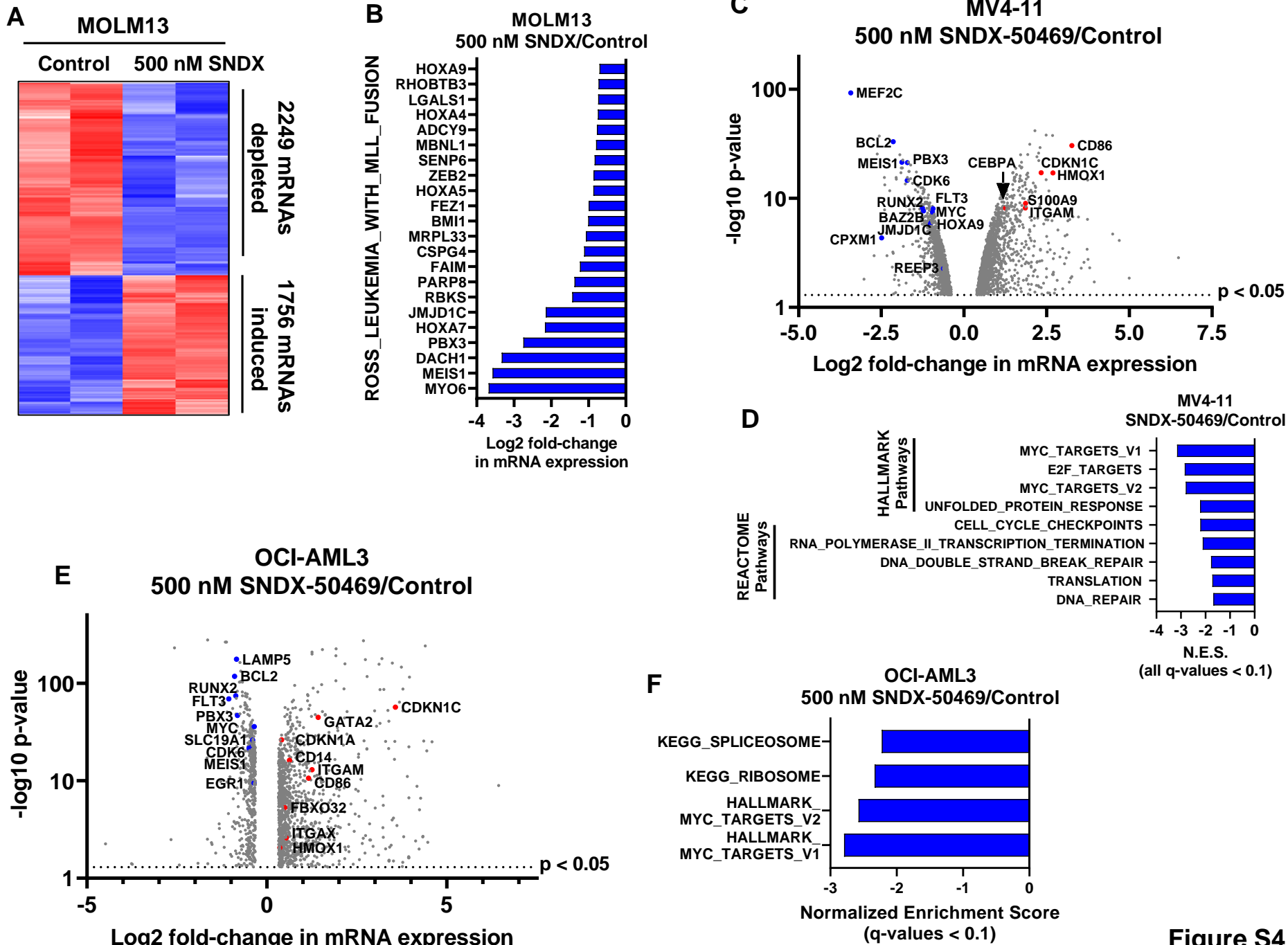
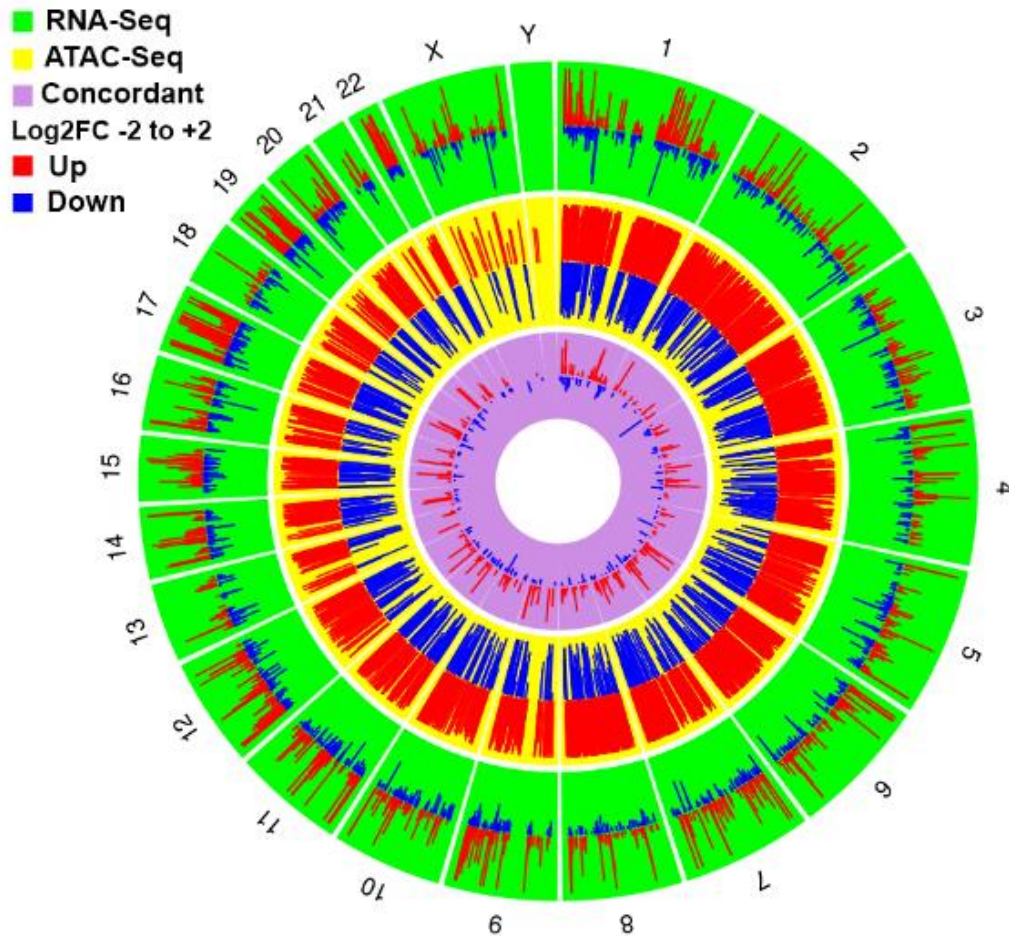


Figure S4

G

OCI-AML3 SNDX-50469/Control



# of genes upregulated in RNA-Seq	2301
# of genes down-regulated in RNA-Seq	2500
# of differential peaks gained in ATAC-Seq	3354
# of differential peaks lost in ATAC-Seq	1134
# of up genes in both RNA-Seq and ATAC-Seq	267
# of down genes in both RNA-Seq and ATAC-Seq	192
# of genes common in RNA-Seq and ATAC-Seq	832

H

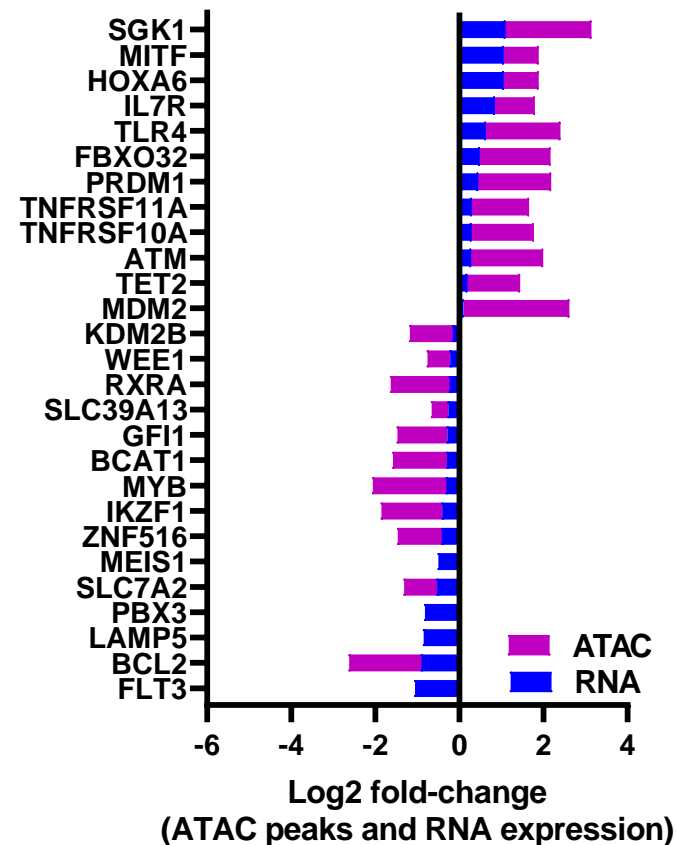
OCI-AML3
500 nM SNDX-50469/Control

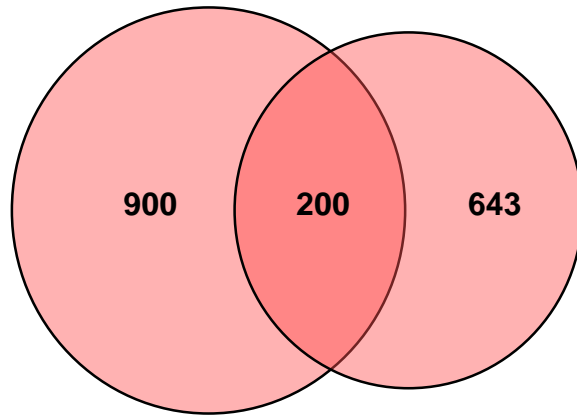
Figure S4

A

SNDX-50469 induced mRNAs

OCI-AML3

MOLM13

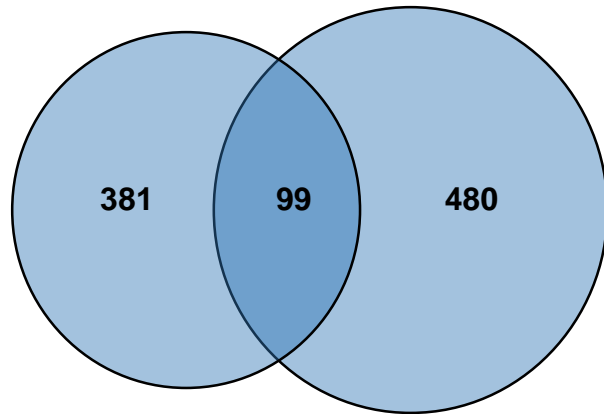


B

SNDX-50469 depleted mRNAs

OCI-AML3

MOLM13



C

Gene Name	OCI3_log2 Fold-Change	MOLM_log2 Fold-Change
ANXA1	0.769126671	2.050580391
METTL7A	1.130841473	0.847360602
TUBA1A	1.131696753	0.344448454
SAMD9L	1.15998037	0.983014002
LRP10	0.586423591	0.412973253
FUCA1	0.951084363	0.431478809
TPPP	1.620478169	0.619654256
KIAA0040	1.618970702	1.50893655
LILRA2	0.643202581	0.913427186
TLR4	0.635016328	1.279735163
ABCA7	0.576437837	0.587335732
IL7R	0.850877104	0.348329468
USP53	0.709446237	0.544774289
C3	0.662770705	1.170914352
F11R	1.018595921	0.485488884
MT2A	0.810602932	0.408295396
KLHL24	0.637013546	0.484316086
SLC43A2	0.59555641	0.50981815
BMF	0.800350424	0.921079652
RAB7B	0.370740315	0.453151312
HELZ2	0.573110271	0.367427521
ARID5B	0.903714225	1.159021156
KIAA0513	0.937634336	1.639889271
BNIP3L	0.387214989	0.764398148
TRAF3IP3	0.581943578	0.584583799
SLA	0.381566838	0.794559452
APOL6	0.494915234	0.484327997
IDS	0.678759958	0.874018668
RAB37	0.480812763	0.718738274
MAP3K12	0.841452642	1.161111127
CDC42EP4	0.511644176	0.475287129
MBNL2	0.661794997	0.777167958
CD37	0.571849756	0.527531943
PIM1	0.960371466	0.393803711
PIAS3	0.435995338	0.470304992
ITPR2	1.00949731	0.794325161
CPNE3	0.38318417	0.344449832
NLRP1	0.454880994	1.838673337
CCNG2	0.446809137	0.878540435
KIFC2	0.614202696	0.353068603
NFKB2	0.410809367	0.463385655
ABTB1	0.663619868	0.835468289
SYNE1	0.836854313	2.893787405
KIAA1551	0.424826036	0.440958201
TSPOAP1	0.443018333	0.685331799
RUBCN	0.396341924	0.404241031
CFP	0.703229456	1.097445997
PDE4DIP	0.632014406	0.651619635
FAM111A	0.341067852	0.333478141
SLC26A2	0.53570467	0.61464032
CXCL10	1.155943052	1.487722805
UBE2L6	0.449416641	0.669729105
NAGK	0.52341085	0.453570925
FCGR2B	1.716012032	2.410834719
PBXIP1	0.353484532	0.479179443
NBR1	0.335671912	0.326441308
CBLB	0.584379329	0.726848329
GCC2	0.464075595	0.466215135
ACSF2	0.761642782	0.63179147
ZNF467	0.724357328	1.149804555
SYNPO	0.588428558	1.773983207
SLC12A6	0.408187986	0.520058354
CLCN3	0.35760623	0.329313288
SV2A	0.376638509	0.403405555
ITGAM	1.250935324	1.193462384
GLTP	0.446658991	0.640877051
IFI6	0.769288621	1.657136986
IFFO2	1.187968924	0.711287958
MYOF	0.461753939	0.807093904



Gene Name	OCI3_log2 Fold-Change	MOLM_log2 Fold-Change
BCAS3	0.465697456	0.825372617
TMEM87B	0.348431114	0.489412108
NTNG2	1.445280839	0.897482732
UACA	0.754659674	0.590032069
ZSWIM8	0.346082636	0.412243771
JUN	0.394618945	0.952660108
NRBP2	0.408903007	0.451528558
APOL2	0.420470922	0.380280201
WDR19	0.604602433	0.390017731
CD86	1.158144941	1.06250525
CX3CR1	0.514037521	2.017295783
CTTNBP2NL	0.49399208	0.70557269
SLC44A2	0.654738008	0.701089744
BBS2	0.362820962	0.607857715
STXBP1	0.448022756	0.687281846
C3AR1	1.221694645	0.932697656
TOM1L2	0.452707302	0.364755292
AKAP9	0.357819474	0.446521618
ZYG11B	0.335492213	0.436903929
PDLIM2	0.433078413	0.513401917
RAB11FIP1	0.342800412	0.527339301
CD244	0.807034237	0.514357051
SLFN5	1.516432134	1.492366991
GPR137	0.421547566	0.578150348
HIPK2	0.330923464	0.727141182
YPEL3	0.521502865	1.335678725
CALCOCO1	0.370902688	0.486639511
ADGRB1	0.924347954	0.511838214
ATP6V0A1	0.394250521	0.328040405
SAT1	0.412683467	0.479306462
SYT11	0.416628995	0.632954886
KIAA1109	0.421602981	0.654416986
ADD3	0.336428991	0.357477814
SRDS5A1	0.408189245	0.655737528
NCOA7	0.425373905	0.391533614
RNF213	0.657762616	0.75886797
RCBTB2	0.442344218	0.510846955
MXD3	0.385632497	0.491572275
FAM49A	0.359203064	0.628440986
GATS	0.786452737	1.656471268
DPYSL3	0.896261707	0.680895133
SLC26A11	0.819788165	4.794263792
TRANK1	0.726684399	1.310873798
PGAP1	0.529706087	1.315518698
ATP7A	0.516784941	0.573020726
CLSTN3	0.495342391	0.427767302
GPR18	0.358532637	0.456048706
JUP	1.462260776	0.852542223
ARRDC3	0.555188435	1.067477118
GN2	0.806043054	0.486493849
ZFYVE26	0.330797044	0.469311262
NCF2	0.881315902	0.811791012
PGM2L1	0.688685588	0.642482906
TLR6	0.66772655	0.727490497
TMEM8B	0.723906022	0.860020147
ABCA5	0.367513971	1.850670448
CLCN5	0.408060293	0.634924917
PAQR8	0.453174445	0.857923376
CYTIP	0.839348561	0.719222686
TLN2	0.821386102	0.438802642
ZFH3	1.096647095	0.95481196
EXD2	0.412304694	0.550006445
C1RL	0.368459366	0.517921031
ARMC9	0.42848912	0.754766431
CCDC186	0.339177733	0.515035873
HCN3	0.574924524	0.632203026
KIF3A	0.372179667	0.89034981
ST3GAL6	0.519346075	0.921253279
FAM161B	0.666461066	0.736229026
RBMS2	0.631748676	0.649310526



Gene Name	OCI3_log2 Fold-Change	MOLM_log2 Fold-Change
PDE4B	0.352456131	0.758254057
LILRB1	0.411427086	0.452965695
MMP25	0.686980358	0.540620268
ID3	0.824744944	1.860681076
PPM1L	0.576138011	0.364537186
TNFSF14	0.553042418	0.658494302
TCP1L2	0.810034588	1.378475524
IZUMO4	0.625807617	0.744764371
DDX60	0.441978755	0.919900684
IL16	0.767902742	0.732064488
NEK1	0.323725029	0.439033443
RAP1GAP2	0.507598612	0.617935404
IL10RA	0.390770673	1.055185292
PCNX2	0.526711998	1.243761557
ZNF697	0.329821733	0.441468191
ZBED6	0.435129938	0.719370258
DNASE2	2.559981297	1.063533372
HERC6	0.49650297	1.603392029
PLXDC2	0.612615596	1.442011086
WDR31	0.387644144	0.829895216
SSBP2	0.363597643	0.795505674
TBC1D2	0.522095257	0.360127881
CLEC12A	1.358228349	0.745613028
AGPAT4	0.766165722	1.255886792
TRIM52	0.378165	0.779334083
ABHD4	0.559804822	0.436279846
GPR68	0.414751909	0.990790546
GIPR	1.685600231	0.776034697
PORCN	0.861686867	0.527197971
AHNAK	0.41599897	0.886870709
ATP8A1	0.521598808	1.129621732
SH2D3C	1.252554528	0.550206054
EFHC1	0.352067154	0.781076831
LILRA1	0.406543436	0.869112137
TXNDC16	0.350555955	0.471645262
LILRB2	1.337436627	1.752720784
NBEAL1	0.40449611	0.927040292
SCIMP	0.451203837	1.407058276
CIITA	0.614624659	1.546655712
JAML	1.478277329	0.876956842
ITGAX	0.533639109	1.090570387
PDE1B	0.463404859	0.575854074
AVPR2	0.565152461	0.918441081
CCDC146	0.767119293	1.423660585
SP110	0.418252735	1.024912162
ANKRD36C	0.419040935	0.596539217
SPATC1	1.312086081	1.796085974
LMTK3	0.989395453	0.952308957
SPACA6	0.386970809	1.334299817
MAP3K14	0.352575841	0.486211771
ABHD8	0.421757524	0.749295326
TSHZ3	0.578717177	0.943820211
PRX	0.423918245	0.743940845
SDS	1.390282554	1.737905939
AIM1	0.561737512	0.445537147
ITPR3	0.525410363	0.348512757
MTMR11	0.355997634	0.466360915
TMEM255B	0.477851949	0.723588463
EML6	0.610815094	2.049094041
RASGRF1	1.407975218	0.839551044
PILRA	0.327575984	0.758696684

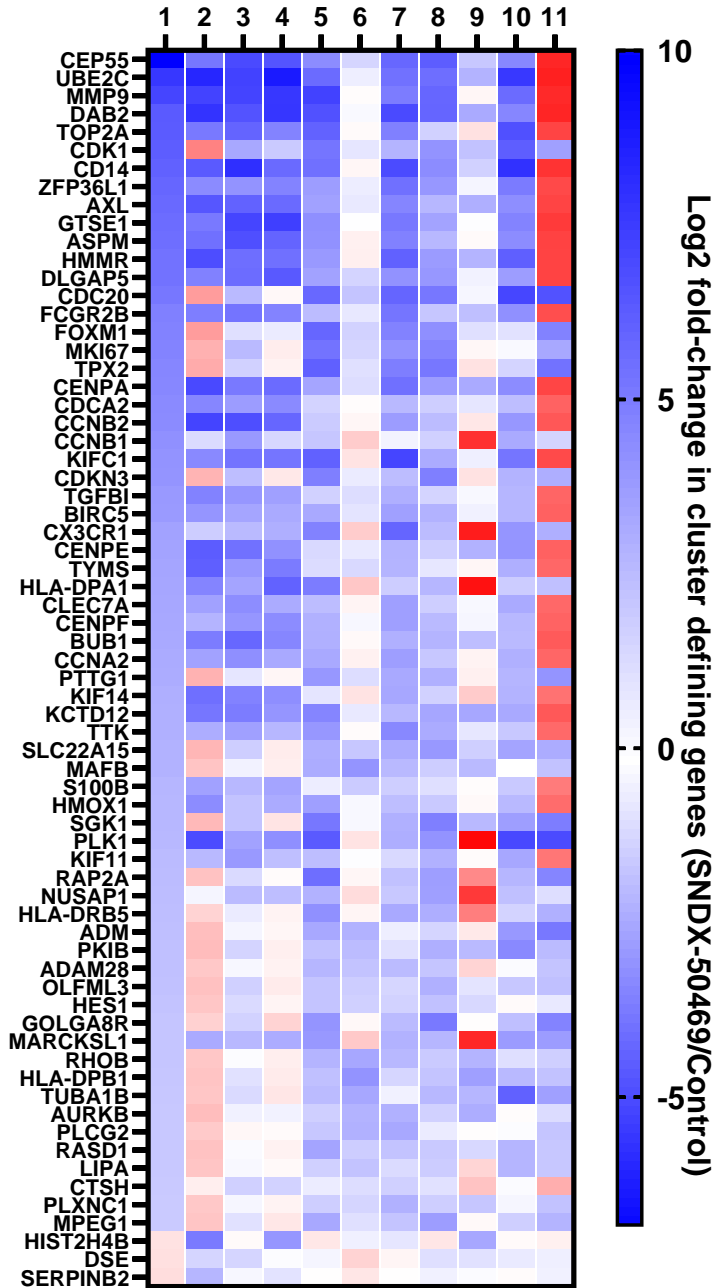
Figure S5

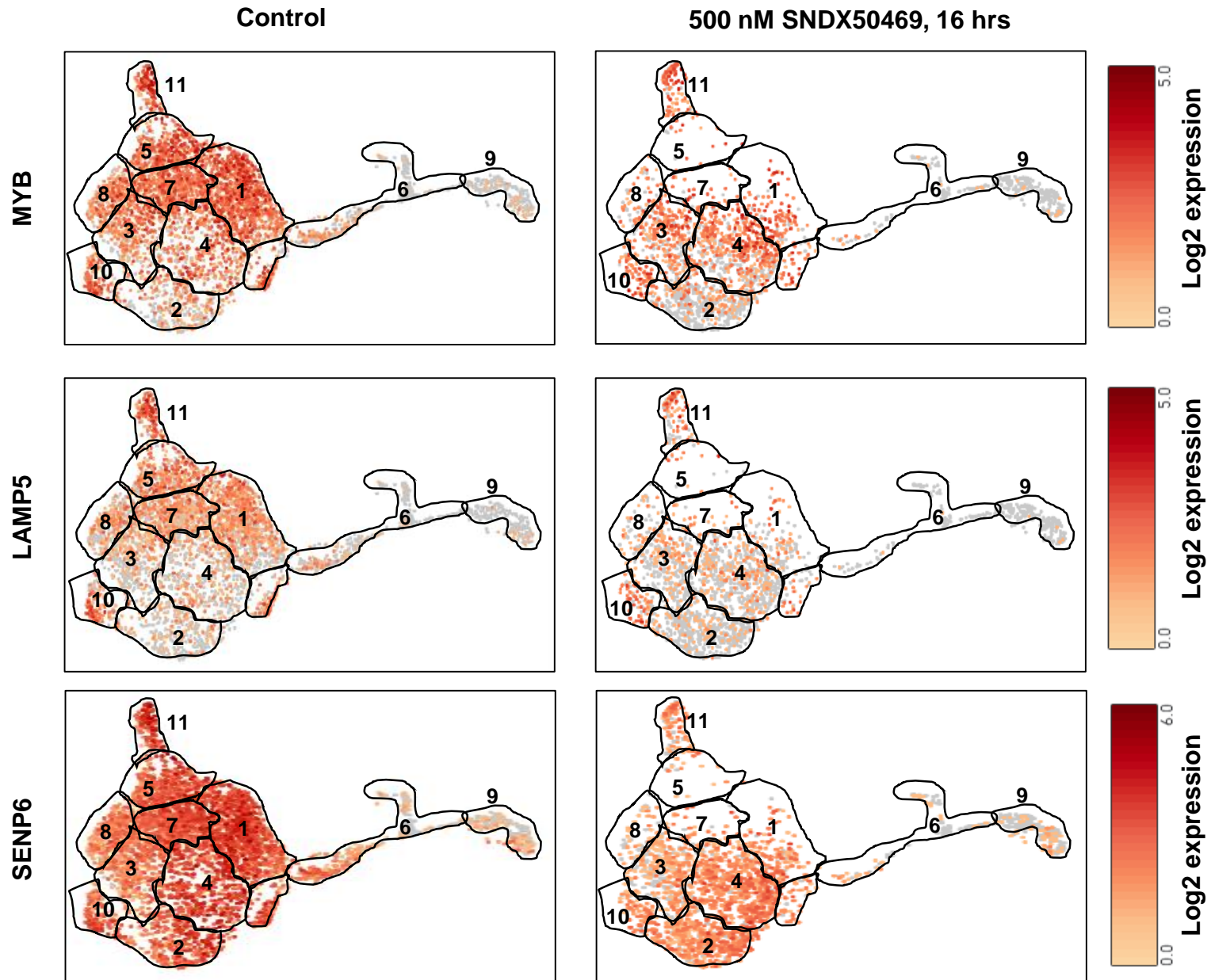
D

GeneName	OCI3_log2 FC	MOLM_log2 FC
CDKN2C	-1.649733229	-0.957504284
PHF10	-1.121464064	-0.570739022
IGF2BP2	-1.155806612	-0.679343221
TMEM255A	-2.570378971	-2.989631346
LAMP5	-0.845916214	-0.768378707
IRF8	-0.749492619	-0.339881248
SATB1	-0.680088531	-0.92339395
CXorf21	-0.598252328	-0.545910616
SATB2	-0.679825687	-0.600778519
SRGN	-0.553921529	-0.4168654
FLT3	-1.056400388	-0.712988005
CPEB2	-1.230555823	-1.809057416
KCNN2	-0.953083024	-0.813782437
FOXP1	-0.750430988	-0.497603164
TESC	-0.859177611	-0.610680802
PBX3	-0.818842026	-1.768859435
SDC2	-0.487149636	-1.067202025
KLHL23	-0.816710615	-0.78709842
MYC	-0.351530754	-0.337674731
REEP3	-0.581024563	-1.441970132
TERT	-0.660329416	-0.324917509
ZNF516	-0.417680197	-0.351410952
DLX1	-0.550081491	-0.730310543
TFB2M	-0.409087985	-0.414146039
SLC25A19	-0.412433634	-0.377046677
NANOS1	-1.193674438	-0.992017796
FAM120AOS	-0.45521356	-0.363490026
HSPA4L	-0.475301018	-0.441551735
CENPV	-0.833750069	-0.586459719
CDK6	-0.434179181	-0.457528672
MEIS1	-0.494833554	-2.592036446
RRP7A	-0.340158808	-0.436506155
DCUN1D5	-0.362309609	-0.333435683
DNAJA4	-0.431822443	-0.440829487
STARD8	-0.615129477	-0.362435997
MRTO4	-0.355331992	-0.427786232
BATF3	-0.851320649	-0.771901131
MRPS34	-0.435247545	-0.362801654
CSPG4	-0.588121242	-0.645501735
ST3GAL4	-0.423082118	-0.354410615
NDUFAF3	-0.370546953	-0.637817861
RPL36AL	-0.330113755	-0.384295181
ZEB2	-0.373498827	-0.492659654
BAG2	-0.58136371	-0.420149031
WDR4	-0.383034064	-0.465727625
SFMBT1	-0.637262679	-0.345642443
CGREF1	-0.428232511	-0.588302825
HS3ST1	-0.520323269	-0.941612428
SFXN4	-0.365622965	-0.621281327
PLD6	-0.387615714	-0.437421361

GeneName	OCI3_log2 FC	MOLM_log2 FC
PSMG1	-0.323615833	-0.424594781
AGMAT	-0.689972746	-0.333246665
TEAD4	-0.363515217	-0.333273264
NOP16	-0.333407476	-0.340139849
ZBTB33	-0.323060432	-0.606023325
CMTM7	-0.418332454	-0.53578187
PIWIL4	-0.458460044	-0.450316448
LHX6	-0.602949475	-0.506947065
GAREM2	-0.471599636	-0.418863173
TIFAB	-1.283306613	-0.671791898
IL15RA	-0.485748542	-0.446254007
CSPG5	-0.580692098	-1.920972963
EGR1	-0.356252851	-1.346300897
AVEN	-0.473762414	-0.33768645
LRFN1	-0.389552782	-0.369222456
CHST10	-0.325282393	-0.360801176
SAP30	-0.436849801	-0.44226863
QPRT	-0.569628604	-0.504319731
RAB33A	-0.624997086	-0.422864464
MYO6	-0.33596582	-2.777965996
BEND3	-0.409590254	-0.411459062
AP1S3	-0.622053183	-0.397109917
CHRM4	-0.801624196	-4.094642204
PPP1R27	-0.606765019	-0.872440061
RHOBTB3	-0.351258823	-0.414934525
C16orf91	-0.323351116	-0.349866938
IGFBP7	-0.39575928	-0.369522524
RNF157	-0.44924468	-0.352607549
FAM89A	-0.447227041	-0.519579501
FAM127C	-0.364217964	-0.379933983
KCNQ4	-0.828723286	-0.708966915
RGS9BP	-0.670167973	-1.04644981
TBC1D30	-0.759982571	-1.106274122
SOCS2	-0.896893553	-2.410567303
HACD1	-0.519382061	-0.463960157
MRPS28	-0.331196482	-0.522708566
SHOX2	-0.496676938	-1.594606875
PPP1R3G	-0.559960037	-0.629169284
PROK2	-1.527030596	-0.542269701
CABLES1	-0.459216227	-0.5528942
TOMM5	-0.366123264	-0.533577587
GAL	-0.454234218	-0.473886456
ITPRIPL1	-0.337822683	-0.488668089
GET4	-0.756694731	-0.454602228
EMID1	-0.394457229	-0.629347219
TXNDC5	-0.530907719	-0.53845581
DLX2	-0.470491862	-0.985056205
GADD45GIP1	-0.339853646	-0.3401186
FAM174B	-0.578203186	-0.4703284

Figure S5

A**MLL-AF9 + FLT3-TKD AML cells
500 nM SNDX/Control****Figure S6**

B**MLL-AF9 + FLT3-TKD AML cells****Figure S6**

MLL-AF9 + FLT3-TKD AML cells

B

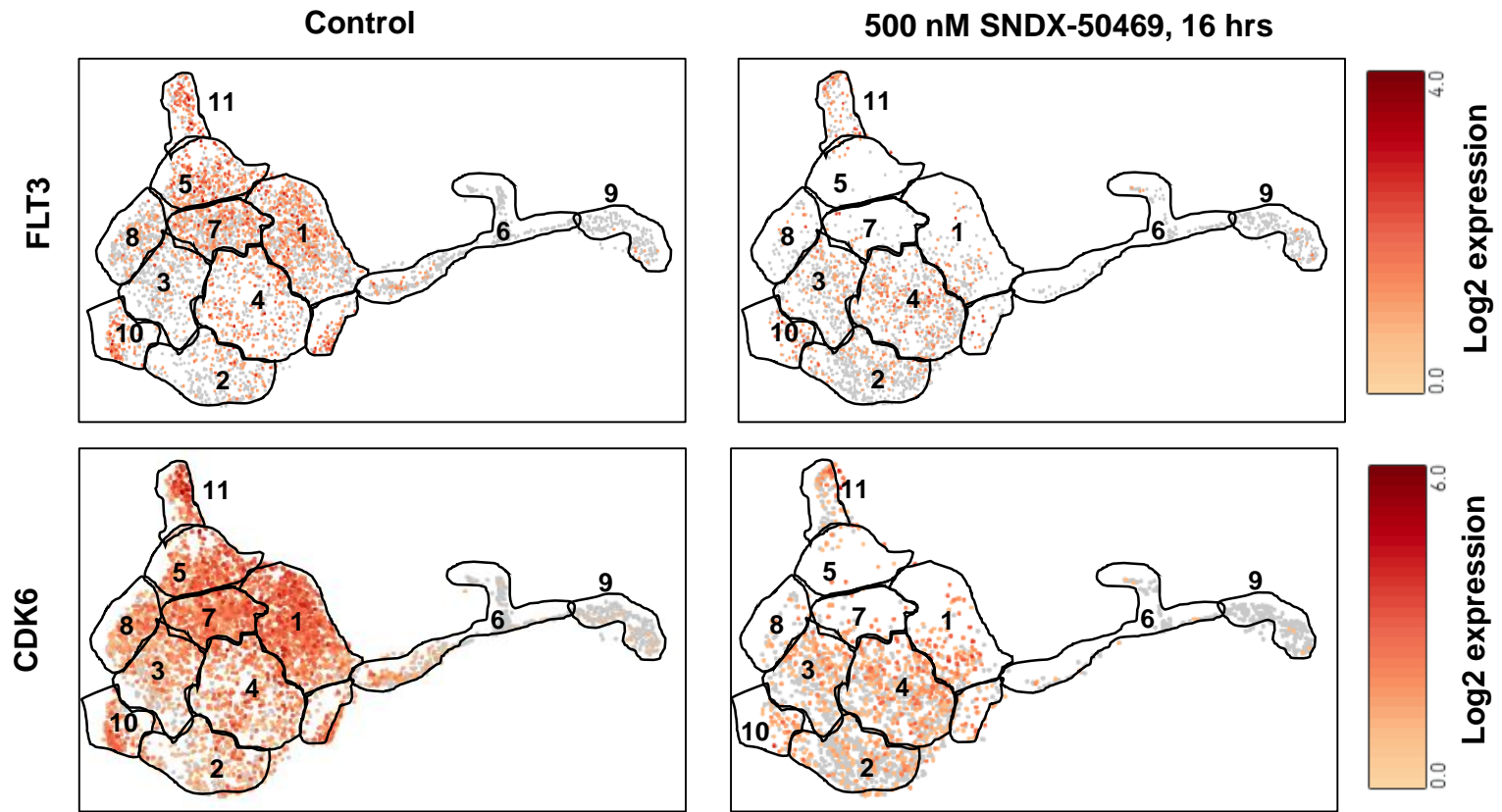
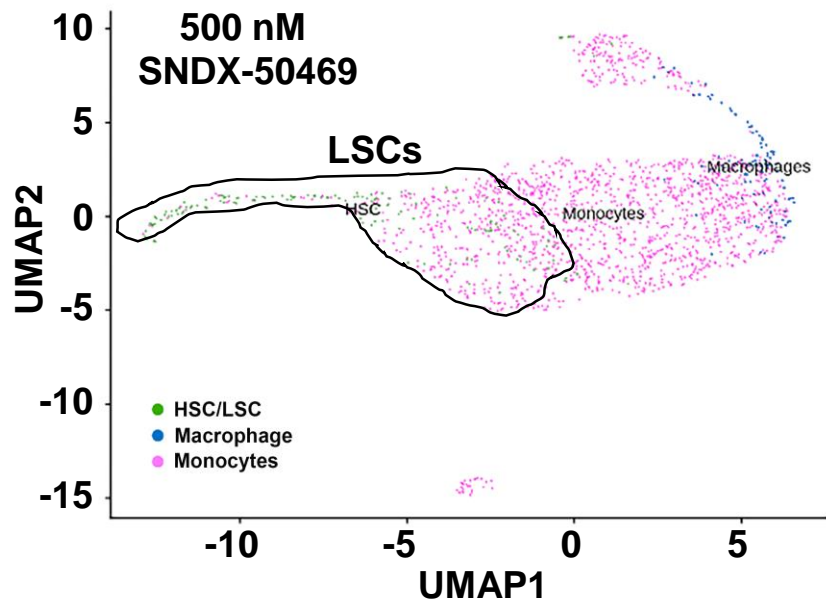
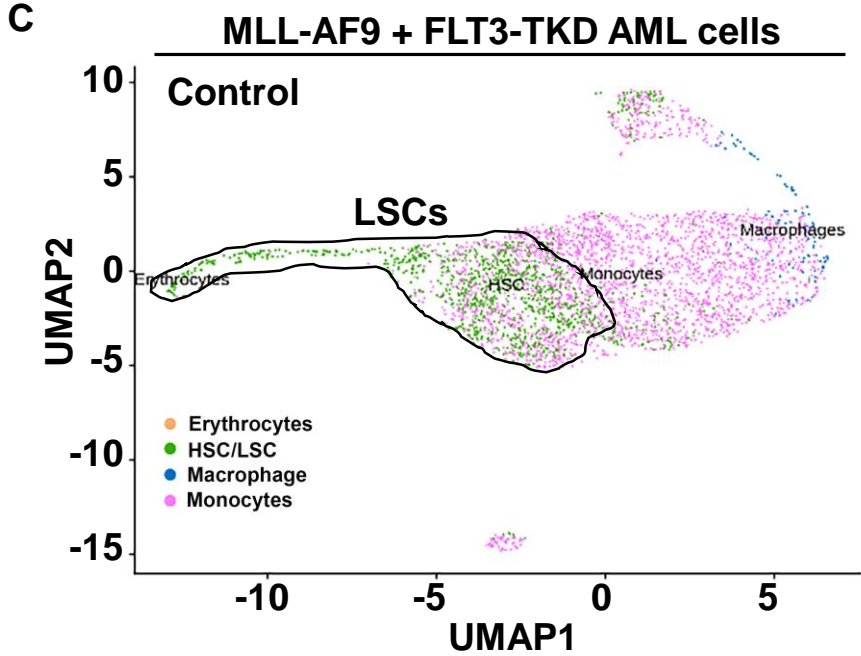


Figure S6



SNDX-50469 treatment decreases the # of cells with an HSC/LSC mRNA signature.

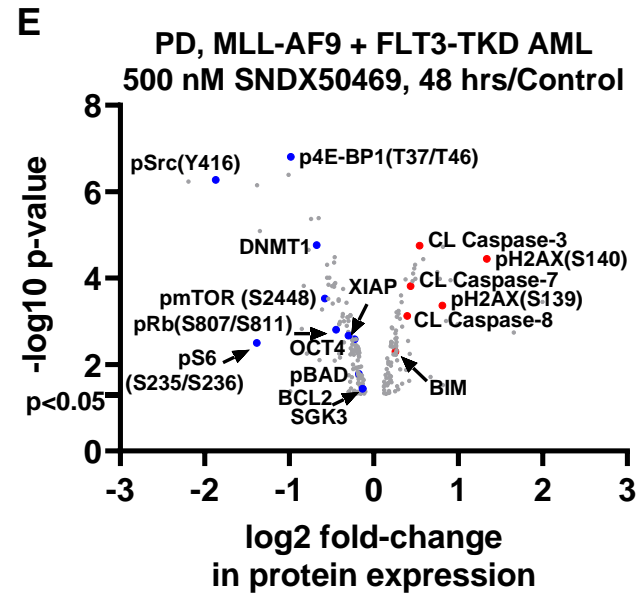
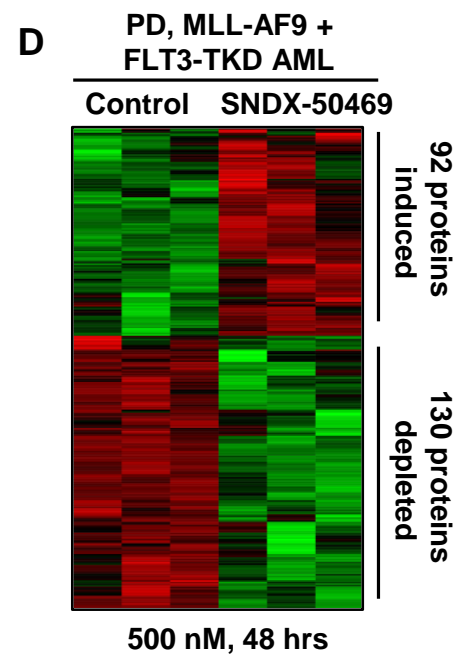
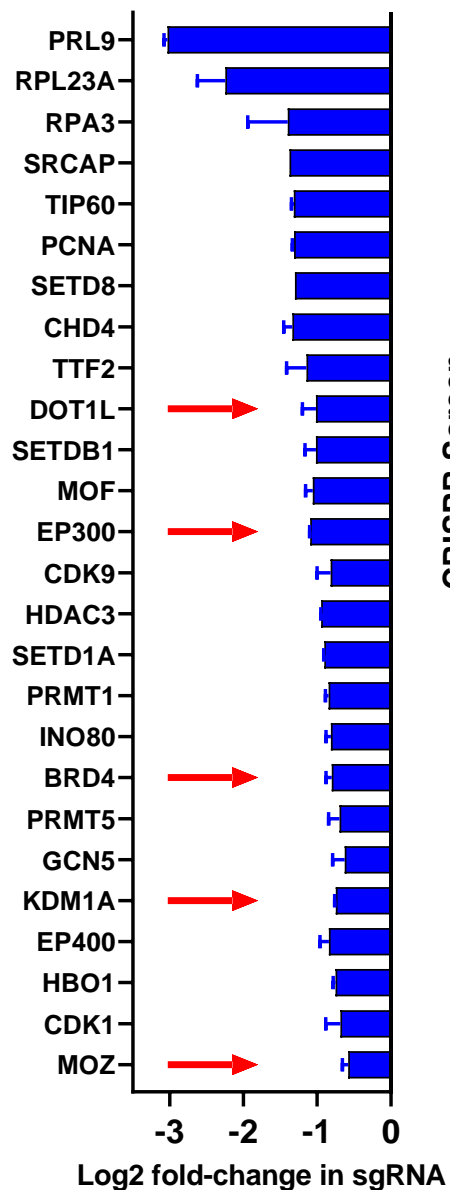


Figure S6

A MOLM13
Day 12/Day 2 Control



B MV4-11
Day12/Day 2 Control

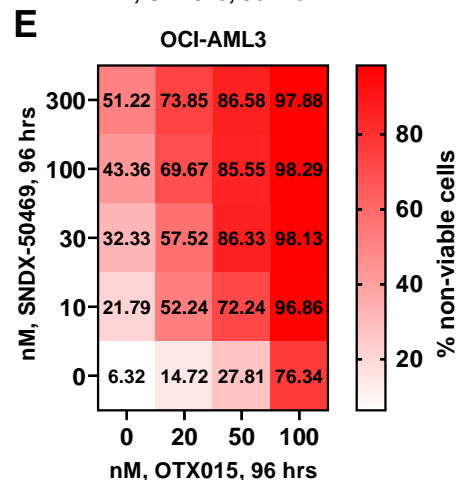
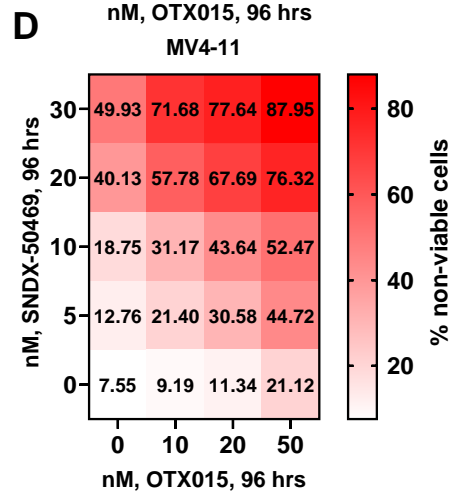
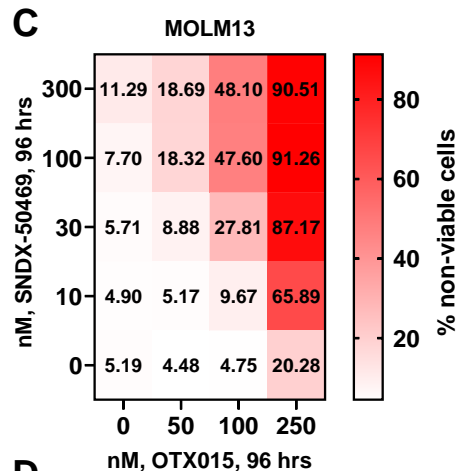
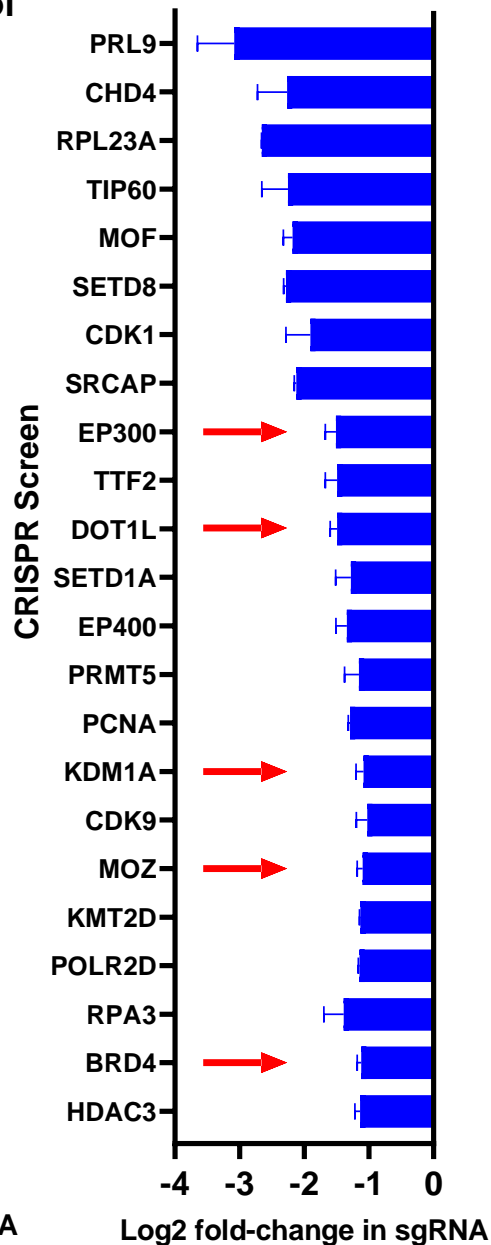
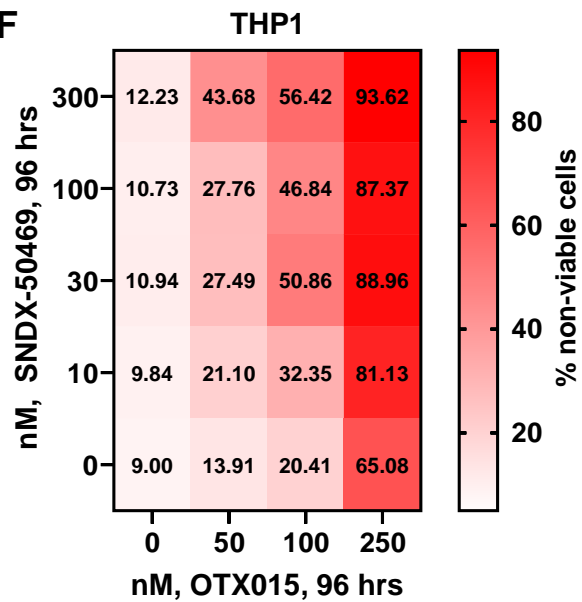
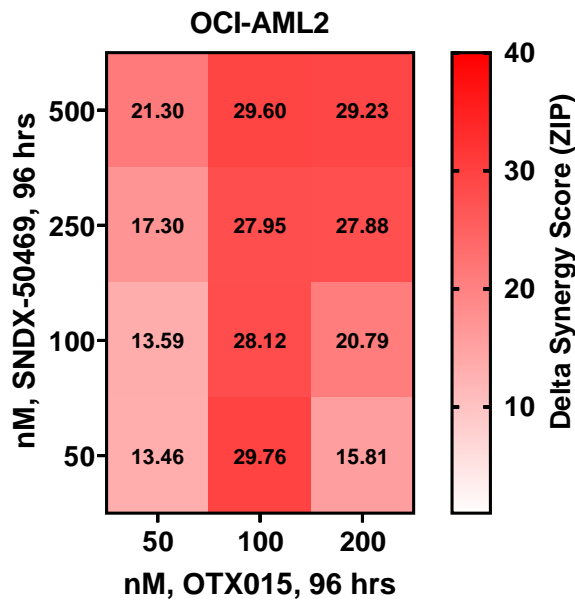
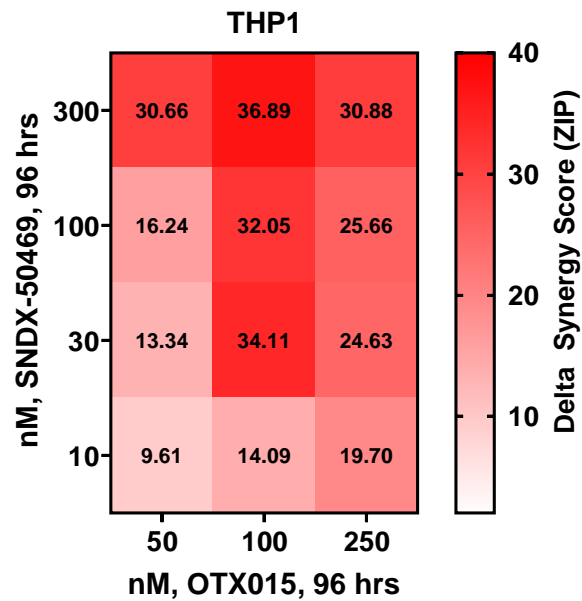
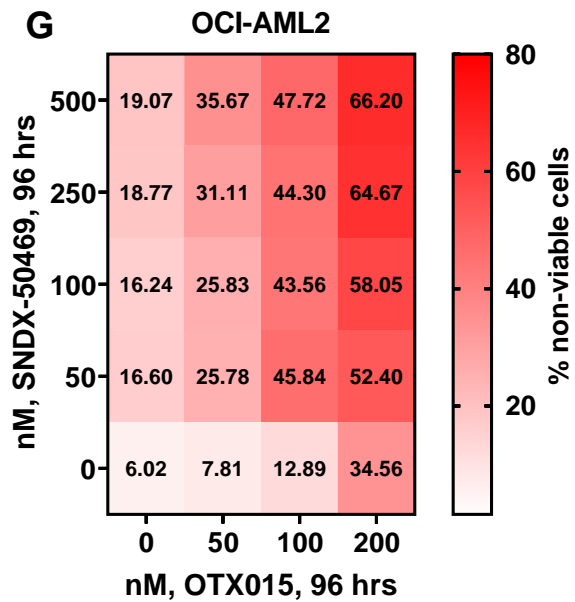


Figure S7

F**G****Figure S7**

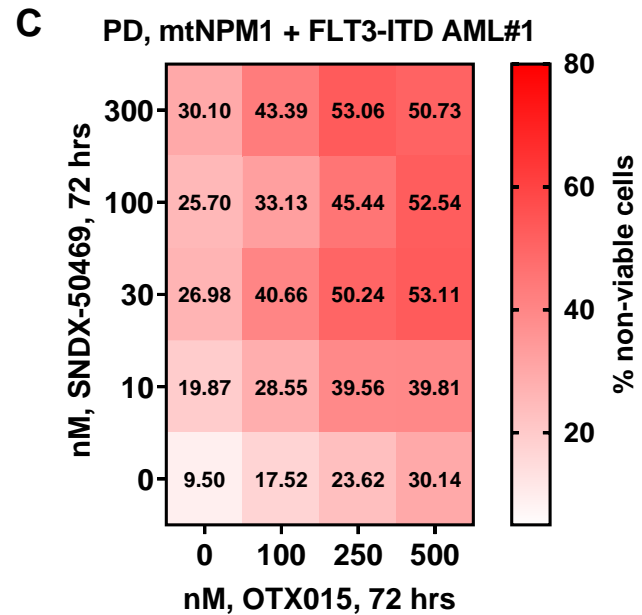
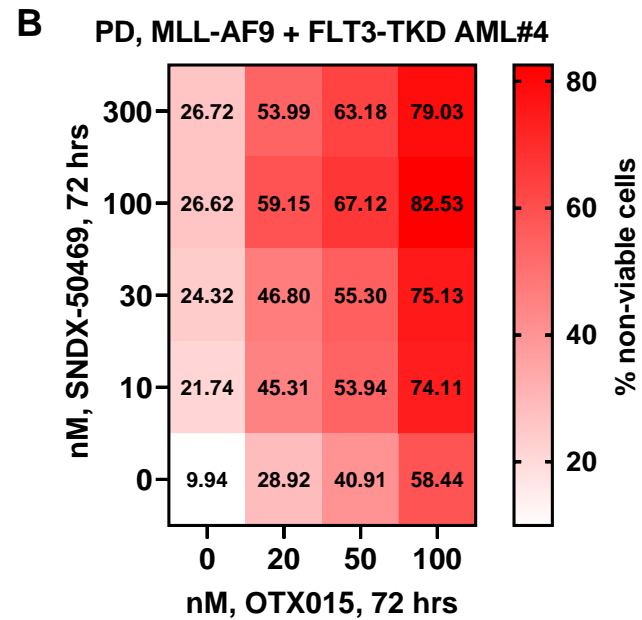
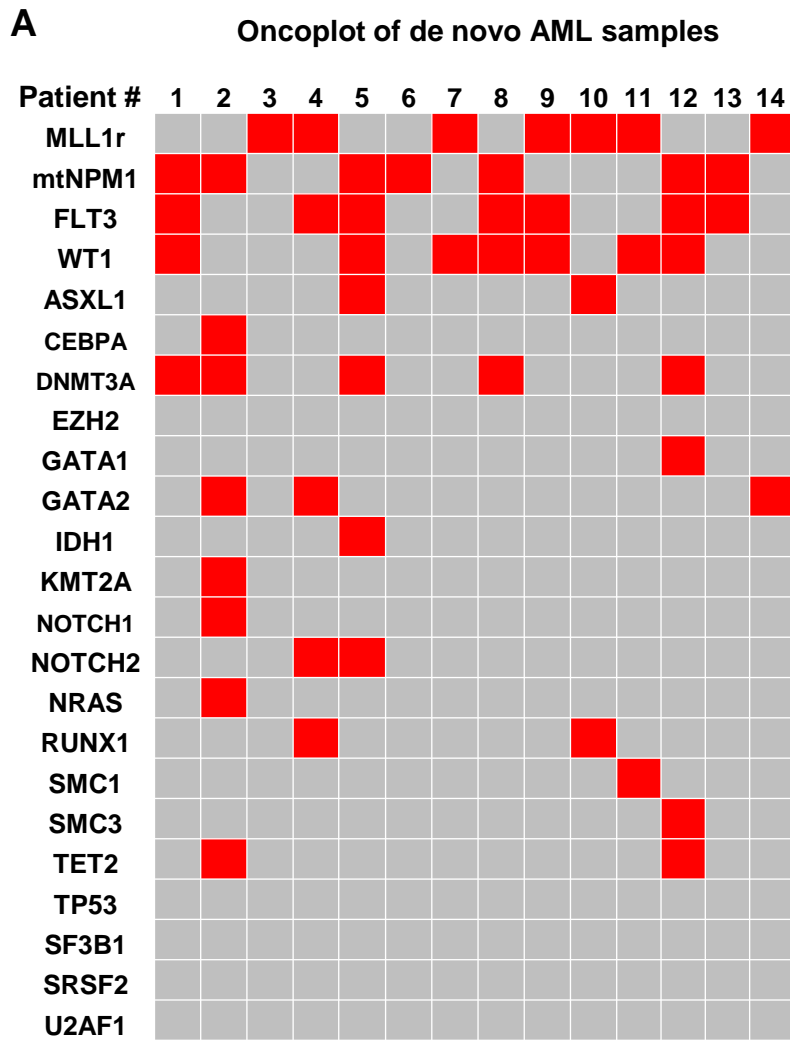


Figure S8

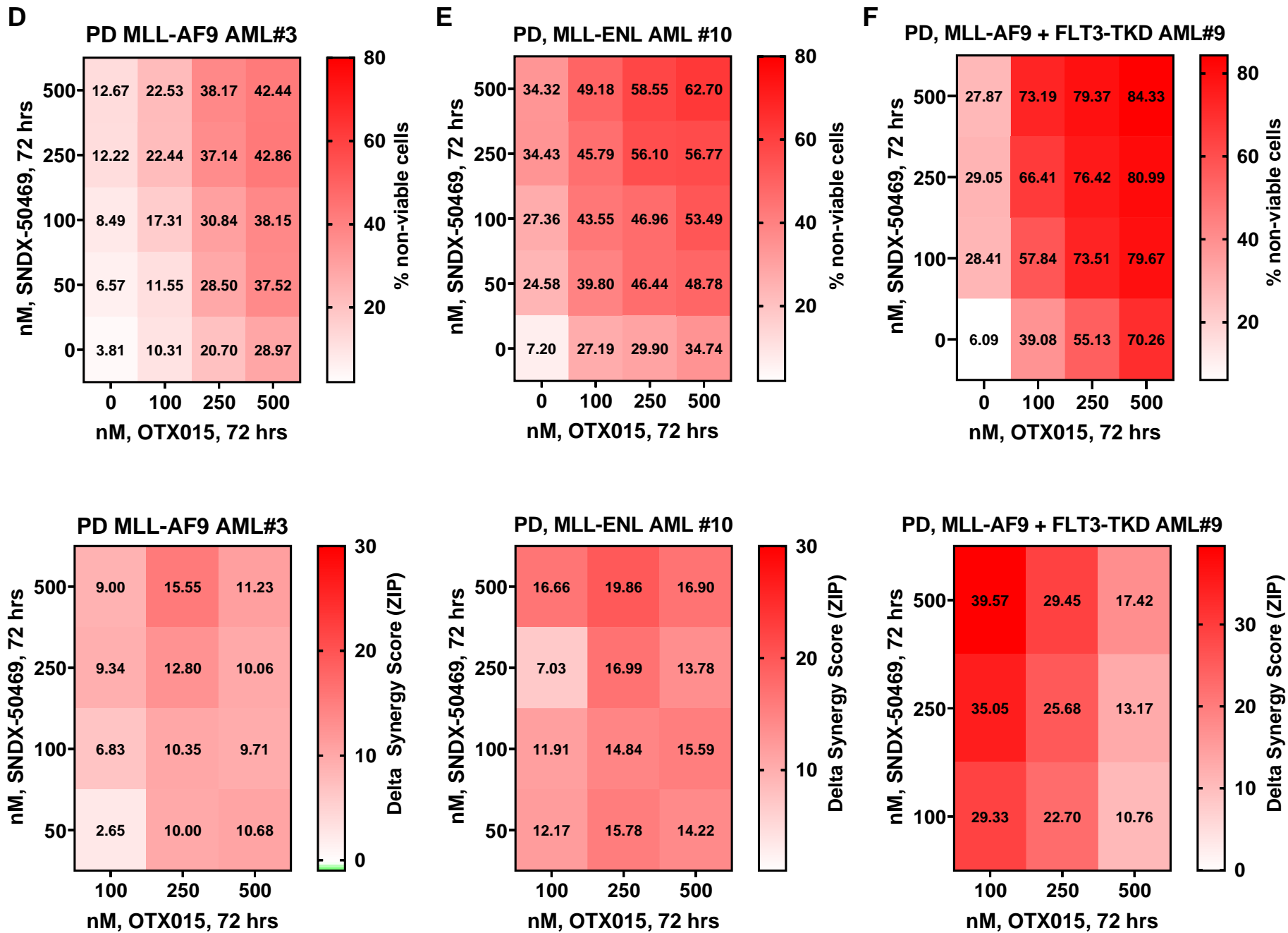
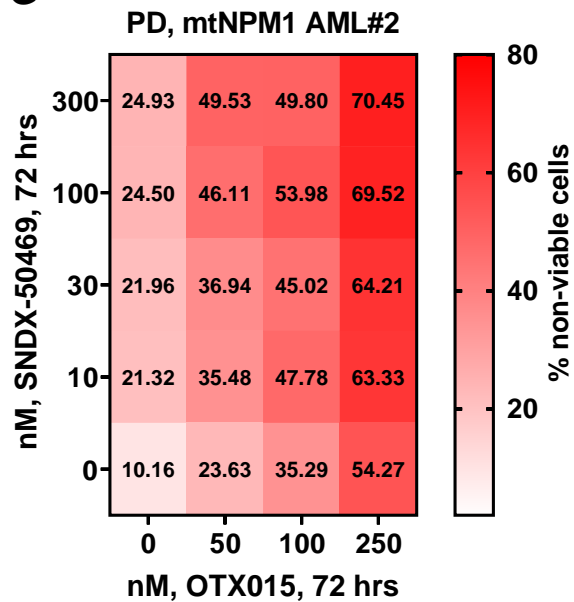
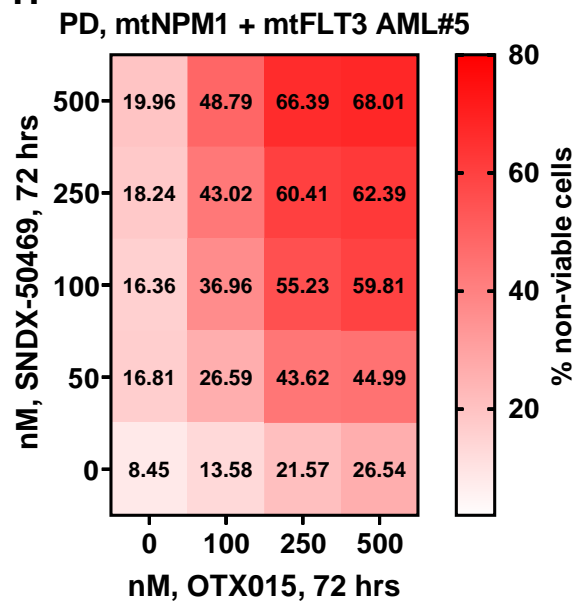
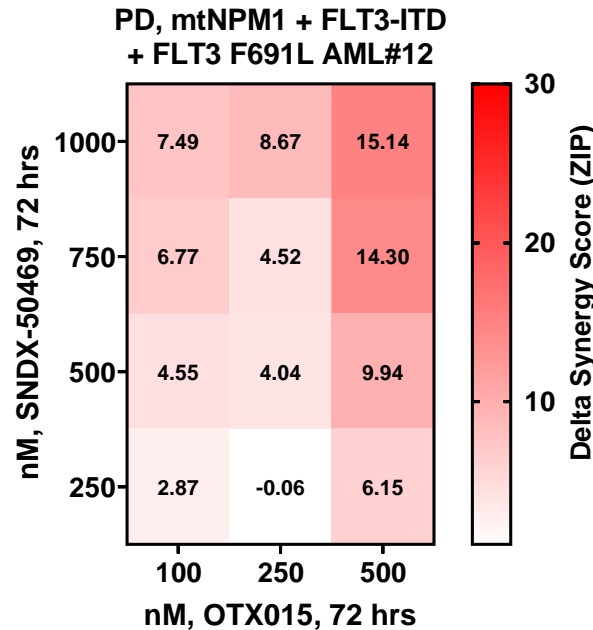
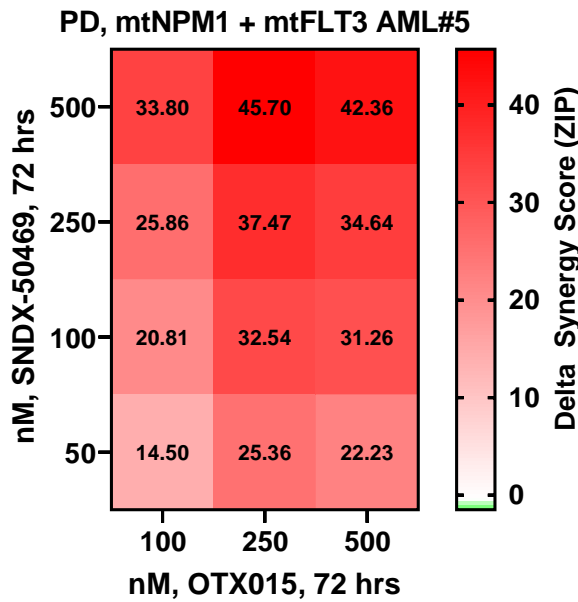
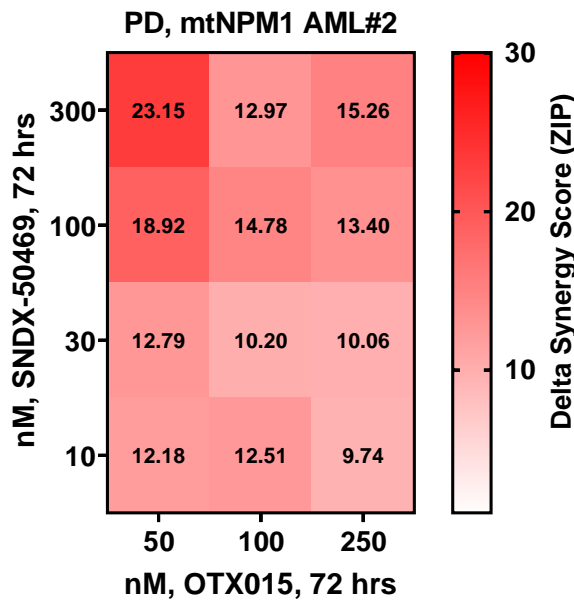
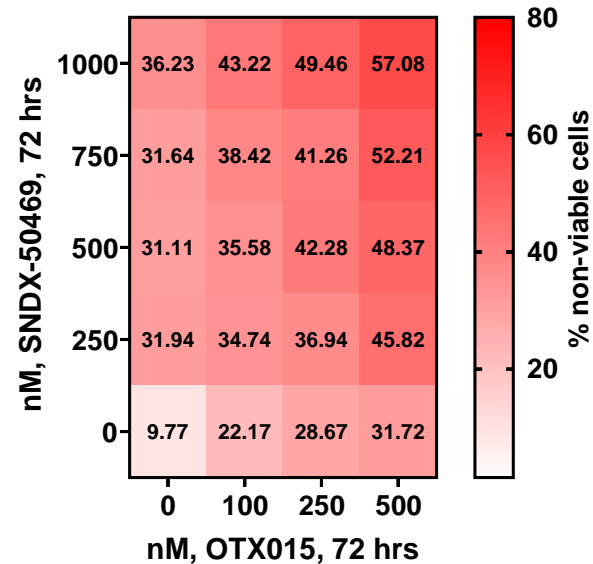
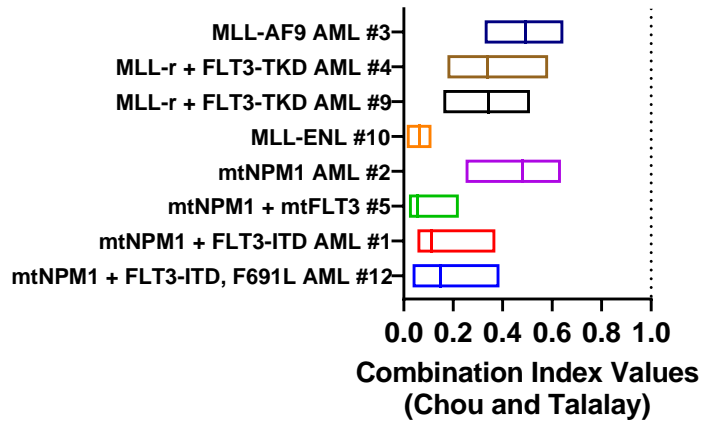
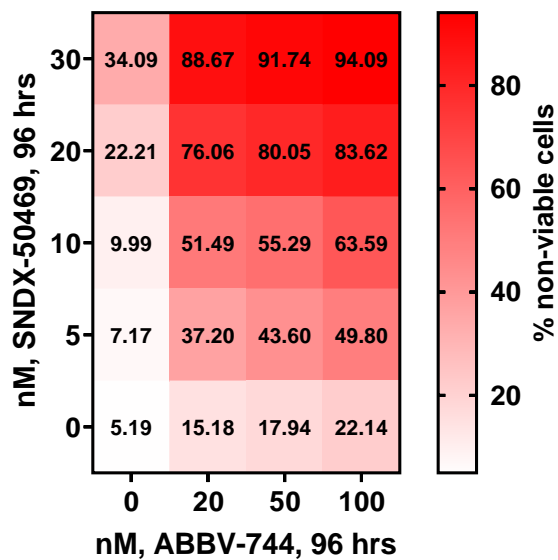
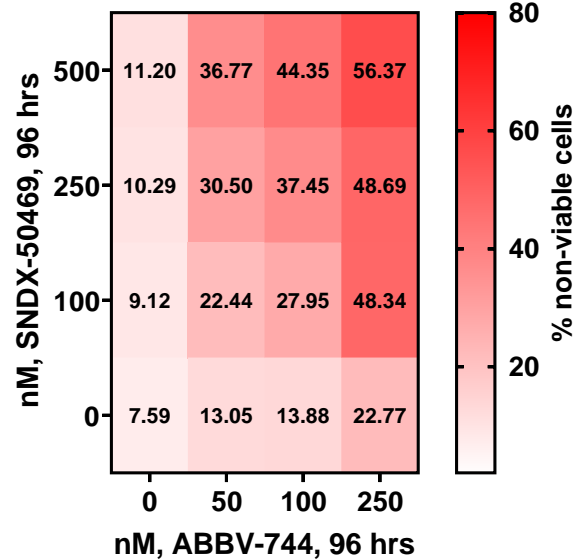
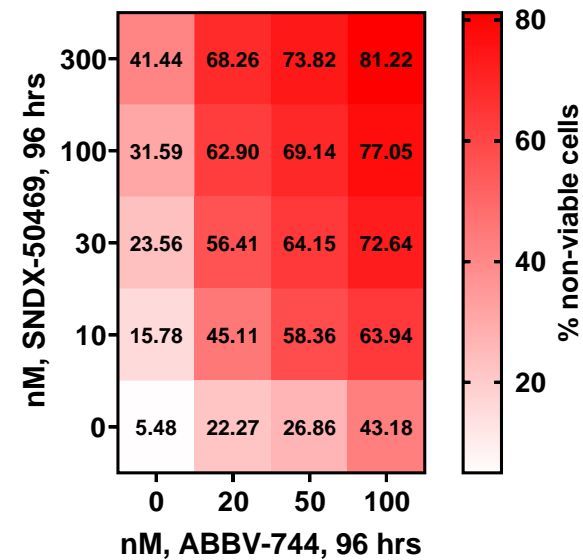
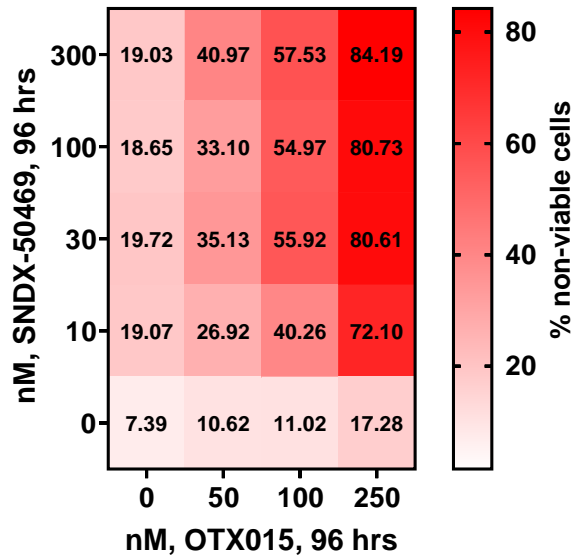
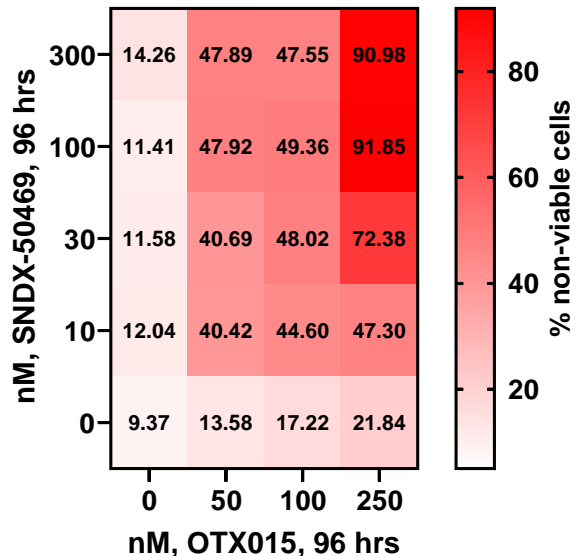


Figure S8

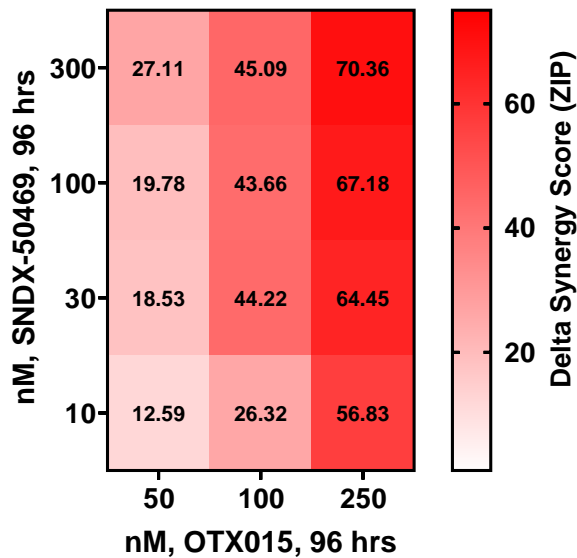
G**H****I****Figure S8**

J**SNDX-50469 and OTX015**

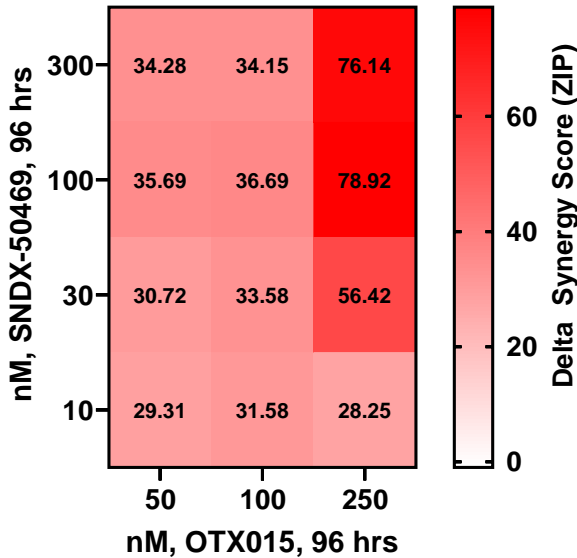
A**MV4-11****B****MOLM13****C****OCI-AML3****Figure S9**

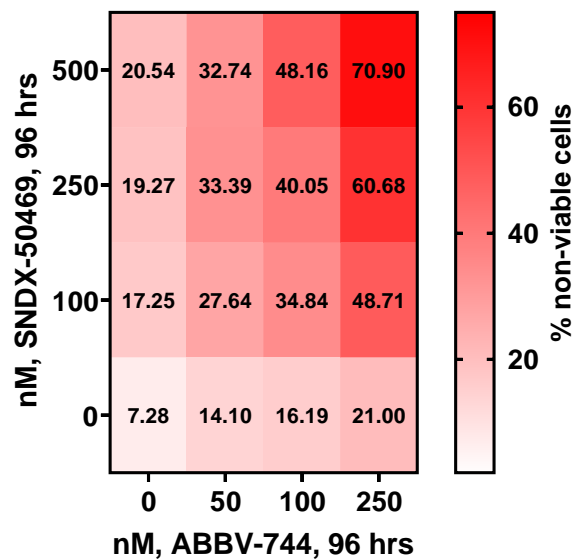
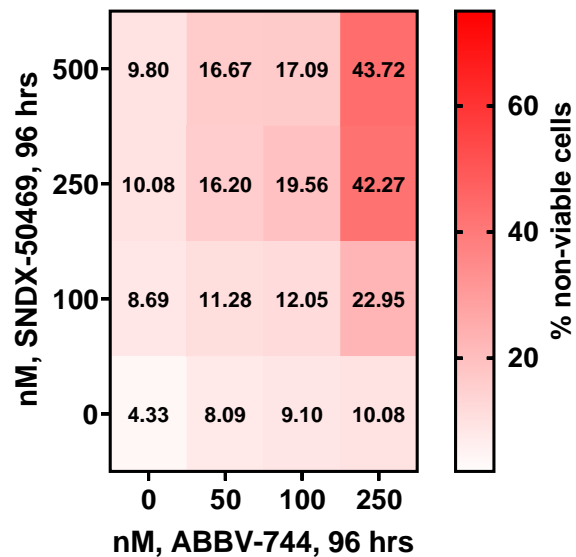
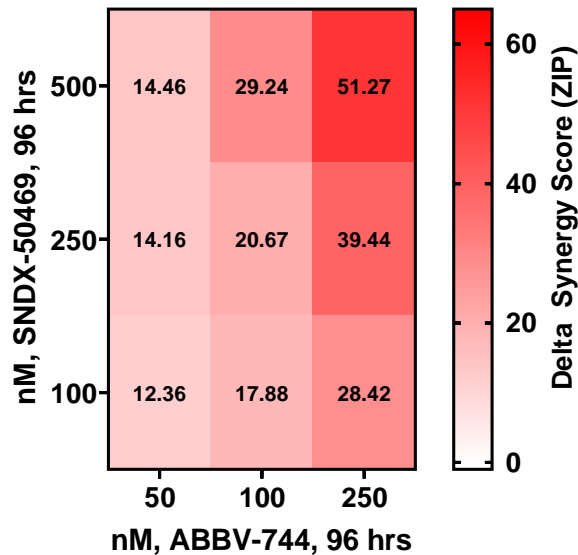
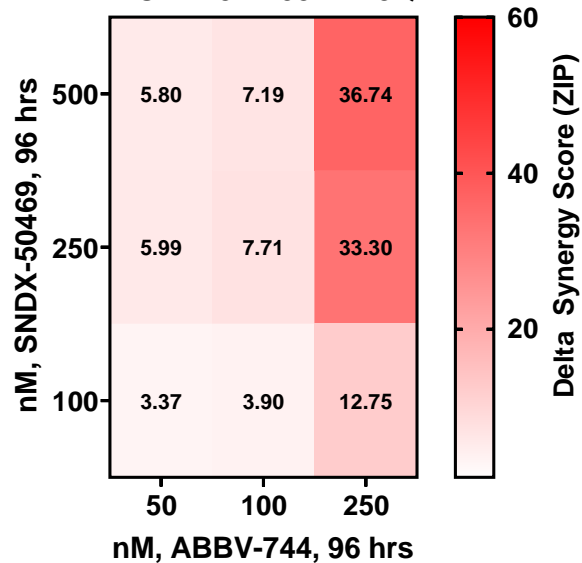
A MOLM13 TP53-R175H**B** MOLM13 TP53-R248Q

MOLM13 TP53-R175H



MOLM13 TP53-R248Q



C**MOLM13 TP53-R175H****D****MOLM13 TP53-R248Q****MOLM13 TP53-R175H****MOLM13 TP53-R248Q**

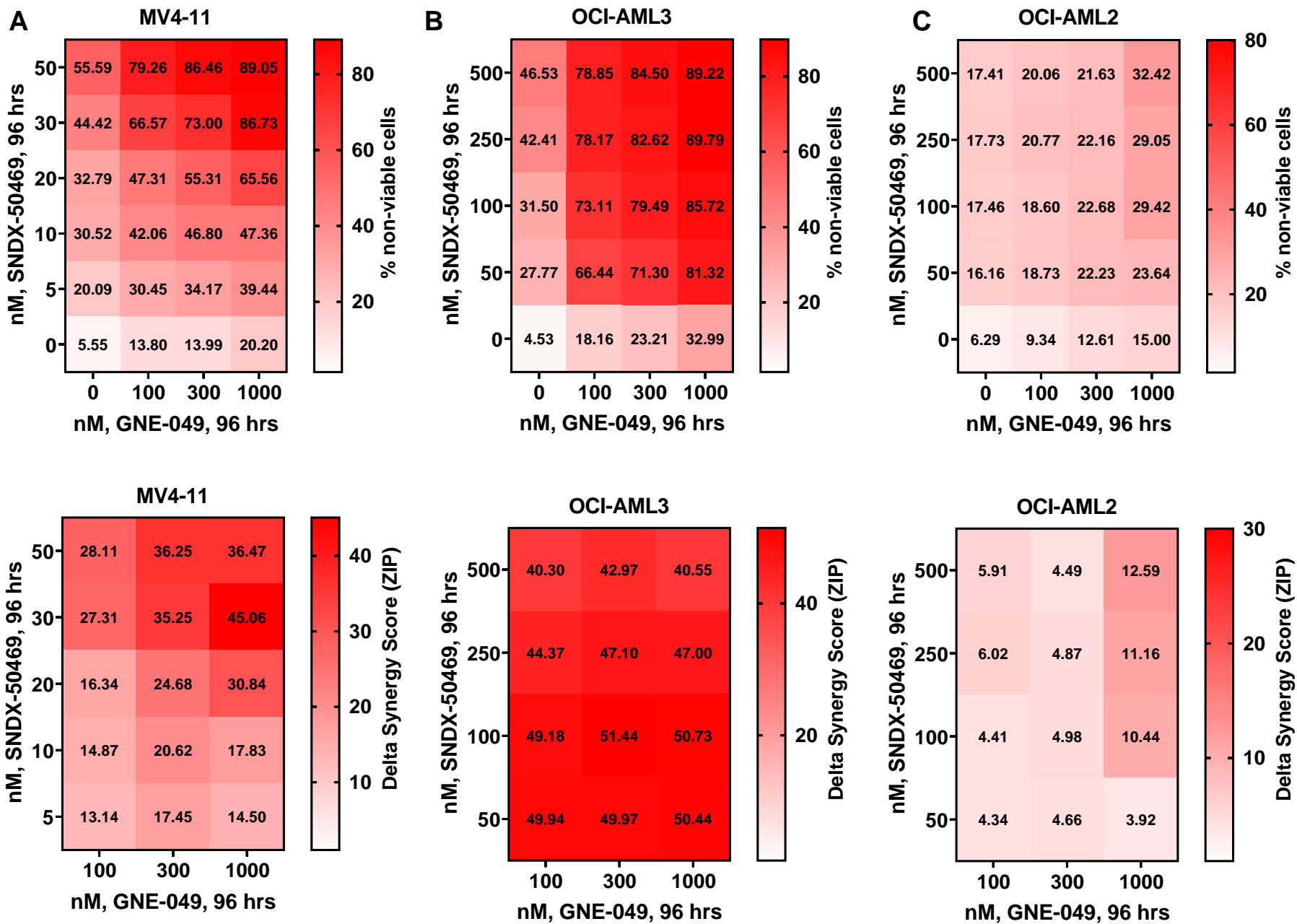


Figure S11

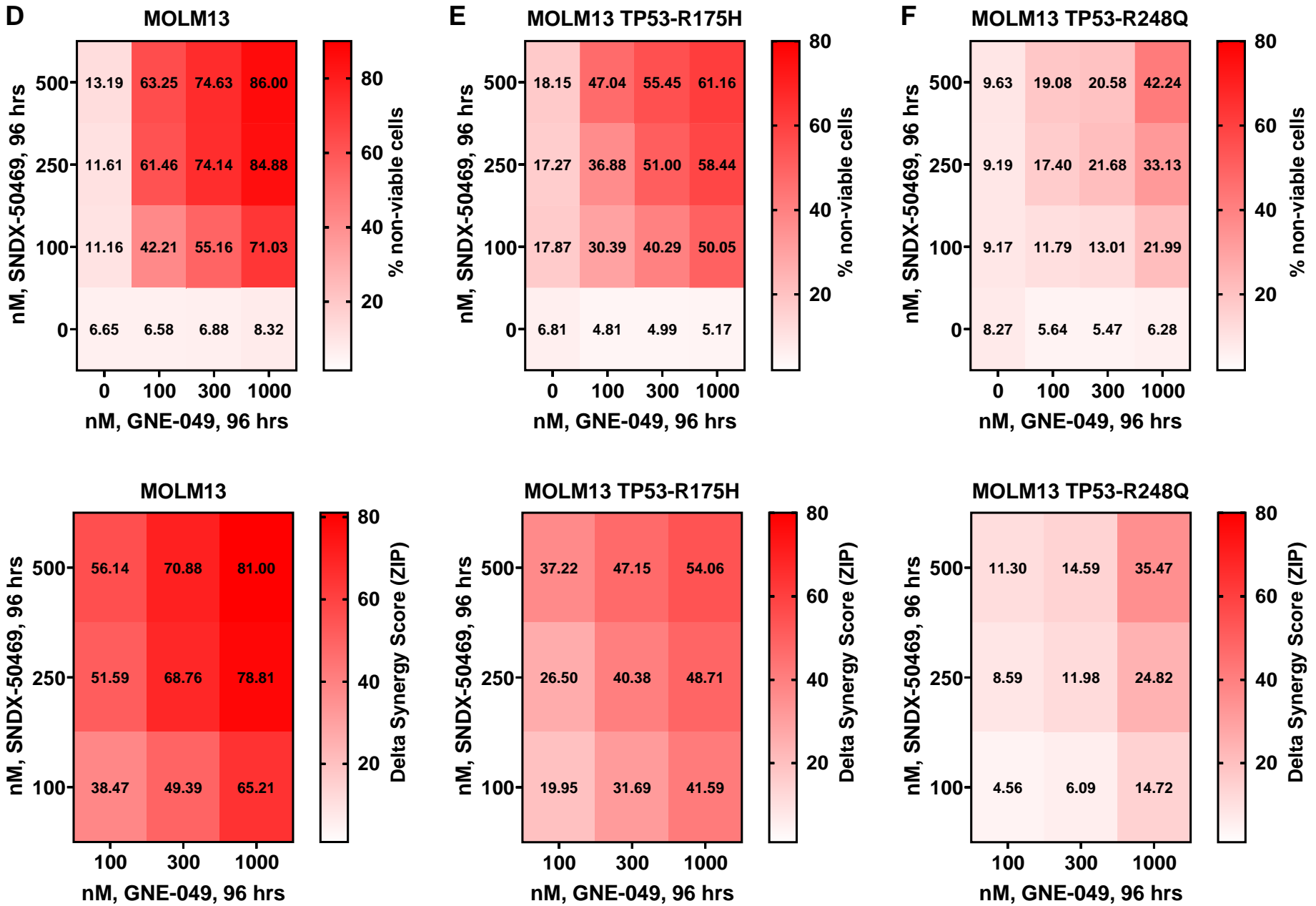
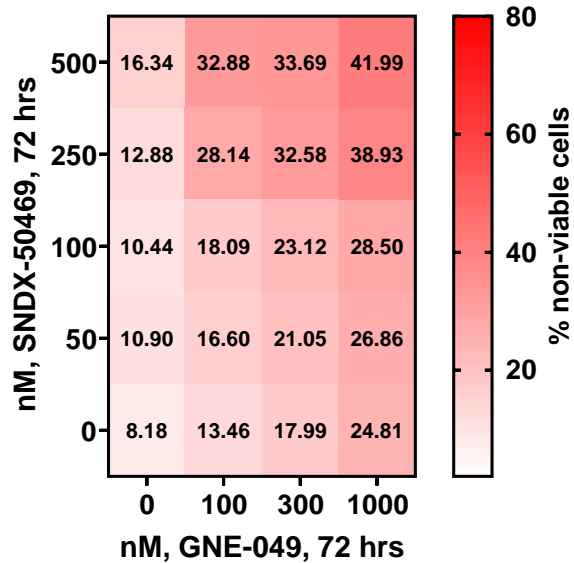
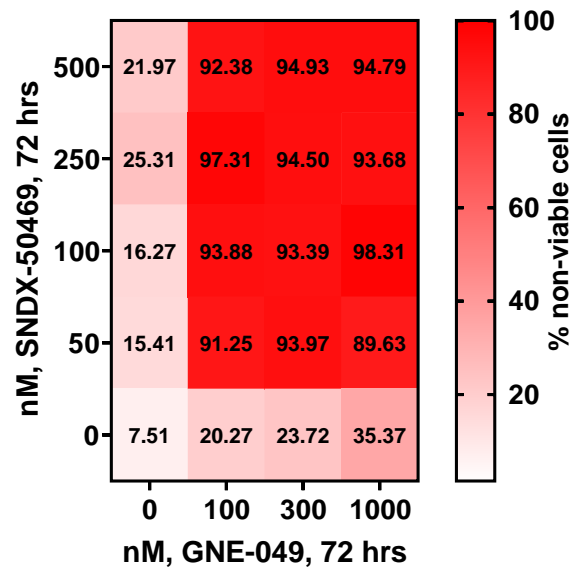
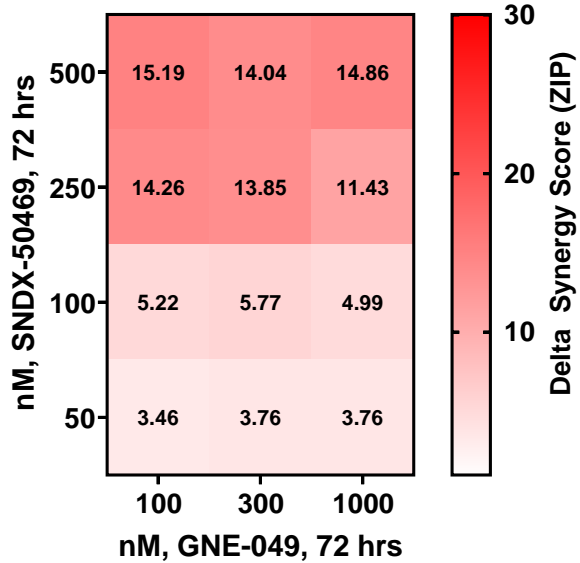


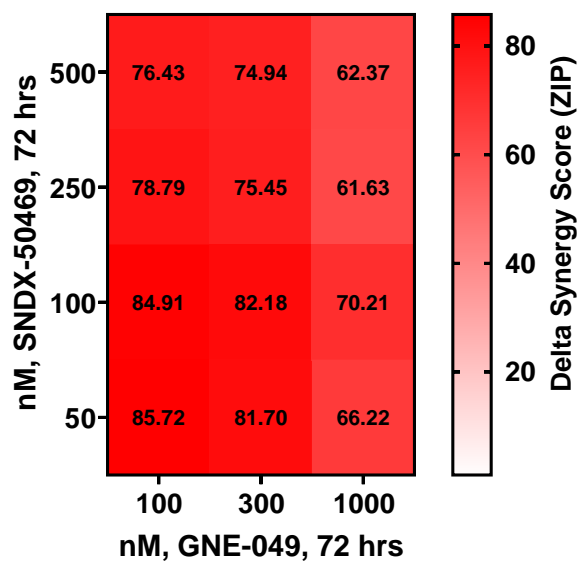
Figure S11

G PD MLL-AF9 AML #3**H** PD MLL-AF9 + FLT3-TKD AML#4

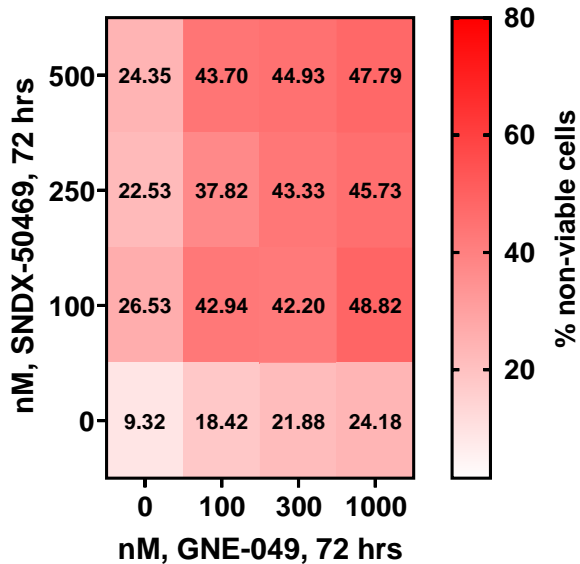
PD MLL-AF9 AML#3



PD MLL-AF9 + FLT3-TKD AML#4

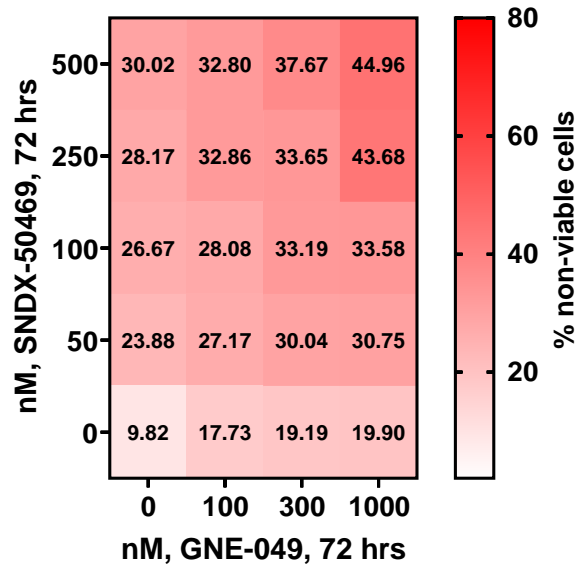


I PD mtNPM1 + FLT3-ITD + F691L AML#12



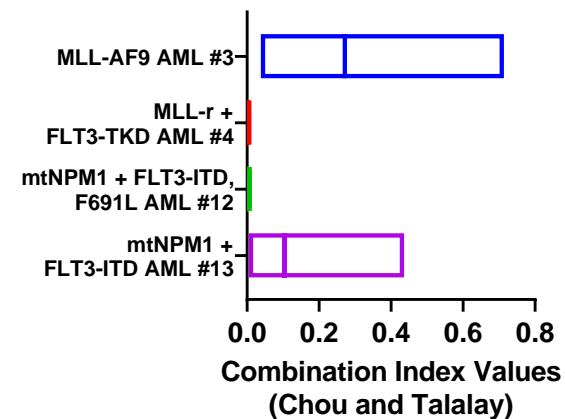
J

PD mtNPM1 + FLT3-ITD AML#13

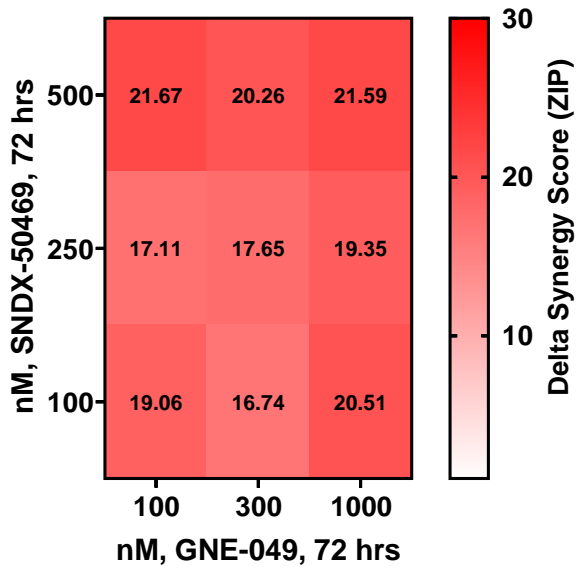


K

SNDX-50469 and GNE-049



PD mtNPM1 + FLT3-ITD + F691L AML#12



PD mtNPM1 + FLT3-ITD AML#13

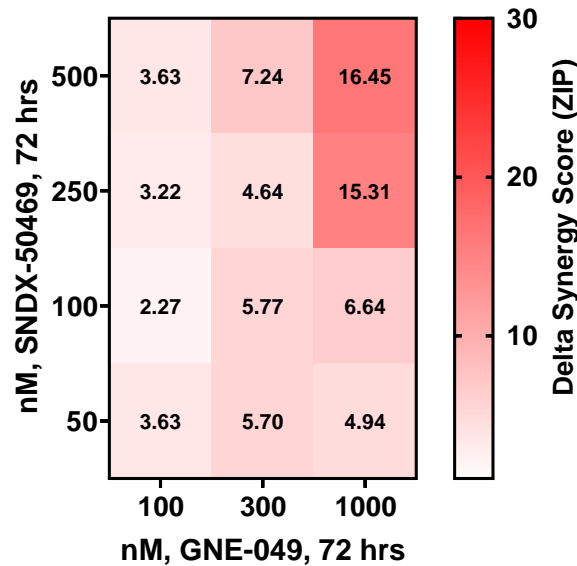


Figure S11

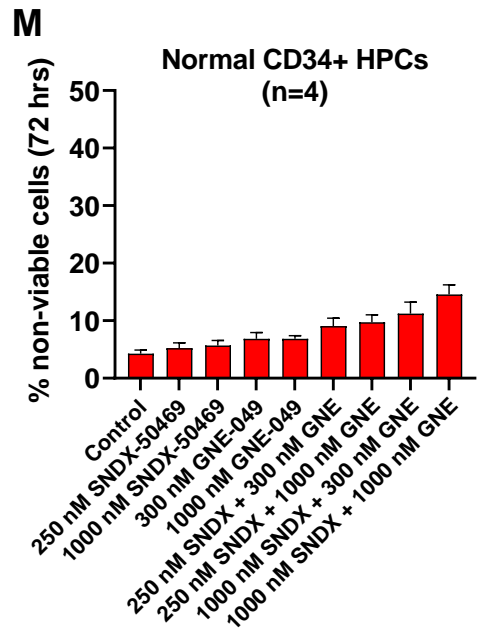
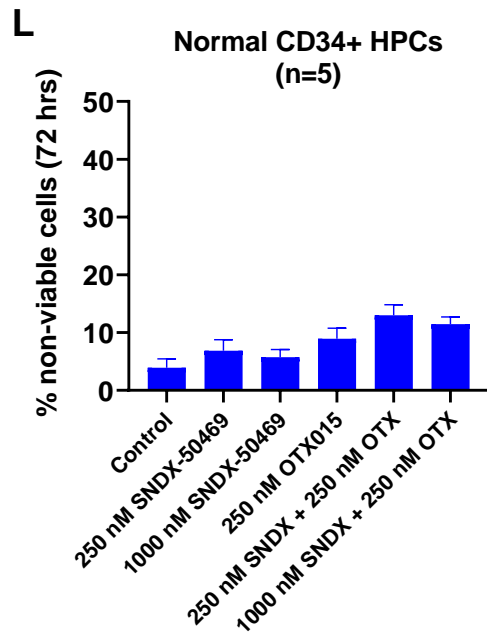


Figure S11

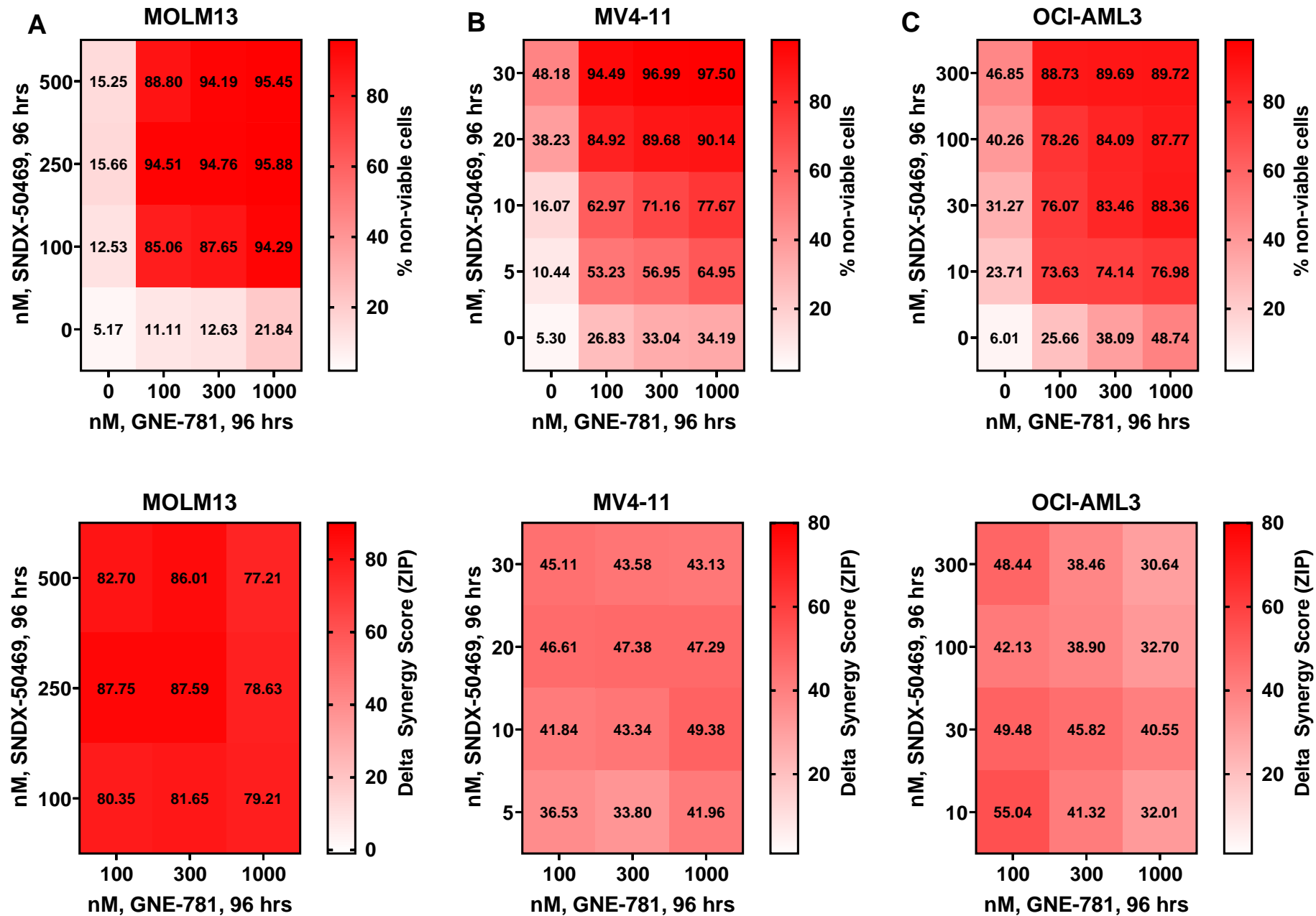


Figure S12

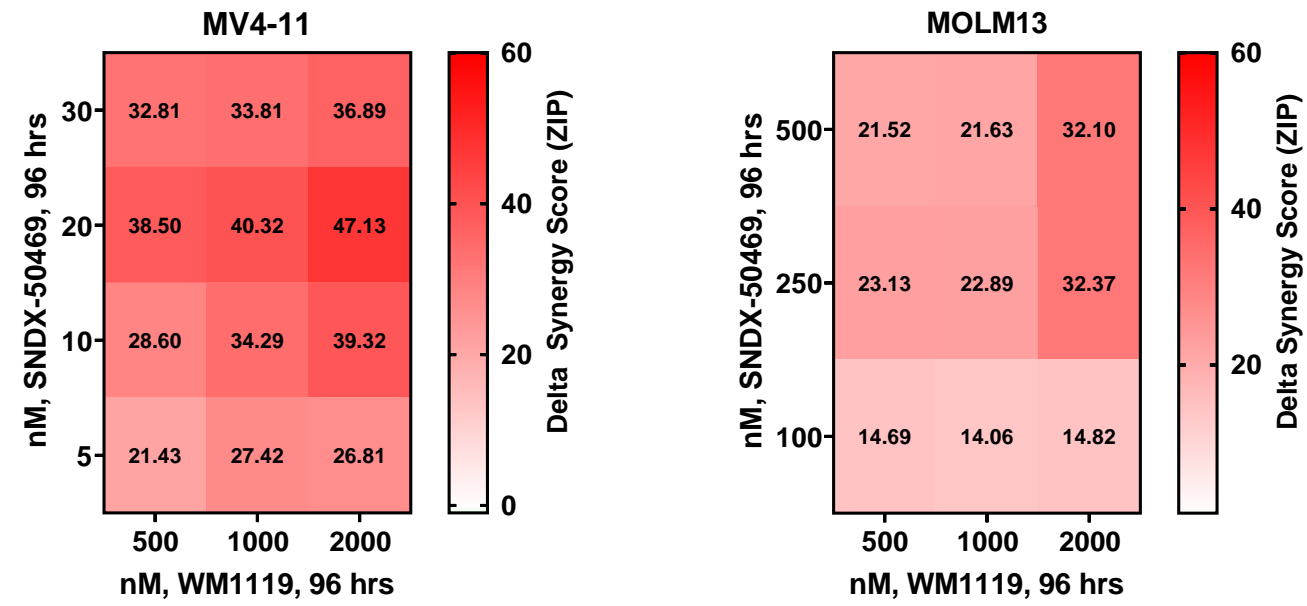
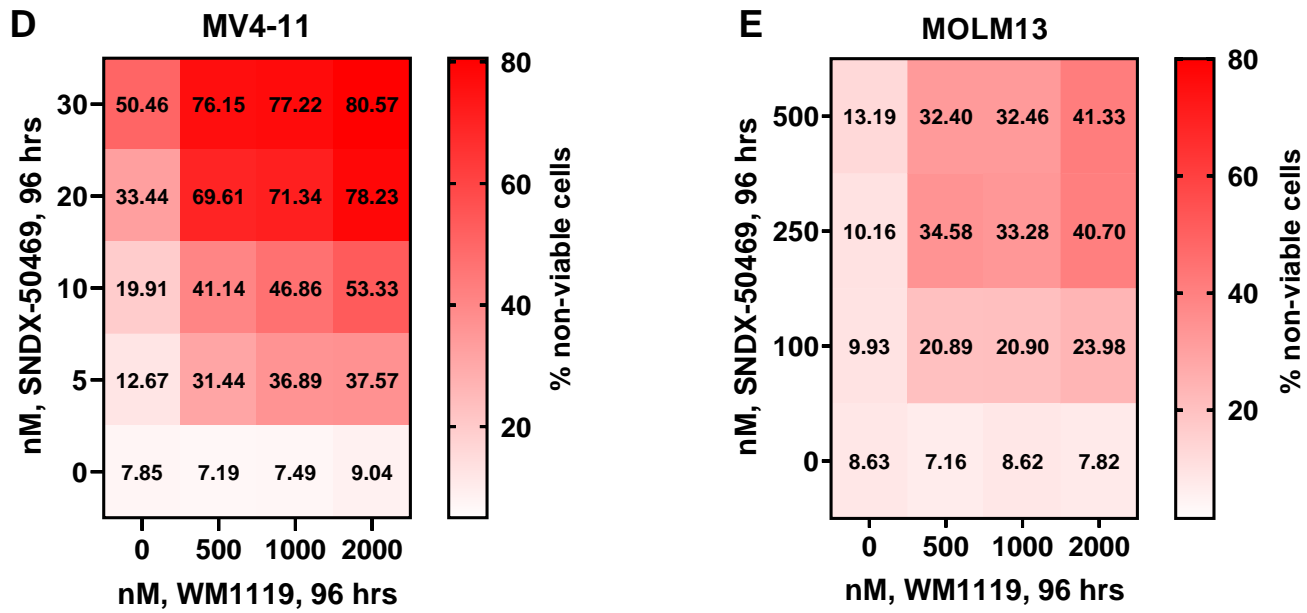


Figure S12

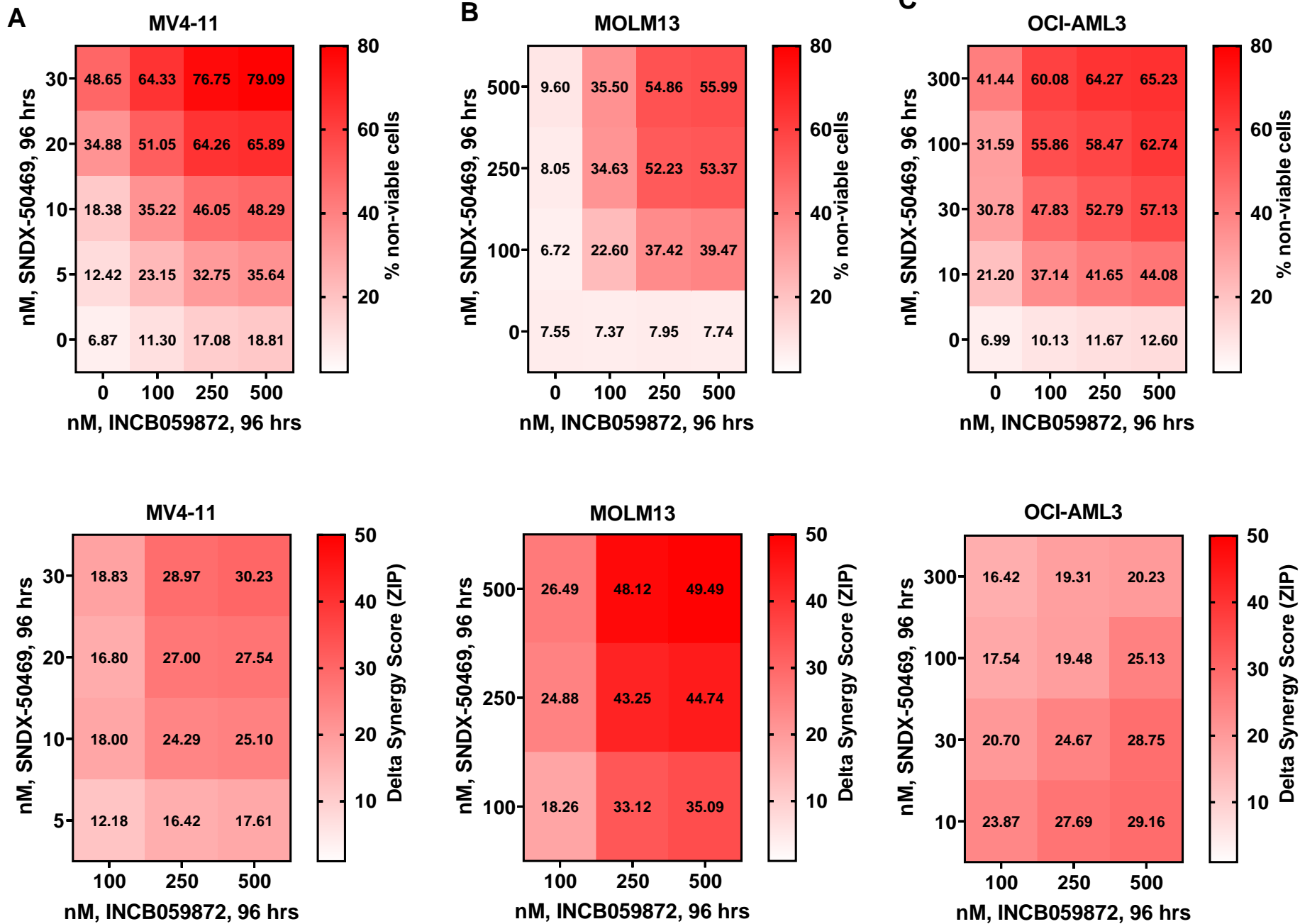
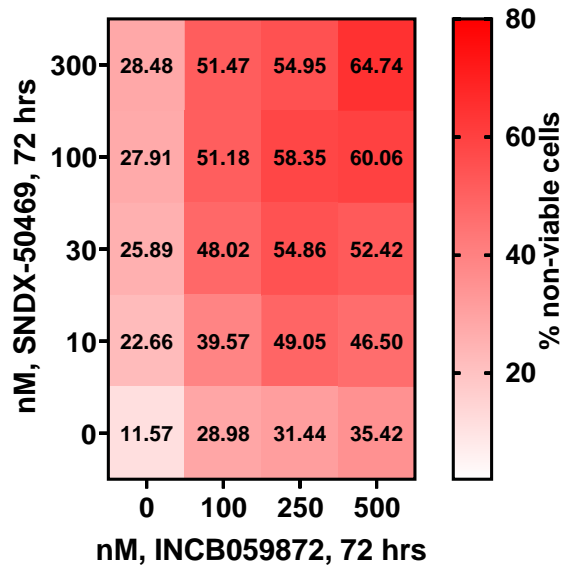
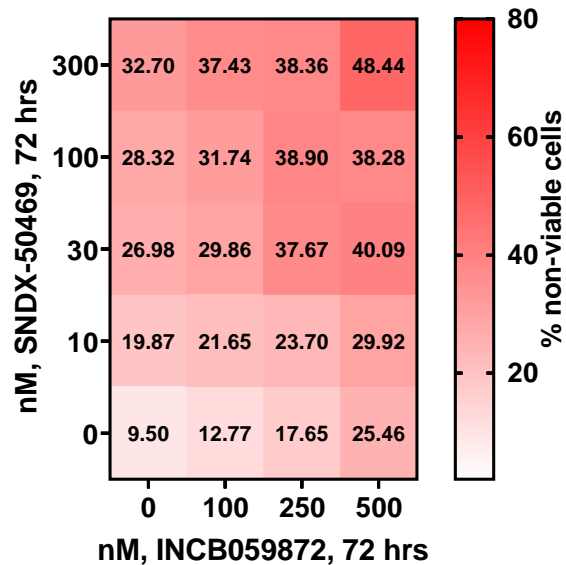
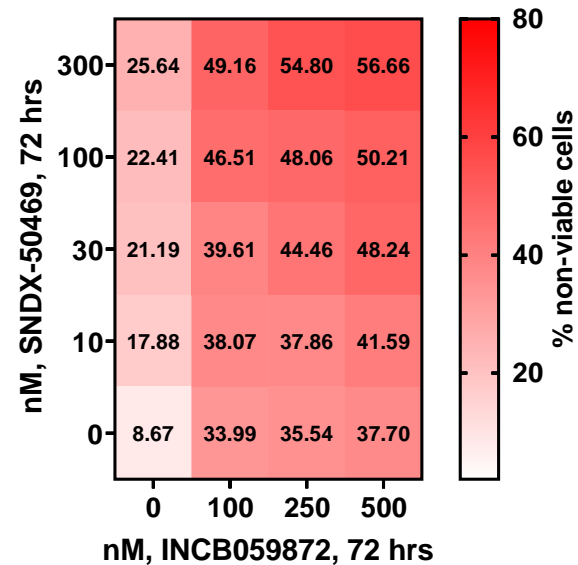
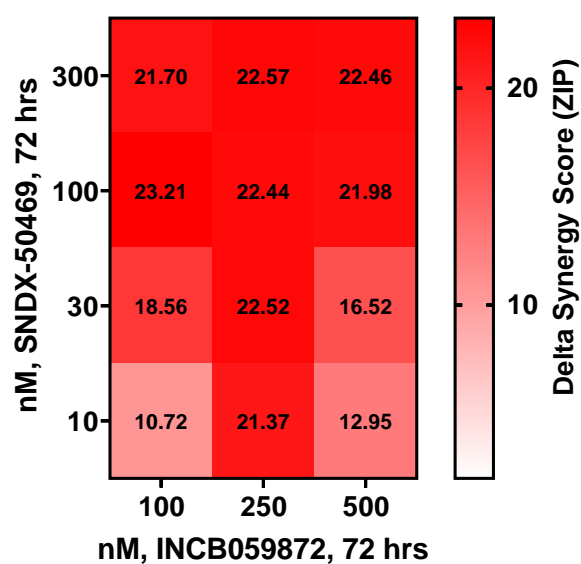
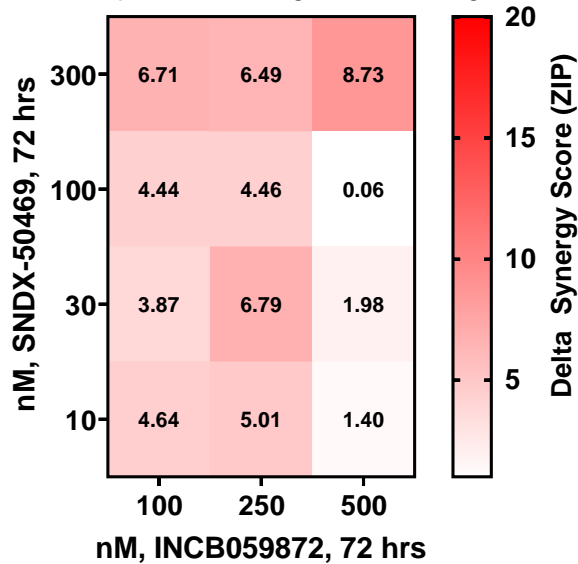
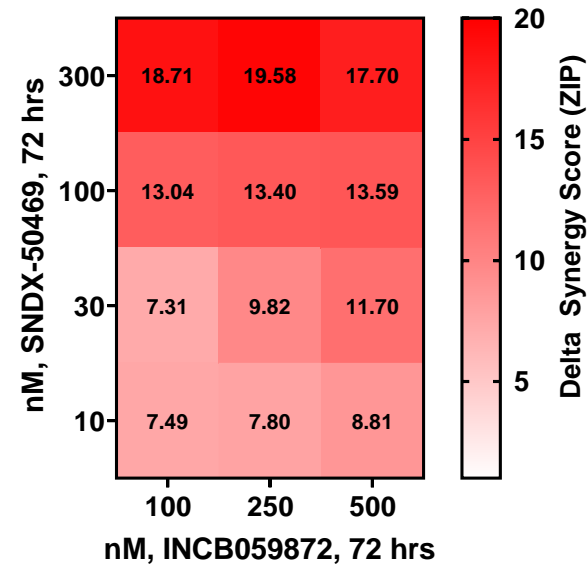
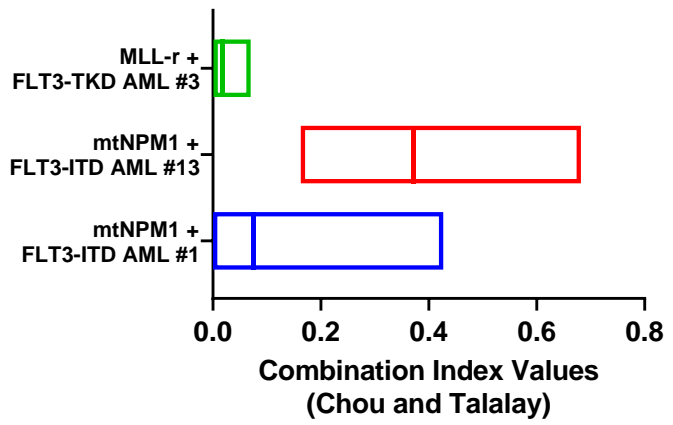
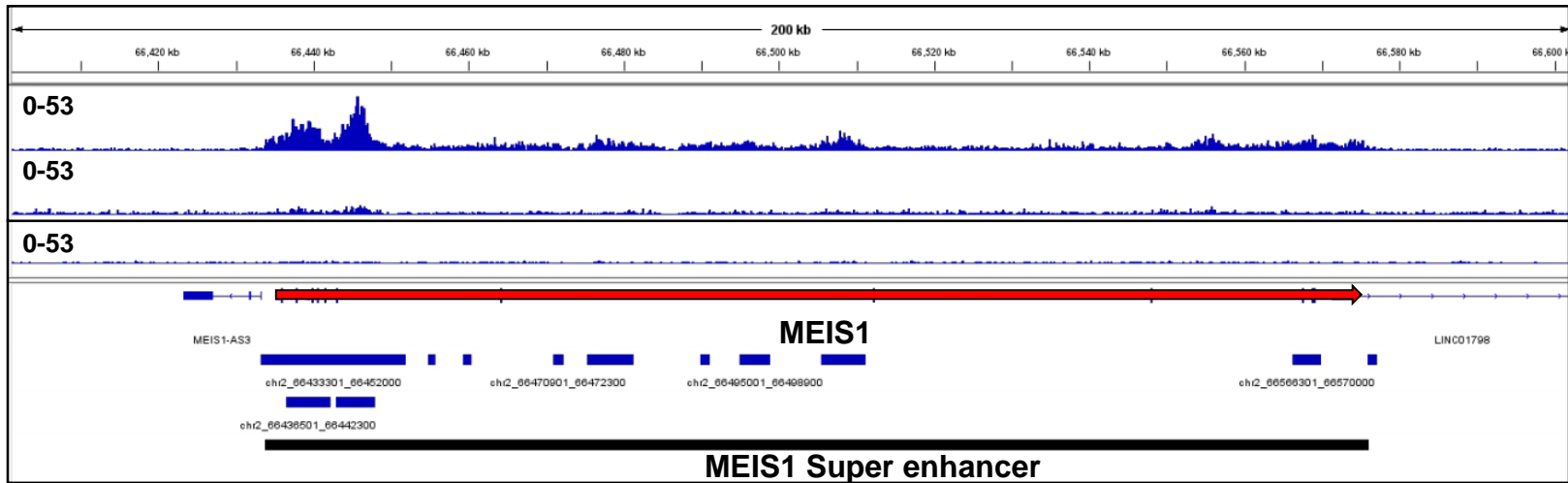
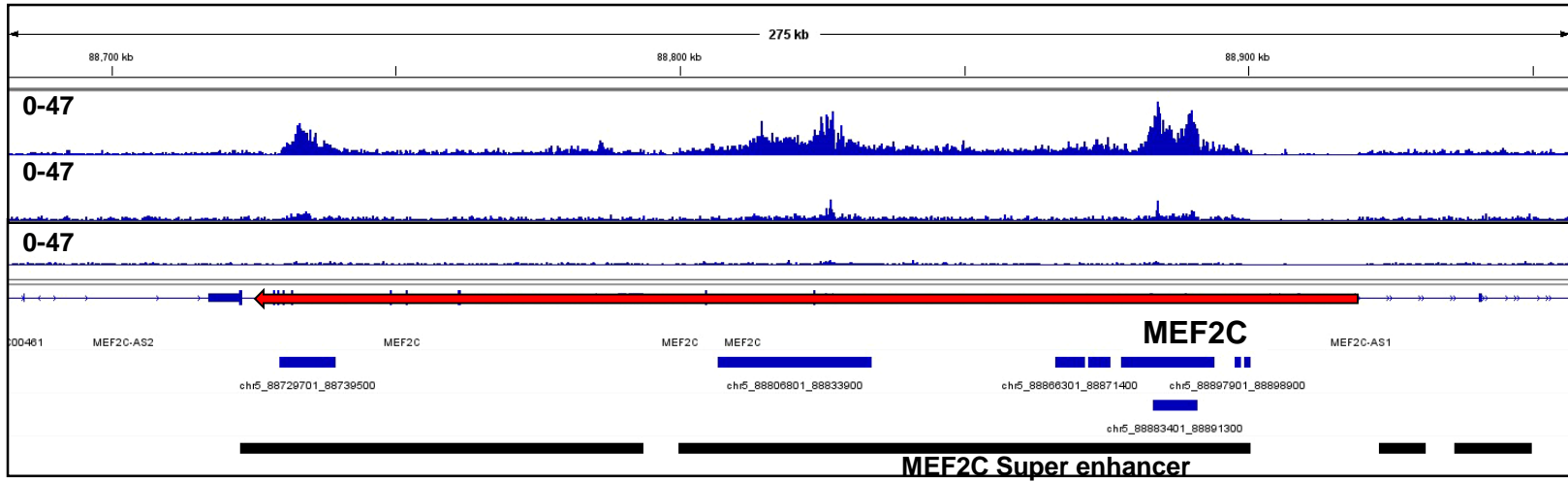
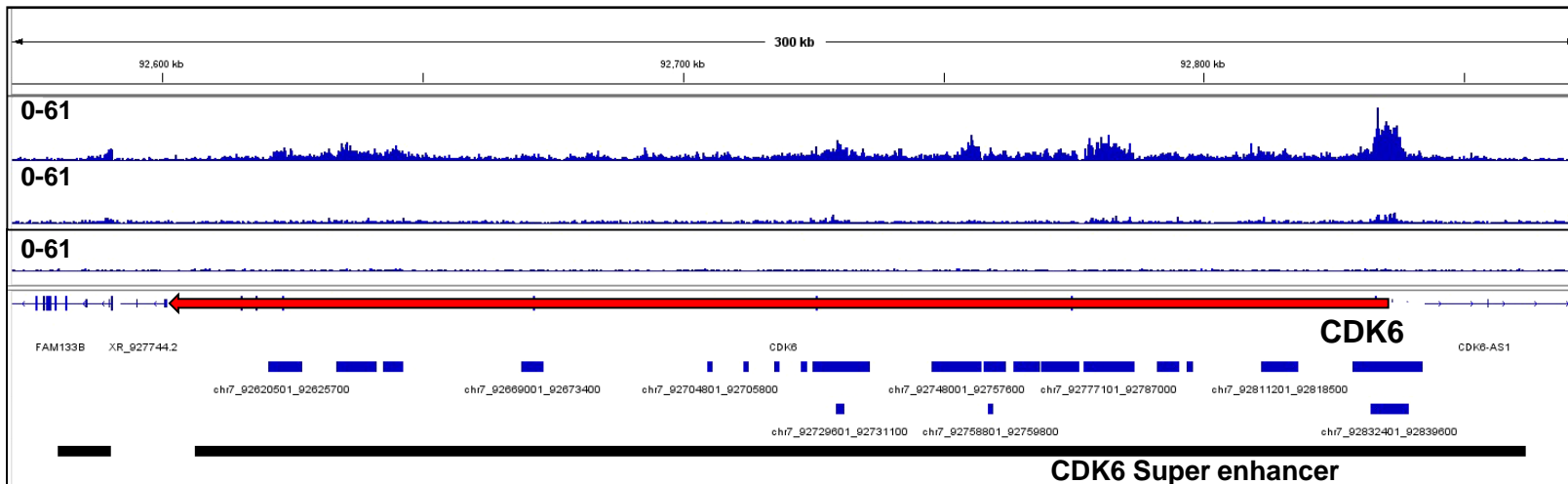
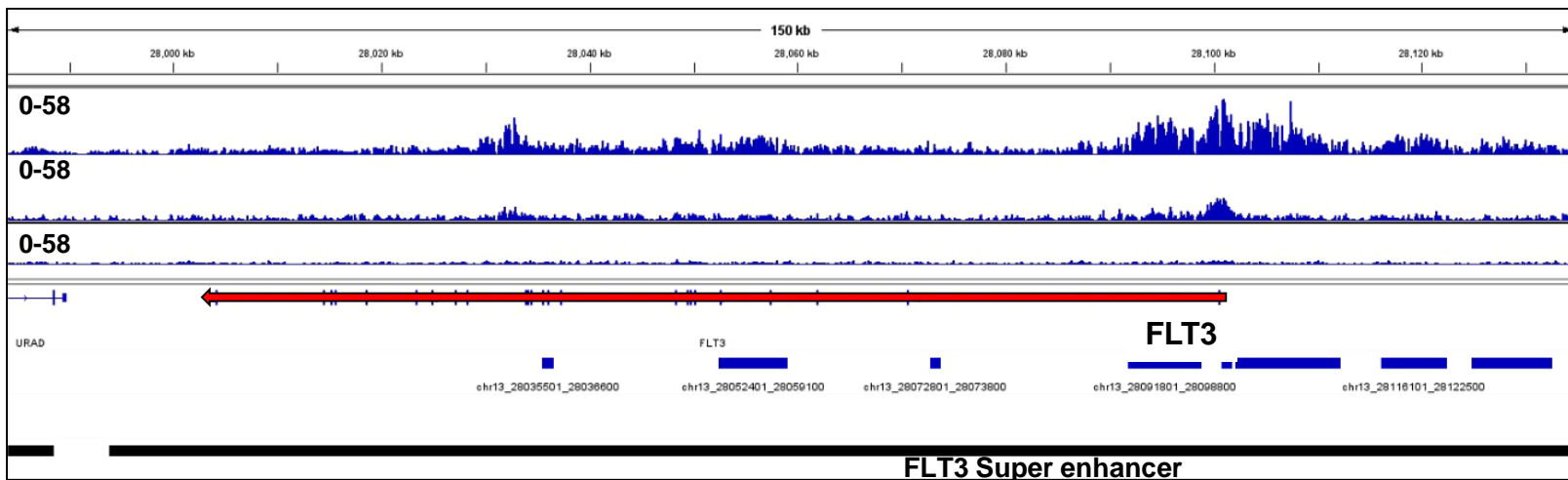


Figure S13

D PD MLL-AF9 + FLT3-TKD AML#4**E PD mtNPM1 + FLT3-ITD AML#13****F PD mtNPM1 + FLT3-ITD AML#1****PD MLL-AF9 + FLT3-TKD AML#4****PD mtNPM1 + FLT3-ITD AML#13****PD mtNPM1 + FLT3-ITD AML#1**

G**SNDX-50469 and INCB**

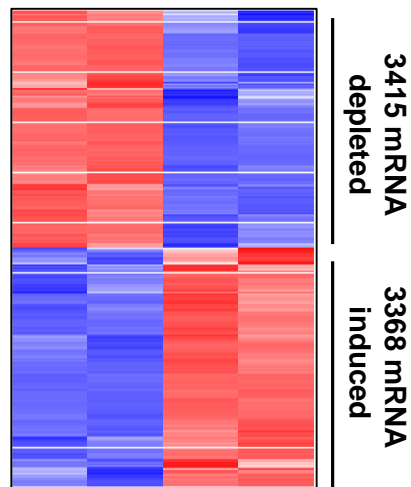
A**MOLM13****B****MOLM13**

C**MOLM13****D****MOLM13**

E

MOLM13

500 nM SNDX SNDX + OTX015



1.25 fold and $p < 0.05$

F