

FIG. 1

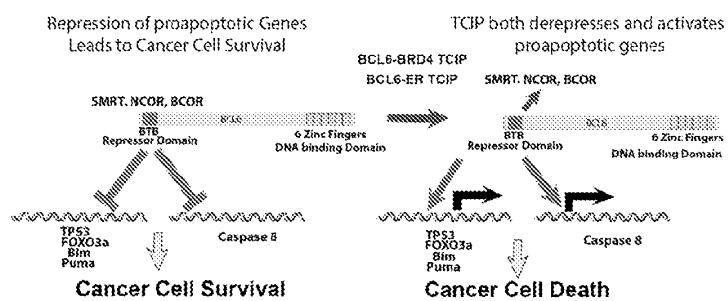
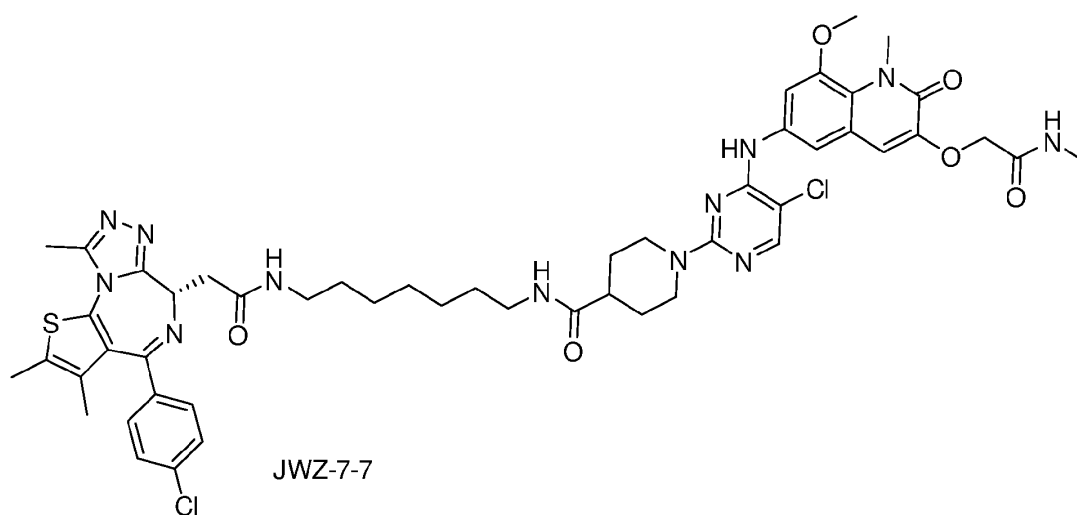


FIG. 2



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FIG. 3

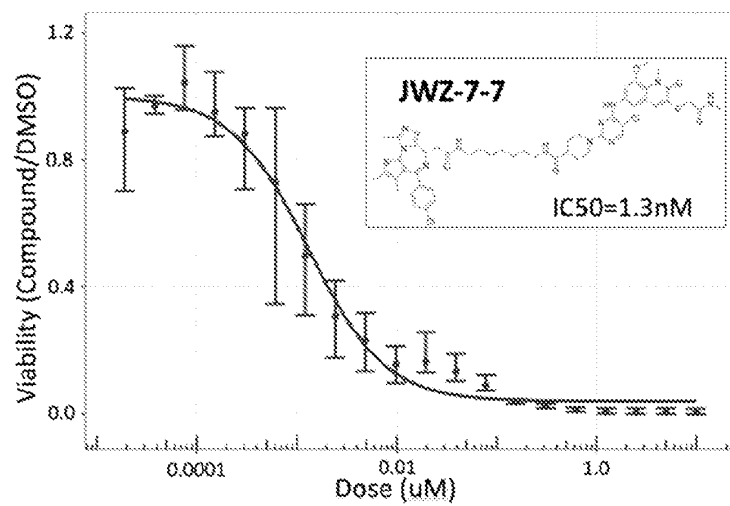


FIG. 4A

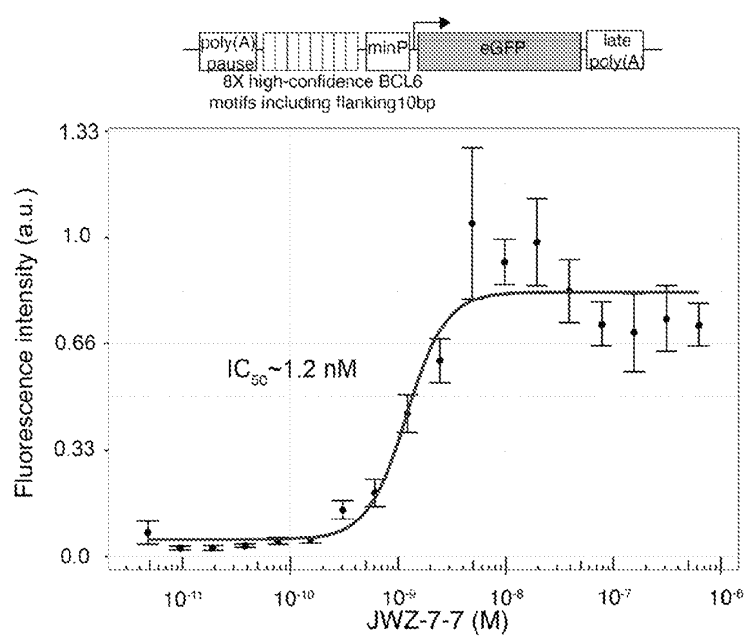


FIG. 4B

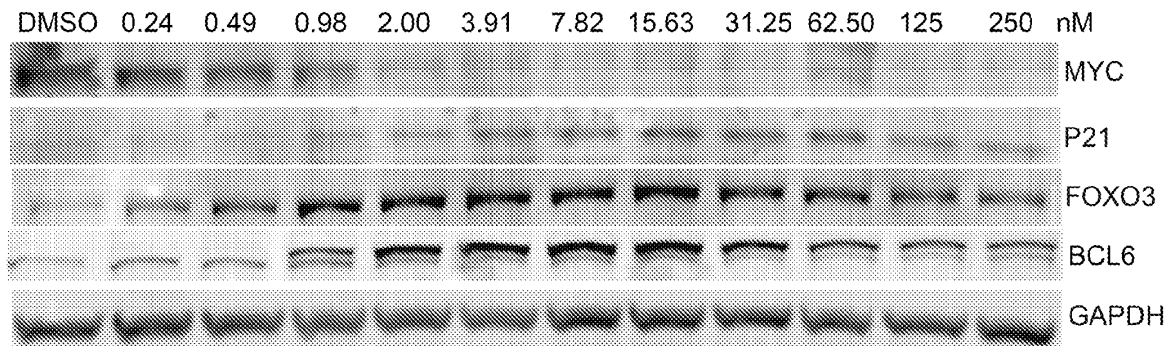


FIG. 5

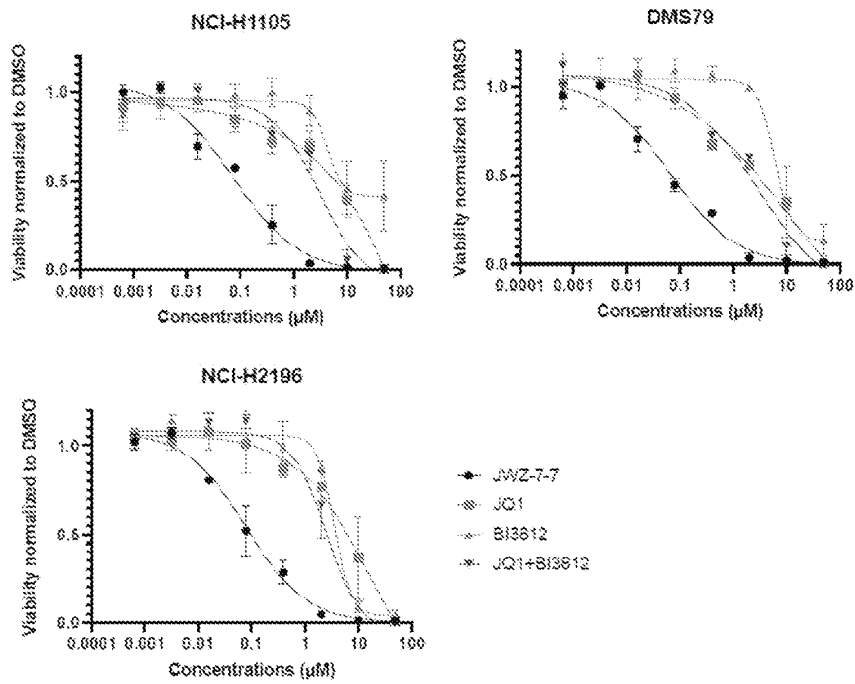


FIG. 6

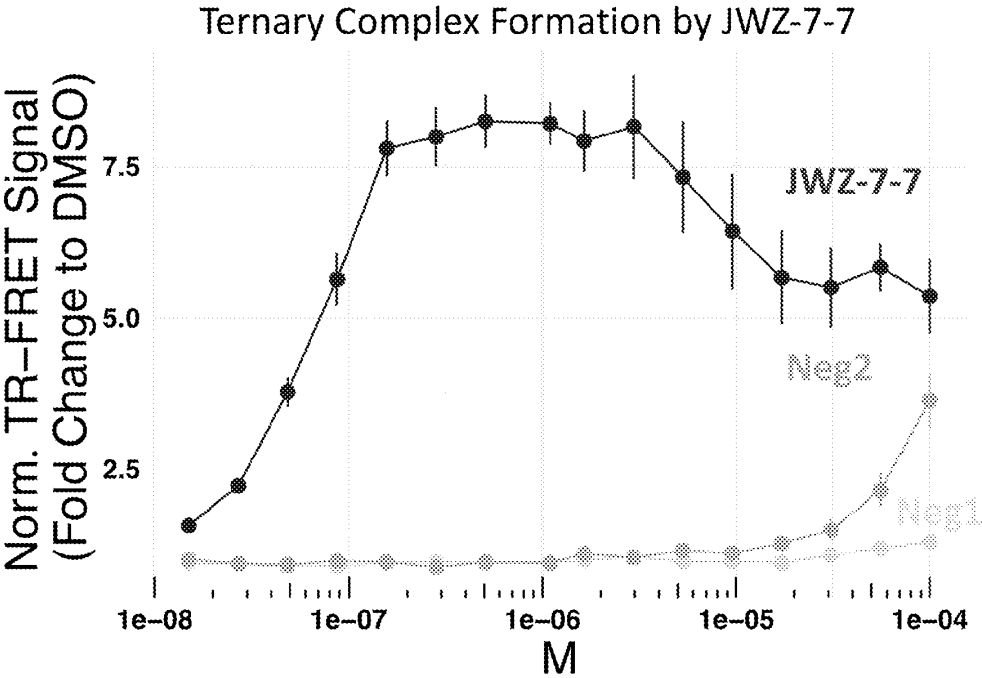


FIG. 7A

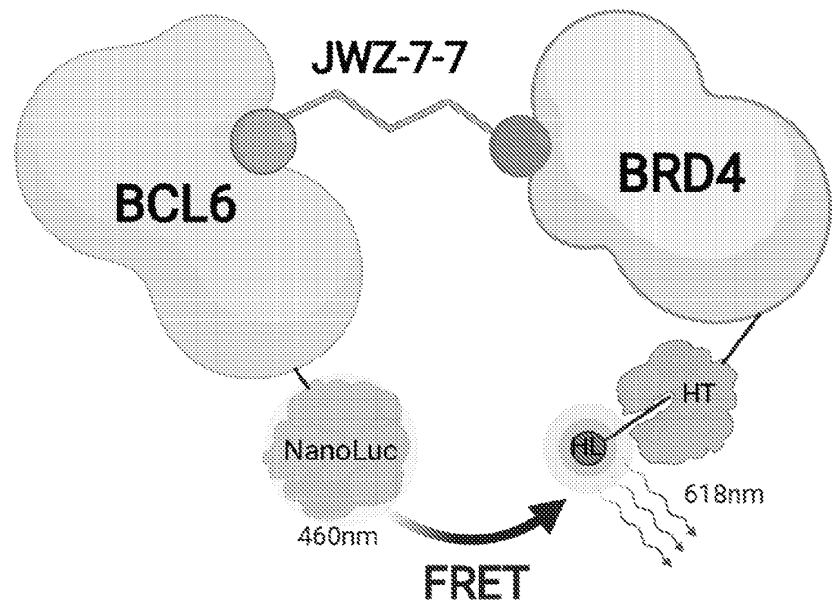


FIG. 7B

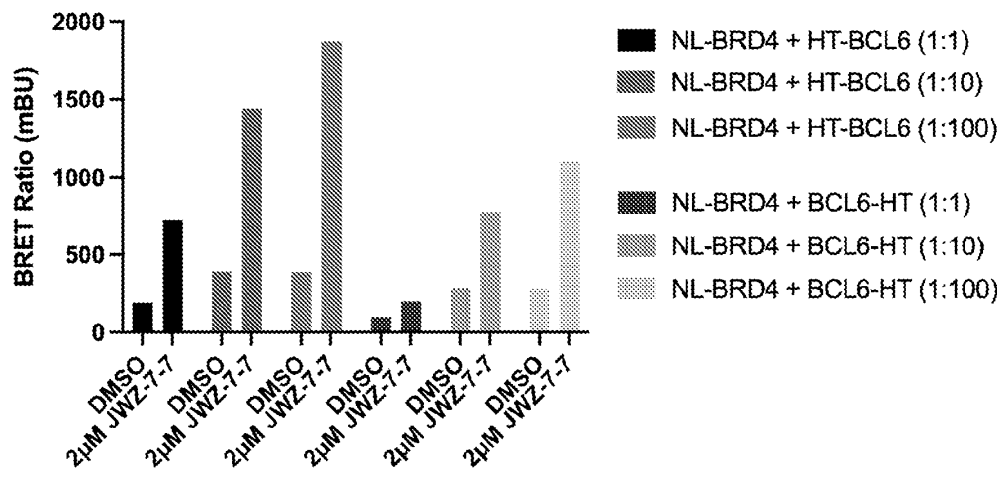


FIG. 8

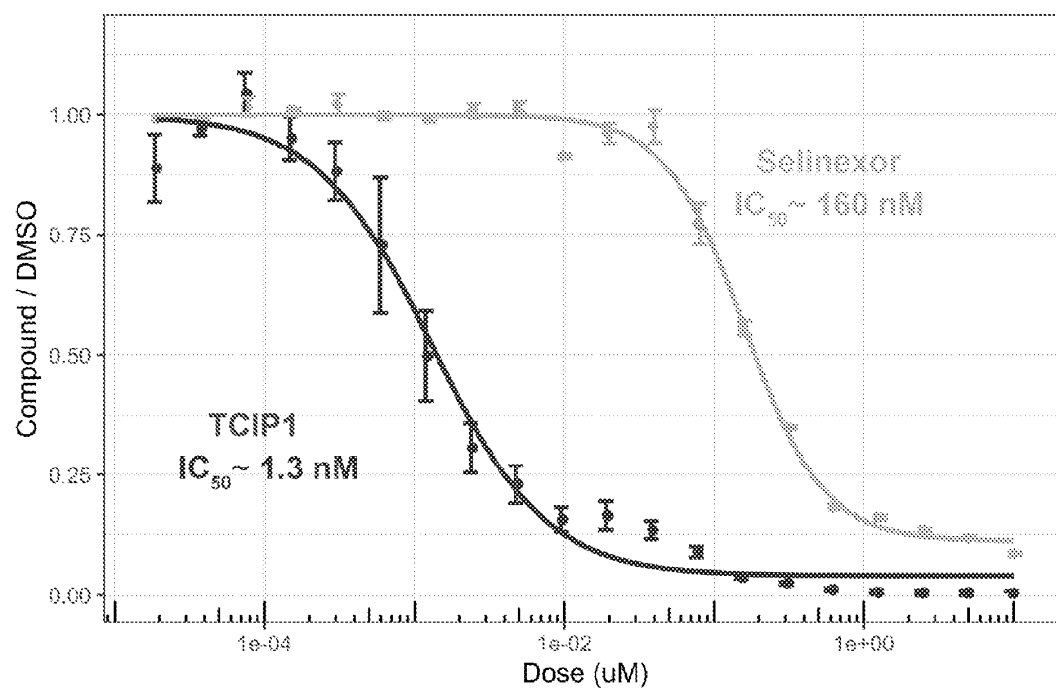


FIG. 9

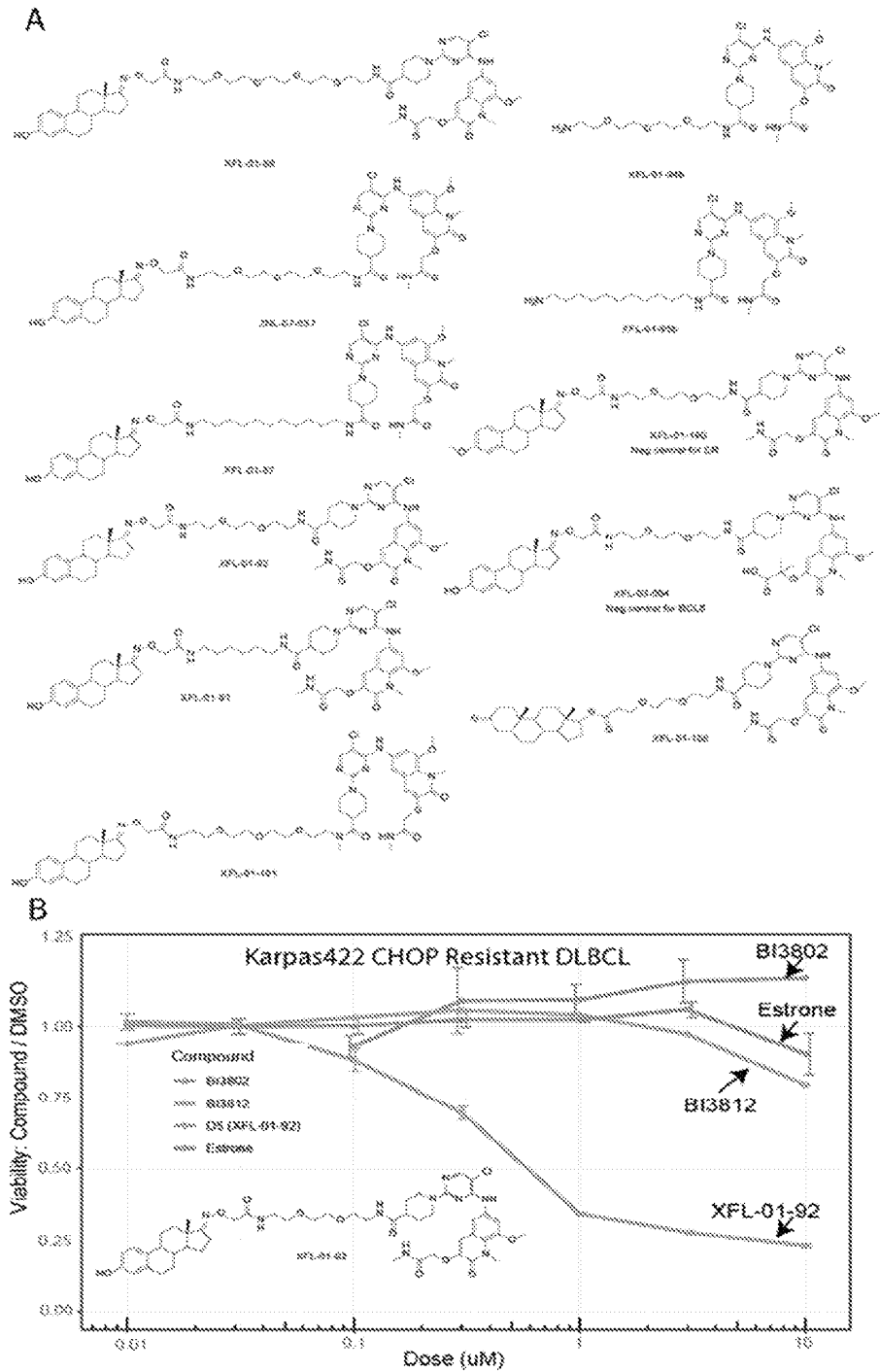


FIG. 10

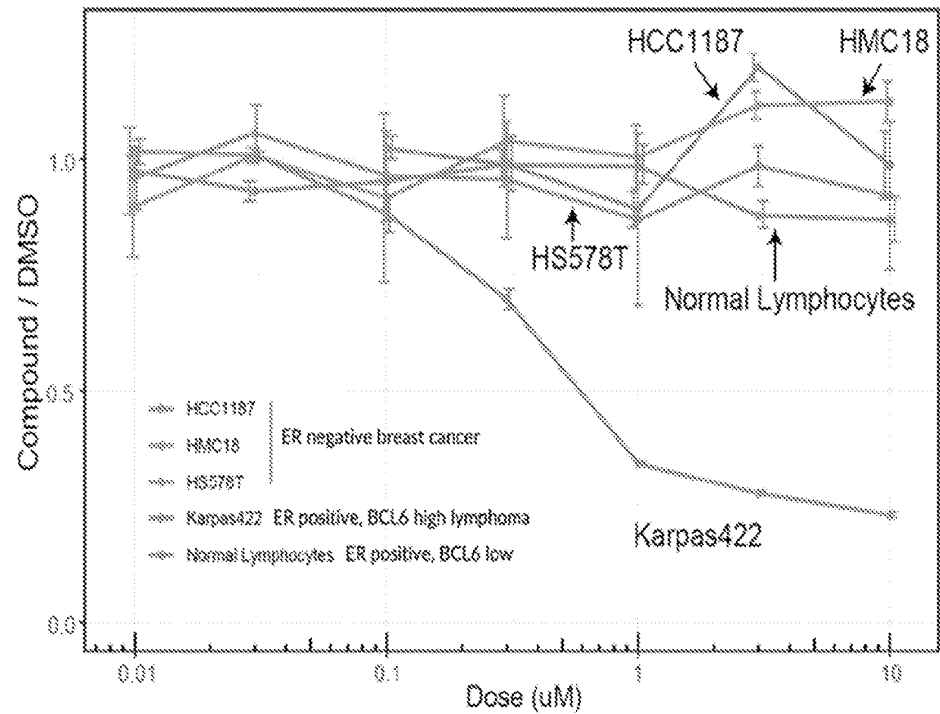


FIG. 11

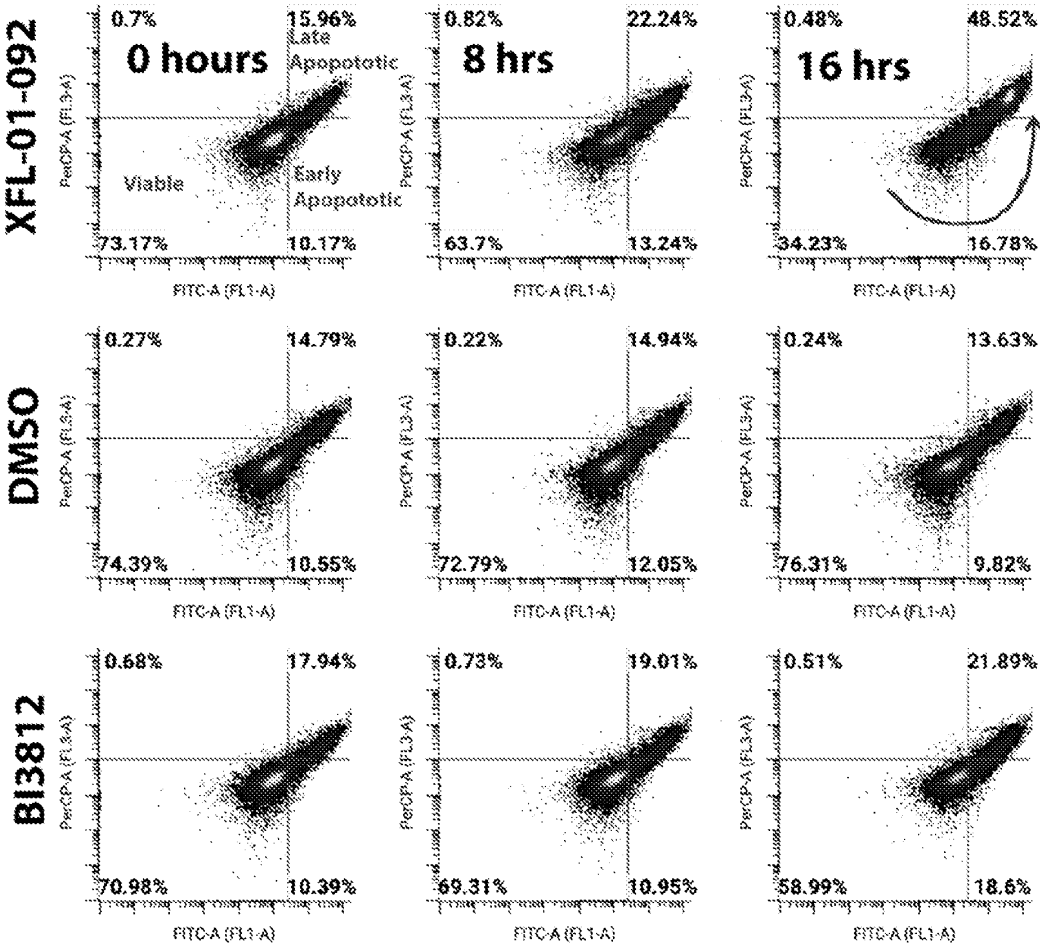


FIG. 12

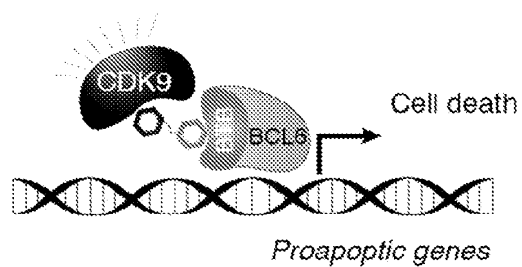


FIG. 13

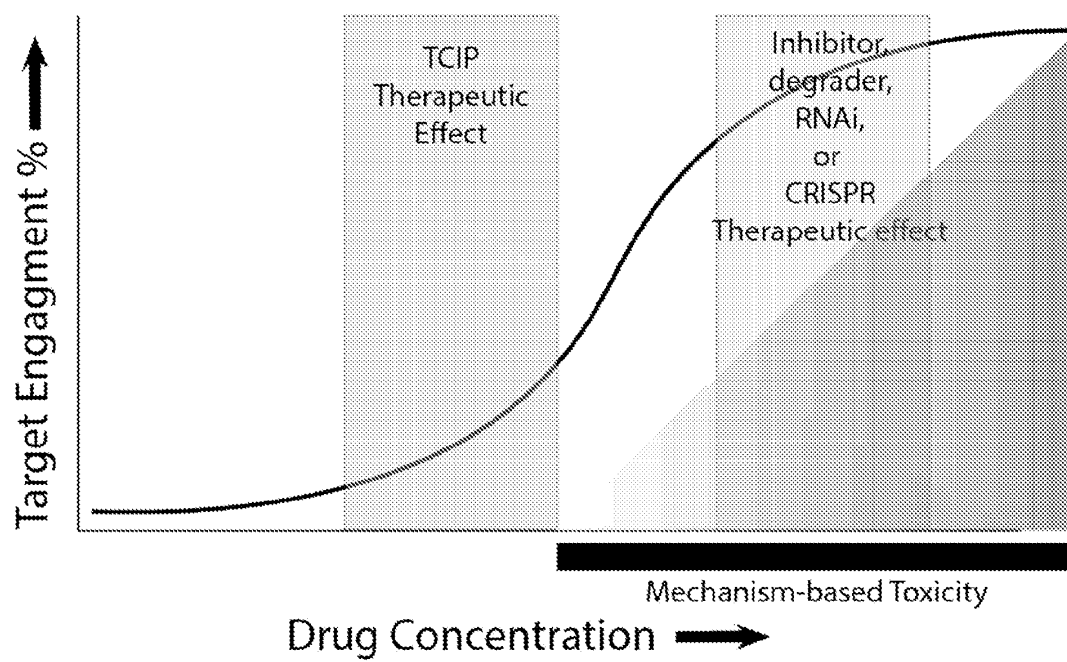
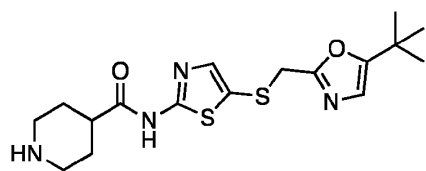


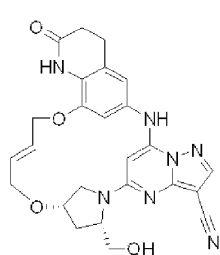
FIG. 14

A)

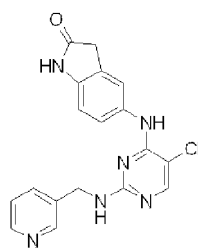


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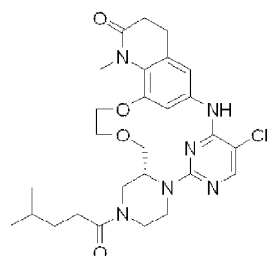
B)



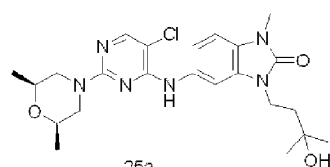
11



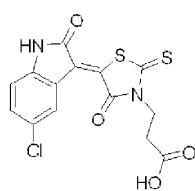
7



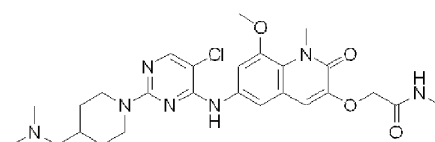
14



25a



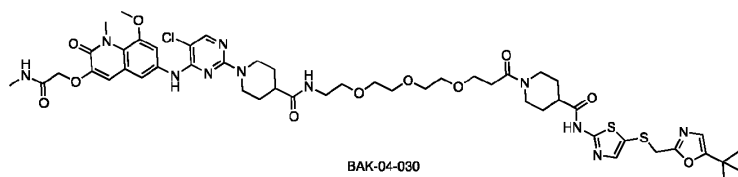
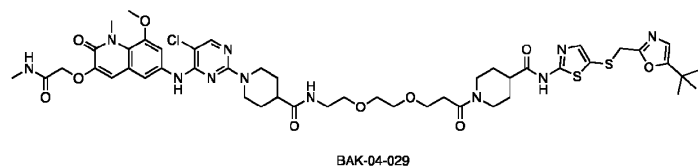
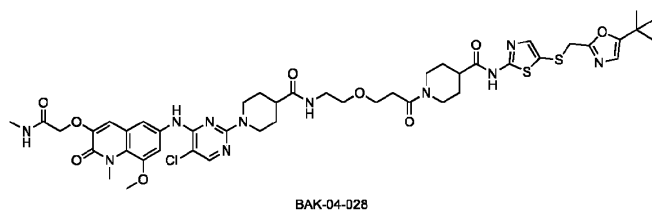
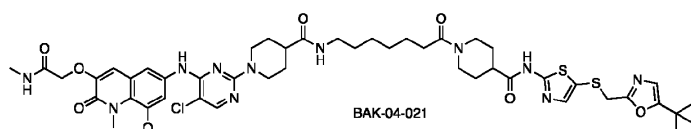
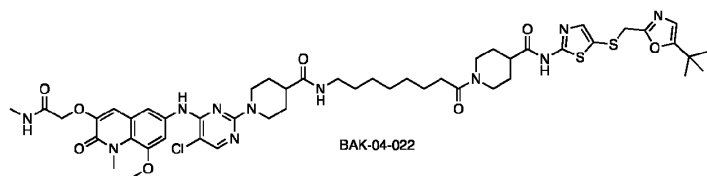
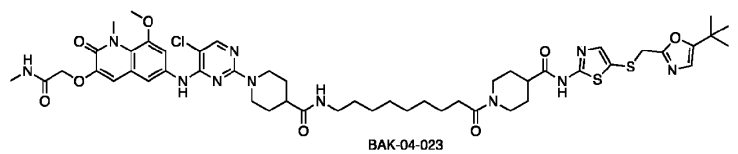
FX1



BI-3812

FIG. 14 Cont.

C)



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FIG. 14 Cont.

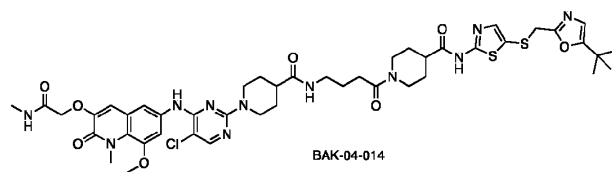
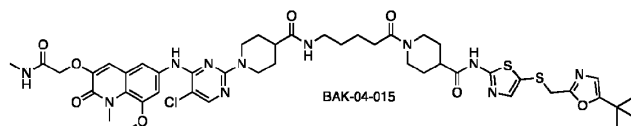
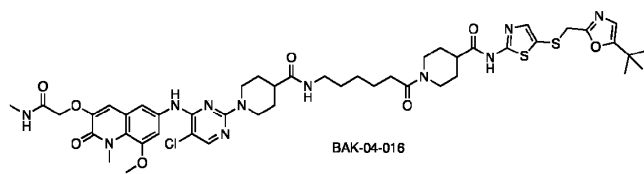


FIG. 15

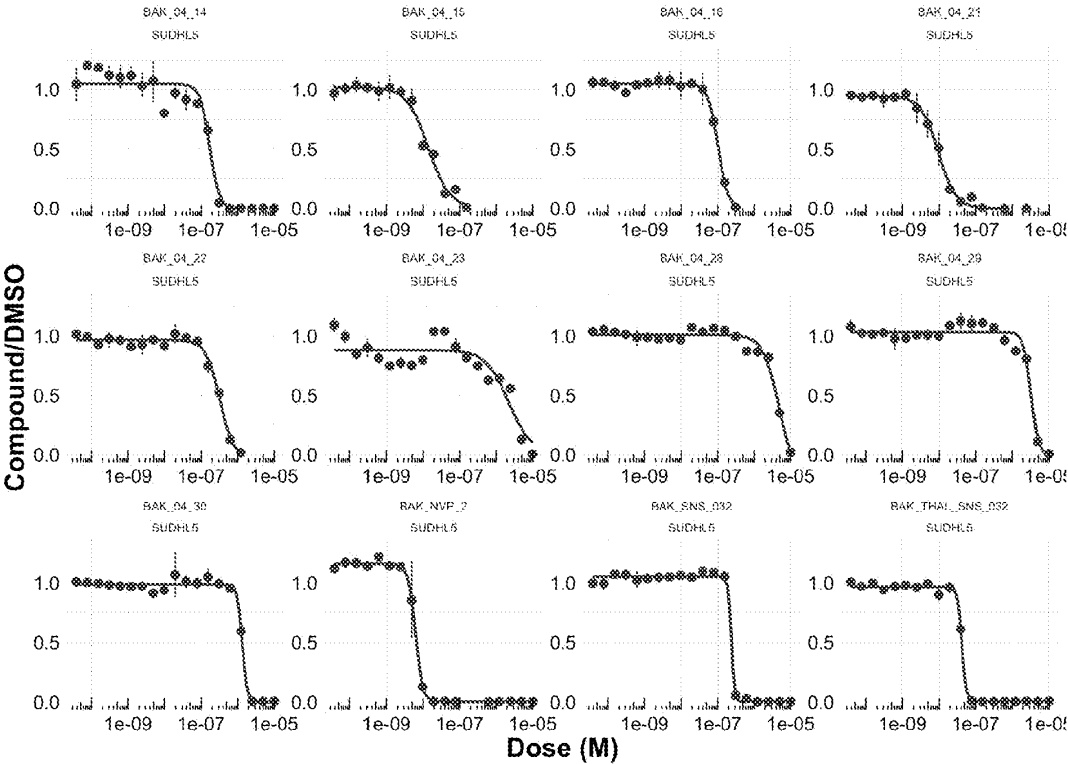


FIG. 16

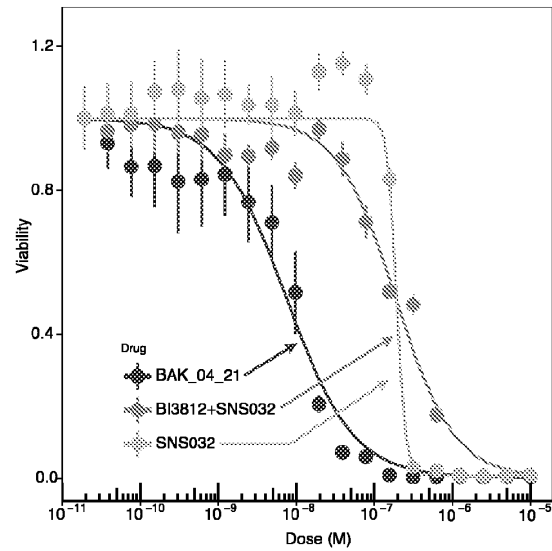


FIG. 17

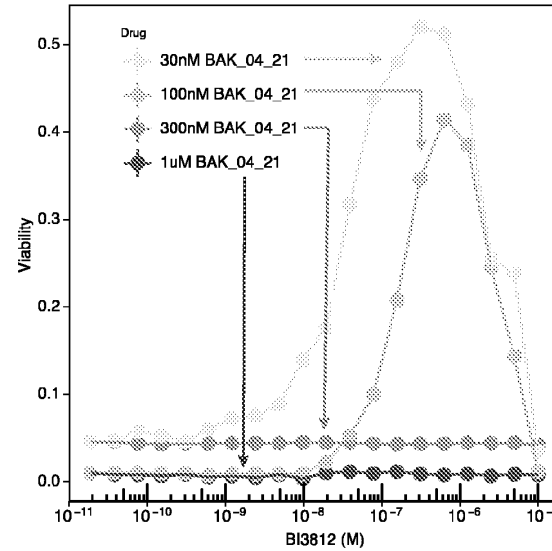


FIG. 18A

CDK9 TCIP CDK9 Inhibitors

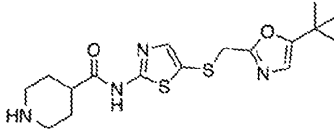
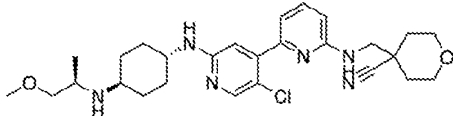
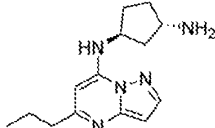
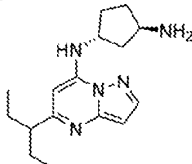
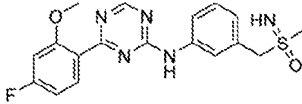
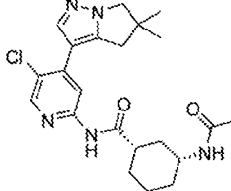
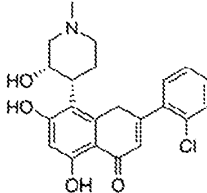
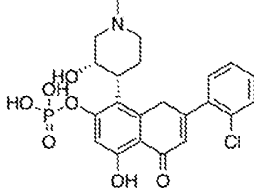
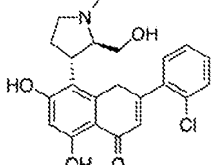
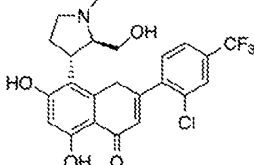
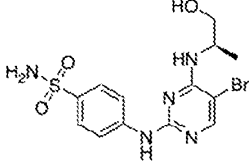
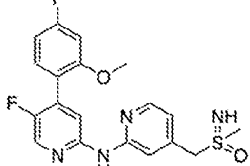
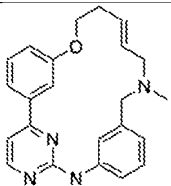
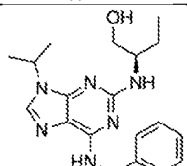
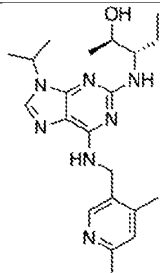
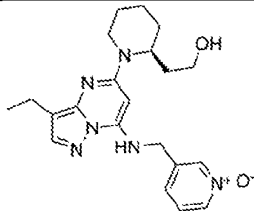
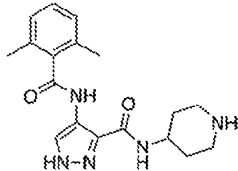
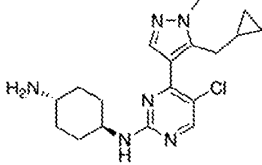
Name	Reference	Structure
THAL-SNS-032	Nature Chem Biol, 2018, 14, 163-173	
NVP-2	WO/2011/01266	
KI-ARv-03	ACS Med. Chem. Lett. 2018, 9, 6, 540-545	
KB-0742	ACS Med. Chem. Lett. 2018, 9, 6, 540-545	
BAY-1143572	ChemMedChem 2017, 12, 1776 - 1793	
AZD-4573	Clin Cancer Res 2020, 26, 922-934.	
Alvocidib	Blood Cancer Journal (2021) 11:175	

FIG. 18A Cont.

TP-1287	Cancer Res (2017) 77 (13_Supplement): 5133	
Rivaciclib	<u>Mol Cancer Ther.</u> 2007 Mar;6(3):926-34.	
Voruciclib	Scientific Reports, 2017, 7, 18007	
ZK-304709	<i>Gut</i> 2009;58:261-270	
BAY-1251152	<u>J Enzyme Inhib Med Chem.</u> 2021; 36(1): 693-706.	
Zotiraciclib (TG-02)	<i>Clin Cancer Res</i> (2021) 27 (12): 3298-3306.	
Selaciclib	Journal of Biotechnology 202 (2015) 40-49	

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FIG. 18A Cont.

Fadraciclib	<u>Leukemia</u> volume 36, pages1596–1608 (2022)	
Dinaciclib	<u>Scientific Reports</u> volume 10, Article number: 18489 (2020)	
AT7519	<u>Oncogene</u> volume 29, pages2325–2336 (2010)	
BTX-A51	<i>Clarivate Analytics Integrity.</i> https://integrity.clarivate.com Blood (2020) 136 (Supplement 1) : 18.	

CDK8 Inhibitors

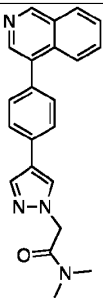
Name	Reference	Structure	Comments
BI-1347	WO2017202719A1		

FIG. 18A Cont.

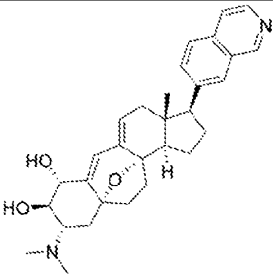
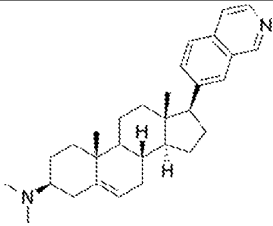
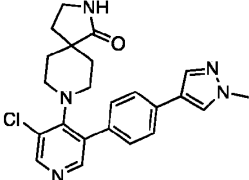
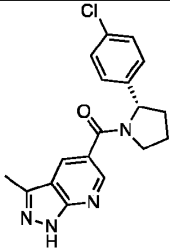
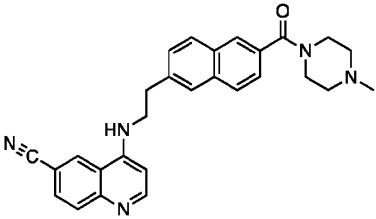
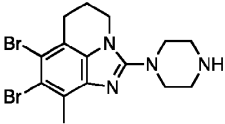
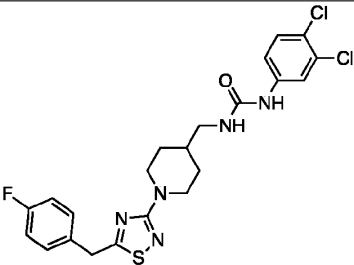
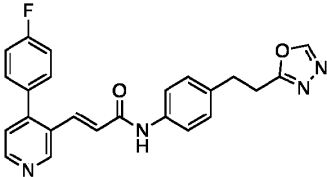
Cortistatin A	ACS Med. Chem. Lett. 2018, 9, 540-545		
JH-VIII-49	ACS Med. Chem. Lett. 2018, 9, 540-545		
CCT251545	Nat Chem Biol 11, 973-980 (2015).		
MSC253818	J. Med. Chem. 2016, 59, 20, 9337-9349		
Senexin C	J. Med. Chem. 2022, 65, 4, 3420-3433		Other derivatives include Senexin A,B
Sel 120-34A	Oncotarget, 2017, Vol. 8, (No. 20), pp: 33779-33795		Phase 1

FIG. 18A Cont.

W-34	<i>Eur J Med Chem.</i> 2017 Mar 31;129:275-286.		
T-814	<i>Oncotarget.</i> 2018 Mar 2; 9(17): 13474–13487.		

CDK7 Inhibitors

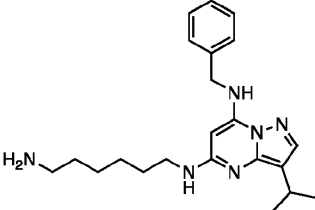
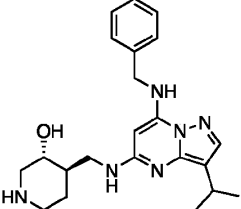
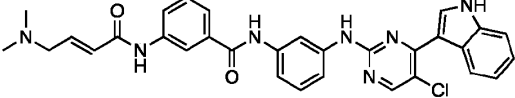
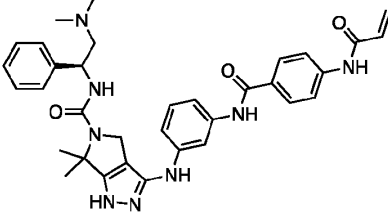
Name	Reference	Structure	Comments
BS-181	<i>Cancer Res</i> (2009) 69 (15): 6208– 6215.		
CT7001	<i>US20160362410A1</i>		
THZ2	<i>Wang et al., 2015,</i> <i>Cell</i> 163, 174–186		Other derivatives include THZ1
YKL-1- 116	<i>Kalan et al., 2017,</i> <i>Cell Reports</i> 21, 467–481		Other Derivatives include YLK-5-124

FIG. 18B

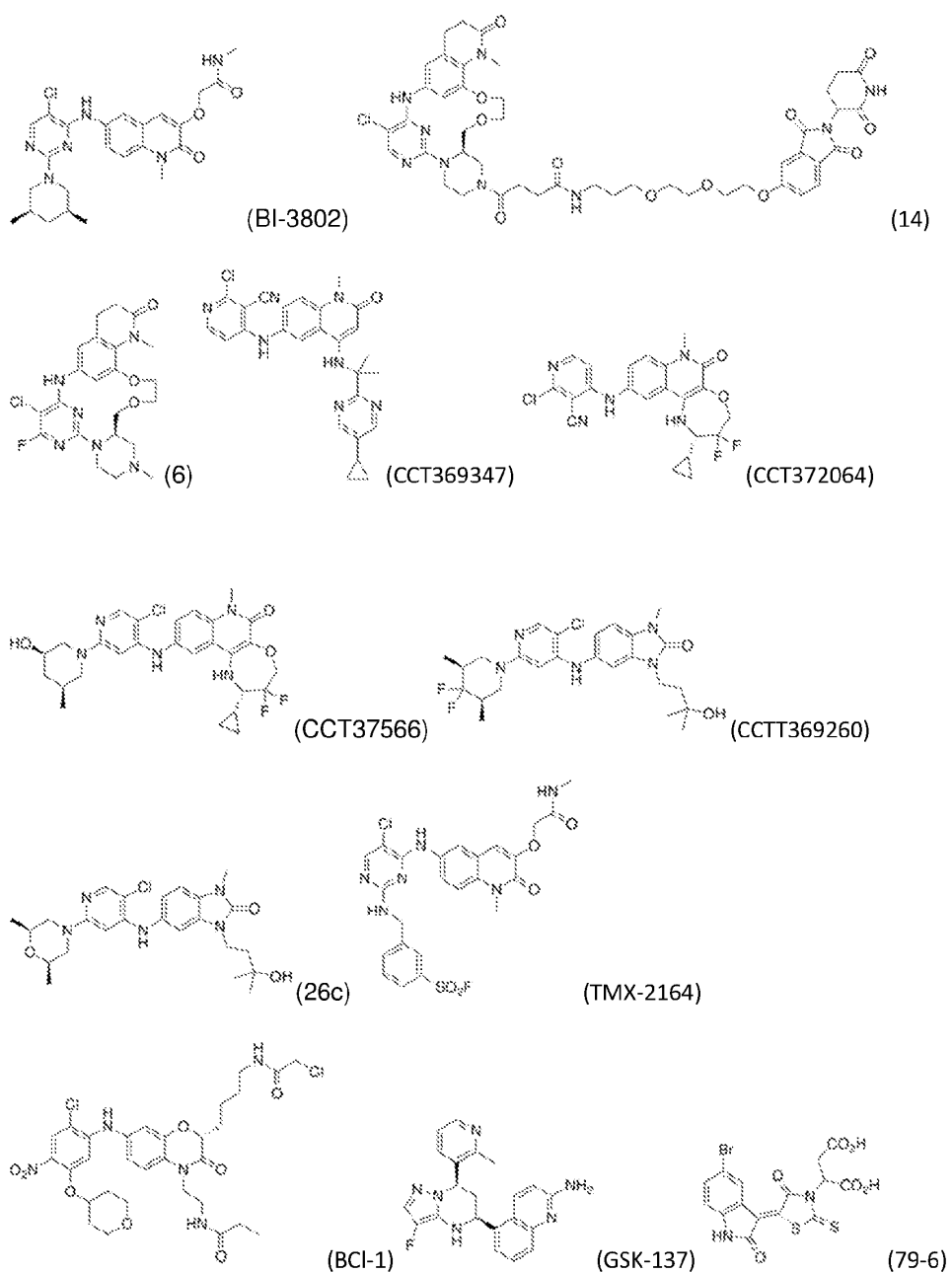


FIG. 19

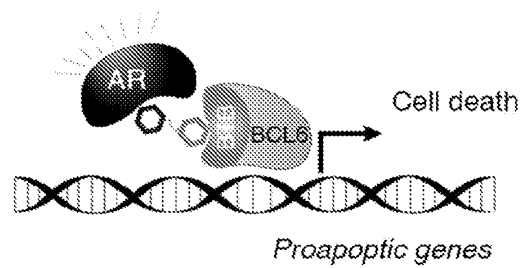


FIG. 20

TCIPs produce a gain of function by diverting signals from the cancer driver to the cell death pathway

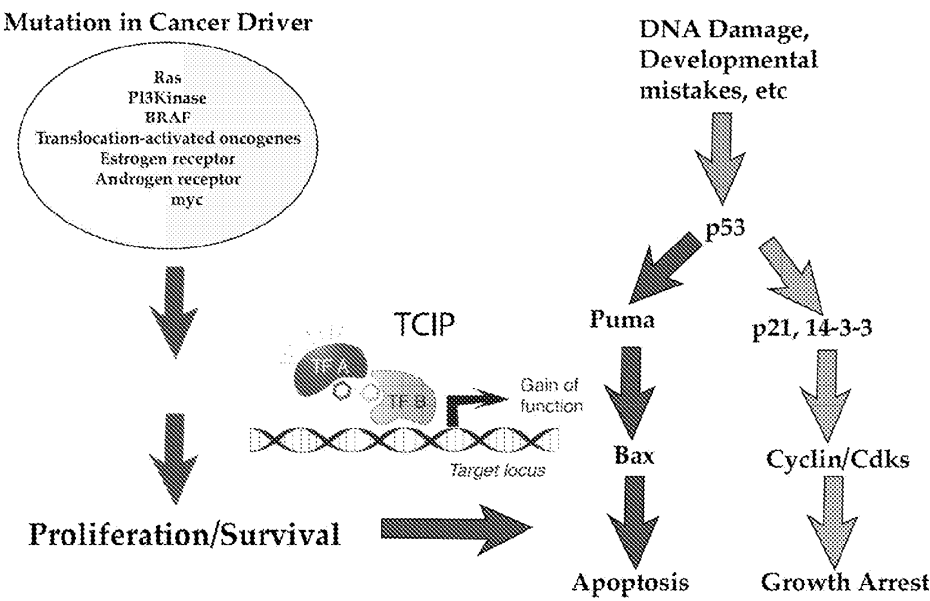


FIG. 21

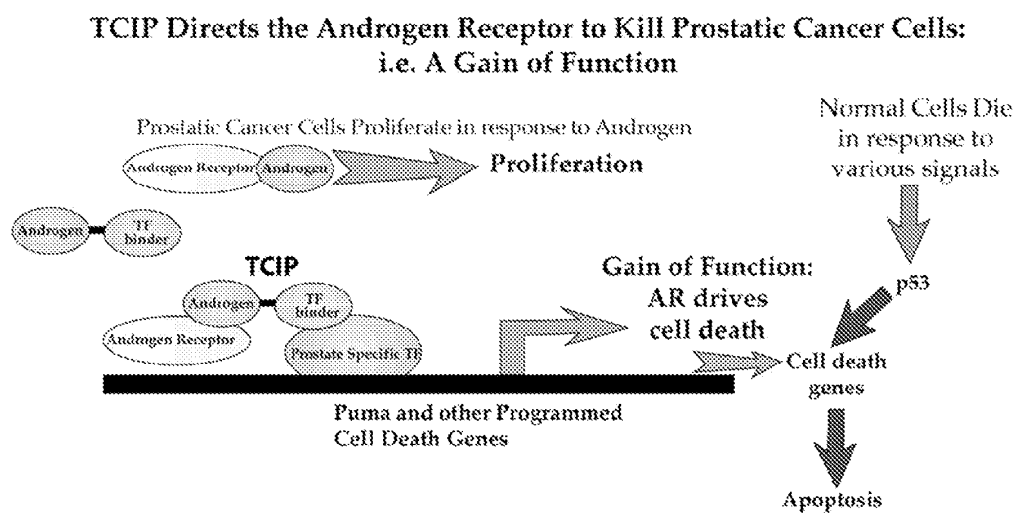


FIG. 22

A.

Name	Reference	Structure	Comments
BI-3812	<i>Cell Reports</i> 2017 , 20, 2860–2875		
BI-3802	<i>Cell Reports</i> 2017 , 20, 2860–2875		monovalent degrader
Cmpd 15	<i>ACS Chem. Biol.</i> 2018 , 13, 3131 - 3141		bivalent degrader
Cmpd 6	<i>ACS Chem. Biol.</i> 2018 , 13, 3131 - 3141		
CCT369347	<i>J. Med. Chem.</i> 2021 , 64, 17079 - 17097		
CCT372064	<i>J. Med. Chem.</i> 2022 , ASAP		

FIG. 22 Cont.

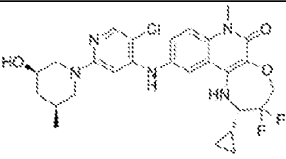
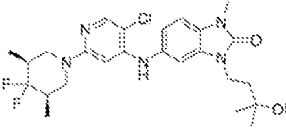
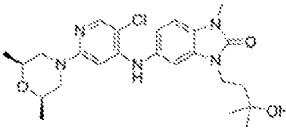
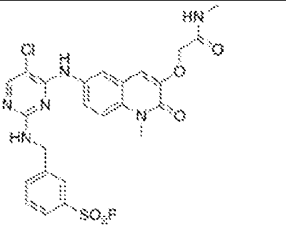
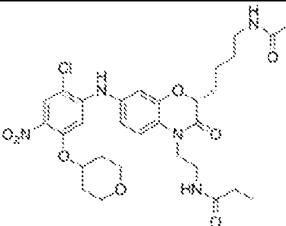
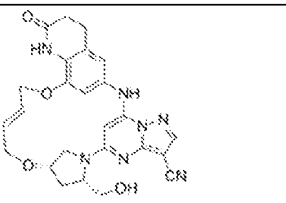
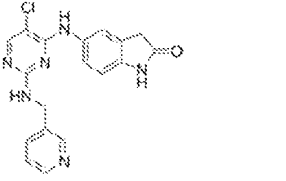
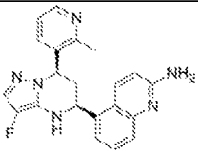
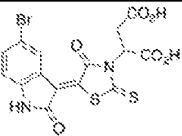
CCT373566	<i>J. Med. Chem.</i> 2022 , ASAP		monovalent degrader
CCTT369260	<i>J. Med. Chem.</i> 2020 , 63, 4047 - 4068		monovalent degrader
Cmpd 26c	<i>J. Med. Chem.</i> 2020 , 63, 4047 - 4068		
TMX-2164	<i>ACS Med. Chem.</i> <i>Lett.</i> 2020 , 11, 1269–1273		covalent, Tyr58
BCI-i	<i>Biochemistry</i> 2018 , 57, 1369–1379		covalent, Cys53
Cmpd 11	<i>J. Med. Chem.</i> 2017 , 60, 4386–4402		
Cmpd 7	<i>J. Med. Chem.</i> 2017 , 60, 4358–4368		

FIG. 22 Cont.

GSK137	<i>J. Biol. Chem.</i> 2021 , 297, 100928		
Cmpd 79-6	<i>J. Med. Chem.</i> 2017 , 60, 4358–4368		

B. Androgen receptor agonists

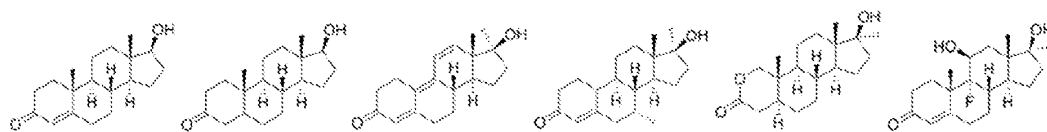
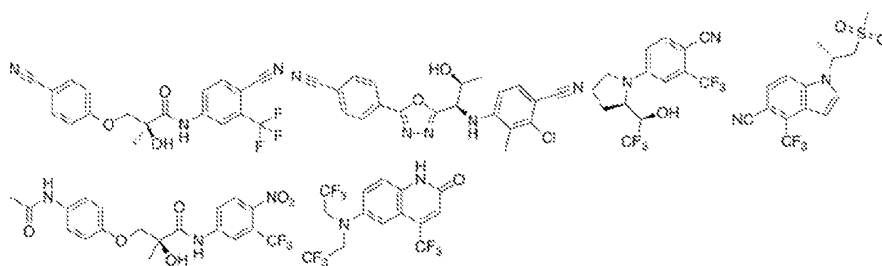
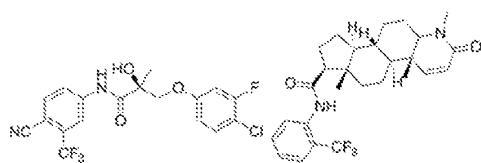
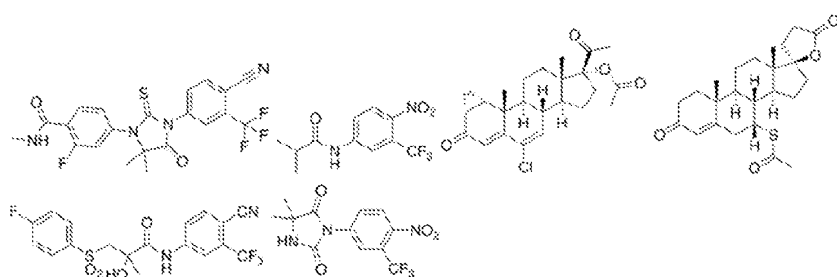
Steroidal*Non-steroidal*

FIG. 22 Cont.



C. Androgen receptor antagonists



D. Linkers

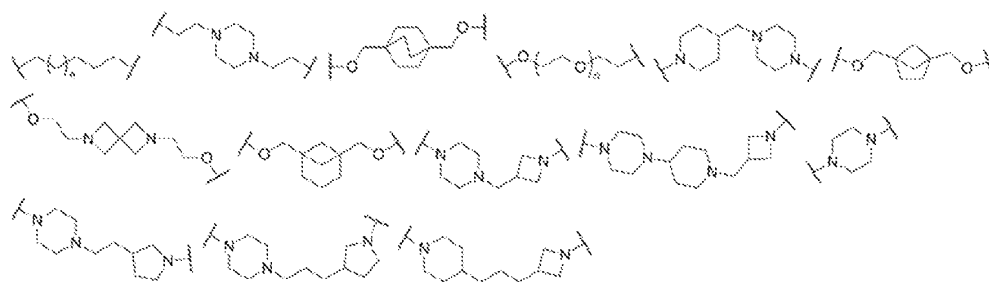
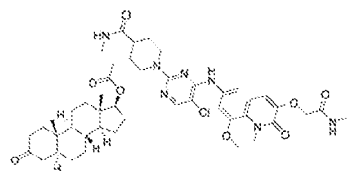
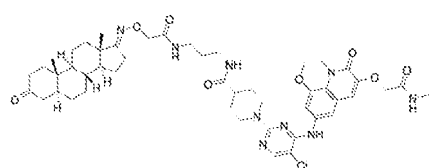


FIG. 23

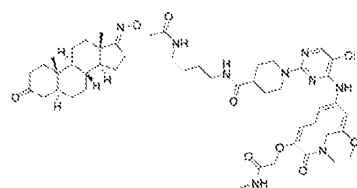
BAK-04-083 (C2)



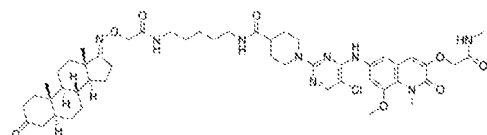
RCS-02-063 (C3)



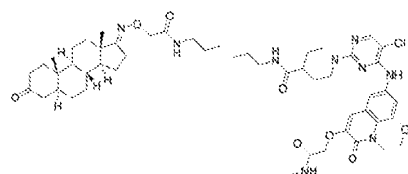
RCS-02-093 (C4)



BAK-04-003 (C5)

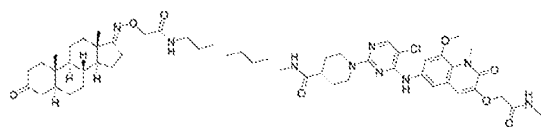


RCS-02-085 (C6)

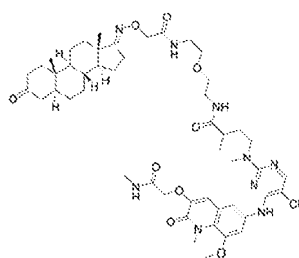


BAK-04-006 (C8)

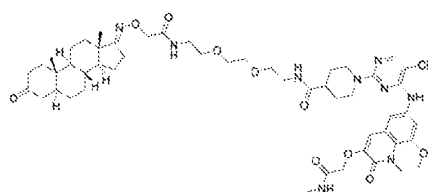
FIG. 23 Cont.



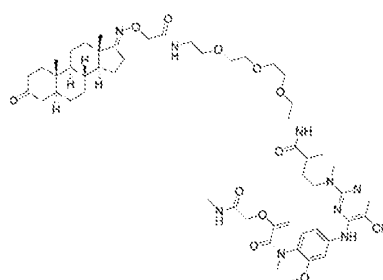
RCS-02-060 (peg1)



RCS-02-058 (peg2)



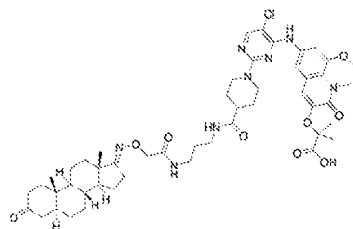
RCS-02-061 (peg3)



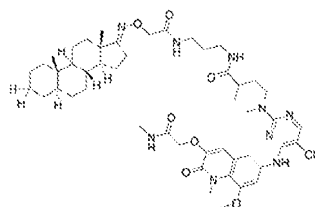
RCS-02-062 (peg4)

FIG. 23 Cont.

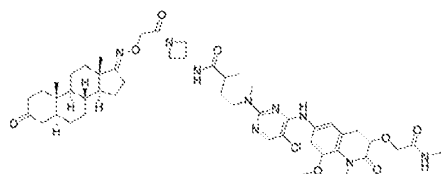
RCS-02-075 (AR-BCL6 neg. control 1)



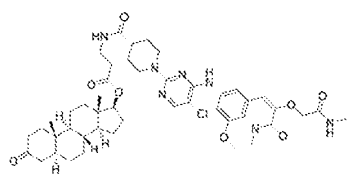
RCS-02-155 (AR-BCL6 neg. control 2)



BAK-04-039

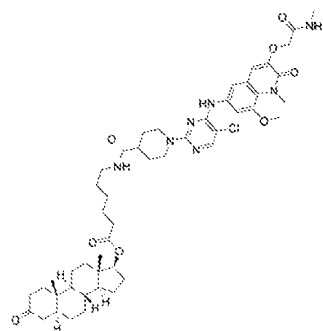


BAK-04-083

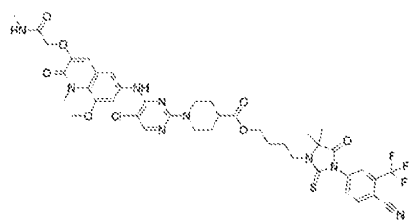


BAK-04-084

FIG. 23 Cont.



RCS-02-160



RCS-02-176

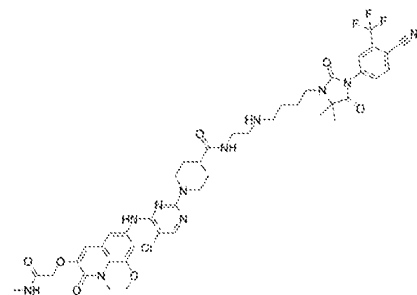


FIG. 24

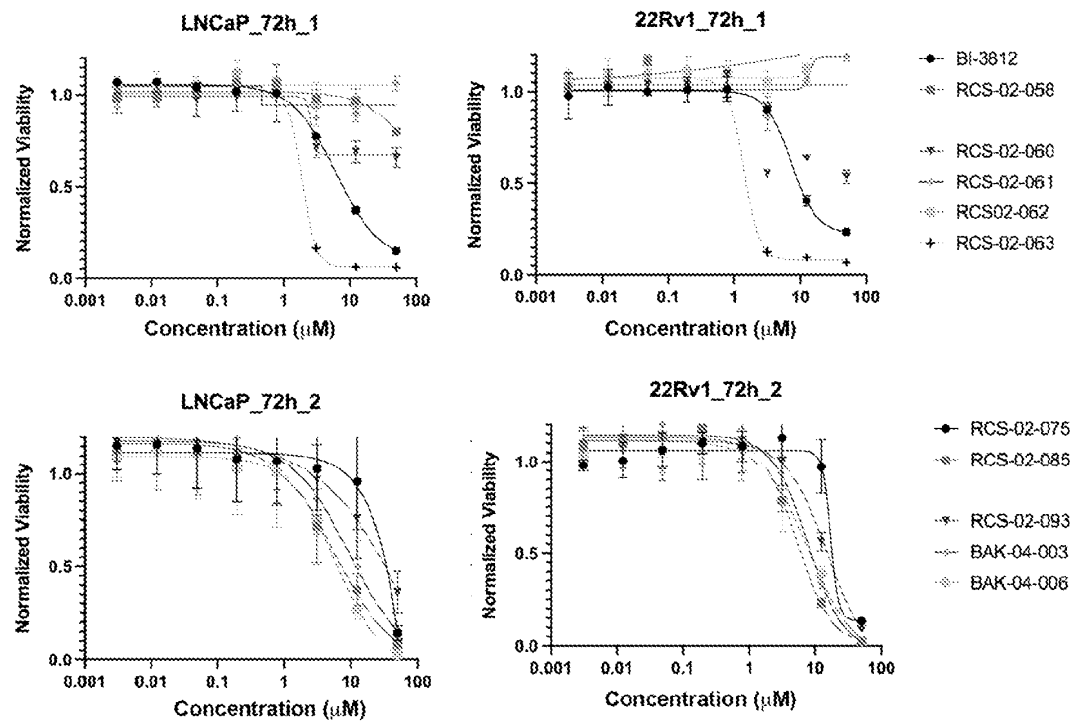
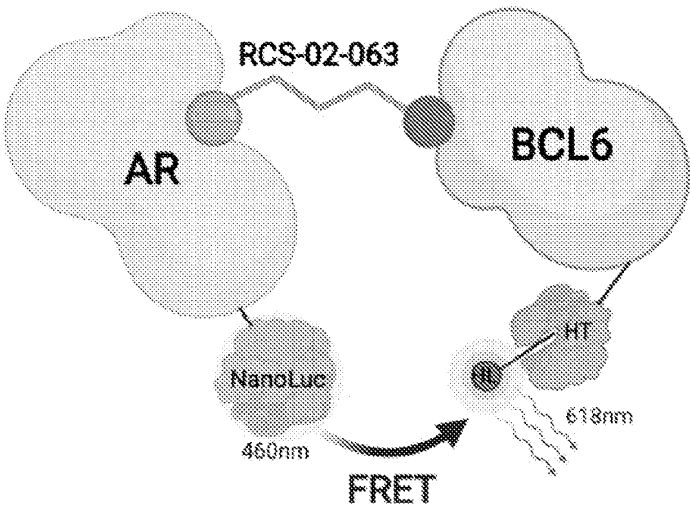


FIG. 25

A.



B.

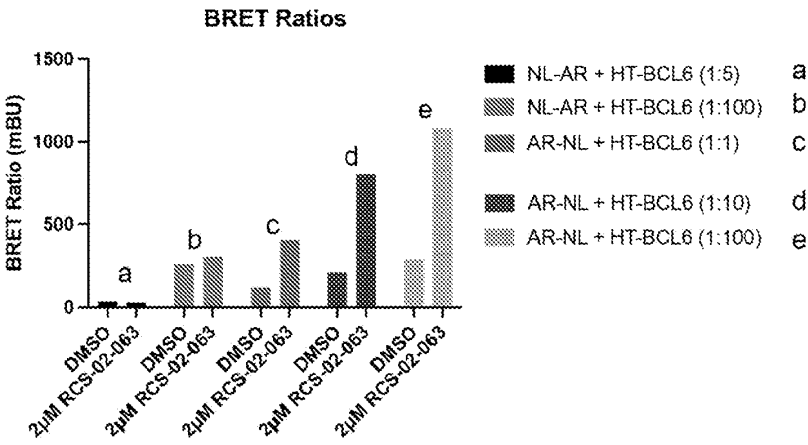


FIG. 26

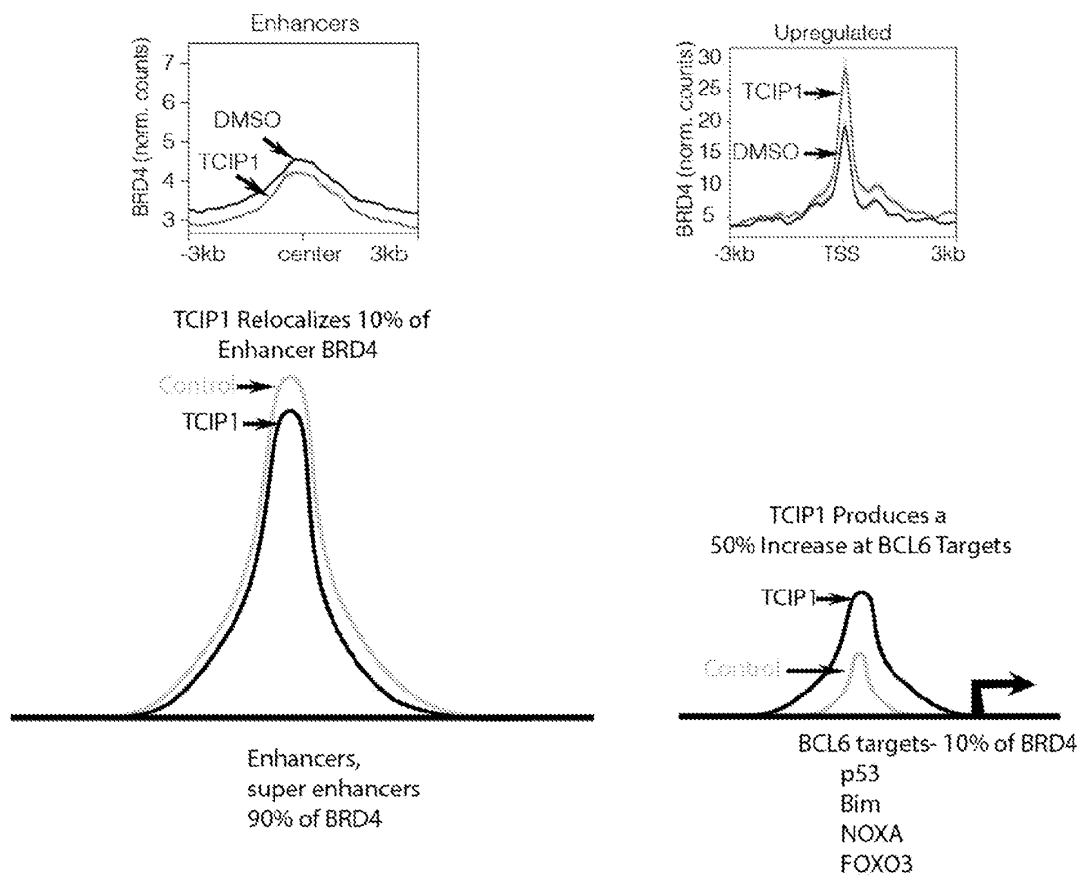


FIG. 27

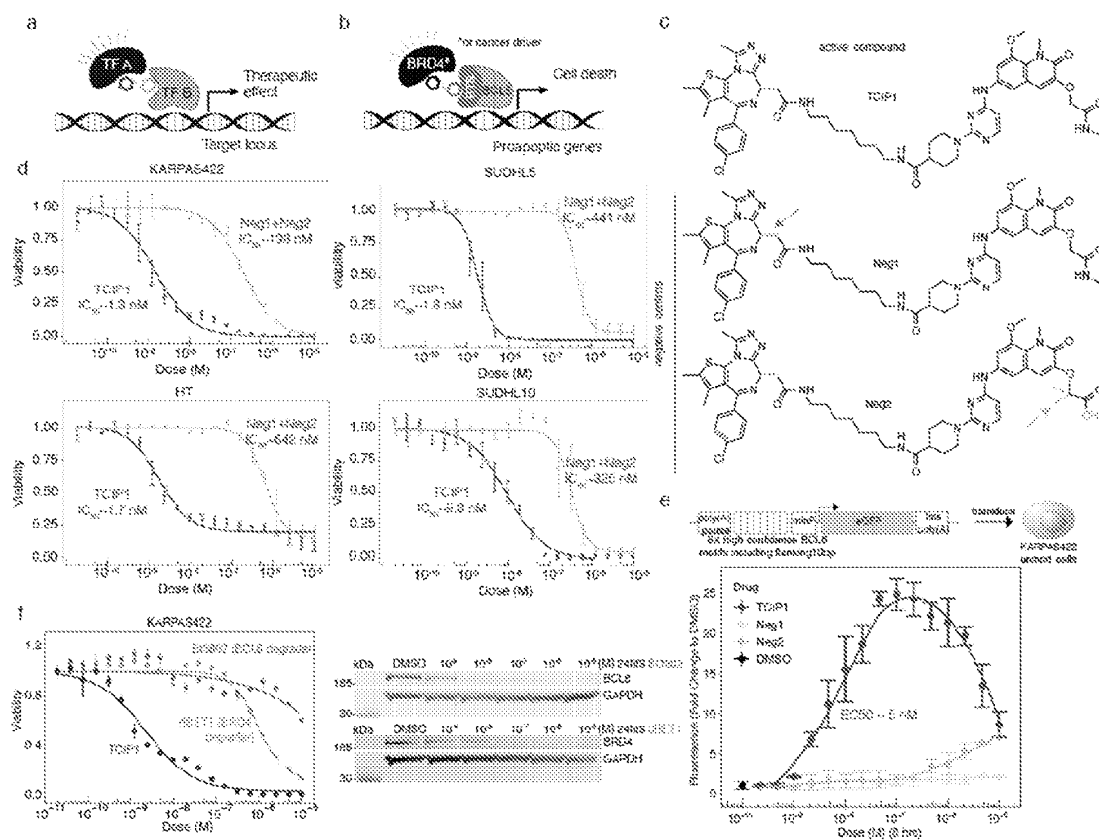


FIG. 28

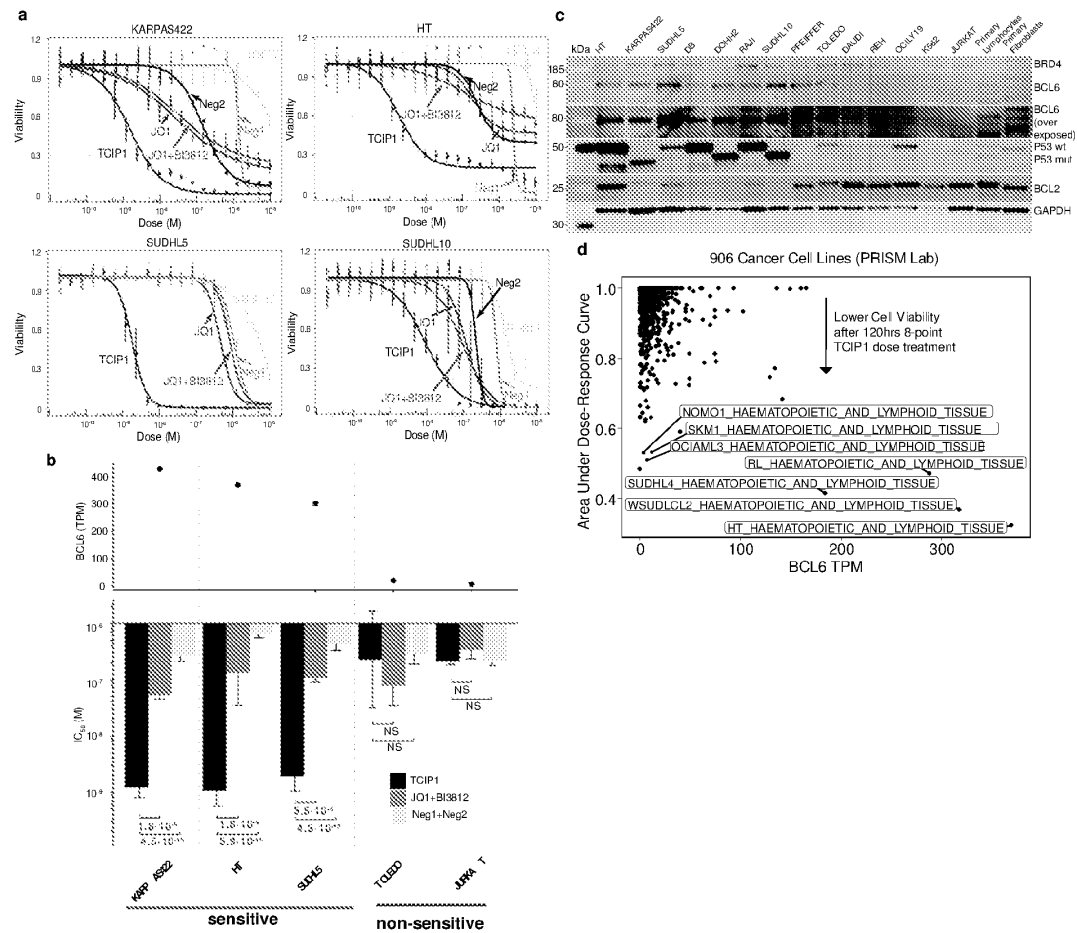


FIG. 29

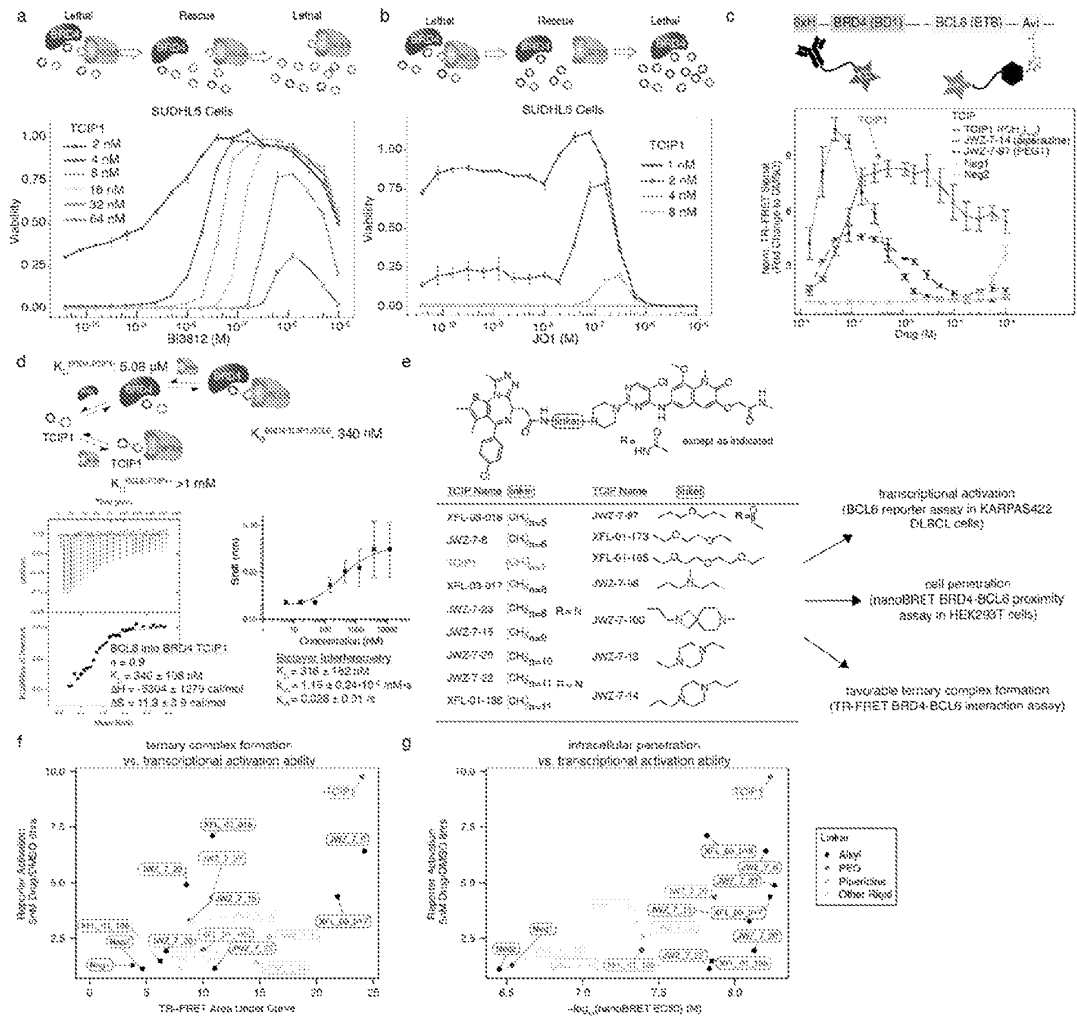


FIG. 30

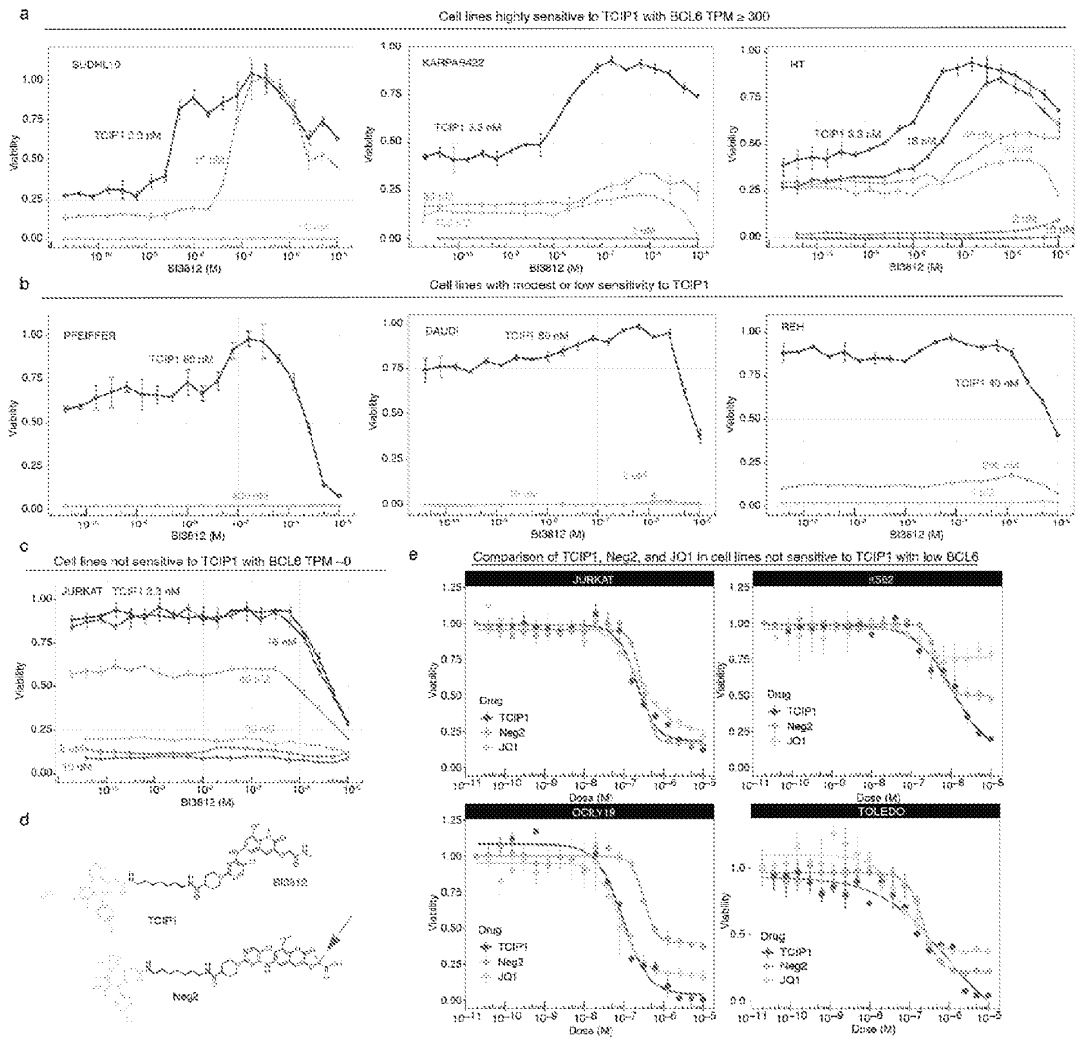


FIG. 31

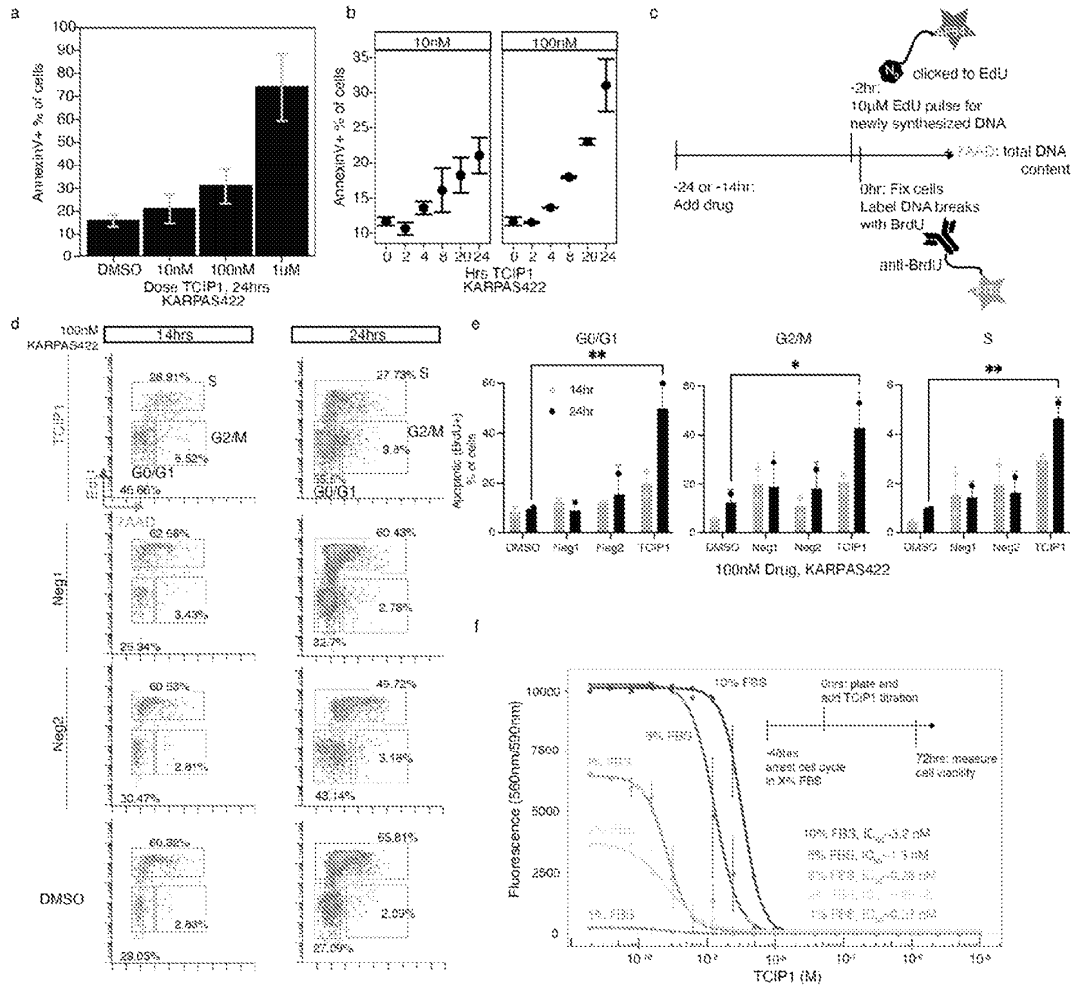


FIG. 32

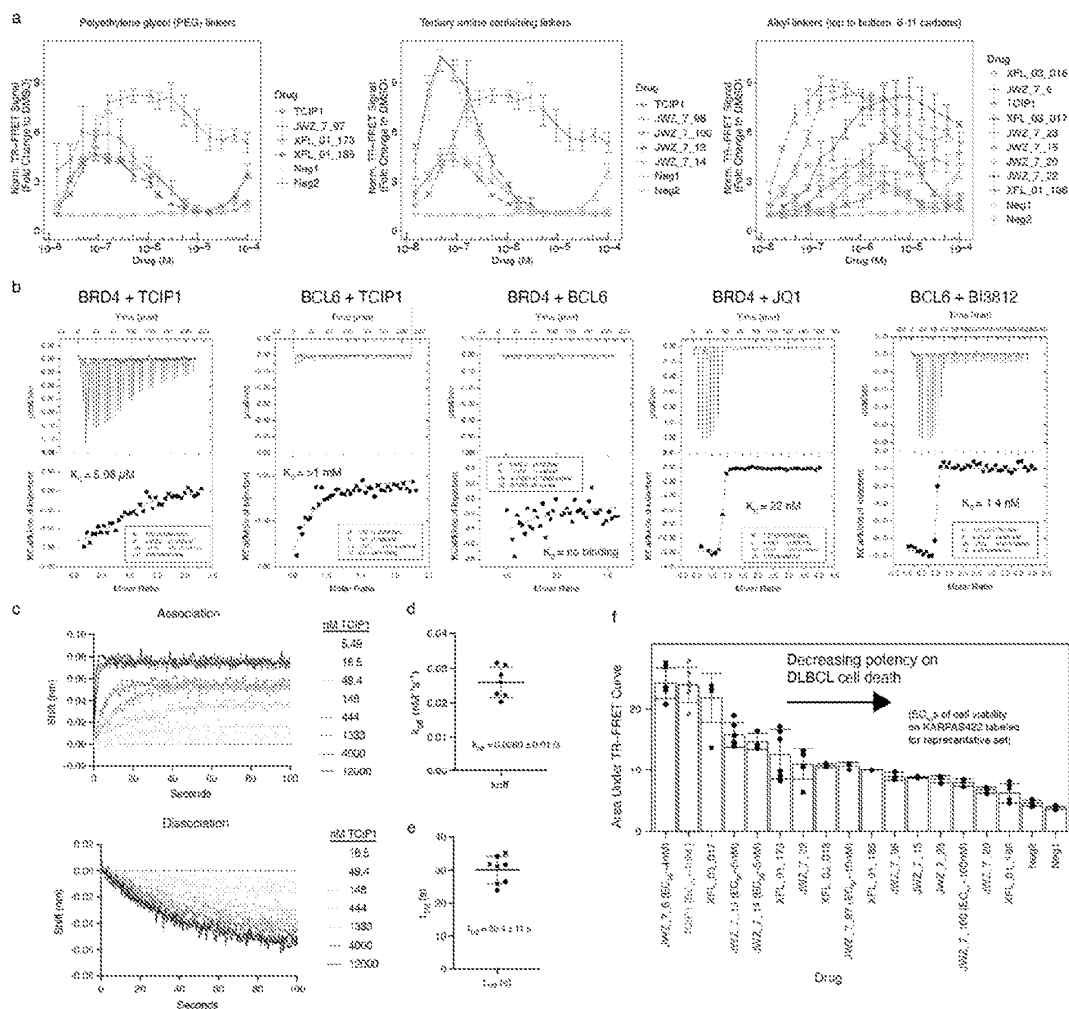


FIG. 33

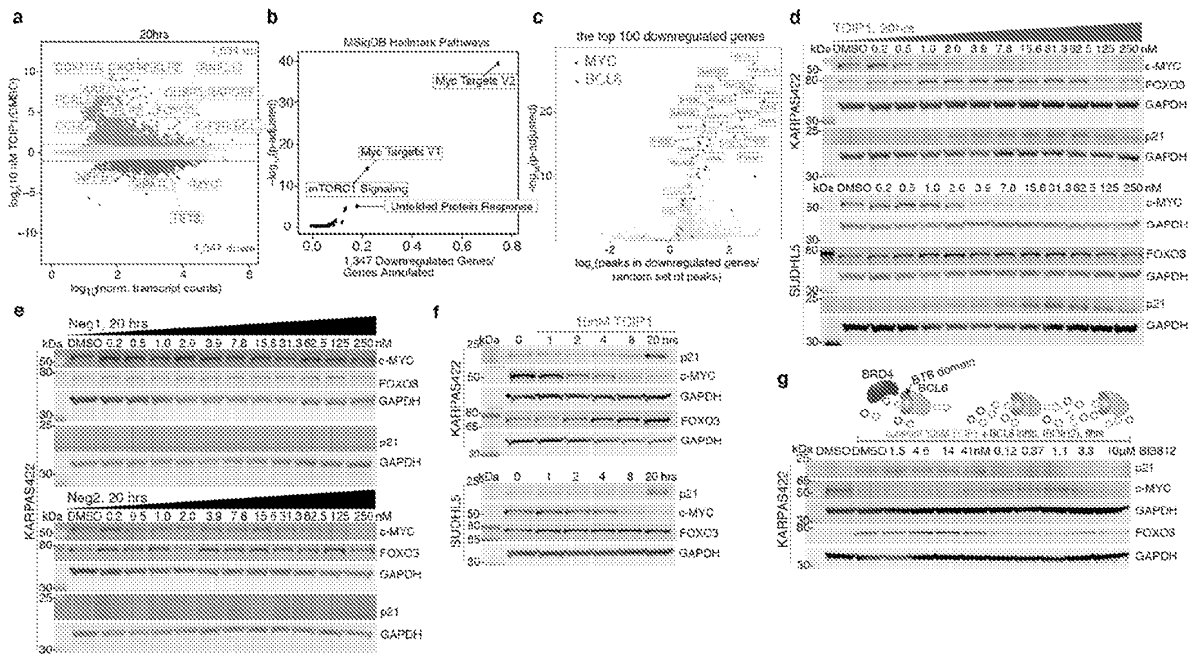


FIG. 34

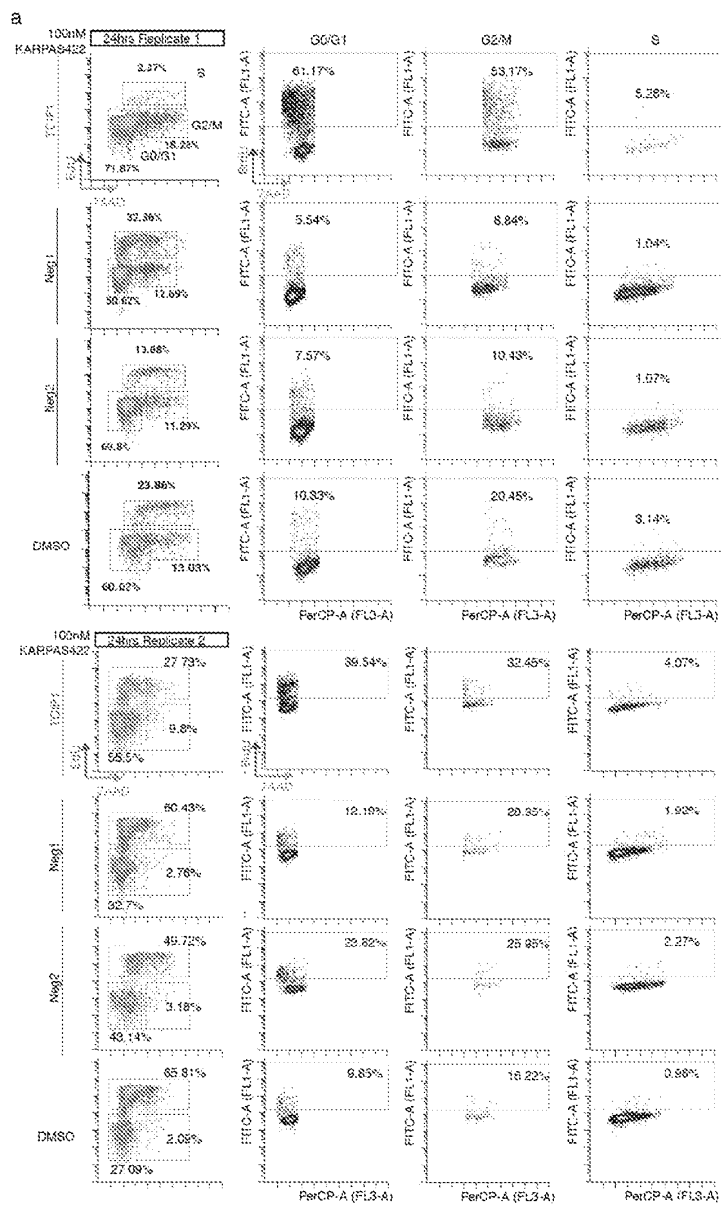


FIG. 36

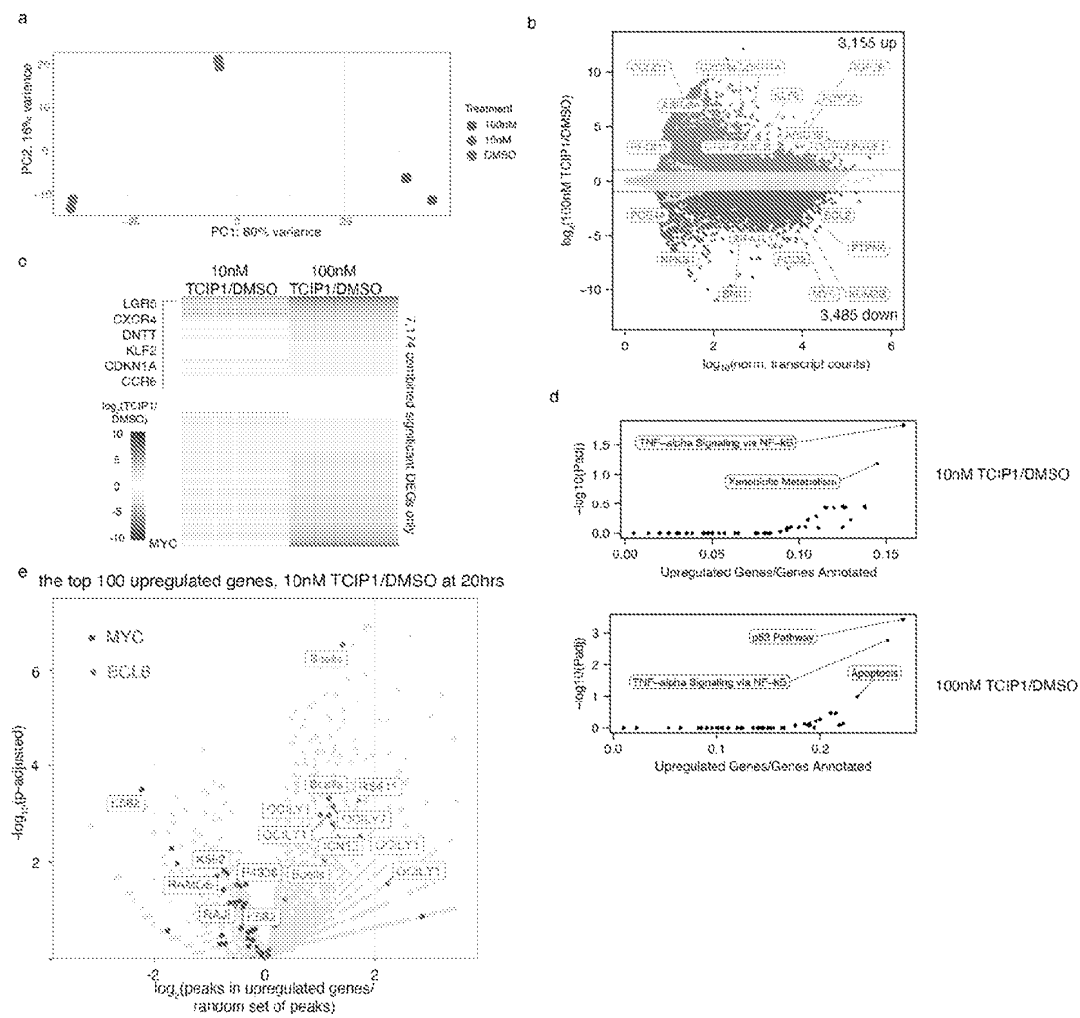


FIG. 37

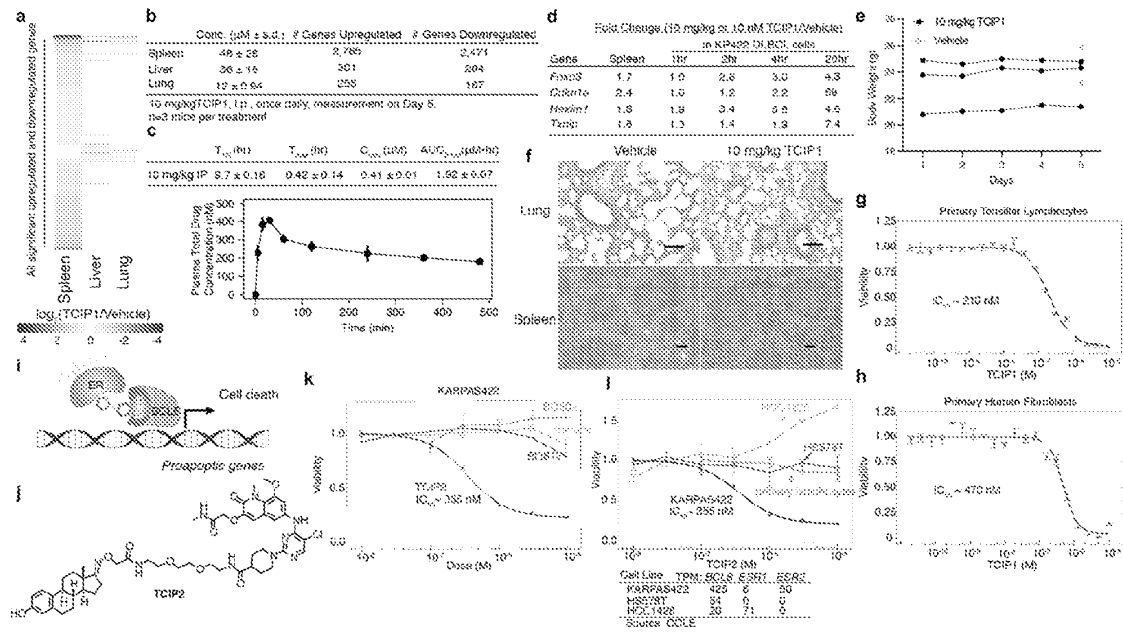
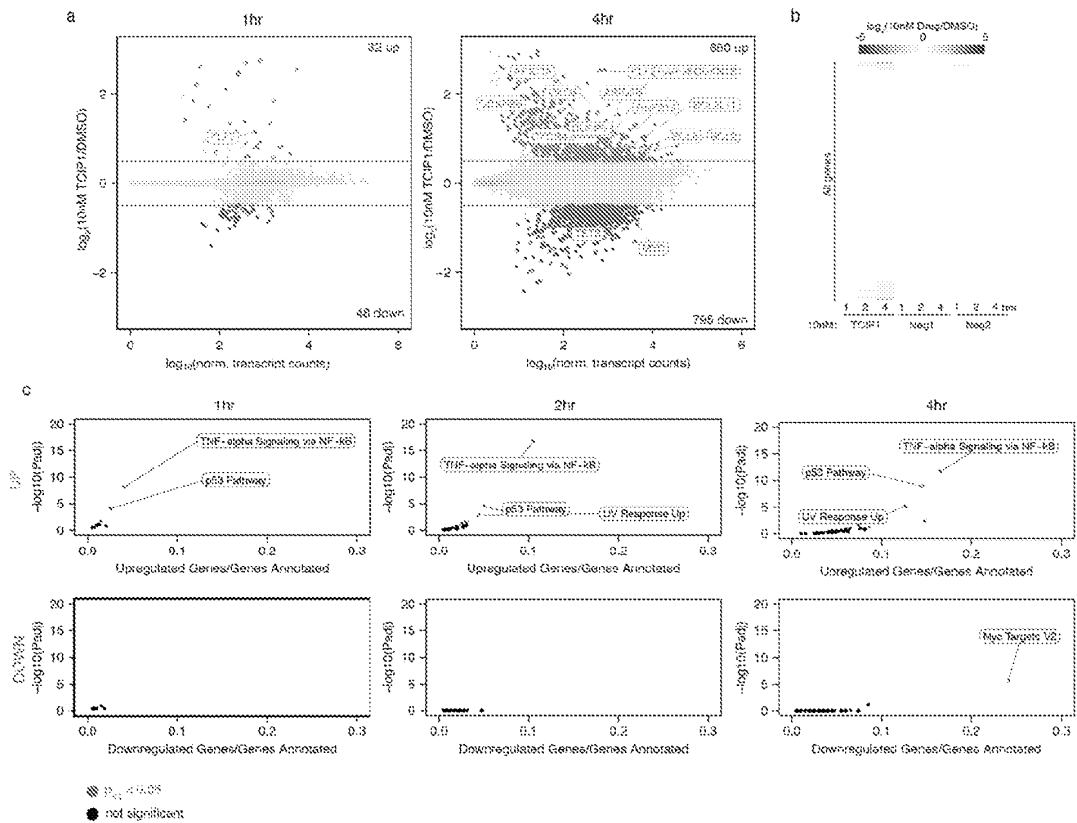


FIG. 38



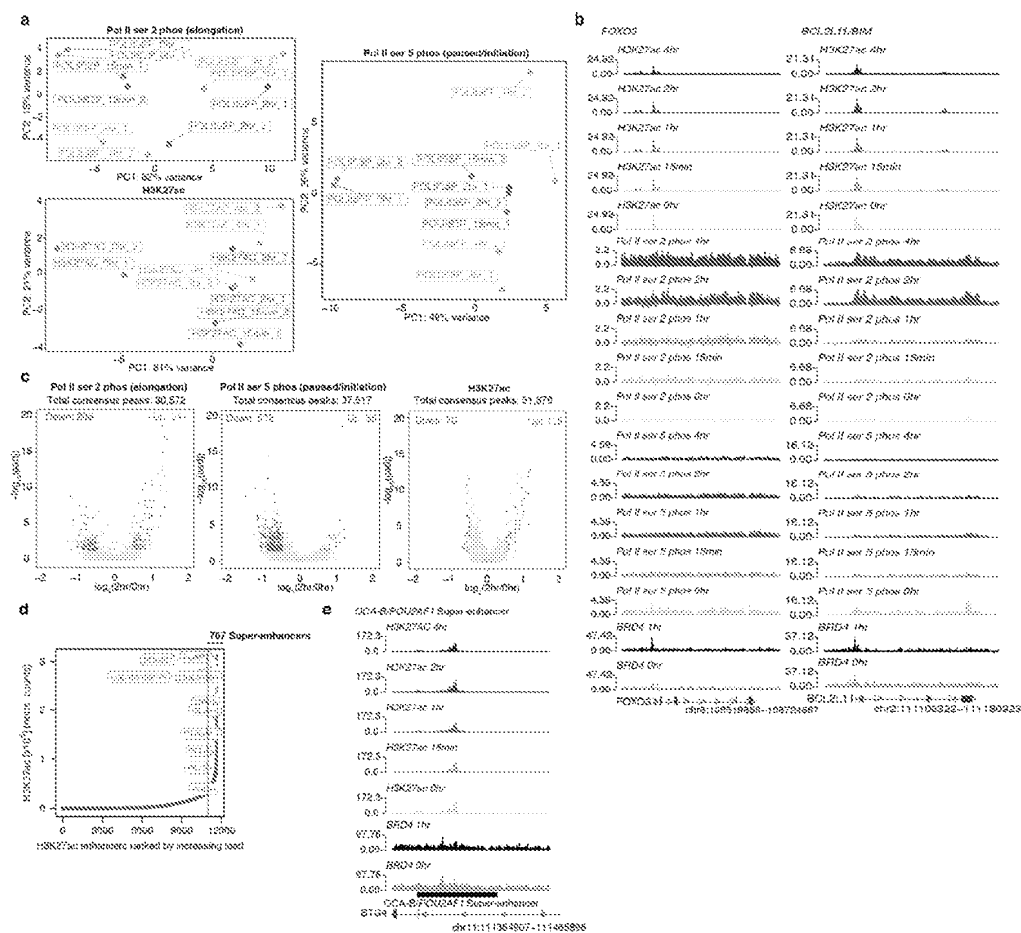


FIG. 40

