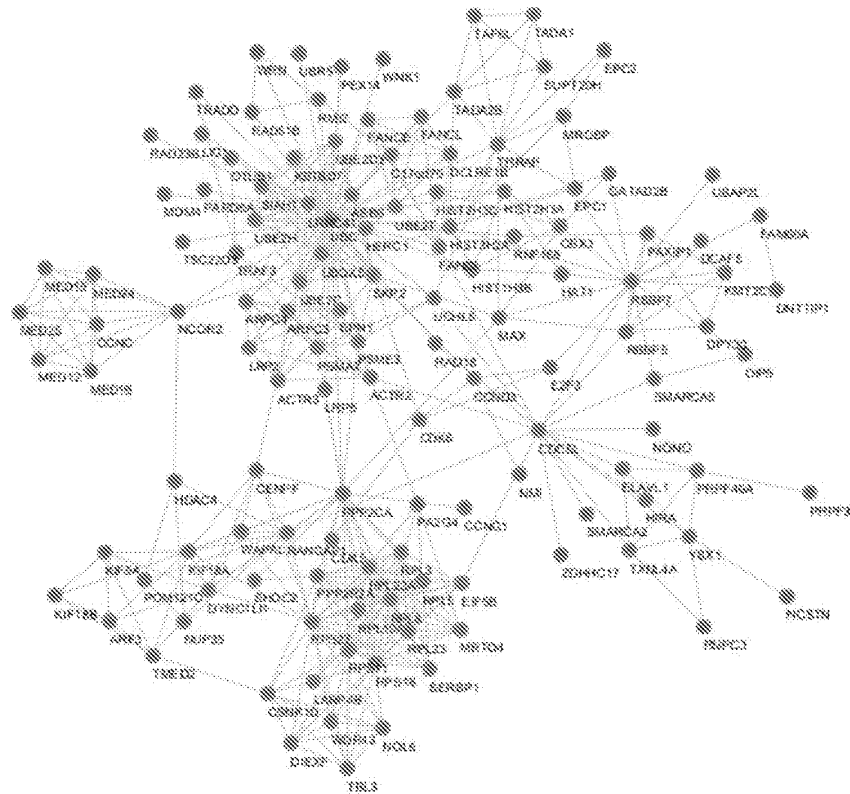


A.



B.

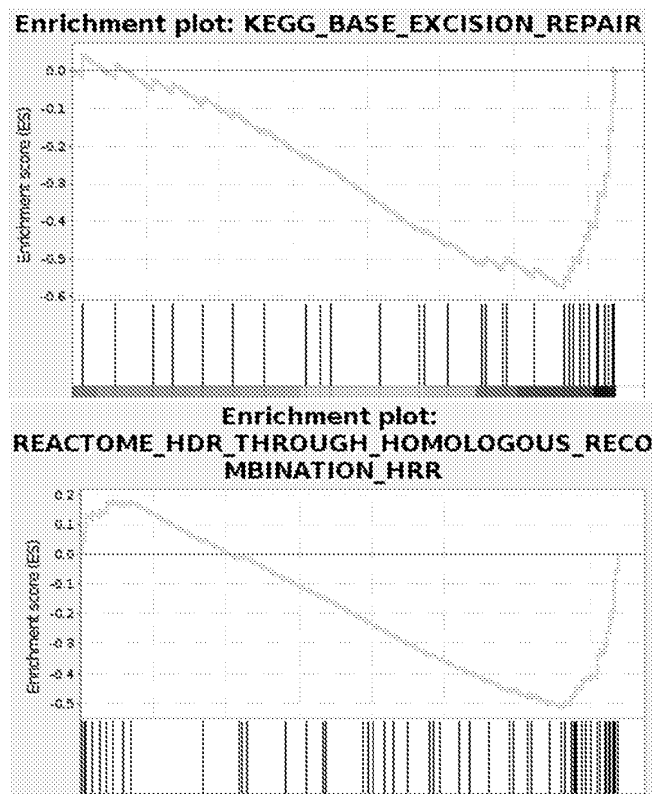


Figure 1

C.

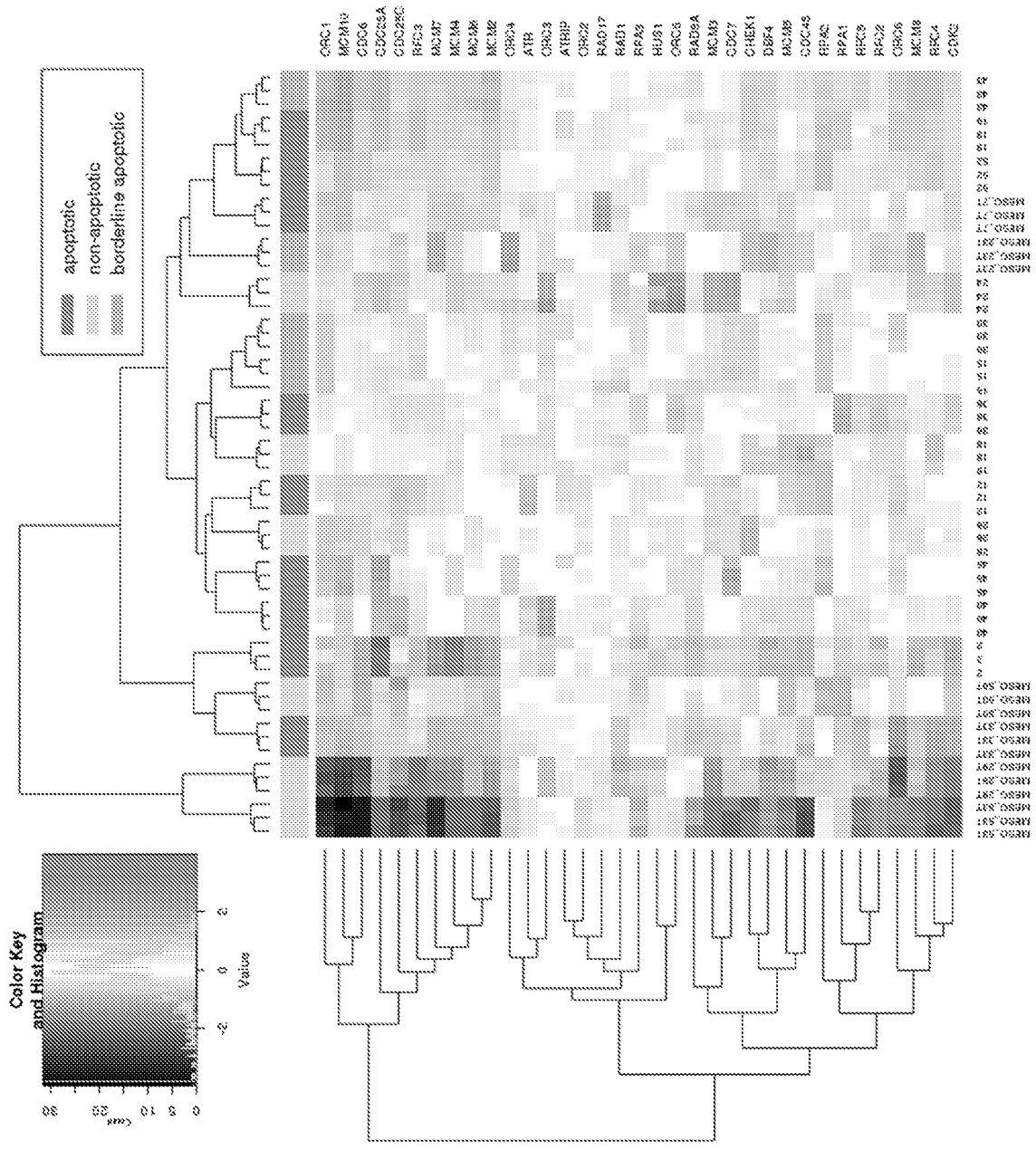
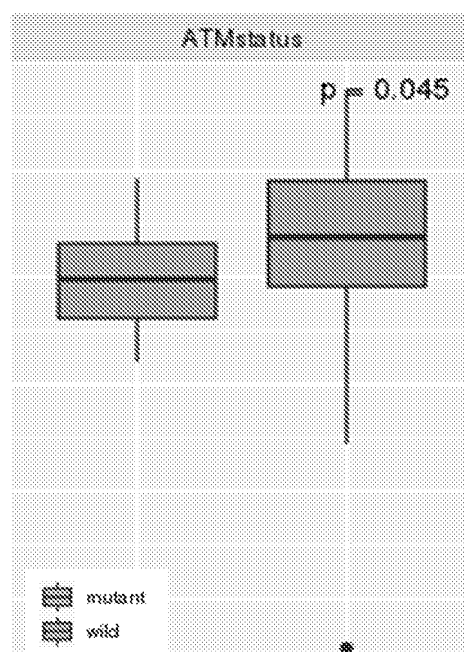


Figure 1

A.



B.

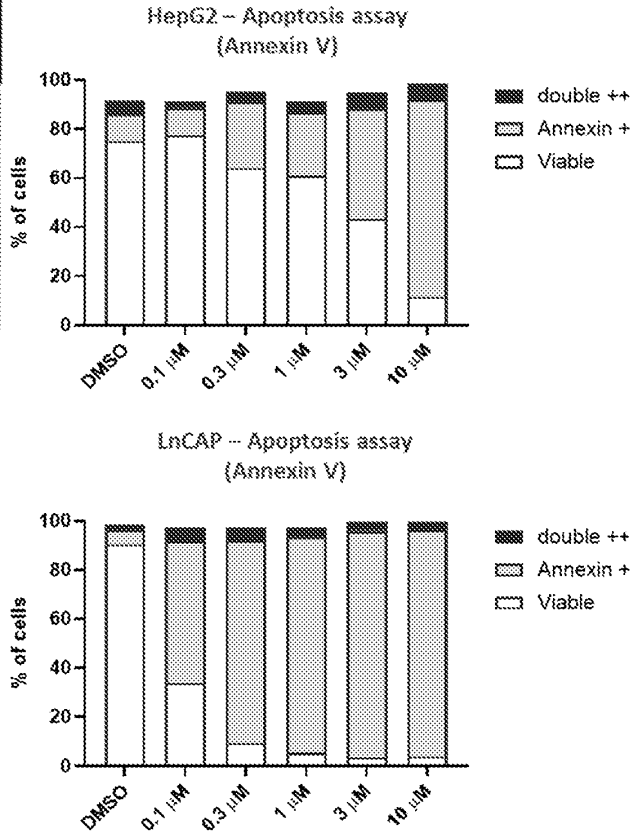
Samples	Type	ATM mutation
12	apoptotic	mutant
19	apoptotic	mutant
2	apoptotic	mutant
36	apoptotic	mutant
40	apoptotic	mutant
45	apoptotic	wild
52	apoptotic	mutant
MESO7T	apoptotic	wild
MESO33T	apoptotic	Wild
18	non-apoptotic	wild
24	non-apoptotic	wild
26	non-apoptotic	wild
MESO29T	non-apoptotic	wild
MESO50T	non-apoptotic	wild
MESO53T	non-apoptotic	wild
15	Borderline apoptotic	wild
30	Borderline apoptotic	wild
43	Borderline apoptotic	mutant
MESO23T	Borderline apoptotic	mutant

Figure 2

C. Cell proliferation

Cell line	Indication	Compound-1 IC50 (μM)
HCC1500	Breast	0.1673
LnCAP	Prostate	0.019
HT-144	Melanoma	0.2636
HepG2	Liver	0.054

D. Apoptosis



E. Modulation of DDR signaling

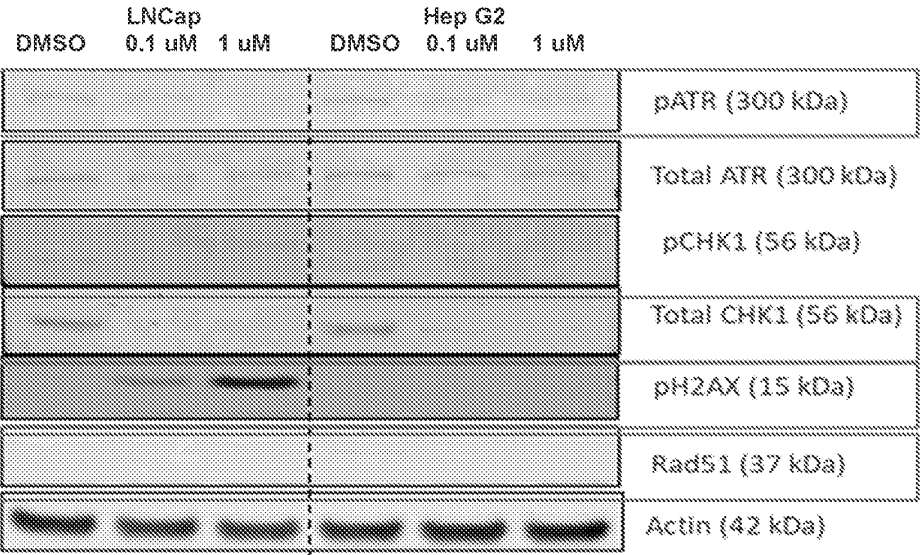


Figure 2

F.

Organoid ID	Tissue origin	TP53 status	BRCA1 Alteration	BRCA2 Alteration	ATM Alteration	Compound #1 IC ₅₀ (μM)
BR9457B	Breast	WT		Yes		0.05
GA6894B	Gastric	WT			Yes	0.075
PA20069B	Pancreas	WT		Yes	Yes	0.07
PA20081B	Pancreas	WT			Yes	0.063
BR5337B	Breast	WT				27
GA0119B	Gastric	WT				12
GA0098B	Gastric	WT				12
PA20079B	Pancreas	WT				20

5

G.

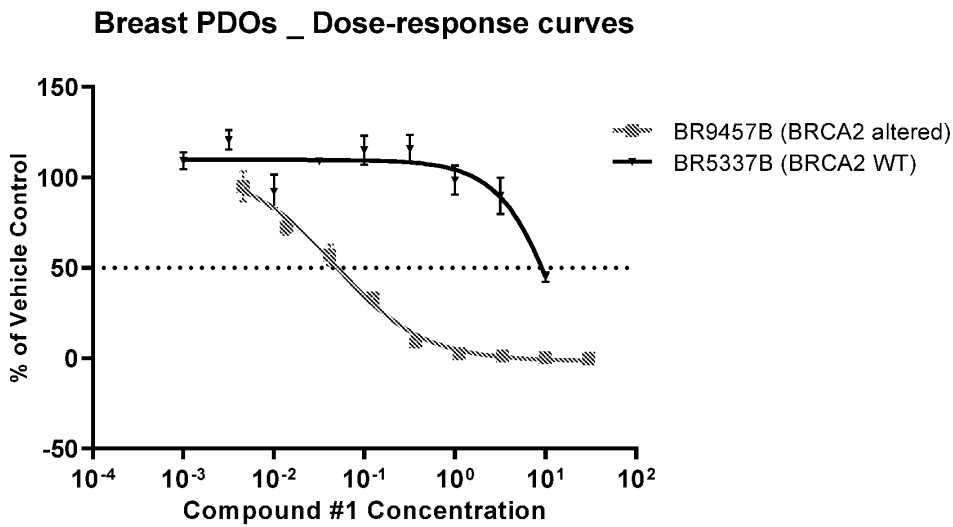
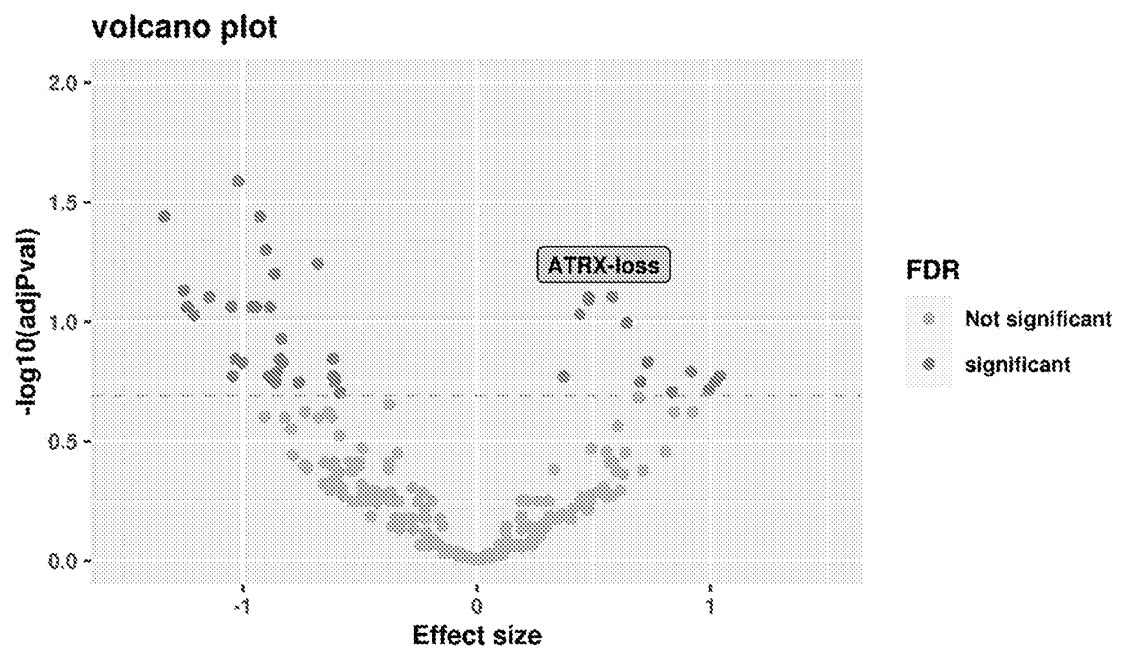


Figure 2

A.



B.

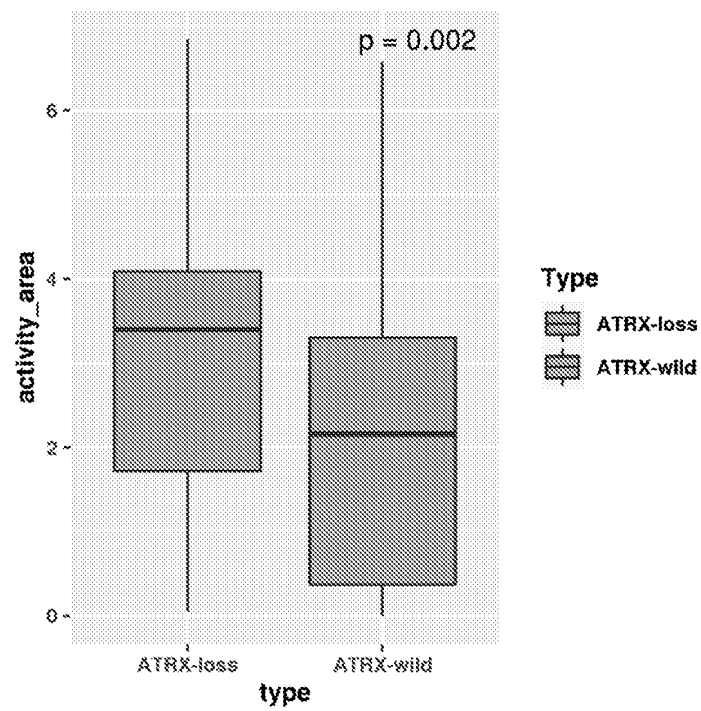


Figure 3

A.

Cell Line	Activity area	Microsatellite status	Tumor mutation burden (Mutations/Mb)	POLD1
HCT116	3.55	MSI-H	70.63	mutant
LOVO	3.41	MSI-H	56.07	mutant
LS180	3.39	MSI-H	66.53	mutant
RKO	3.00	MSI-H	81.4	wild
SW48	2.99	MSI-H	66.07	mutant
CW2	2.81	MSI-H	237.83	mutant
GP2D	2.68	MSI-H	-	mutant
SNU-1	3.51	MSI-H	51.53	mutant
SNGM	6.58	MSI-H	58.77	wild

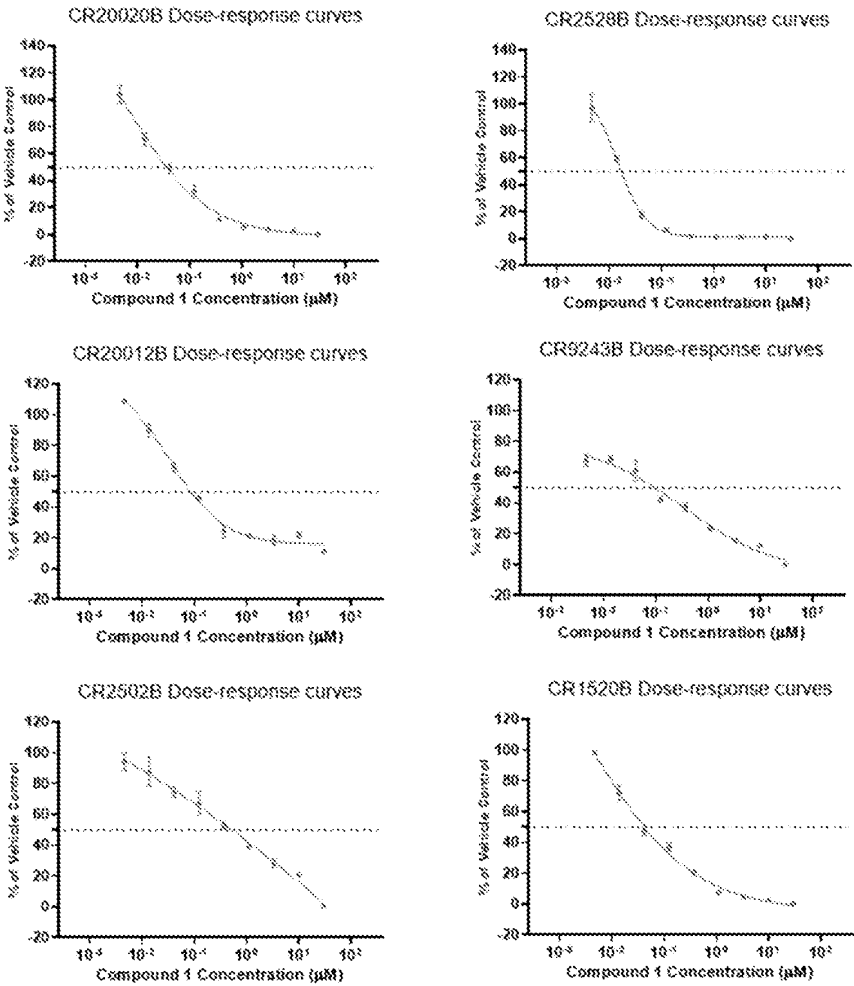
B.

MSI-H Cell lines	Indication	Compound #1 IC50
CW2	CRC	0.5824 μ M
SW48	CRC	0.5682 μ M
RKO	CRC	0.5970 μ M
LS180	CRC	0.1550 μ M
LOVO	CRC	0.4329 μ M
HCT116	CRC	0.1022 μ M
SNU-1	Gastric	0.0858 μ M
SNGM	Endometrial	0.1106 μ M

Figure 4

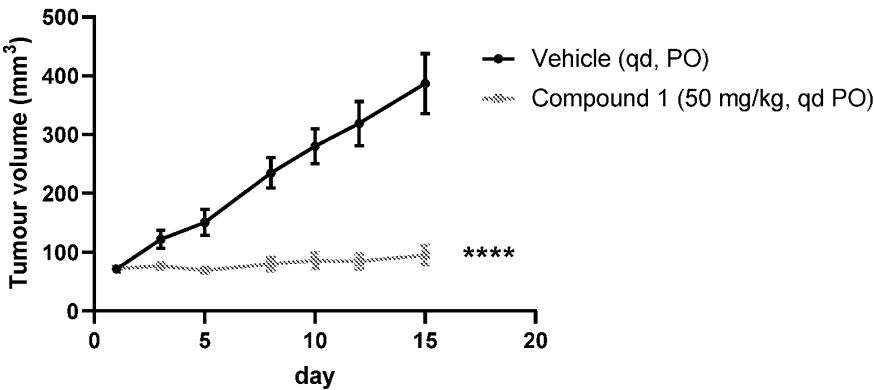
MSI-H Patient-derived organoids

C.



D.

HCT116 xenograft



**** p-value < 0.0001 vs vehicle by 2way ANOVA

Figure 4

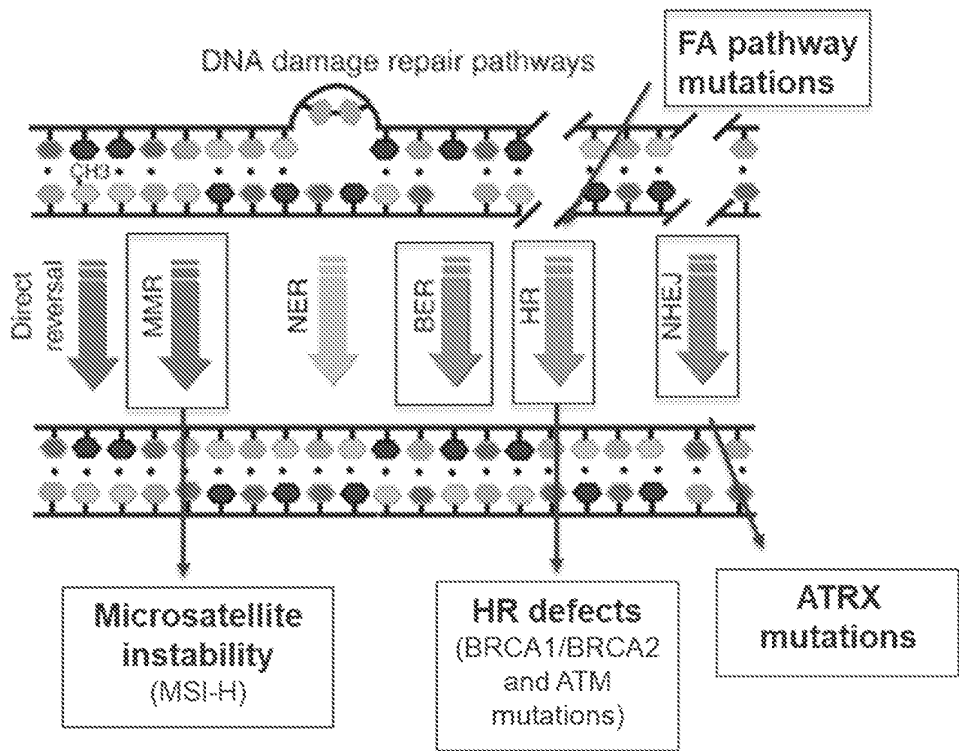


Figure 5

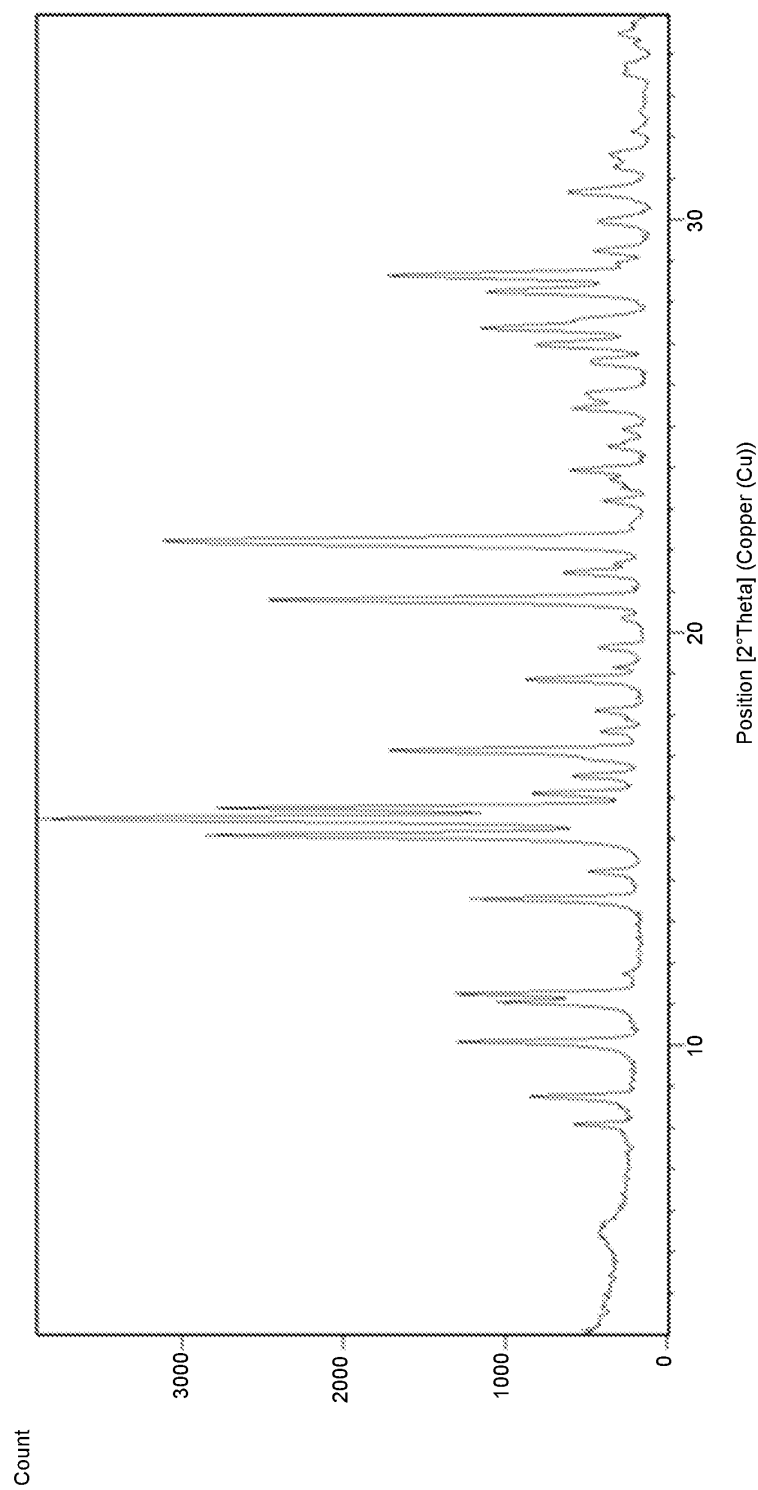


Figure 6

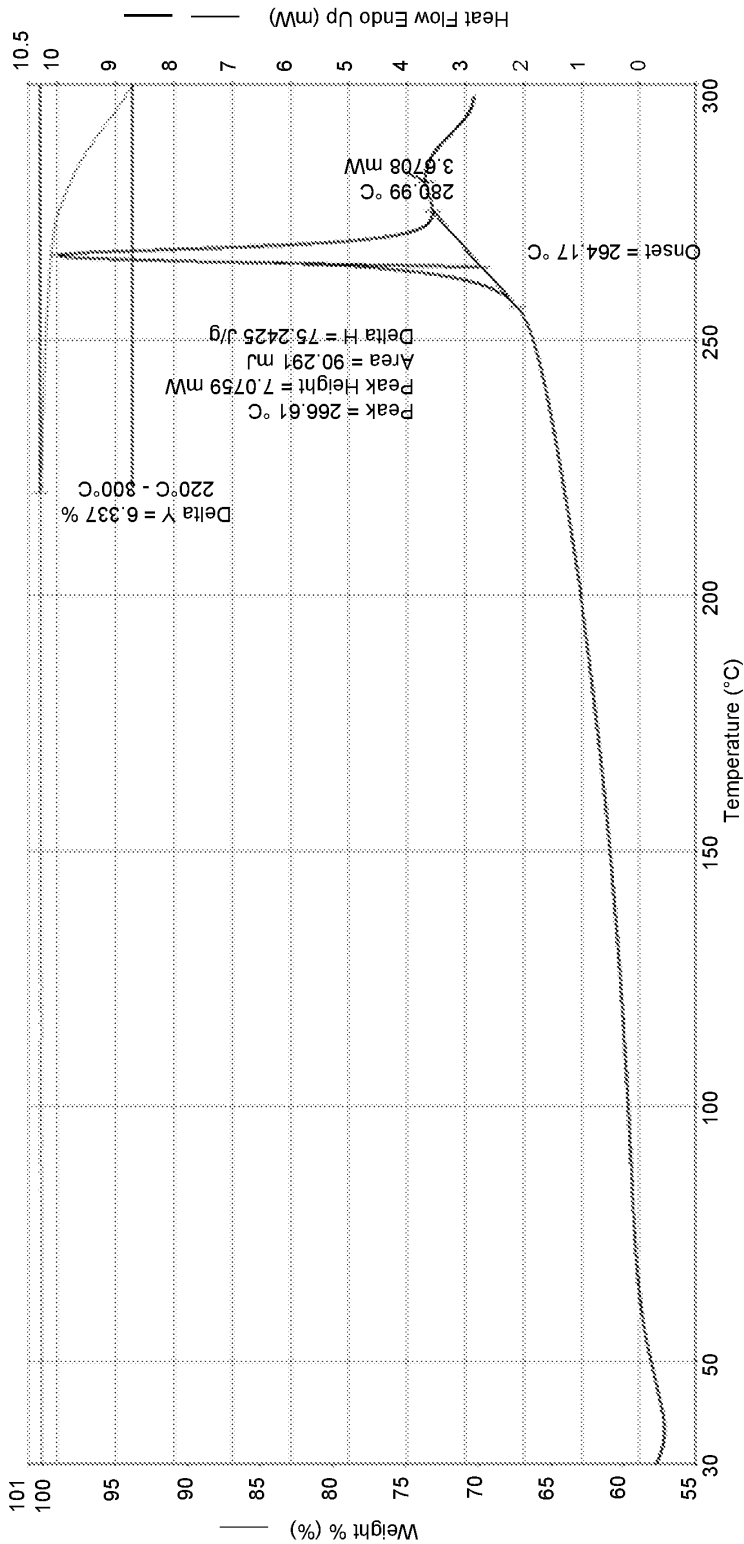


Figure 7