

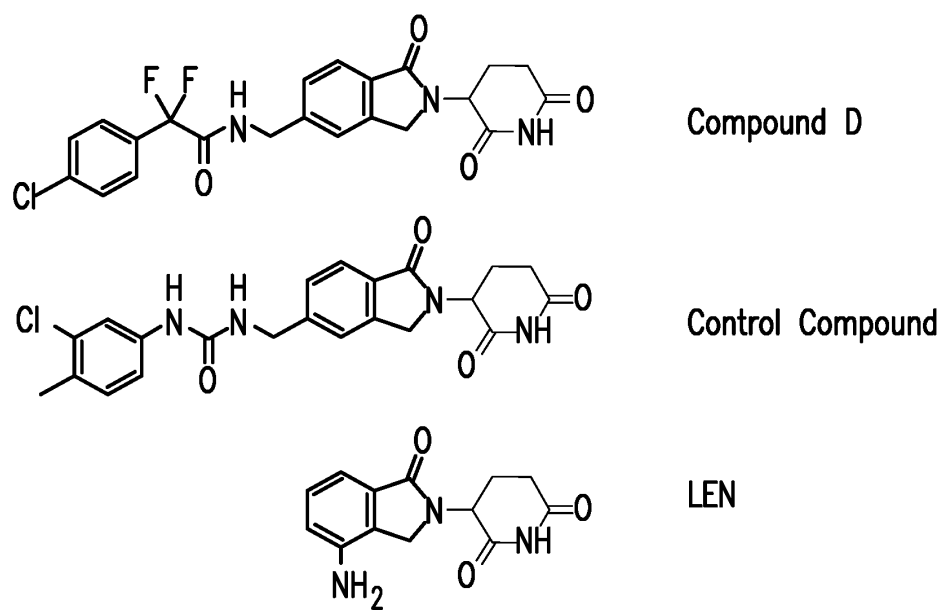


FIG. 1A

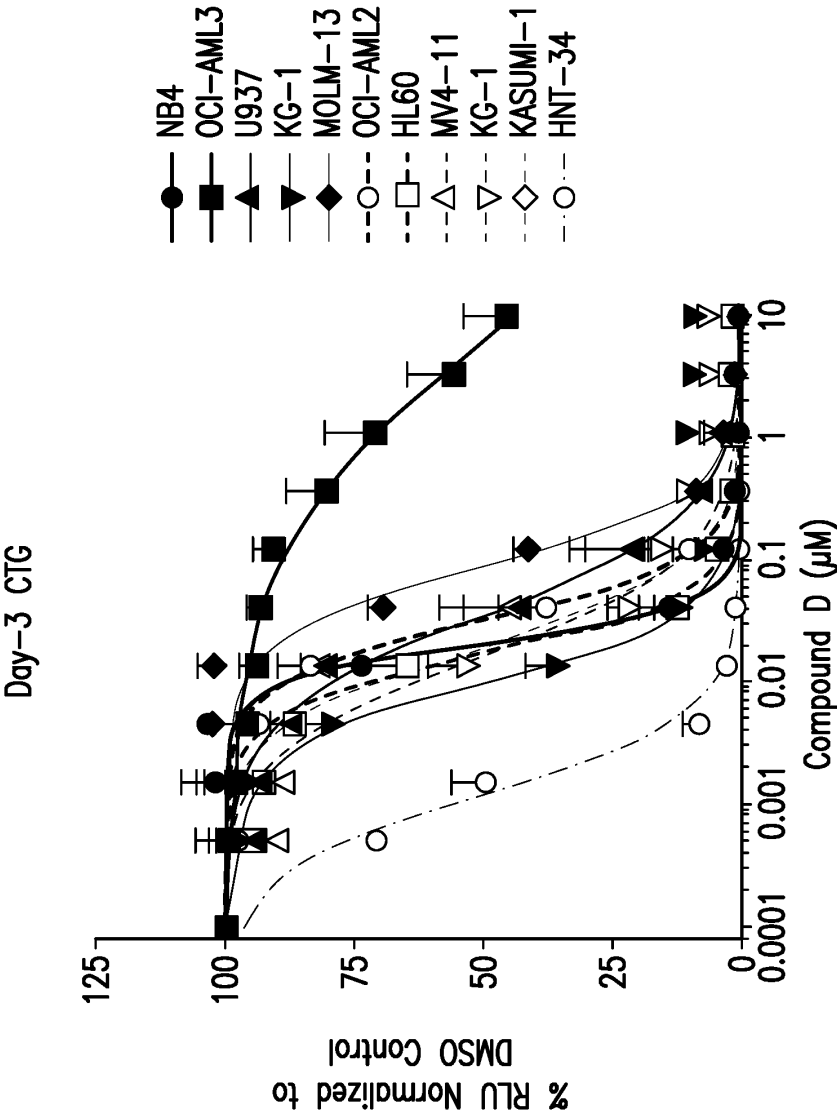


FIG. 1B

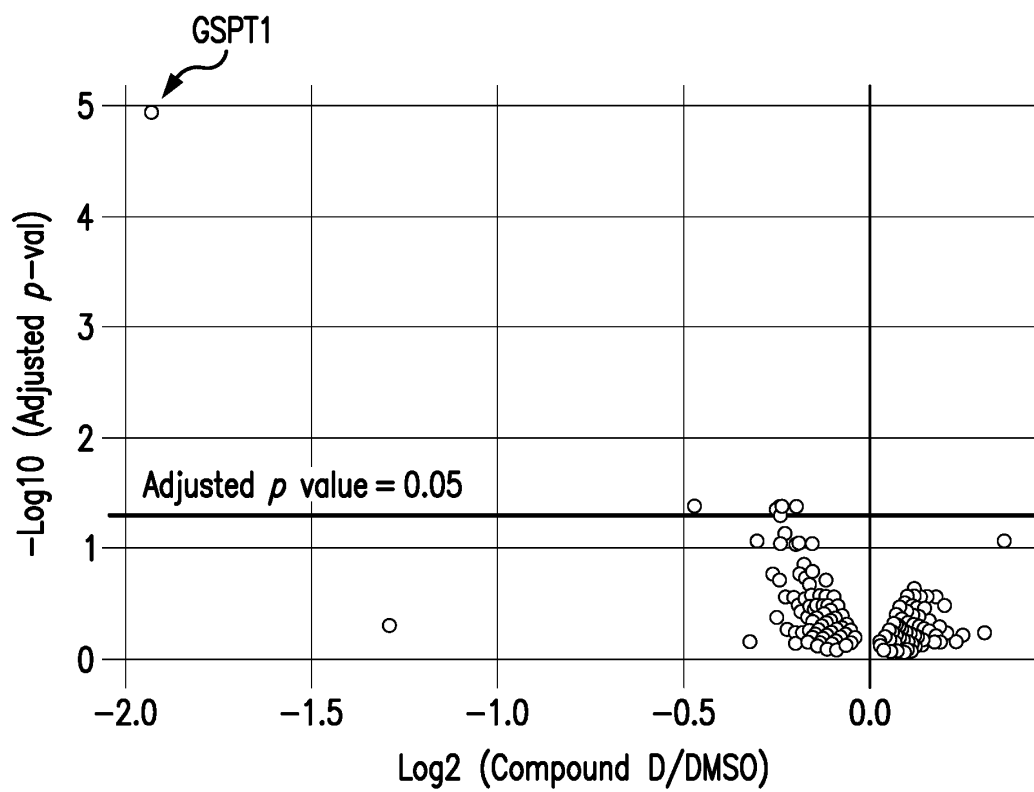


FIG. 2A

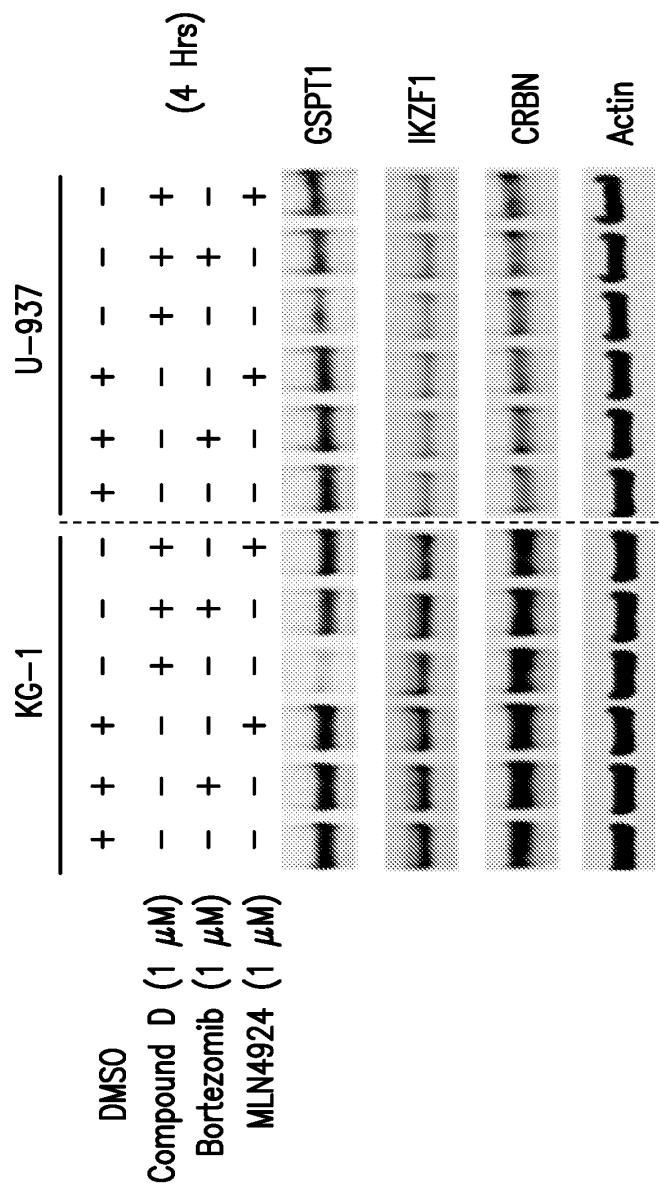


FIG. 2B

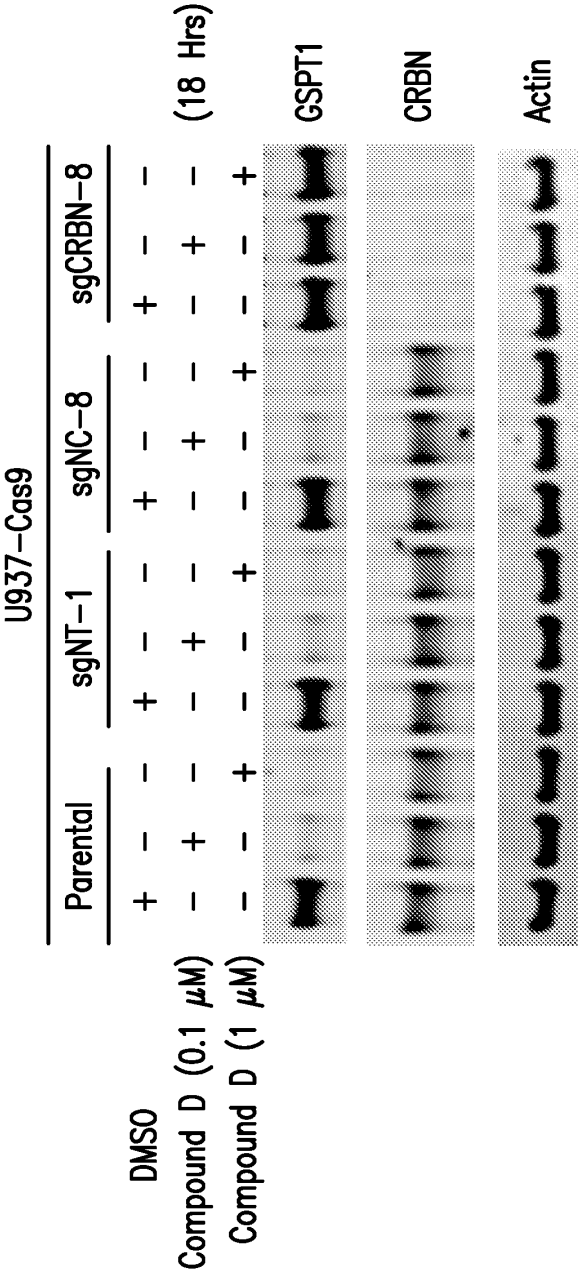


FIG. 2C

U937-Cas9
CTG, Day-3

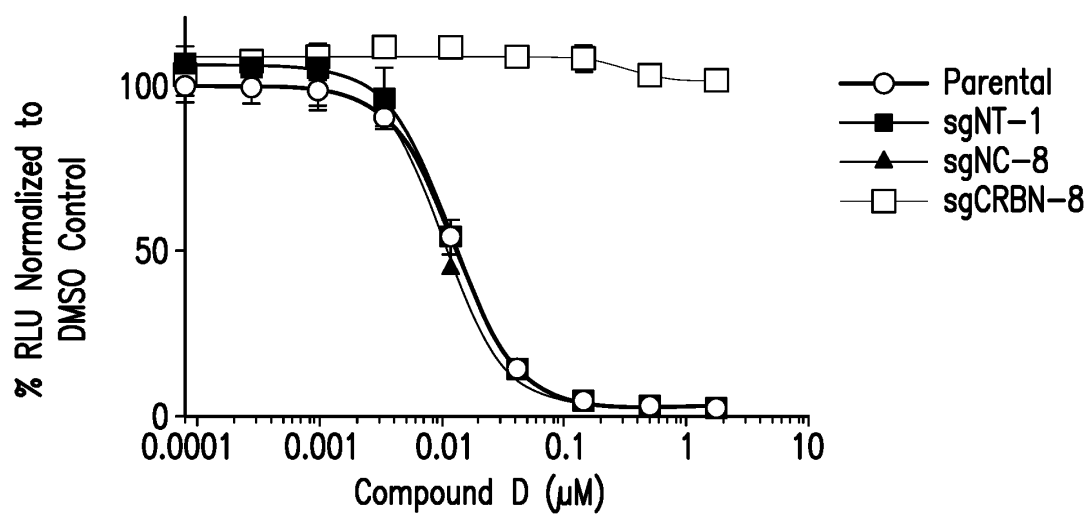


FIG. 2D

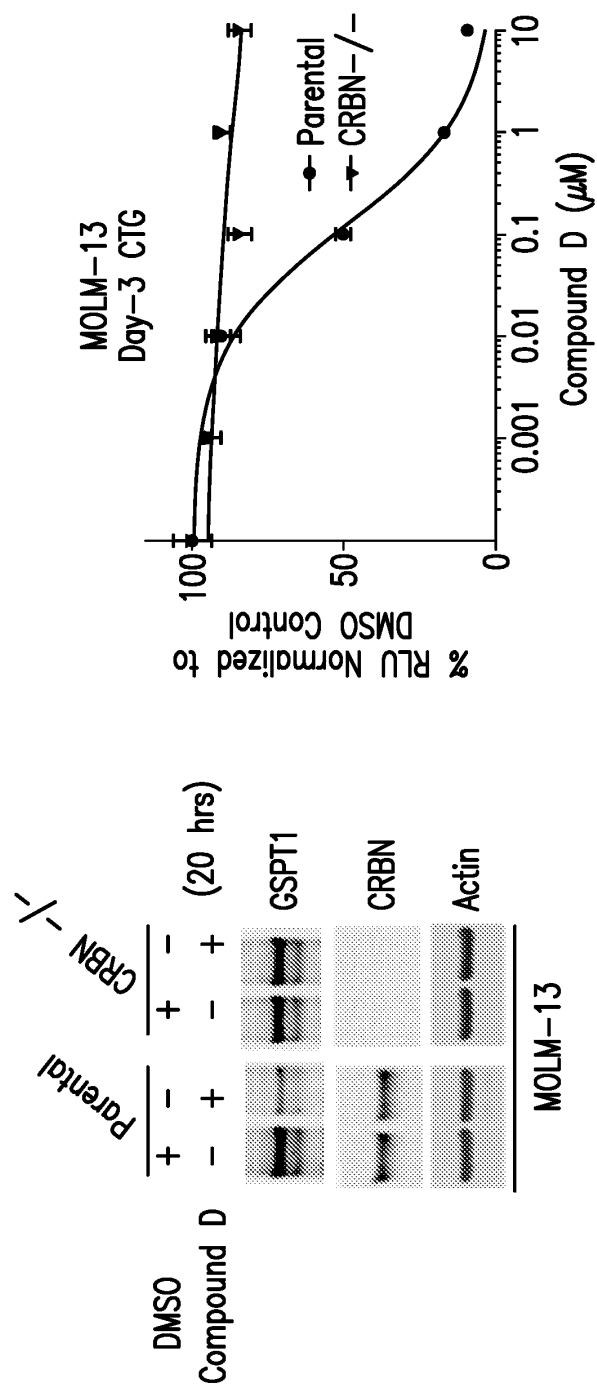


FIG. 2E

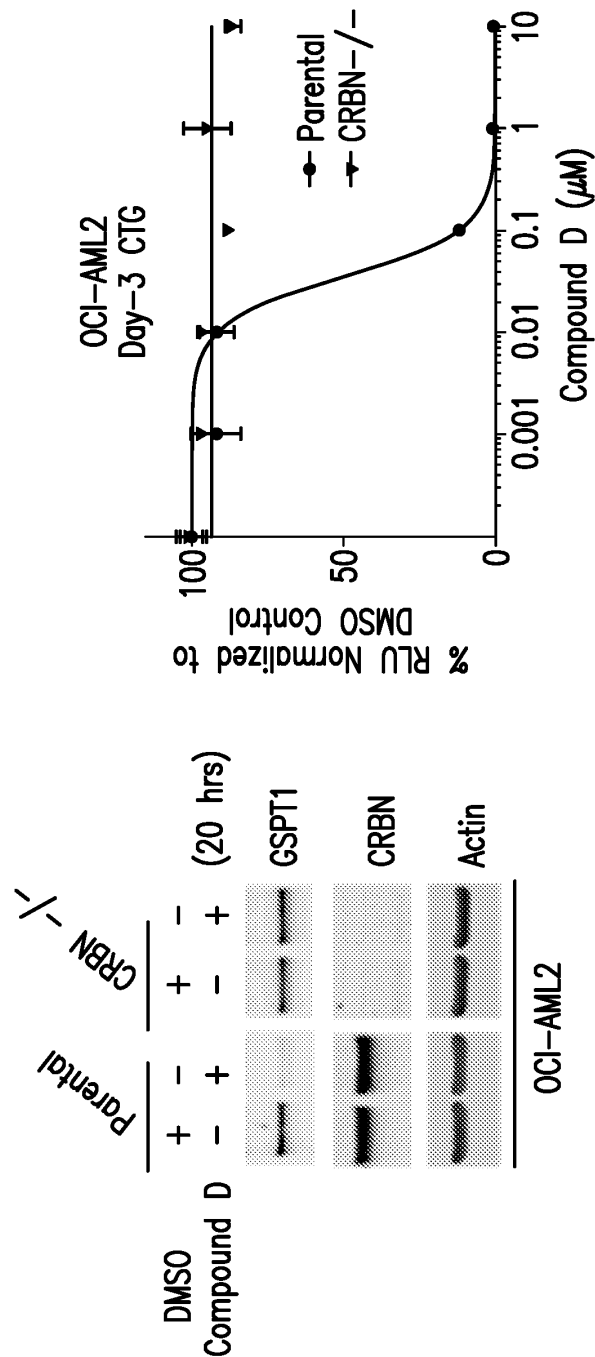


FIG. 2F

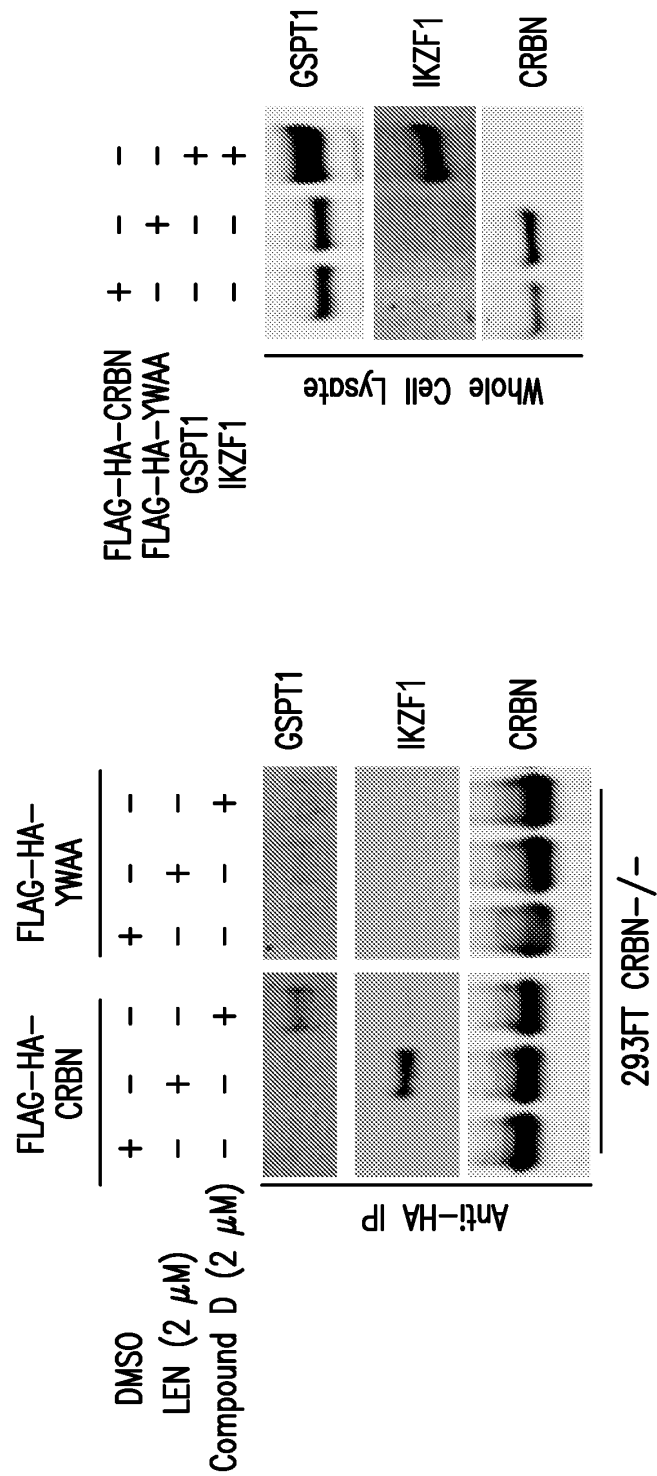


FIG. 3A

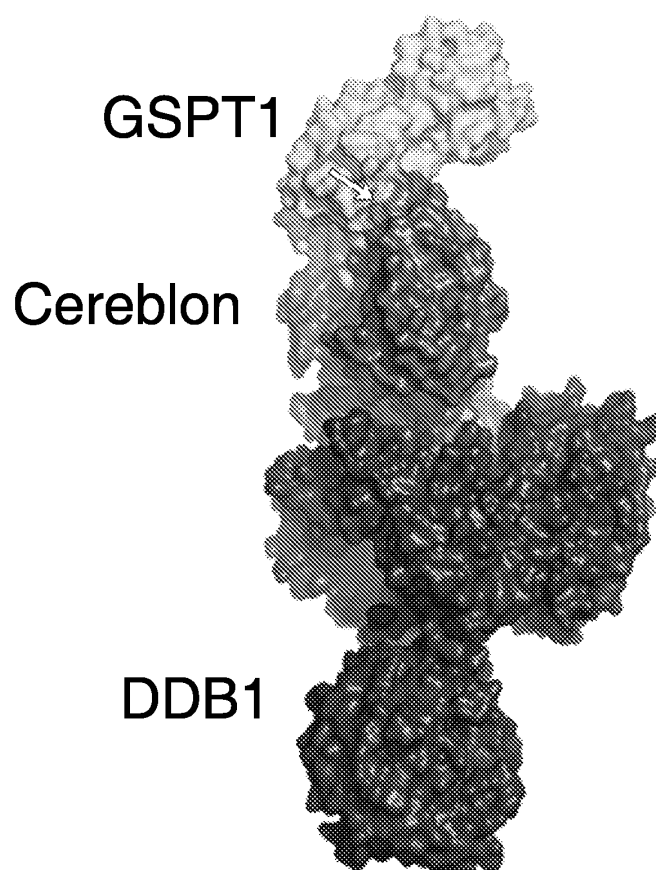


FIG. 3B

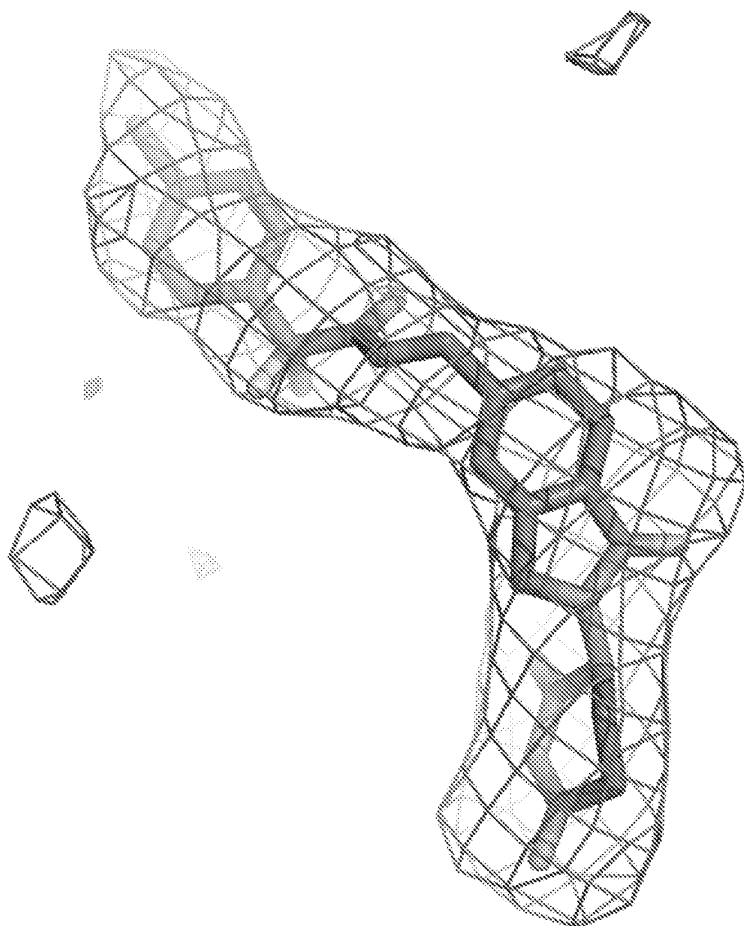


FIG. 3C

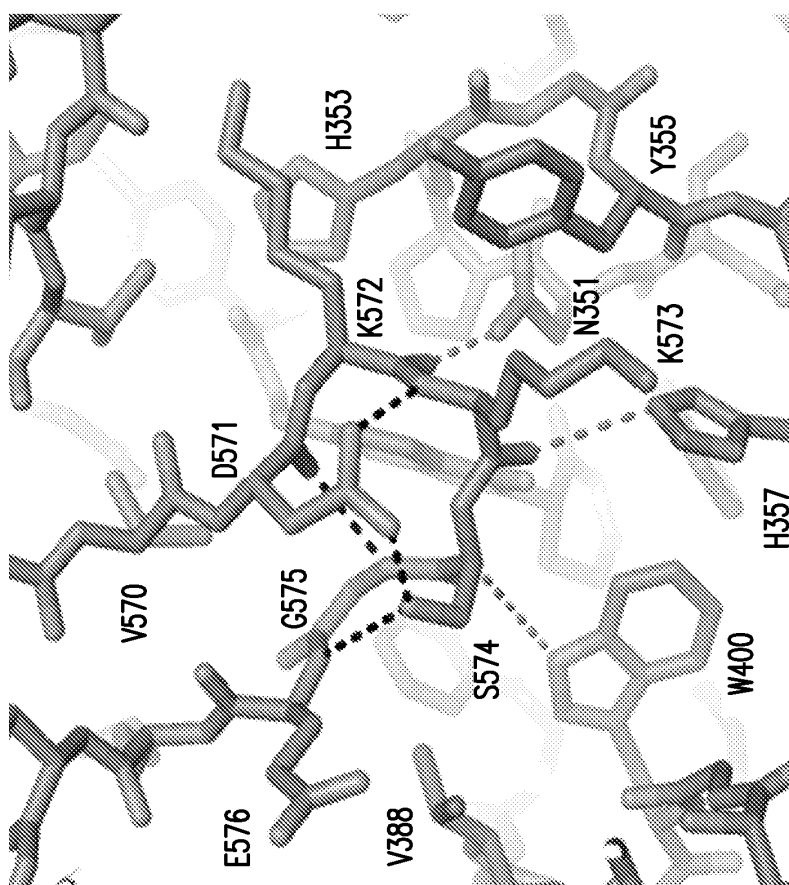


FIG. 3D

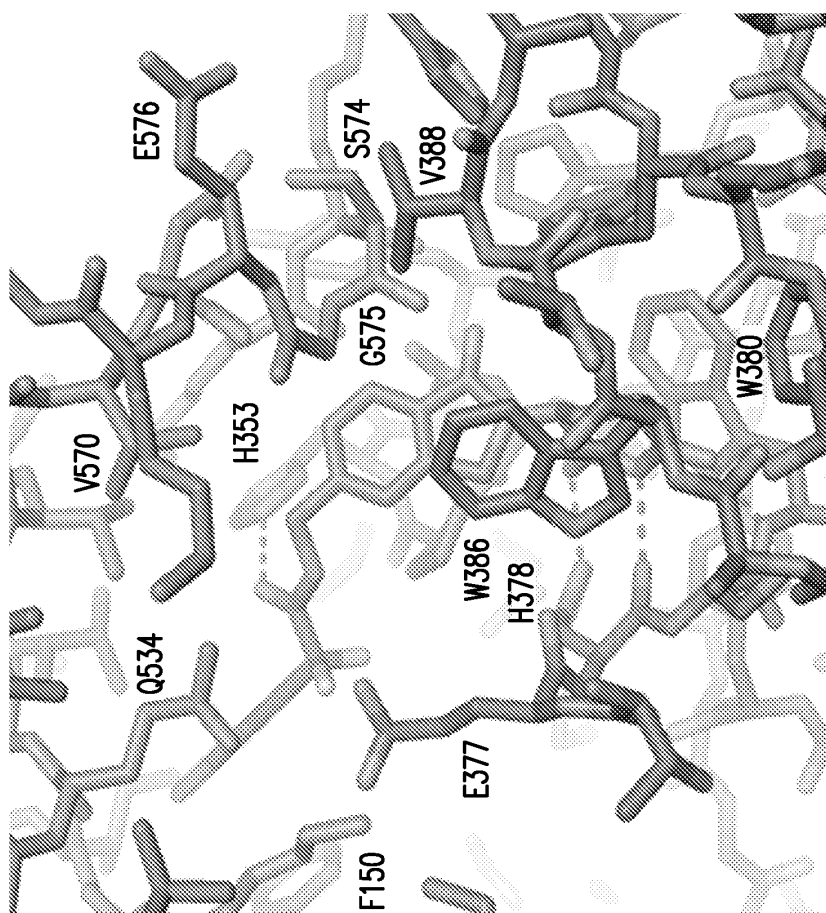


FIG. 3E

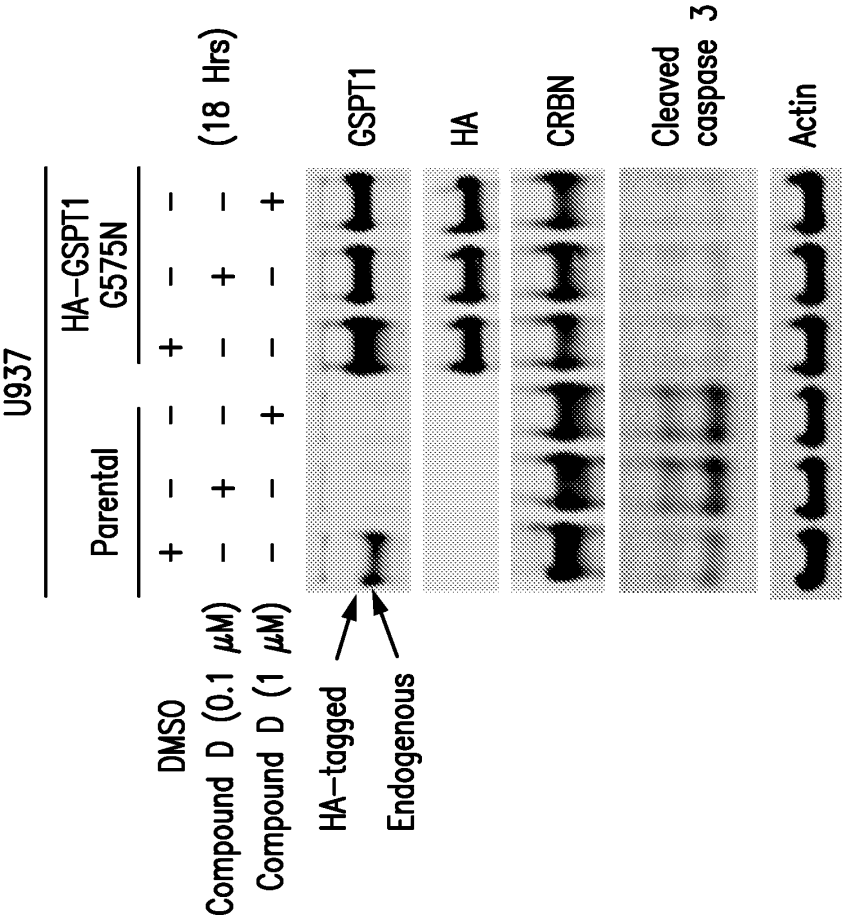


FIG. 3F

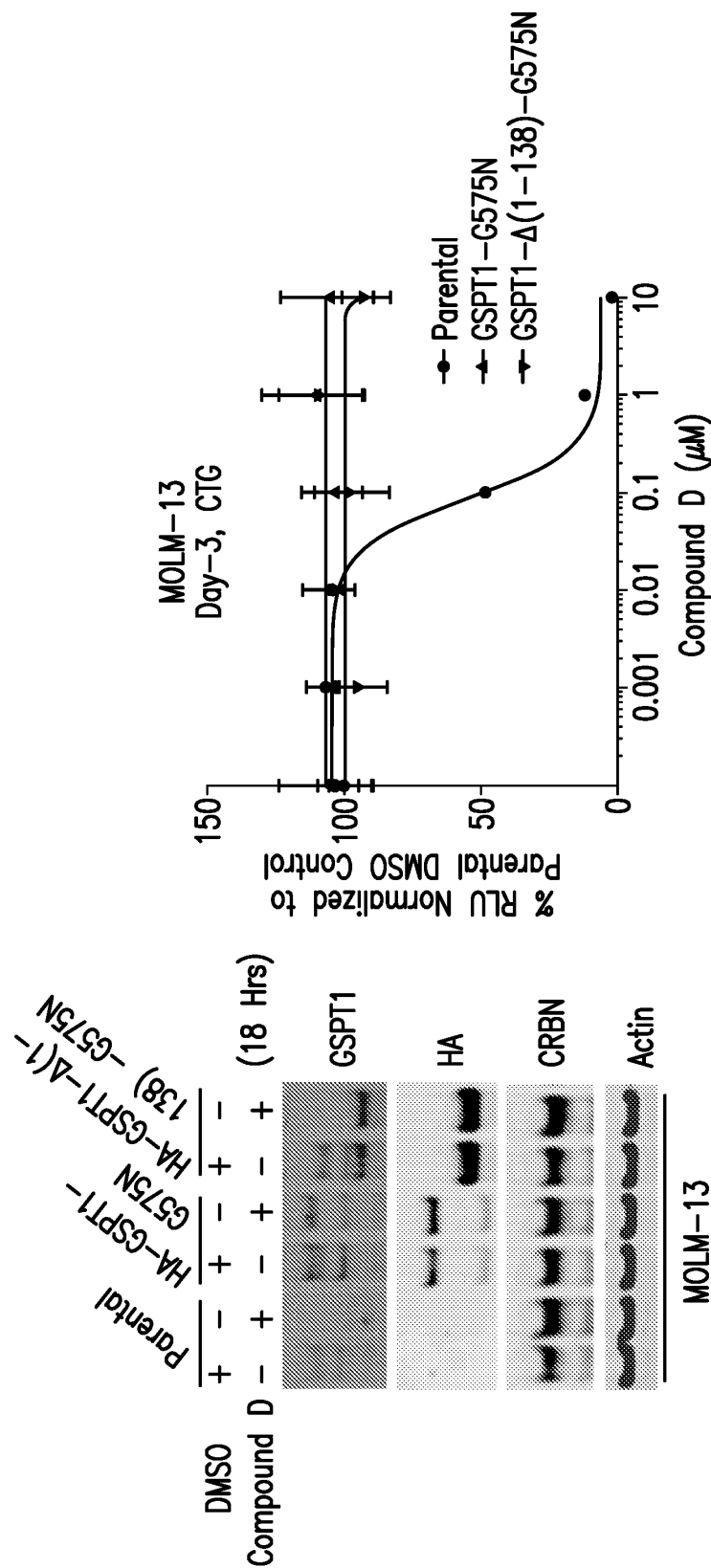


FIG. 3G

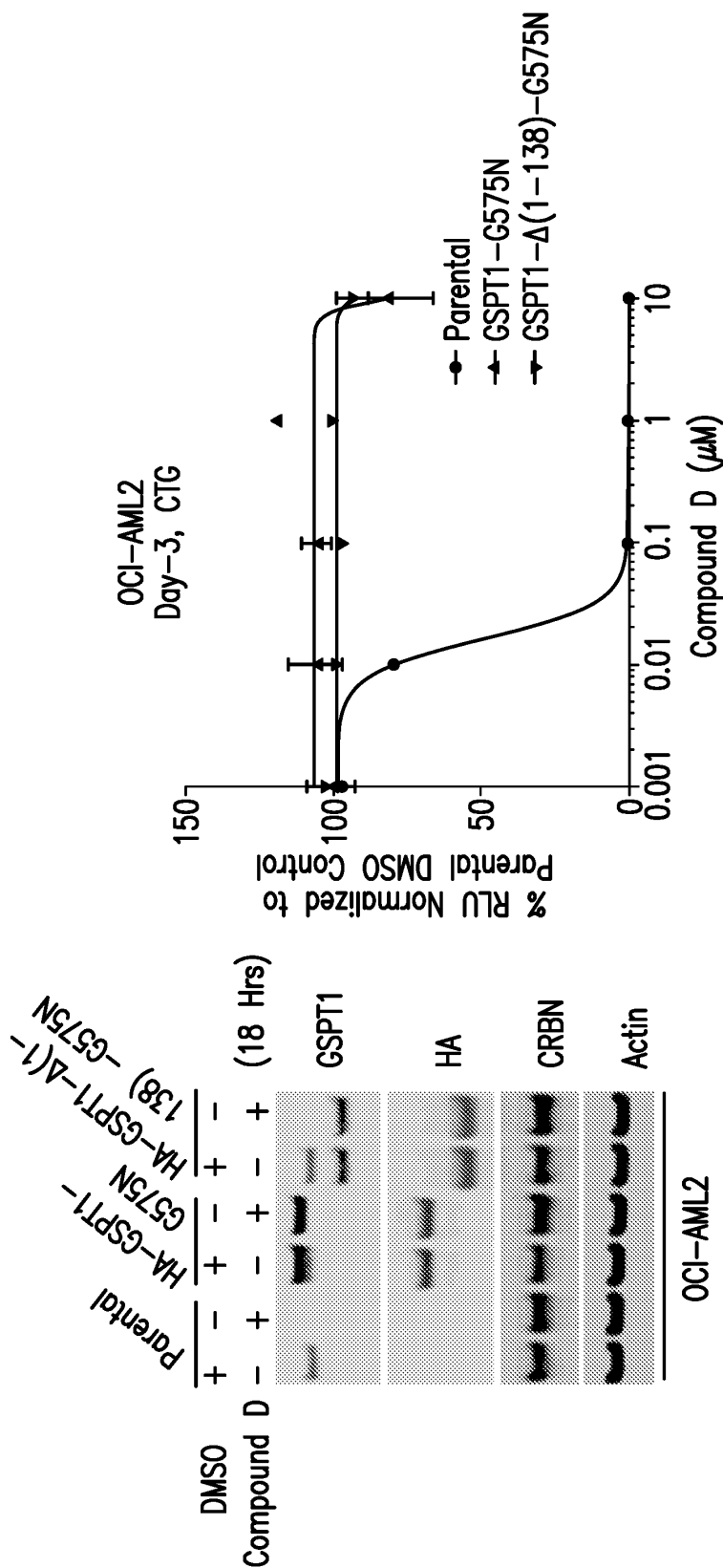


FIG. 3H

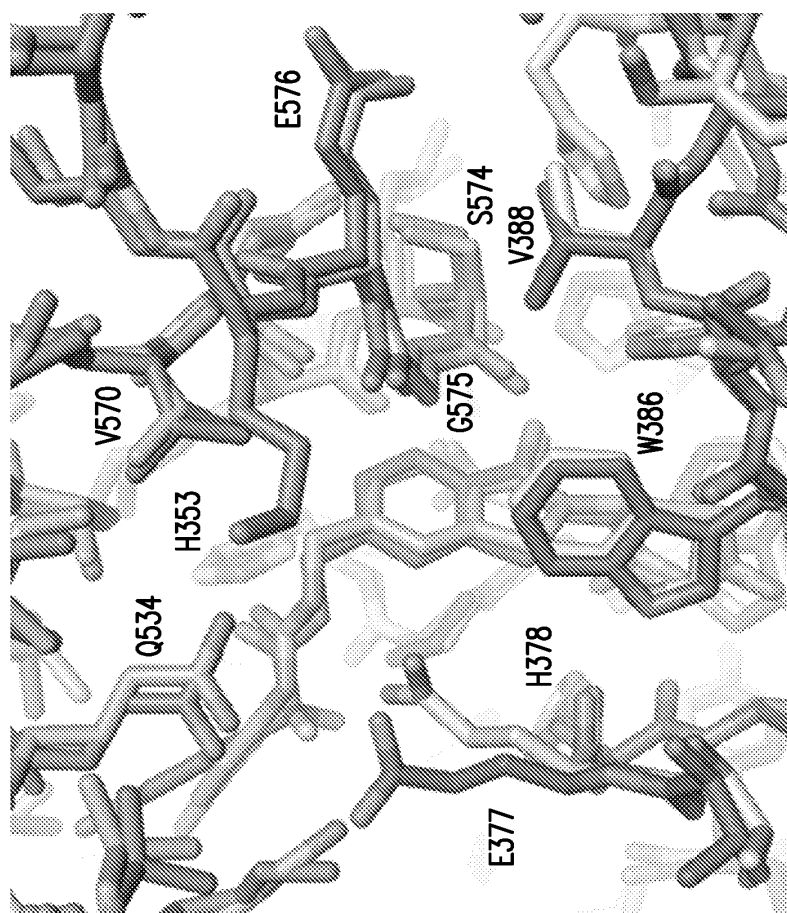


FIG. 3I

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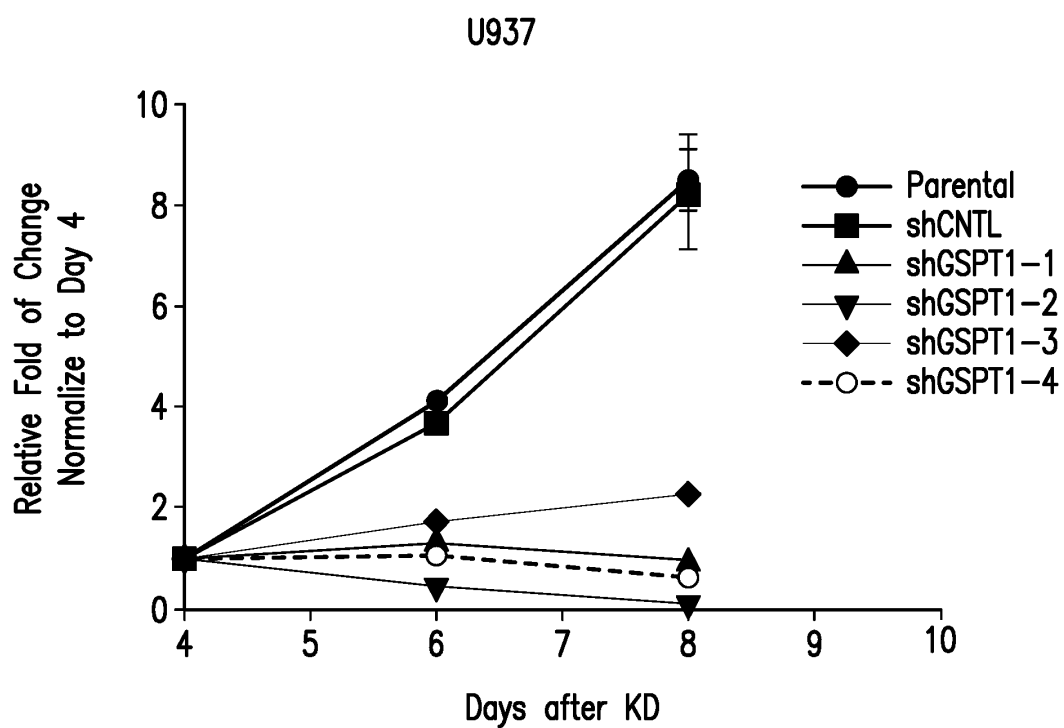


FIG. 3J

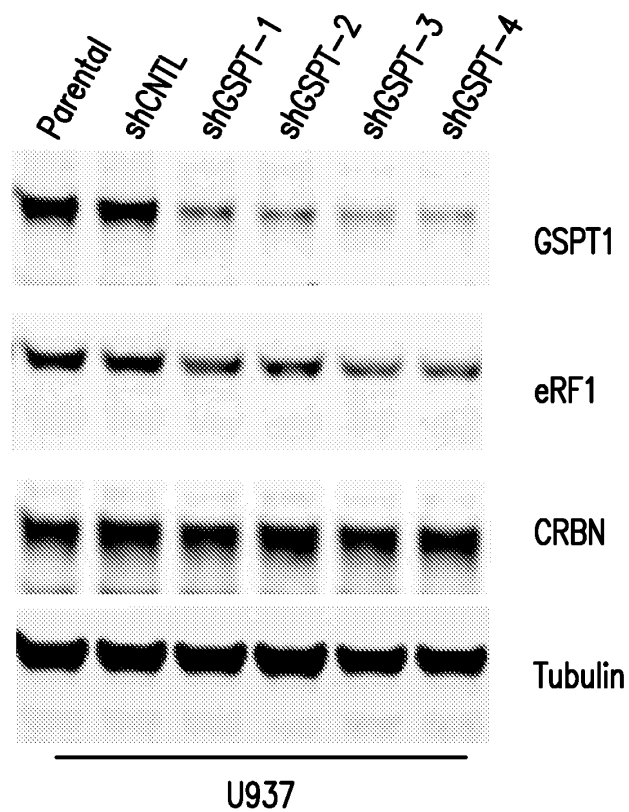
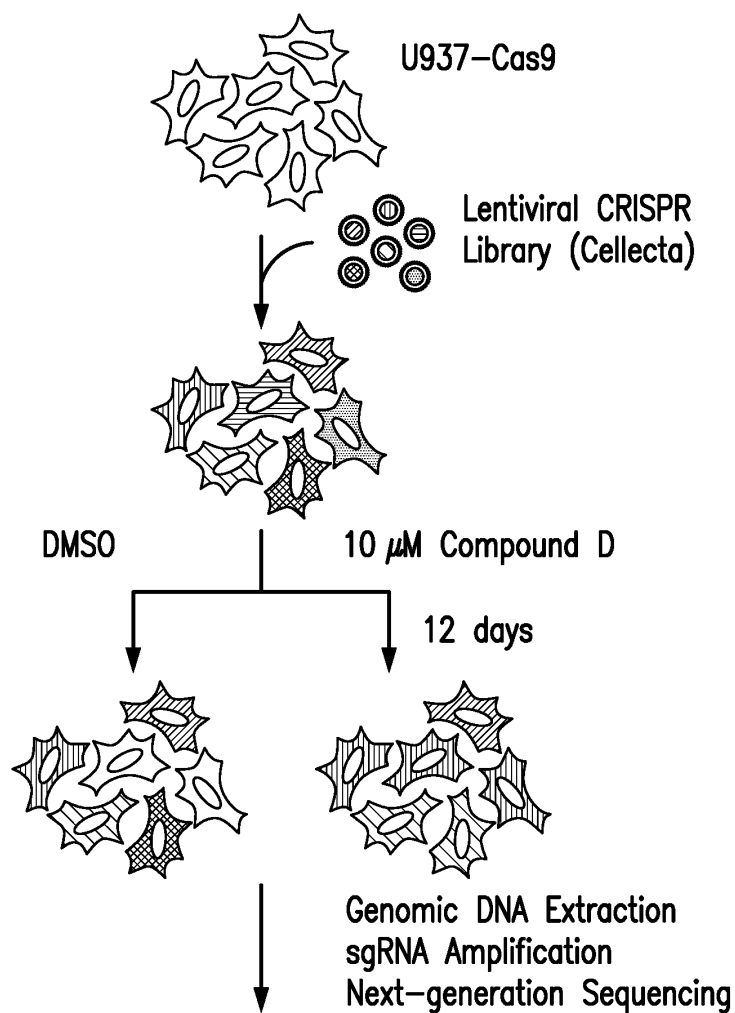


FIG. 3K



$$\text{Gene Score} = \frac{1}{n} \sum_{i=1}^n \log_2 \text{FC sgRNA}_i (\text{Compound D/DMSO})$$

FIG. 4A

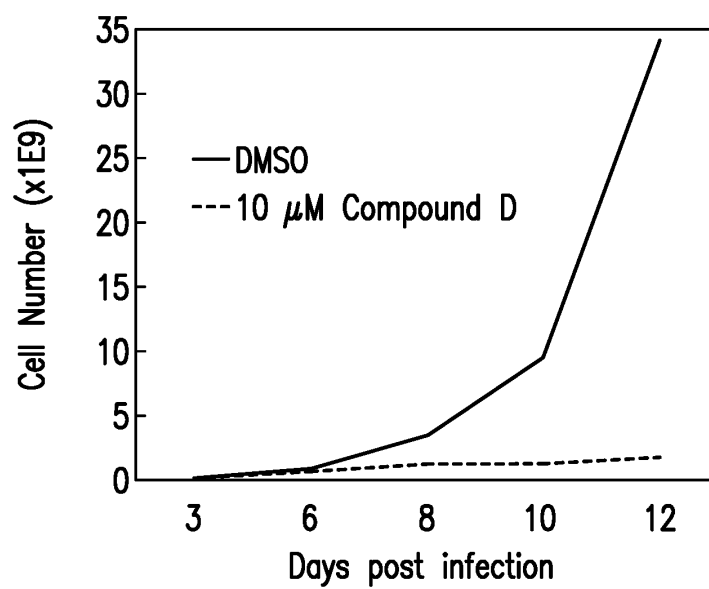


FIG. 4B

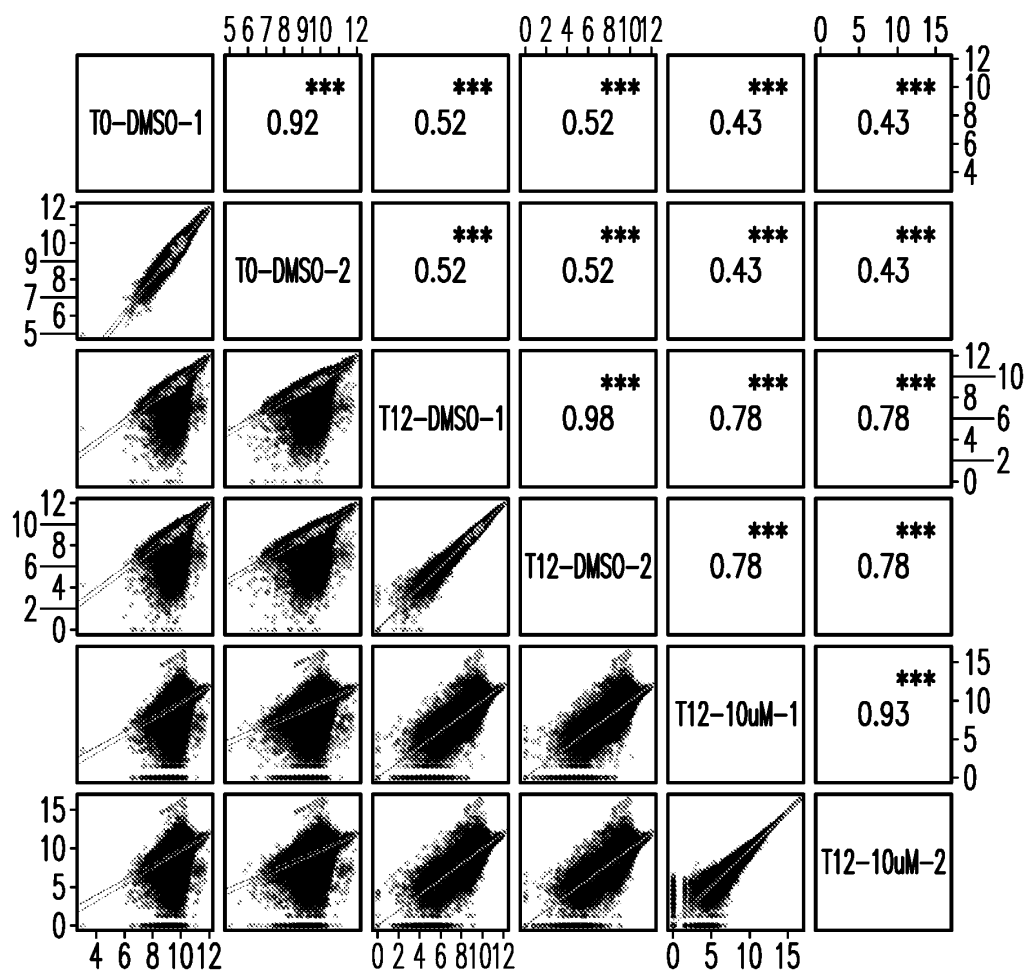


FIG. 4C

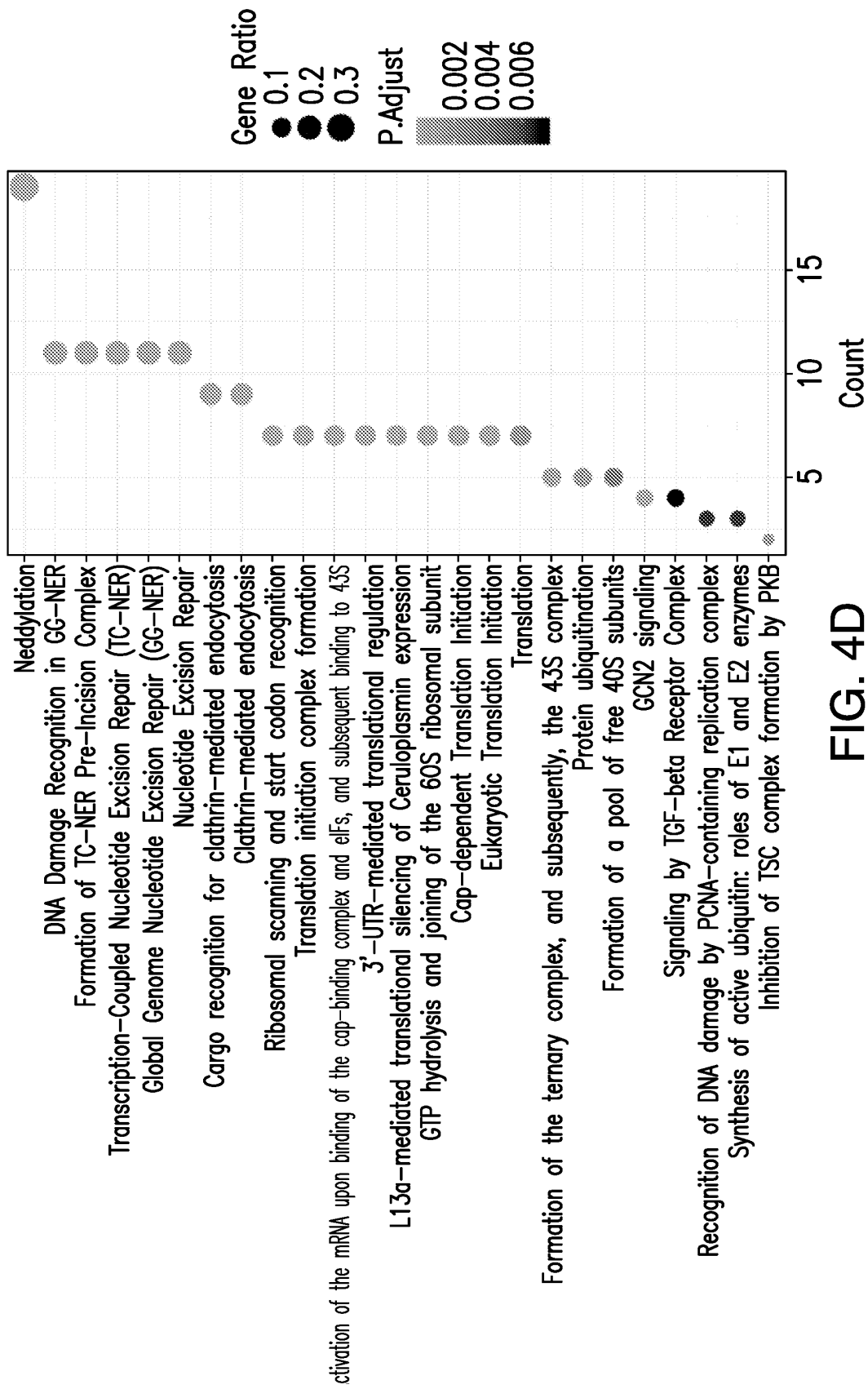


FIG. 4D

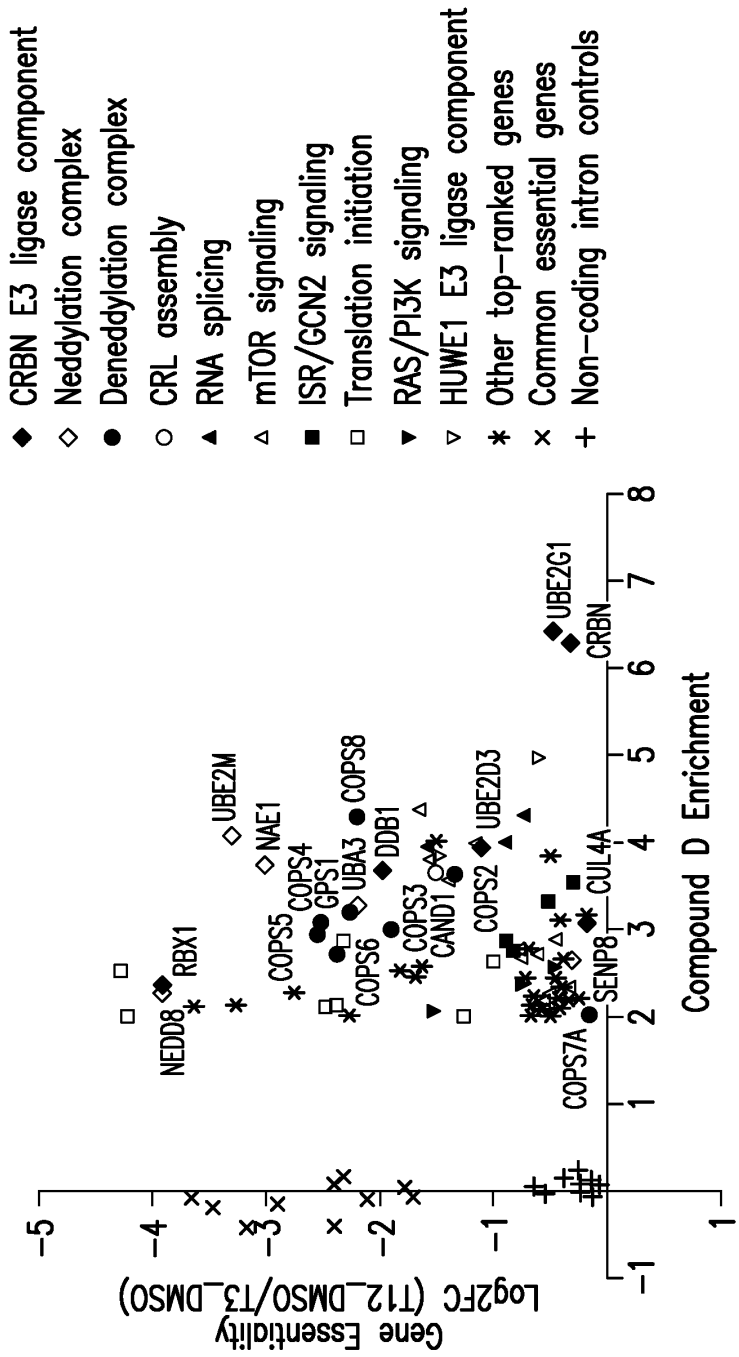


FIG. 4E

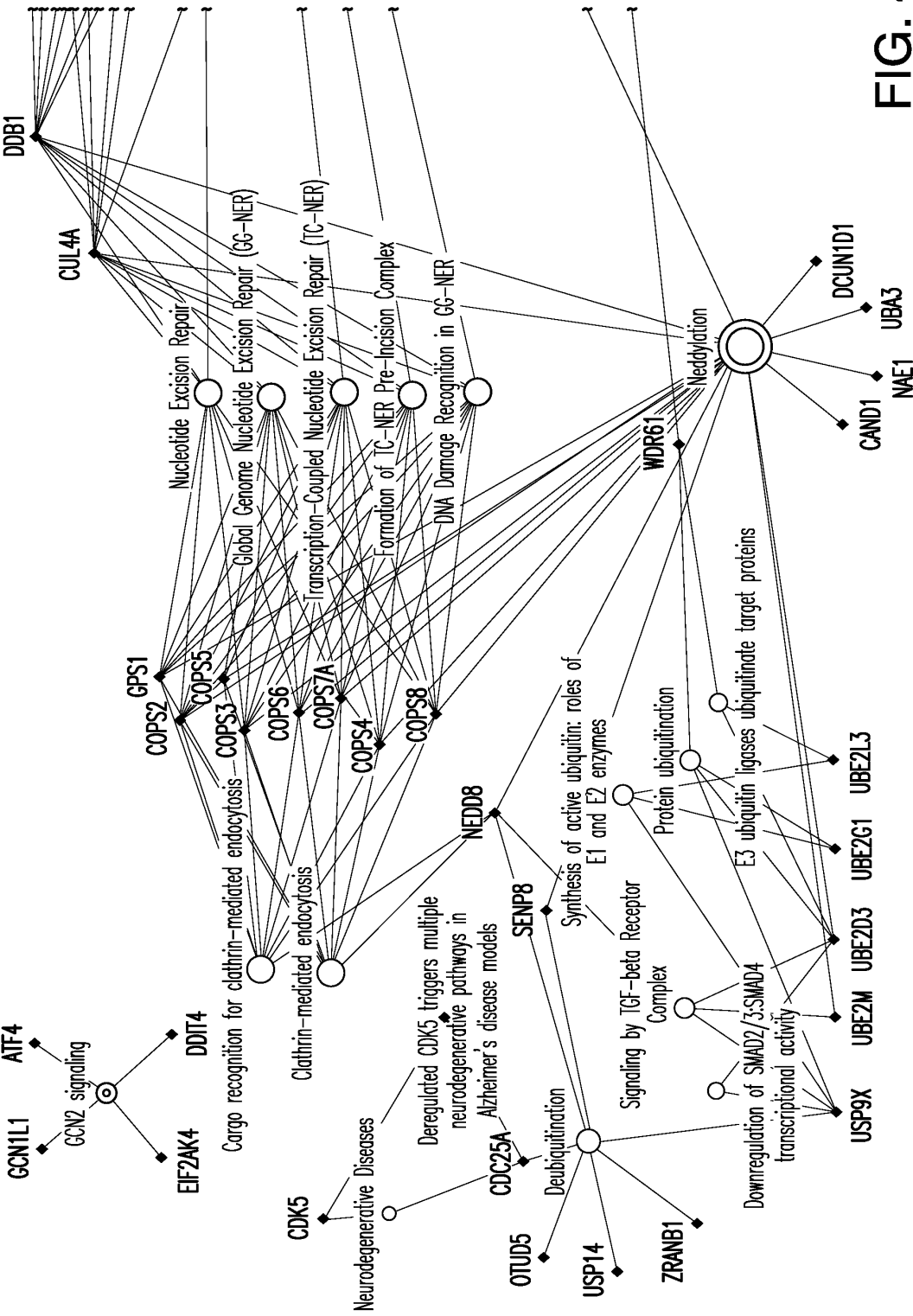


FIG. 4F

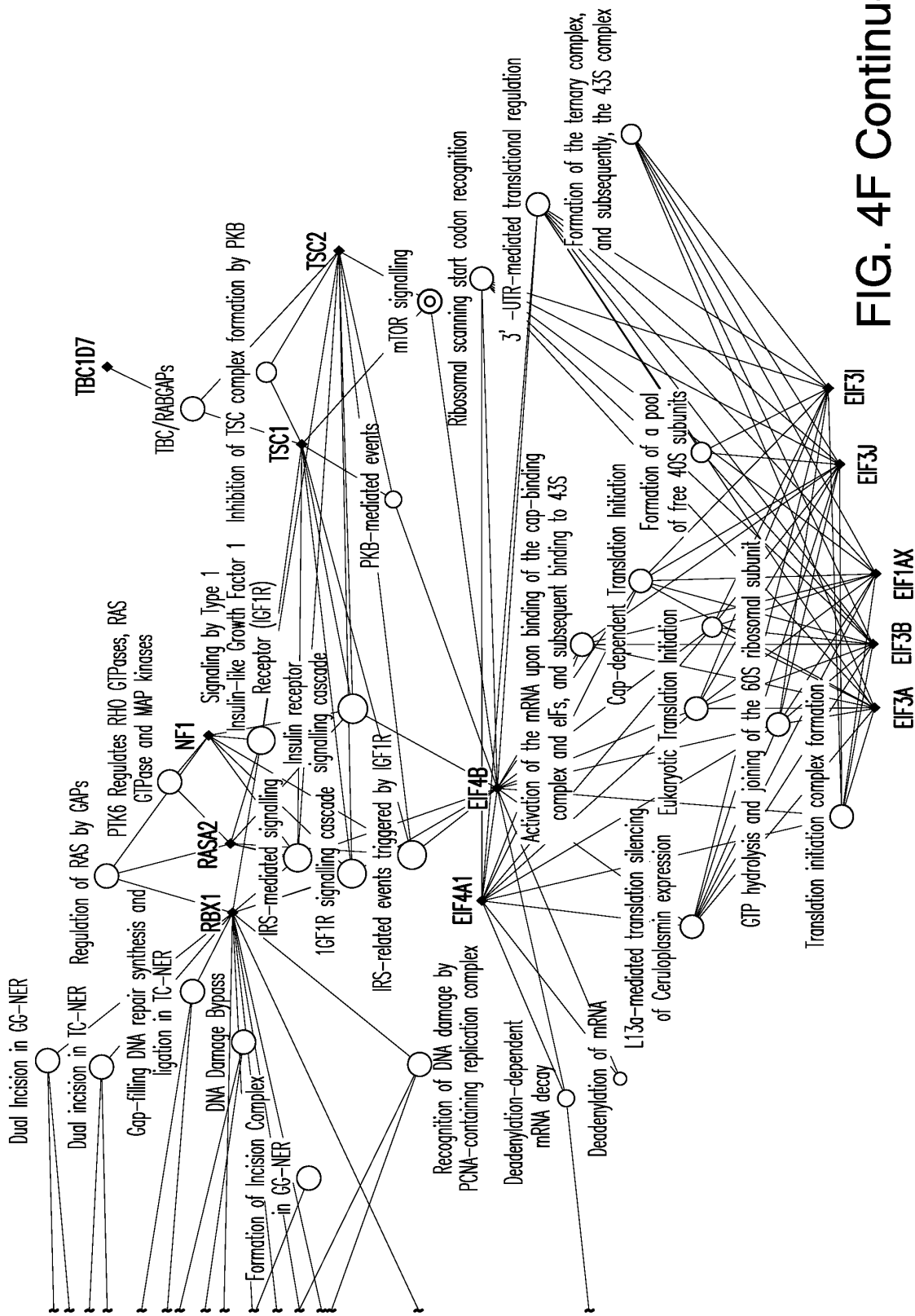


FIG. 4F Continued

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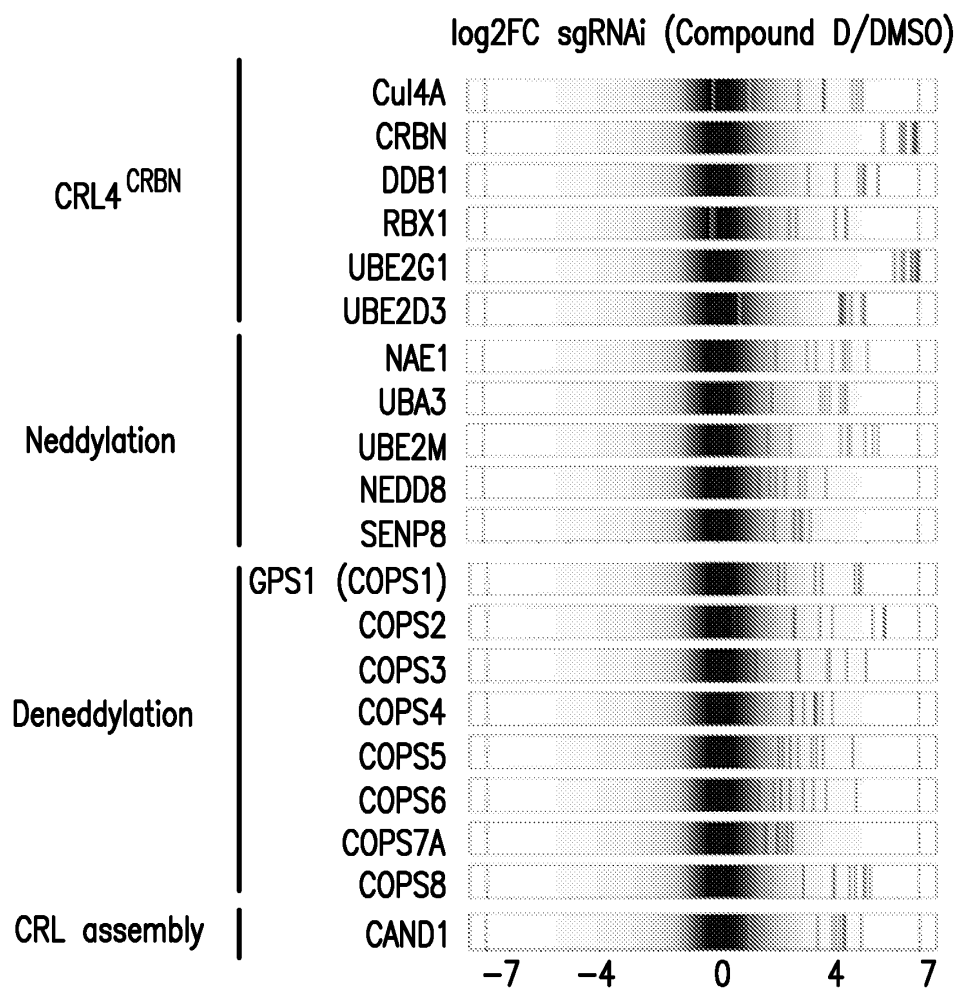


FIG. 4G

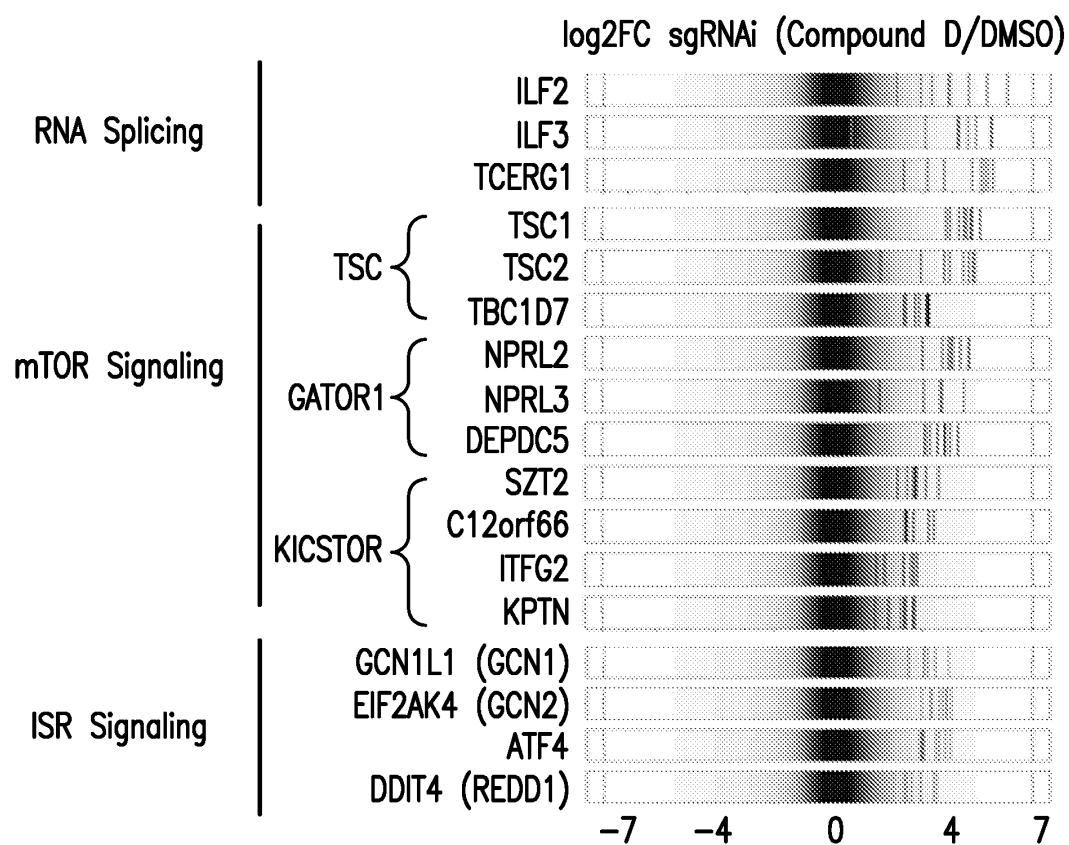


FIG. 4H

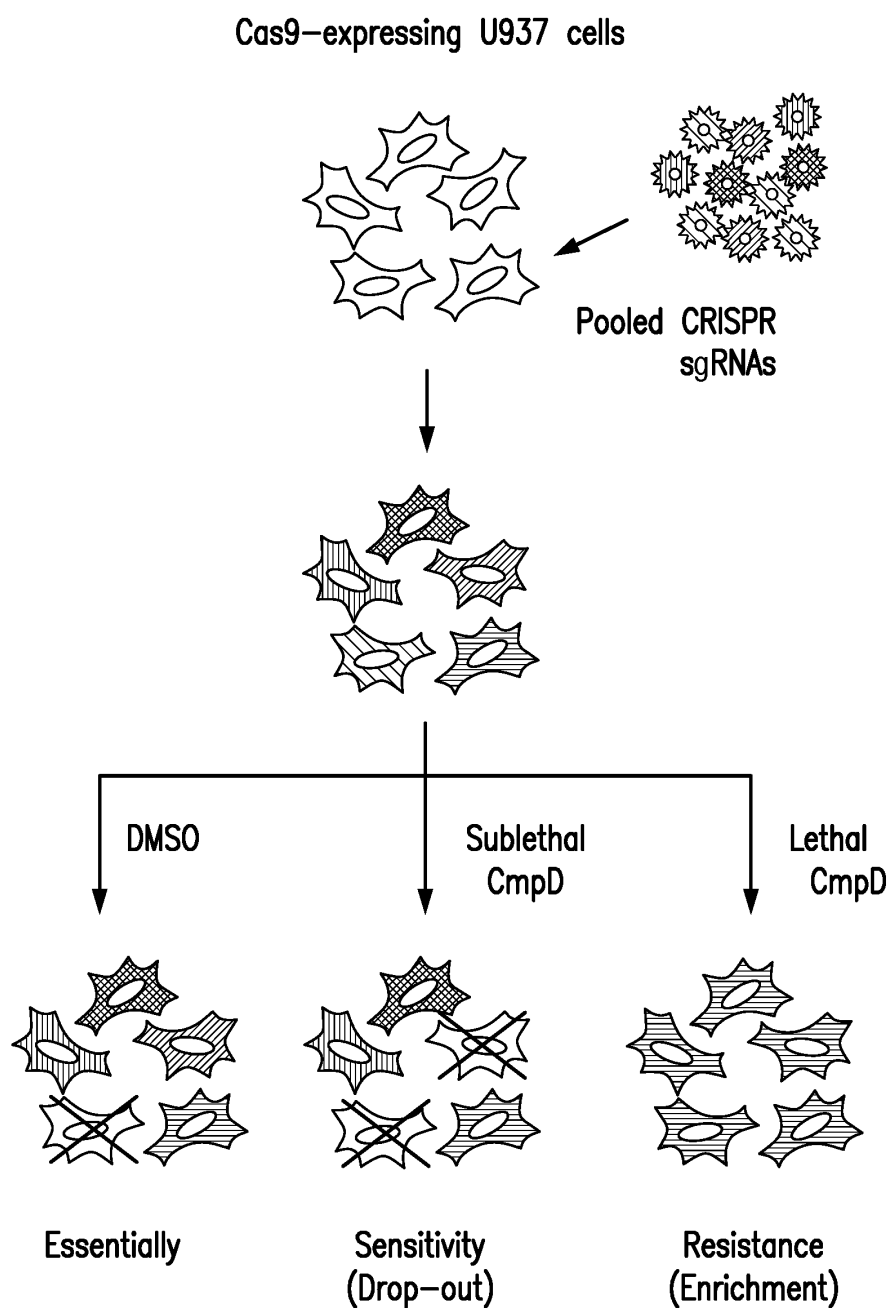


FIG. 5A

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U937 Genome-Wide CRISPR Screen
Gene Drop-Out or Enrichment [LOG2(Fold-Change)]

GENE	D8 DMSO vs D3 DMSO	D12 DMSO vs D3 DMSO	Resistance				Sensitivity			
			D8 100nM [CmpD] vs D8 DMSO	D8 1 μ M [CmpD] vs D8 DMSO	D8 10 μ M [CmpD] vs D8 DMSO	D12 100 nM [CmpD] vs D12 DMSO	D12 1 μ M [CmpD] vs D12 DMSO	D12 10 μ M [CmpD] vs D12 DMSO		
CRBN	-0.25	-0.32	0.42	1.24	1.66	1.02	5.22	6.29		
TSC1	-0.66	-1.65	0.19	1.10	1.39	0.52	3.70	4.38		
ILF3	-0.44	-0.89	0.14	0.74	0.94	0.40	3.52	4.00		
ILF2	-0.86	-1.57	0.19	0.71	1.08	0.49	3.29	3.95		
TSC2	-0.61	-1.56	0.17	0.99	1.19	0.37	3.10	3.82		
ATF4	-0.36	-0.51	0.11	0.57	0.81	0.56	2.64	3.32		
EIF2AK4 (GCN2)	-0.08	-0.30	0.38	0.82	1.19	0.96	2.53	3.54		
DDIT4	-0.60	-0.83	0.15	0.57	0.70	0.45	2.07	2.76		
GCN1L1	-0.36	-0.89	0.32	0.62	0.97	0.74	1.79	2.86		
RPTOR	-0.94	-1.88	-0.44	-0.88	-1.23	-0.56	-1.27	-1.54		
MTOR	-1.12	-1.89	-0.78	-1.39	-1.64	-1.20	-2.53	-2.04		
RICTOR	-0.37	-0.71	-0.67	-1.46	-1.47	-1.47	-2.66	-2.67		
GSPT1	-2.15	-3.06	-1.77	-1.43	-2.15	-1.66	-1.81	-2.97		
DDX5	-0.91	-1.50	-2.58	-3.36	-3.43	-2.88	-4.22	-4.48		

Essentiality

FIG. 5B

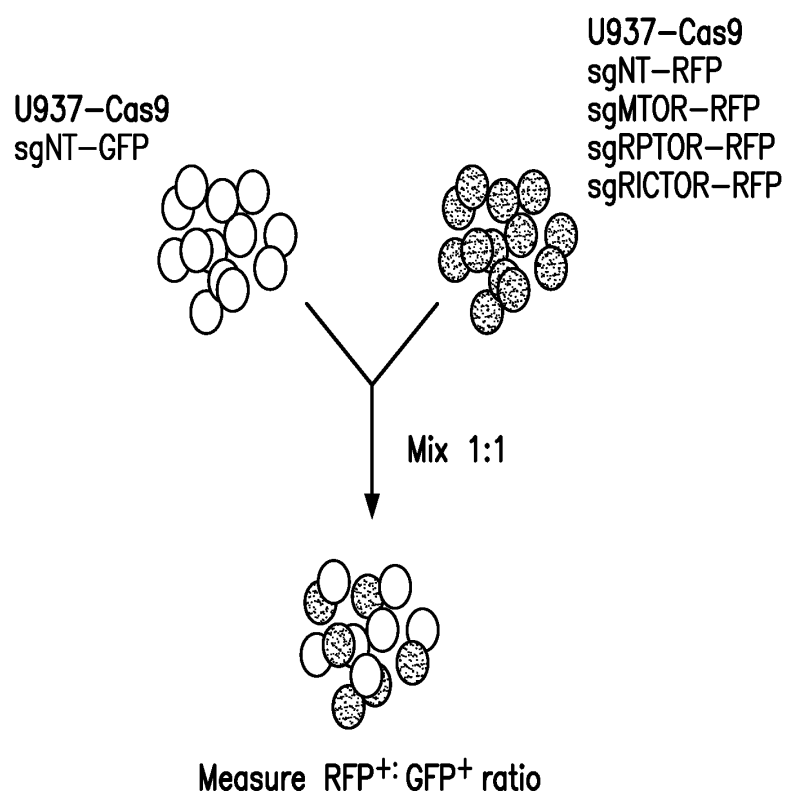


FIG. 6A

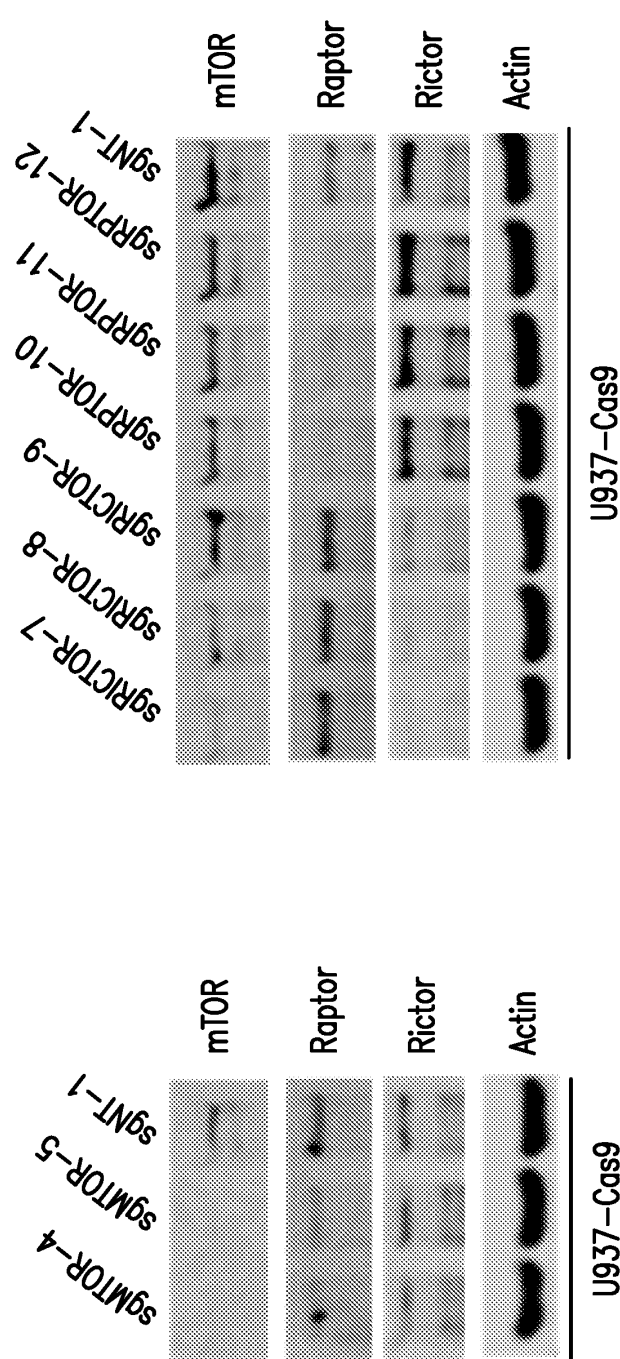


FIG. 6B

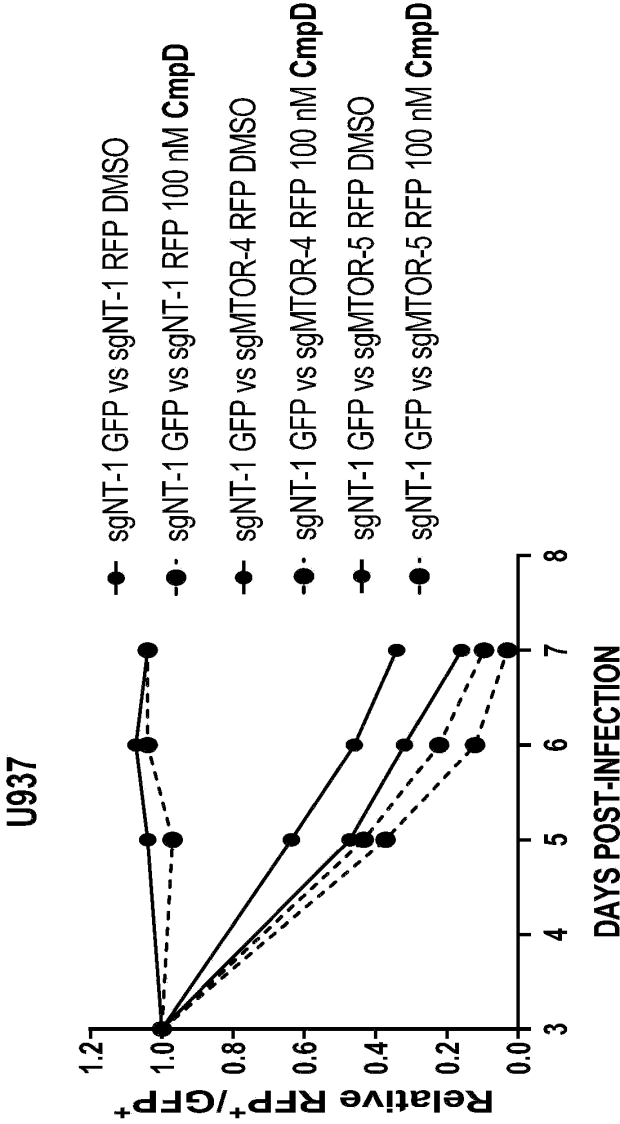


FIG. 6C

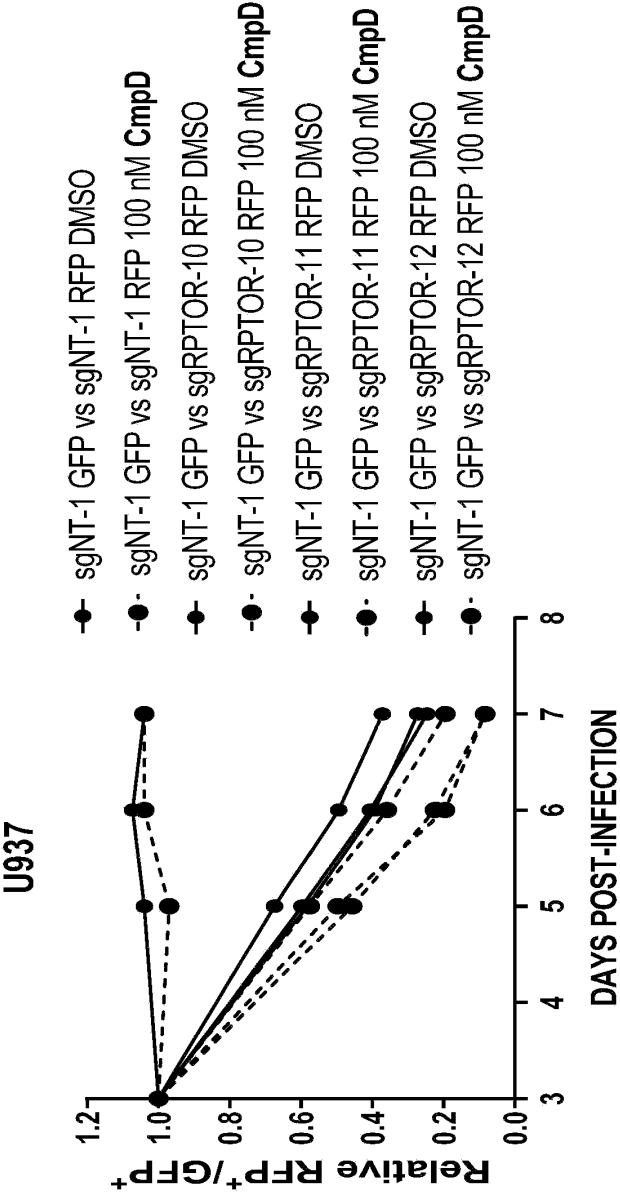


FIG. 6D

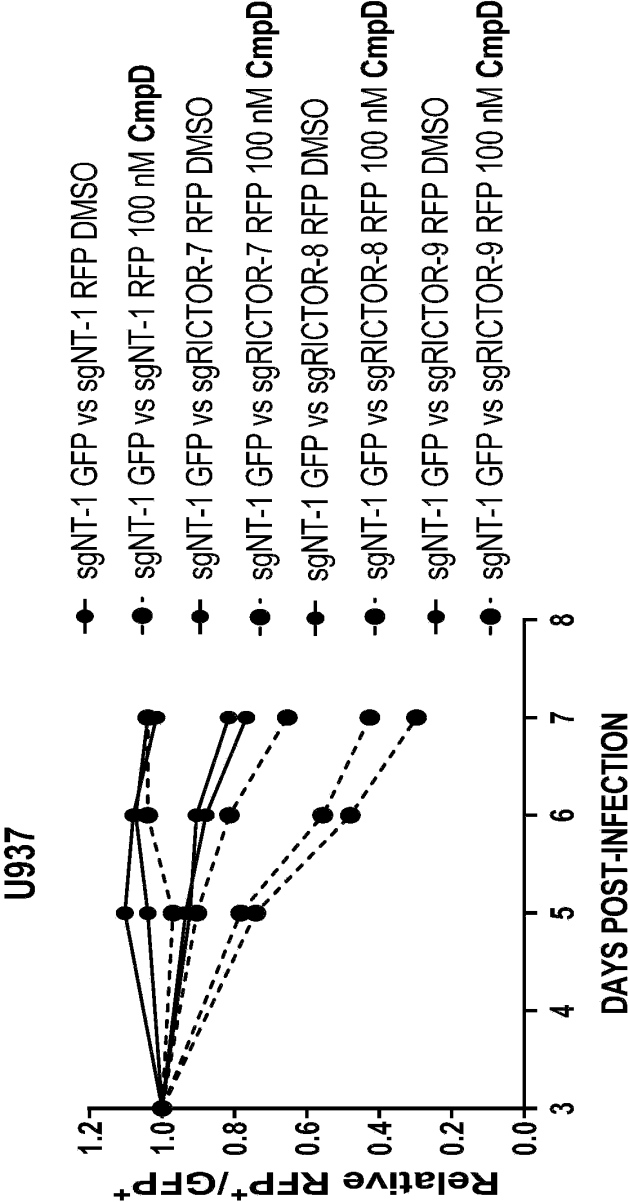


FIG. 6E

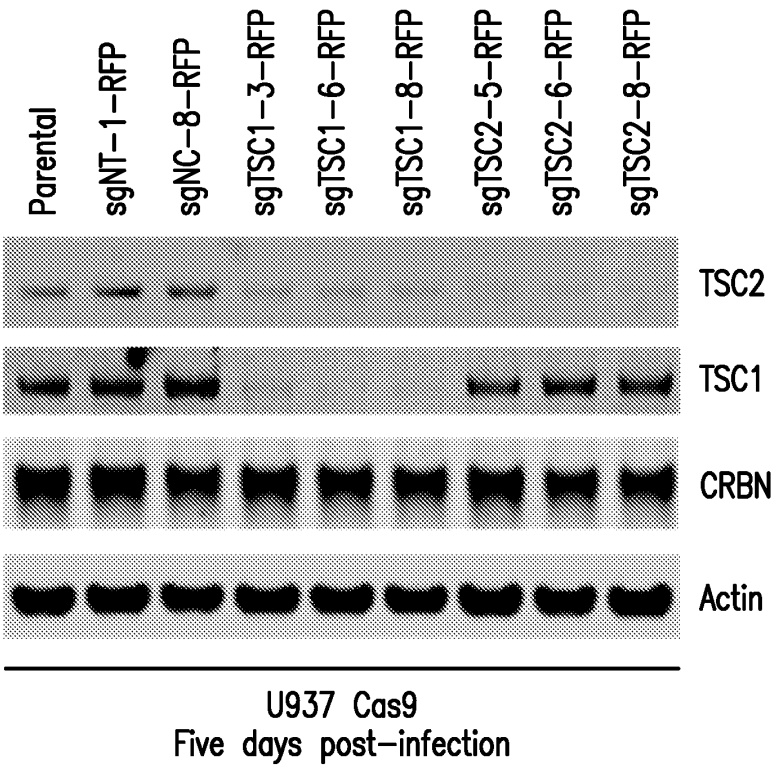


FIG. 7A

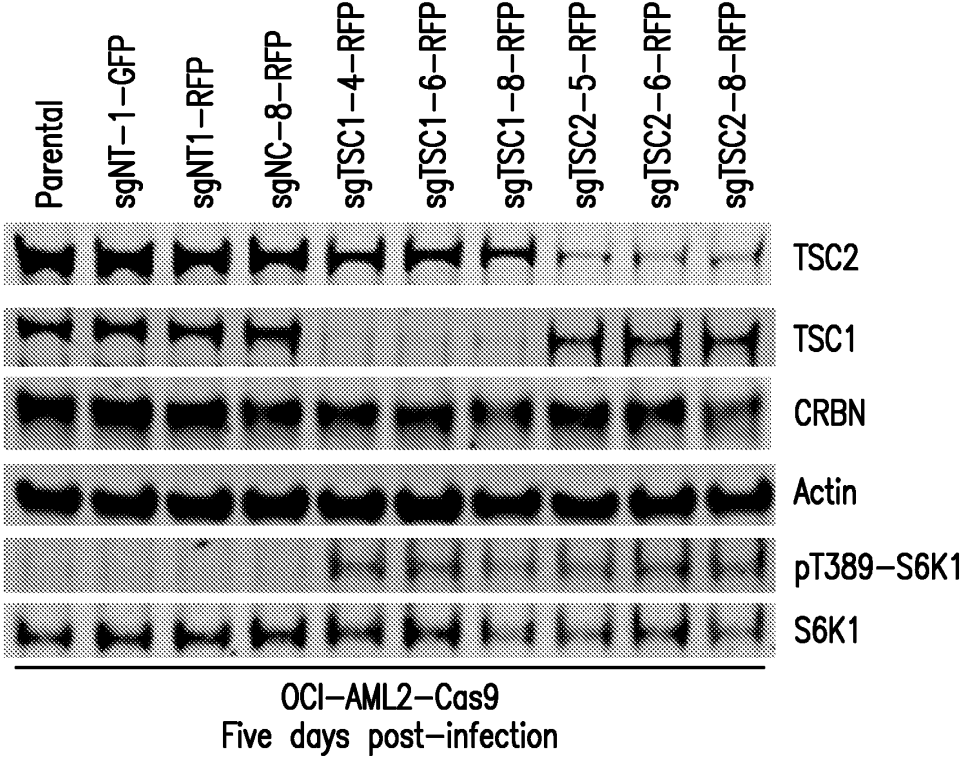
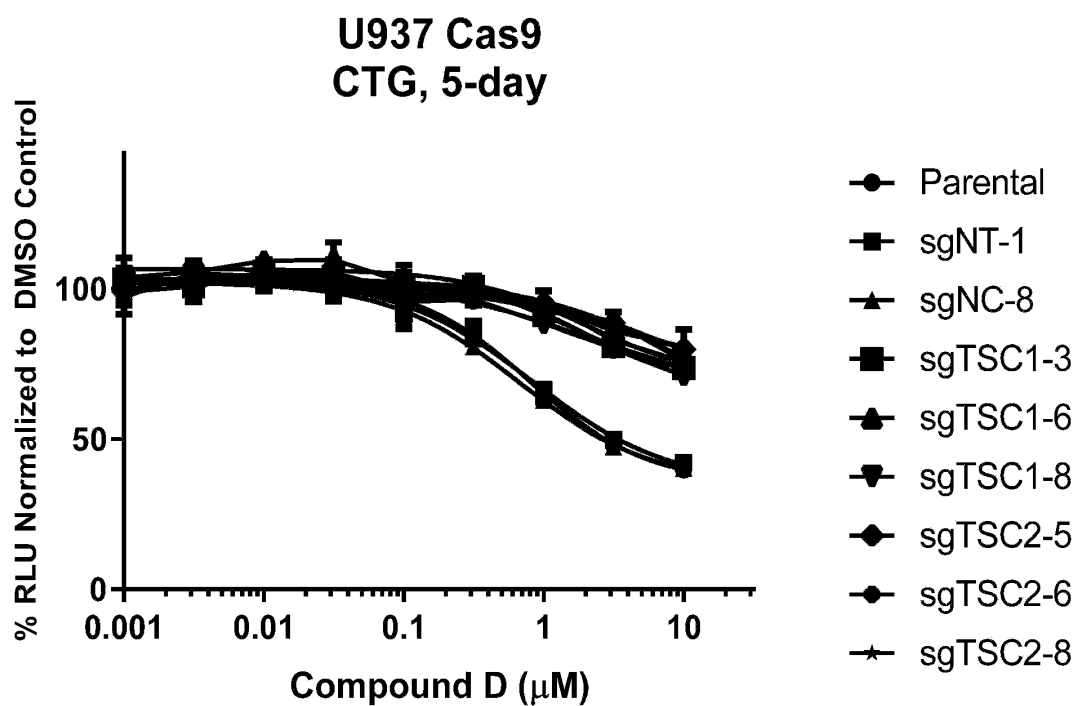
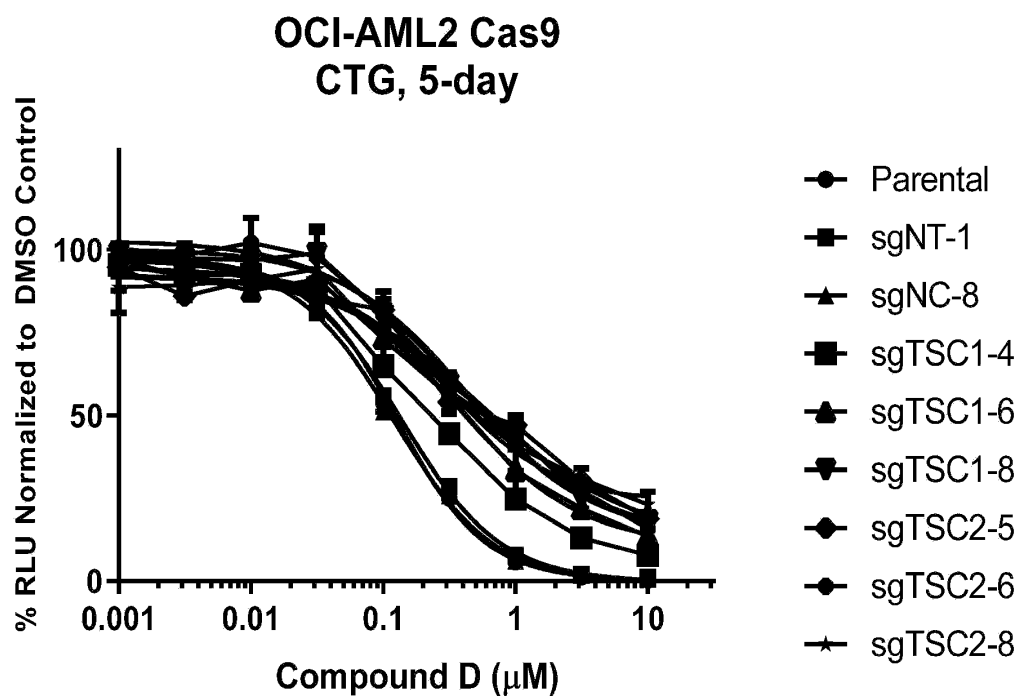


FIG. 7B

**FIG. 7C**

**FIG. 7D**

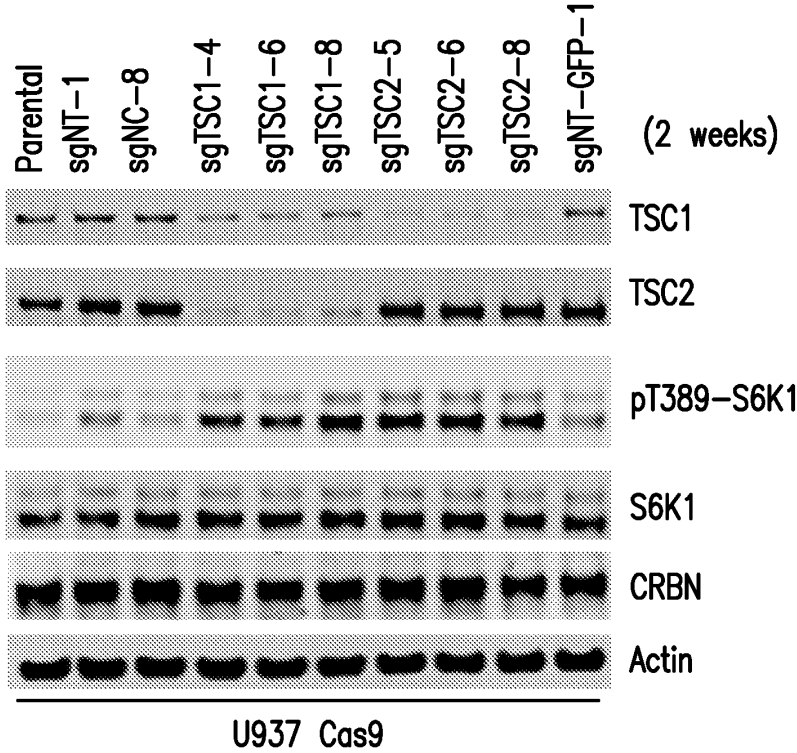


FIG. 7E

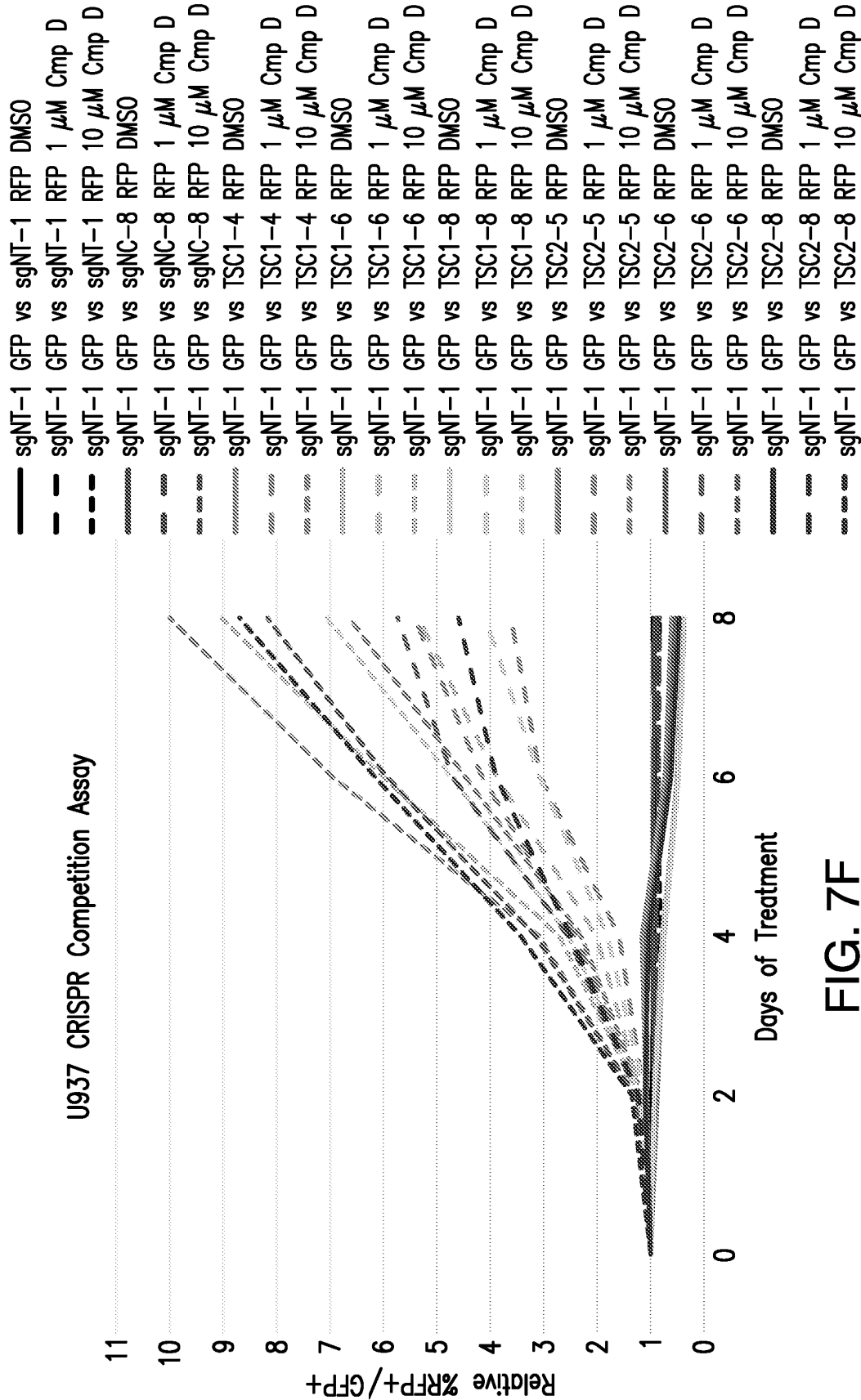


FIG. 7F

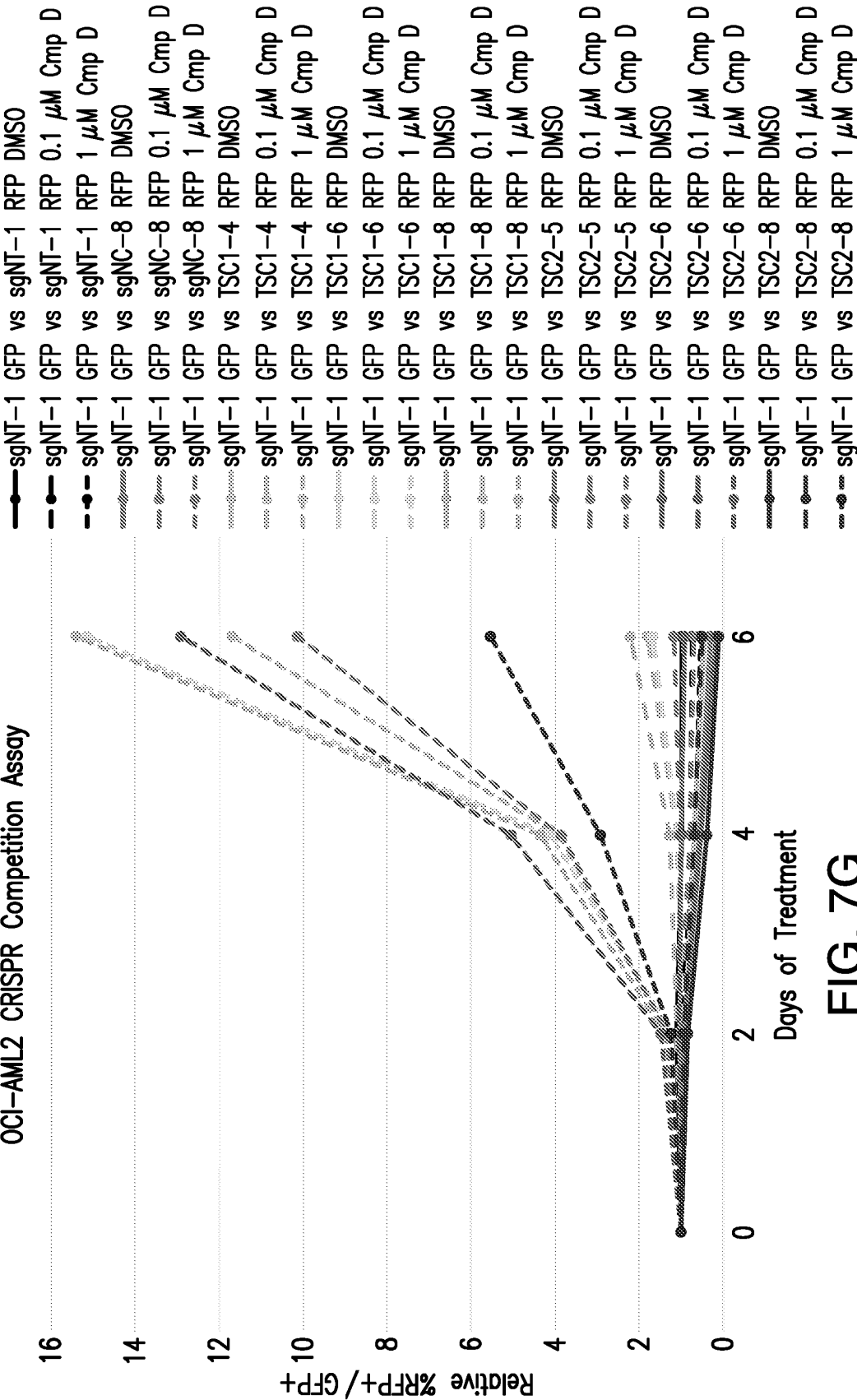


FIG. 7G

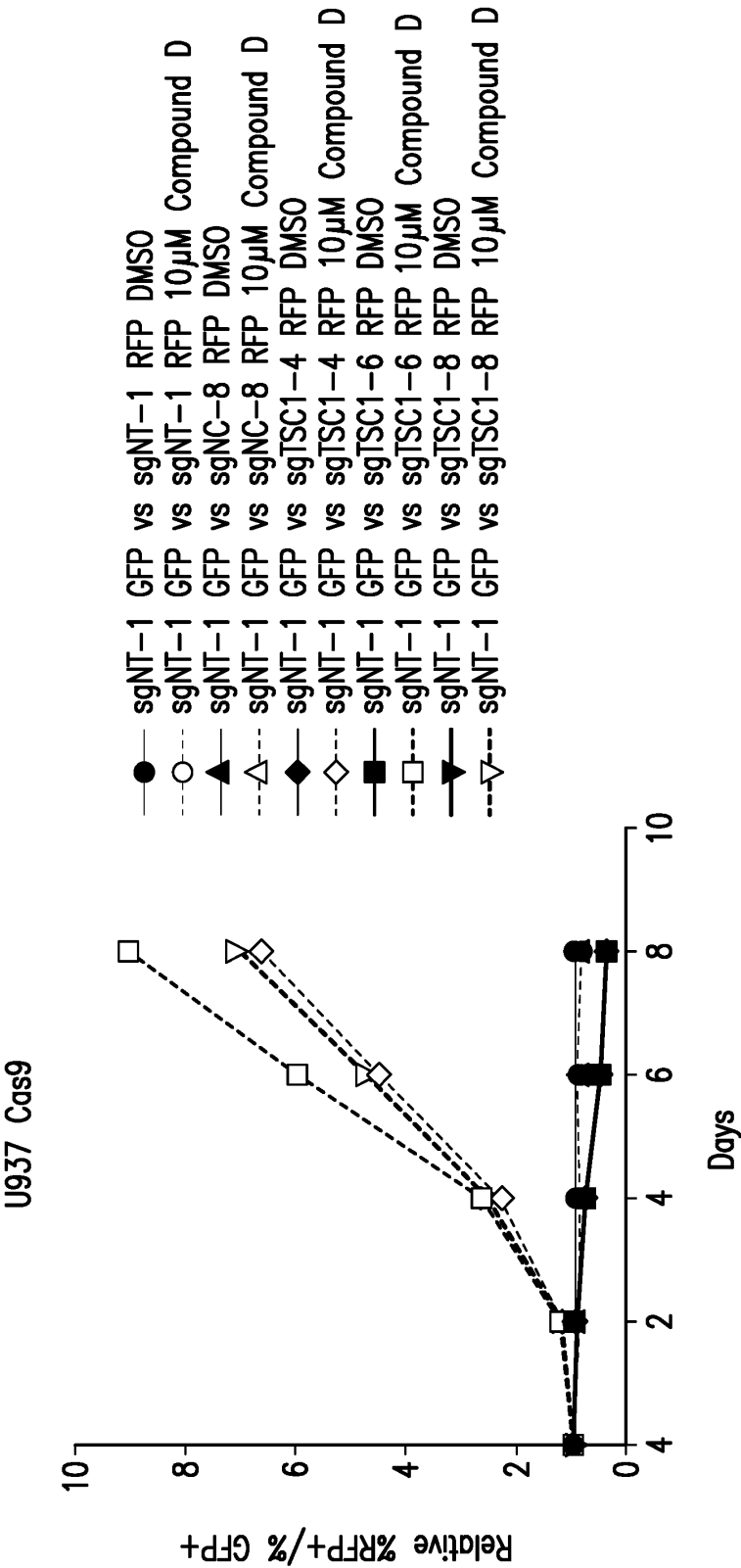


FIG. 7H

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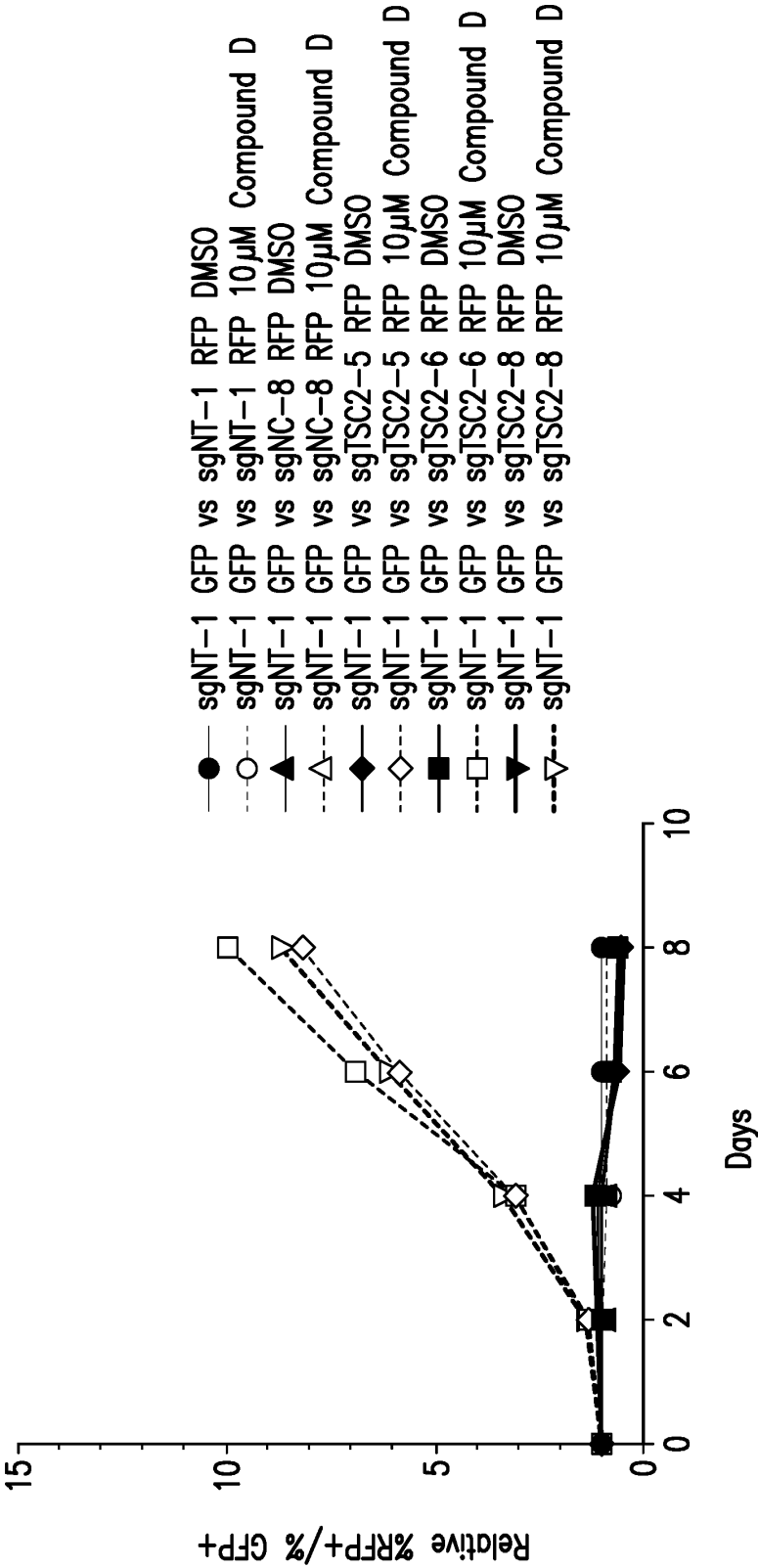


FIG. 7I

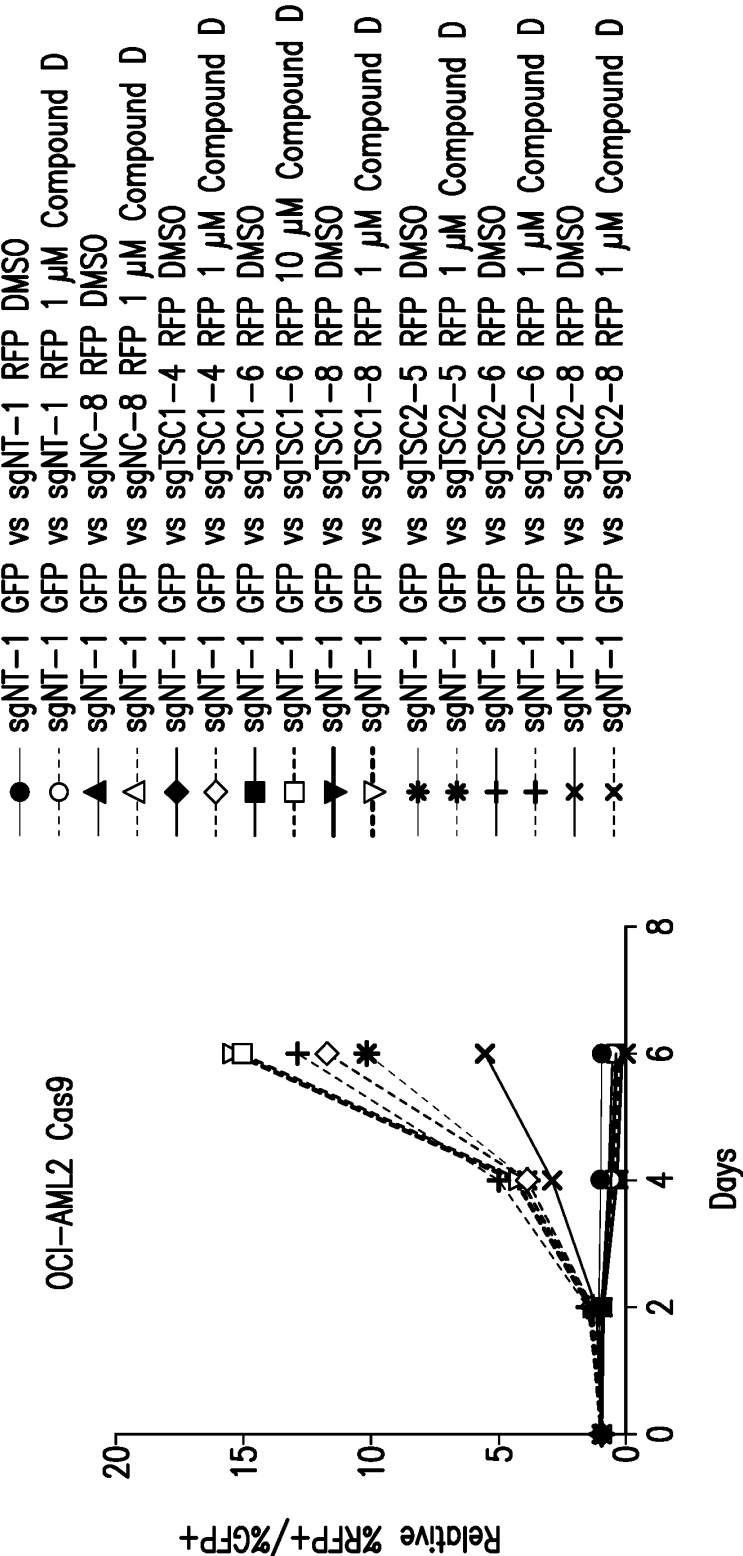


FIG. 7J

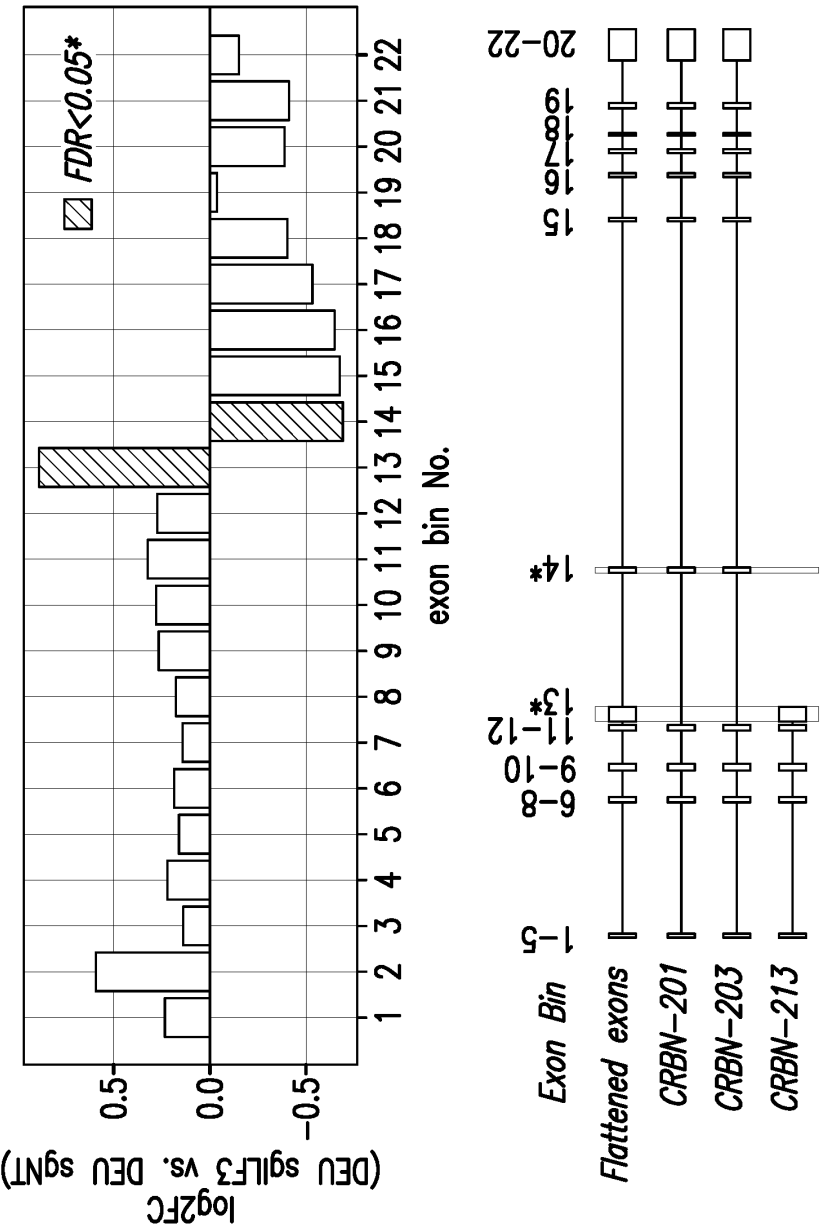


FIG. 7K

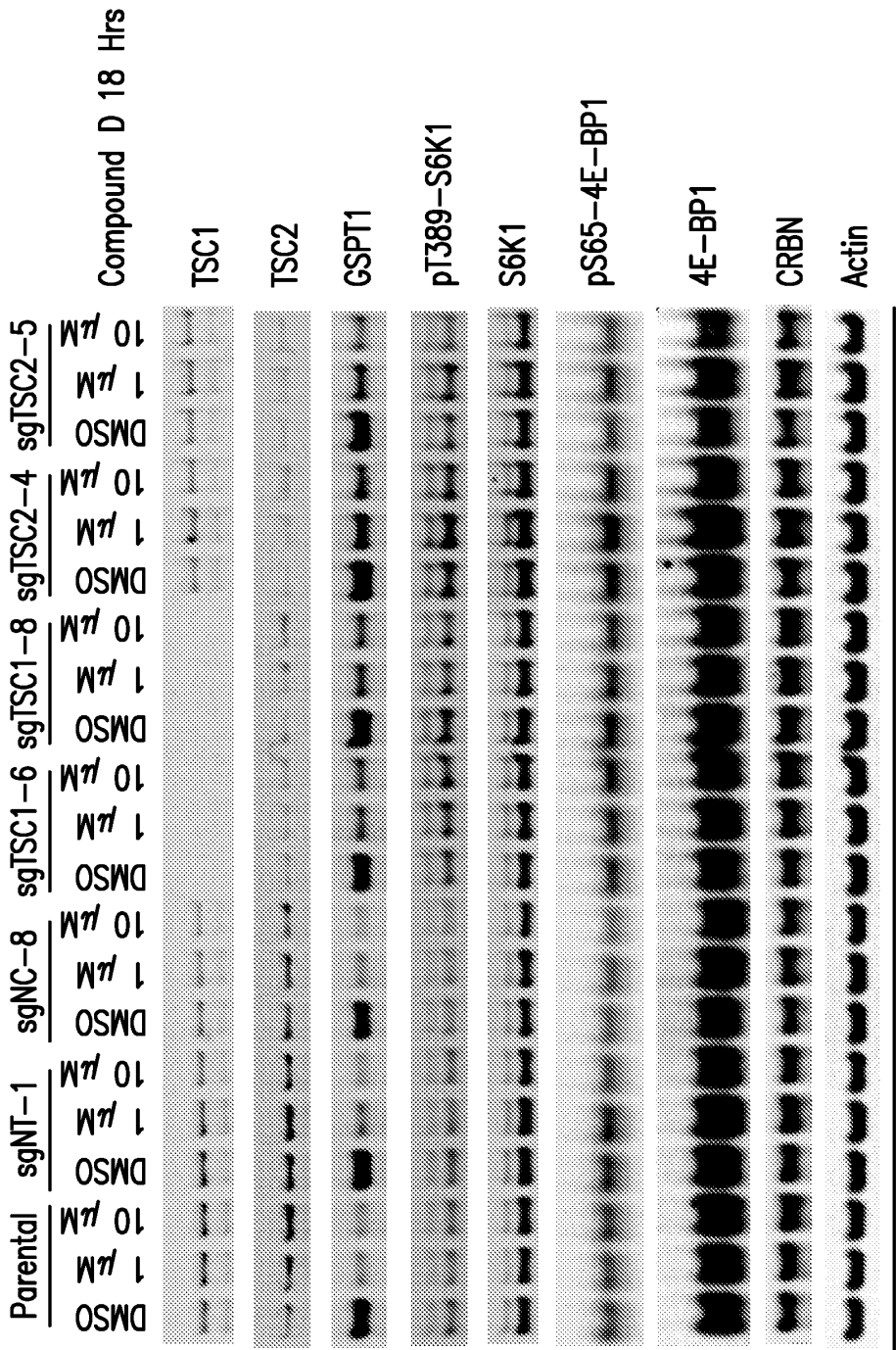


FIG. 8A

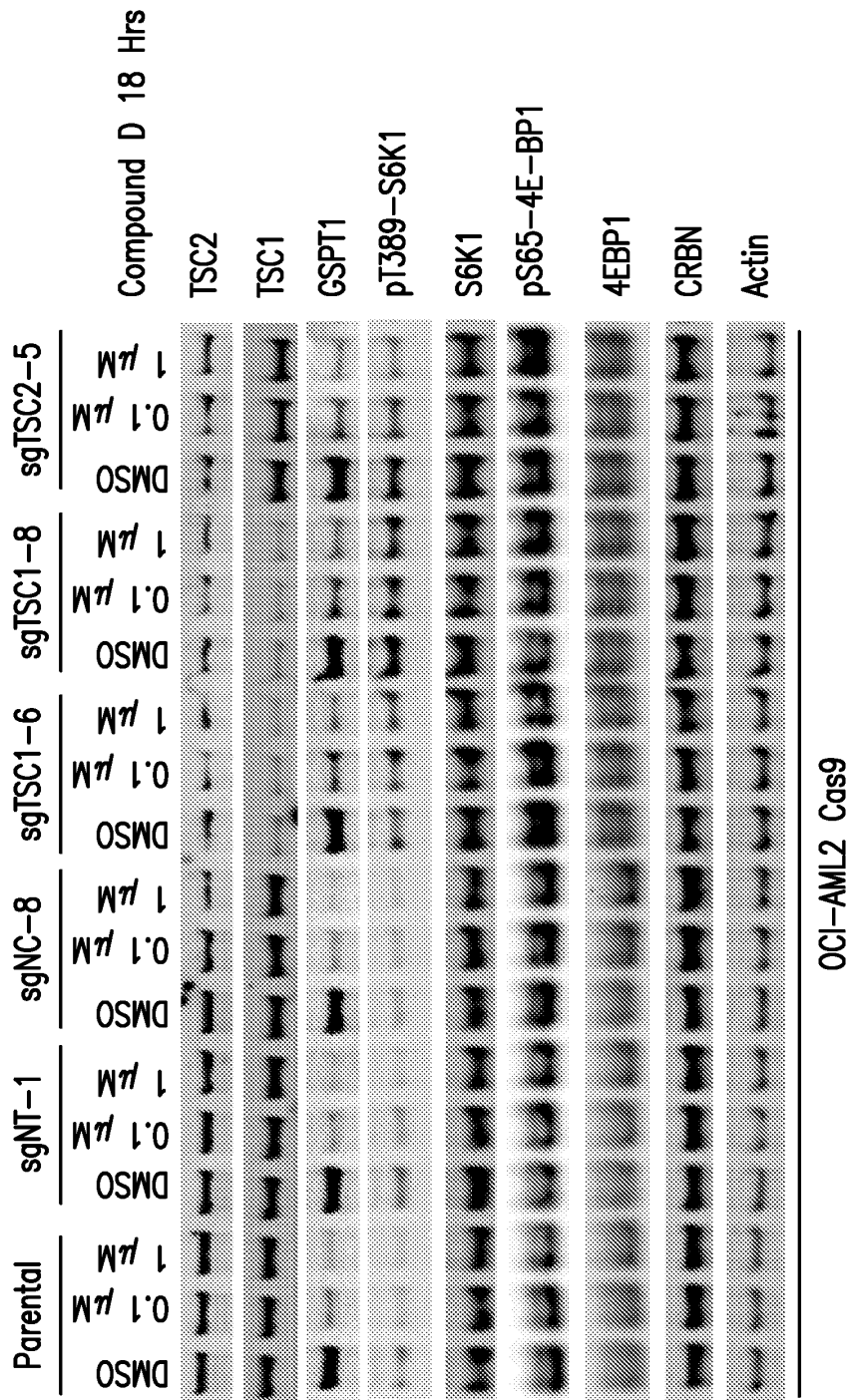


FIG. 8B



FIG. 8C

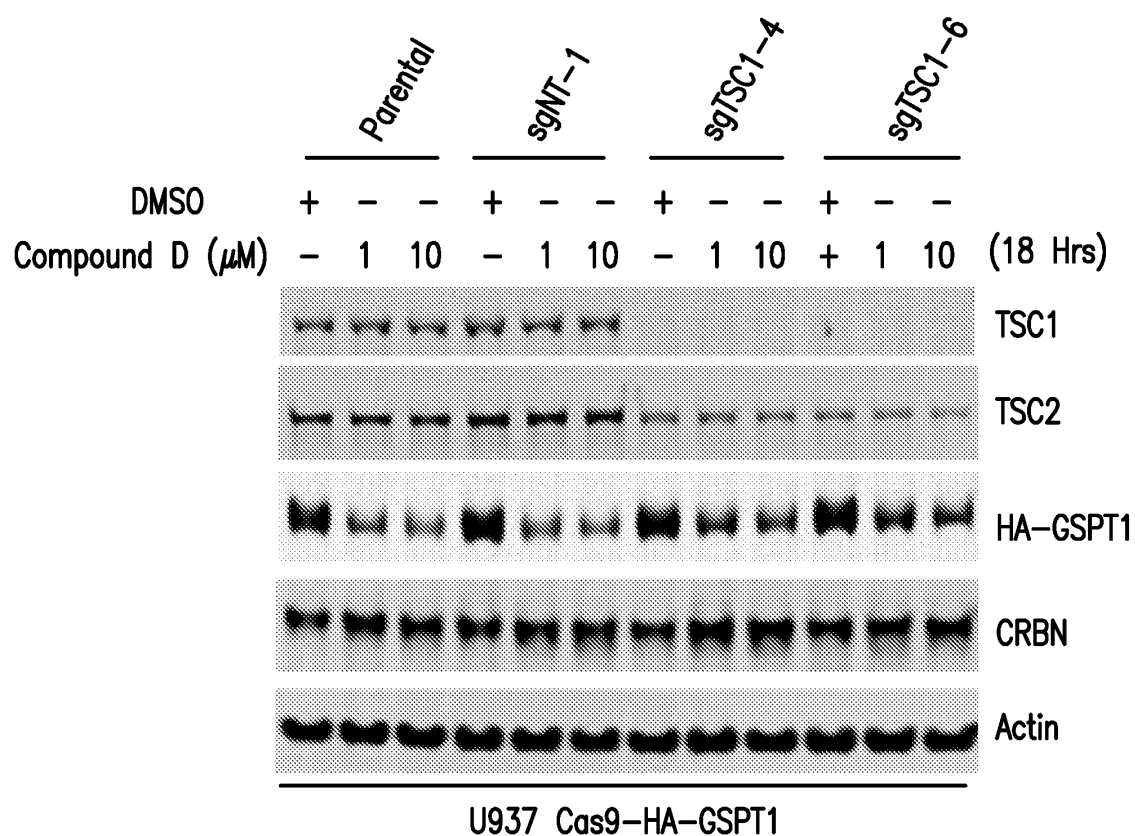


FIG. 8D

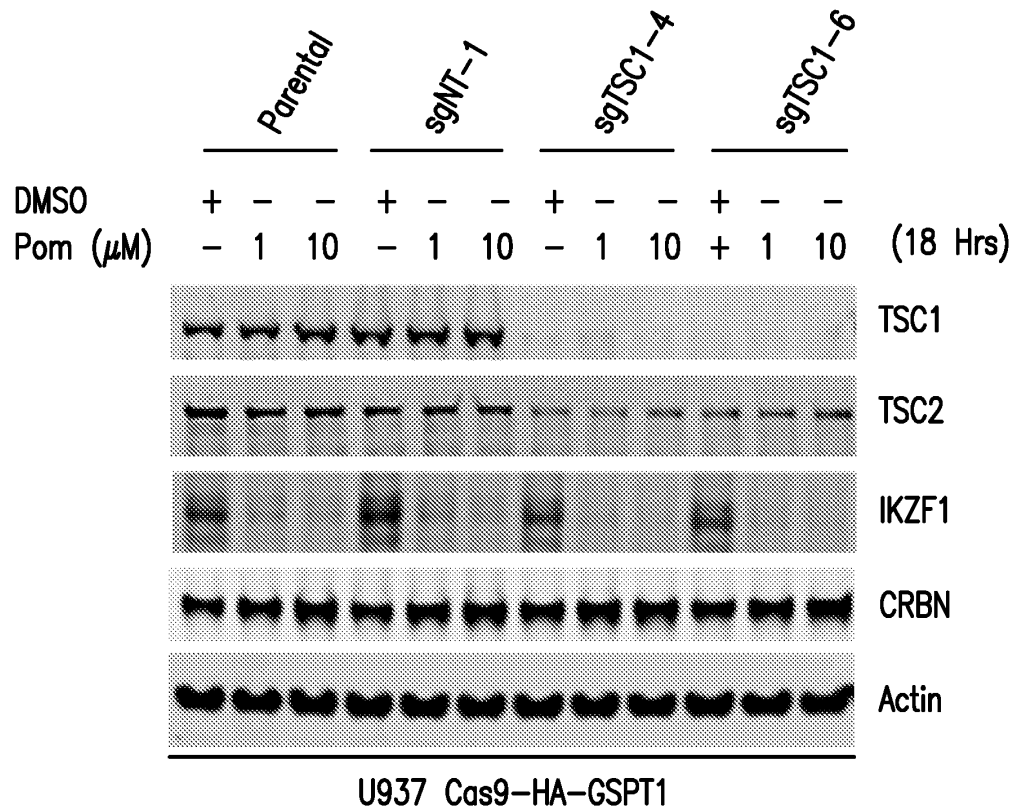


FIG. 8E

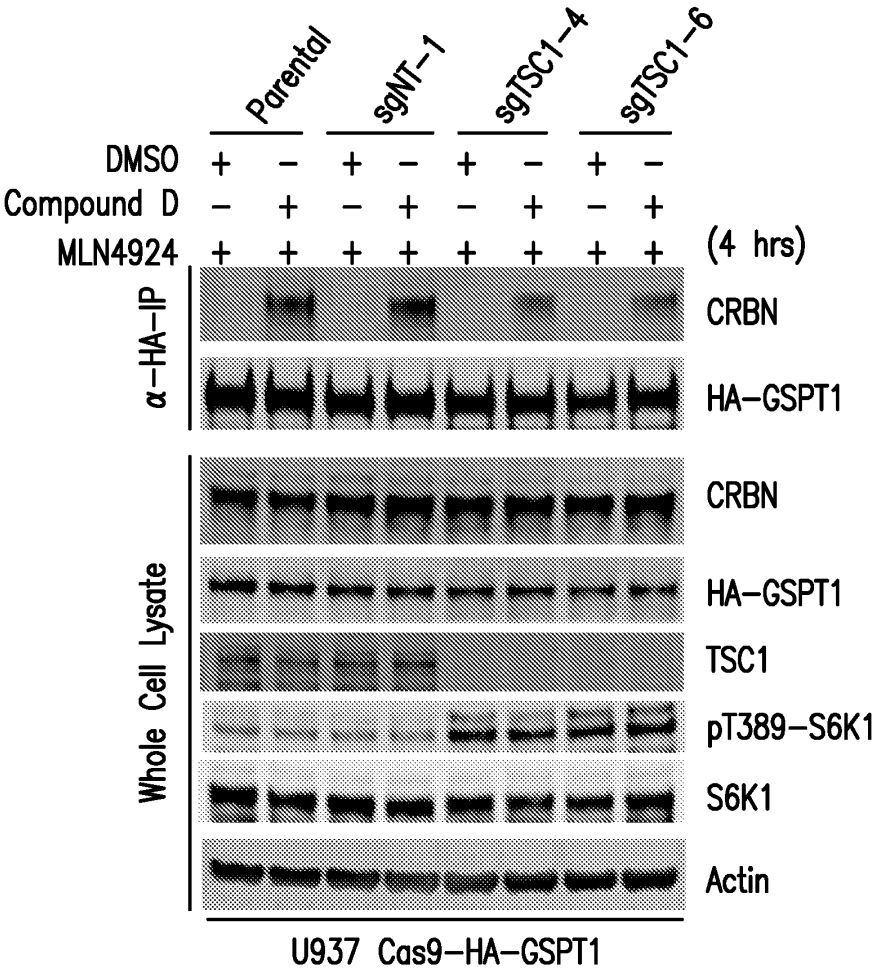


FIG. 8F

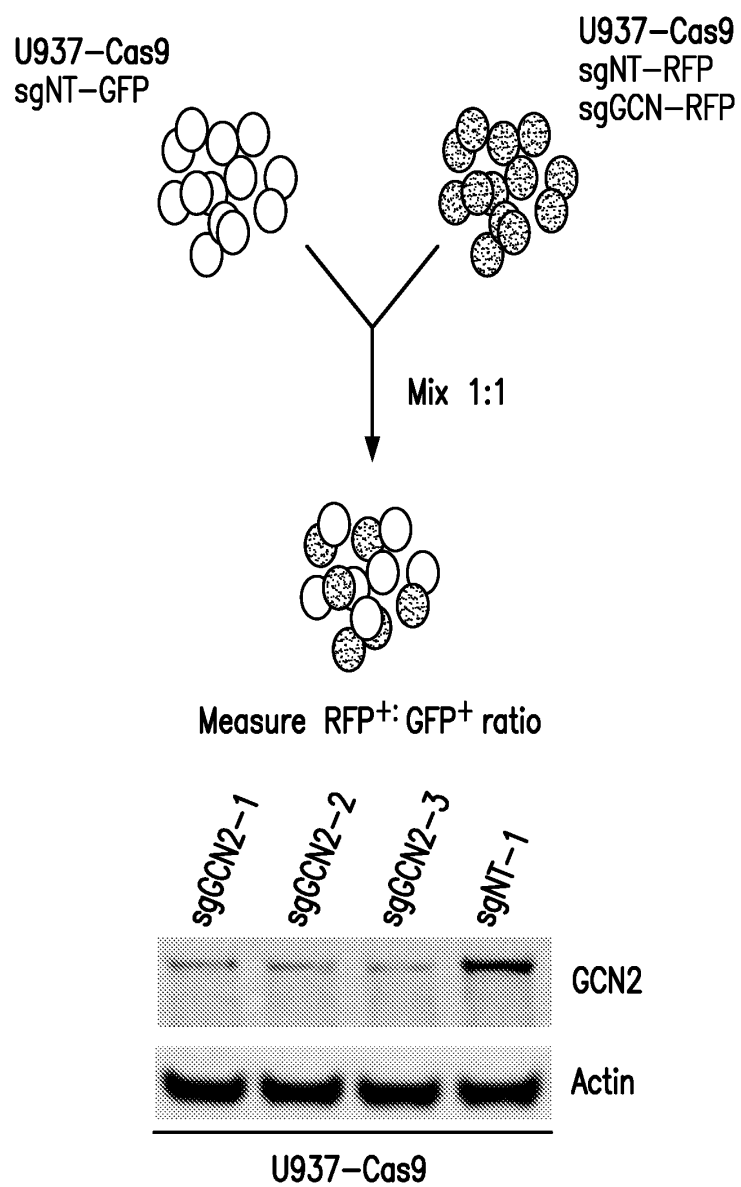


FIG. 9A

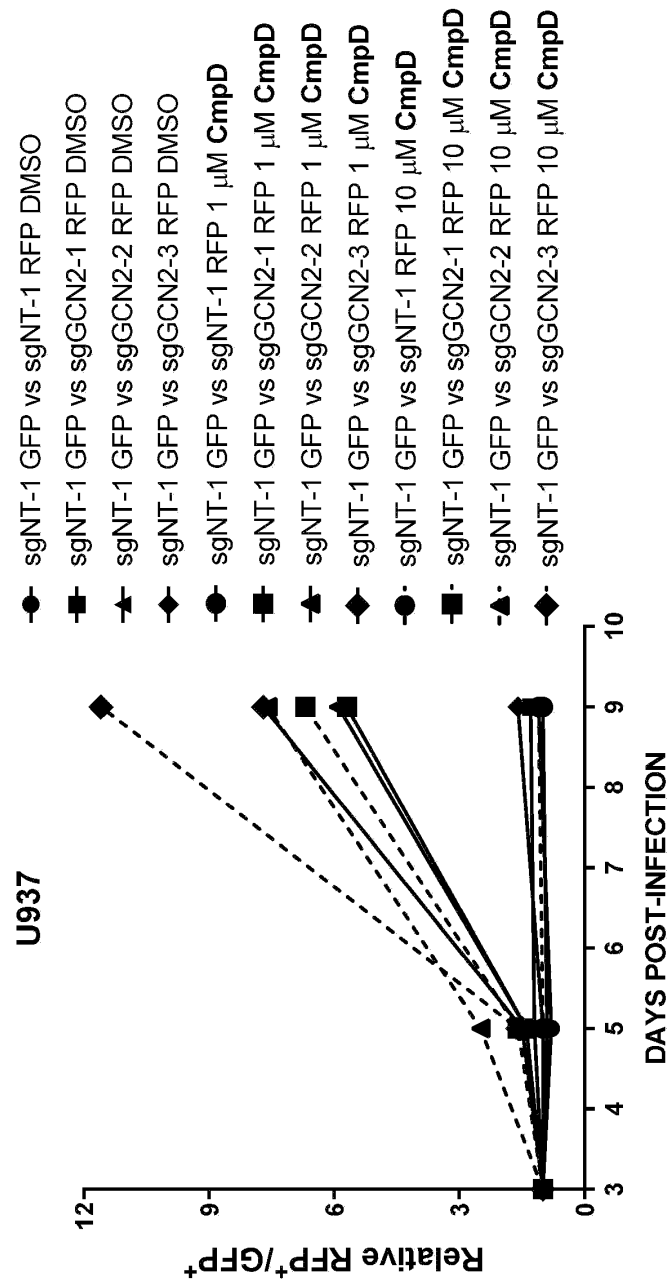
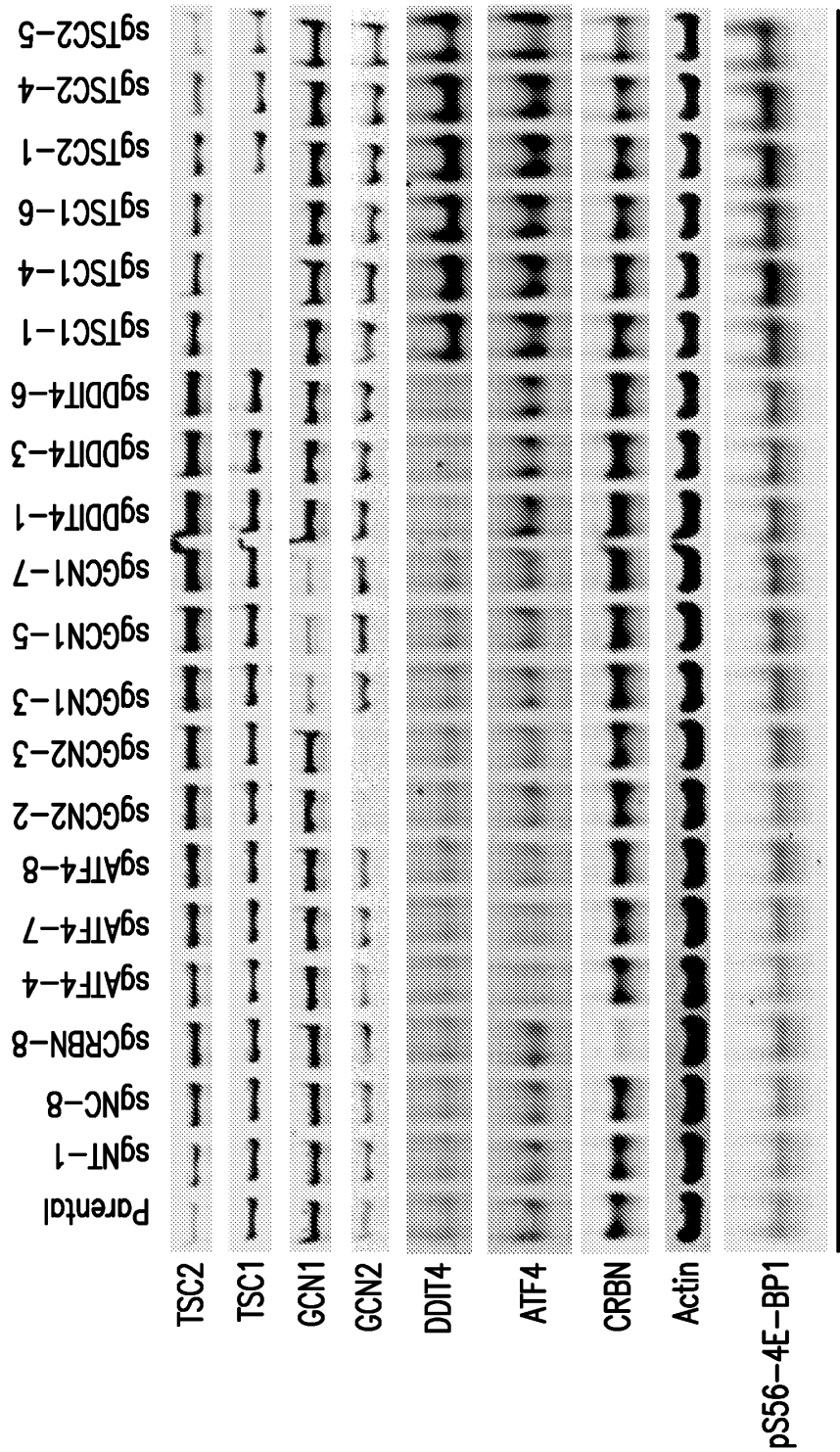


FIG. 9B



U937-Cas9

FIG. 9C

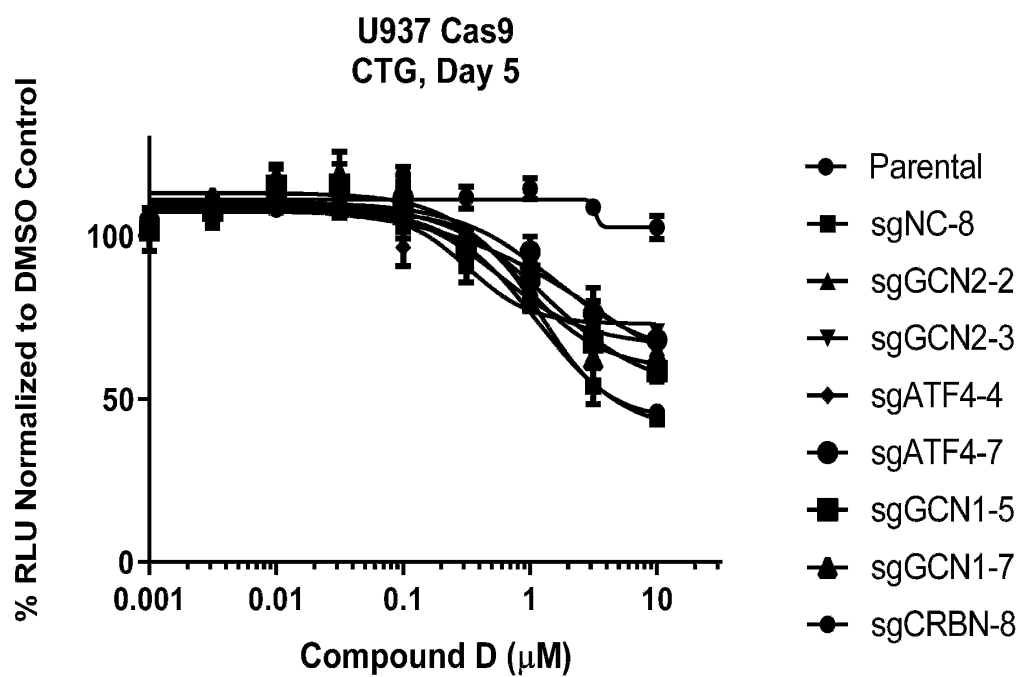
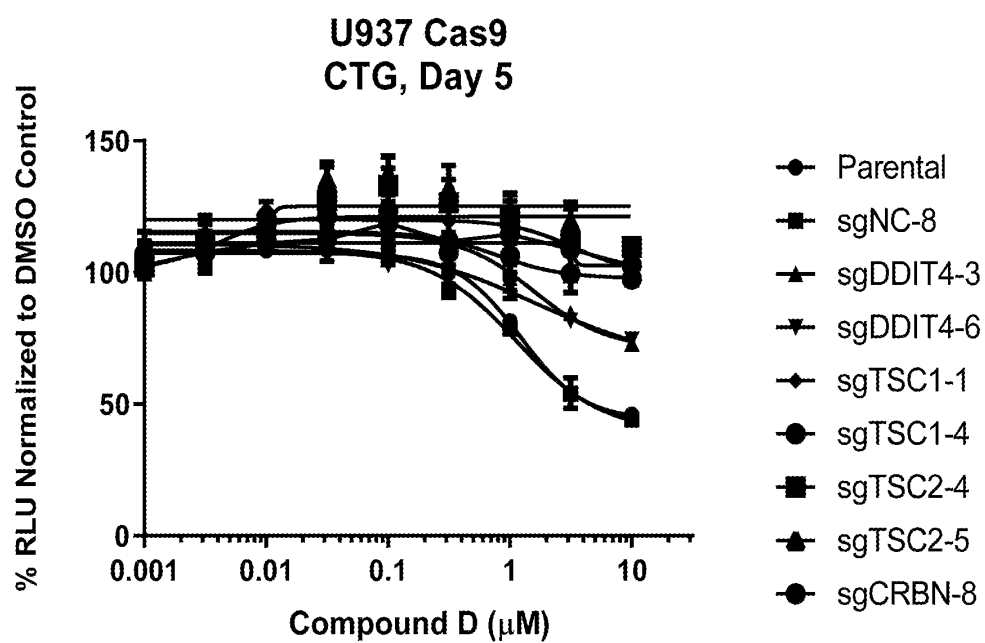


FIG. 9D

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**FIG. 9E**

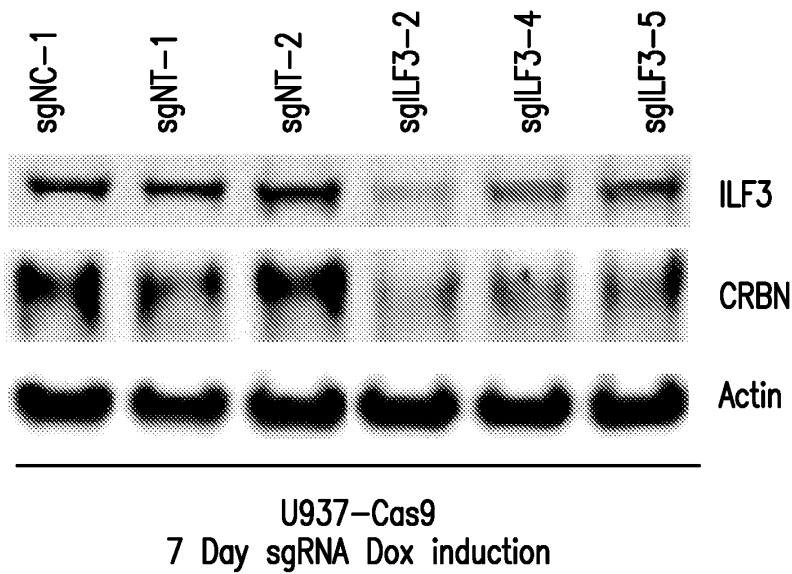


FIG. 10A

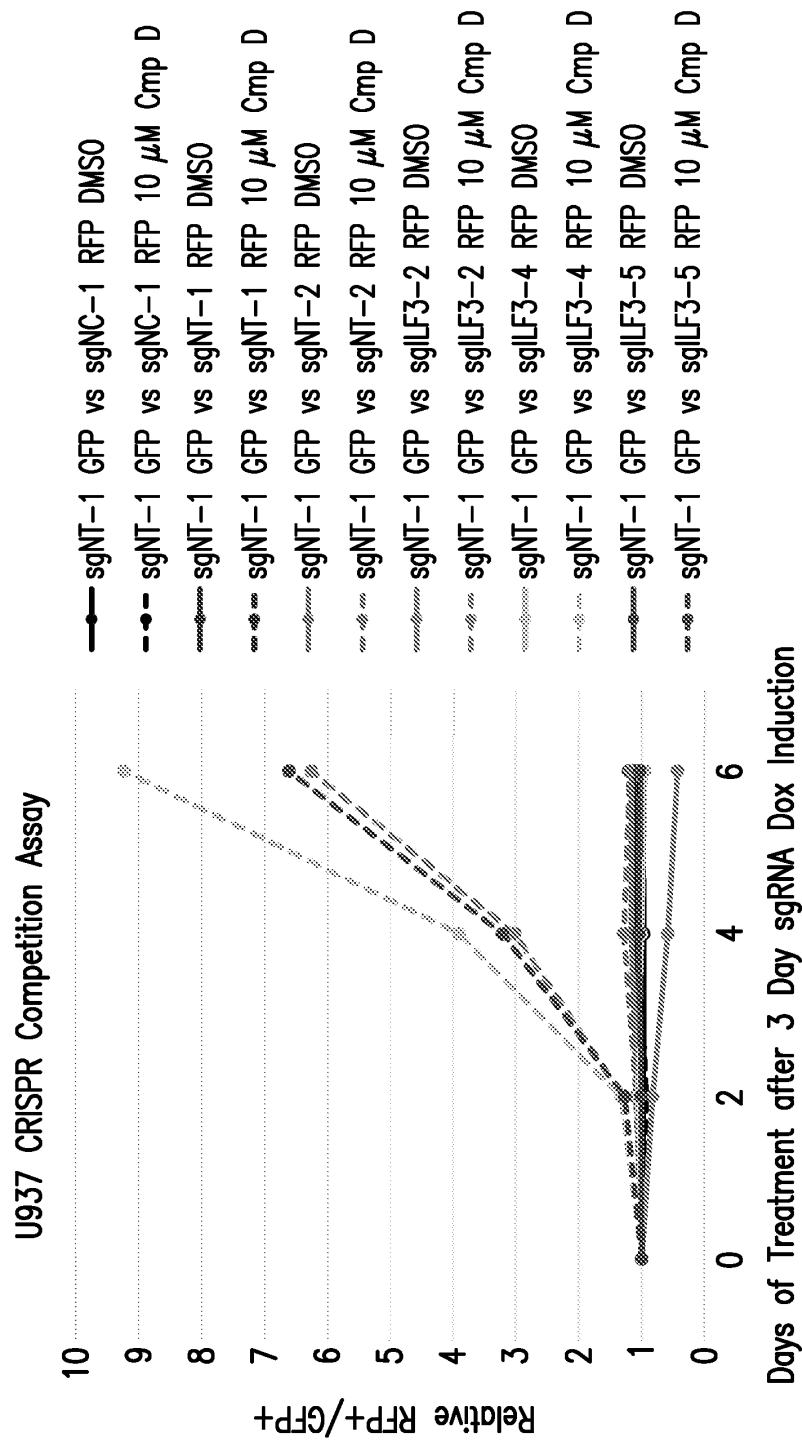
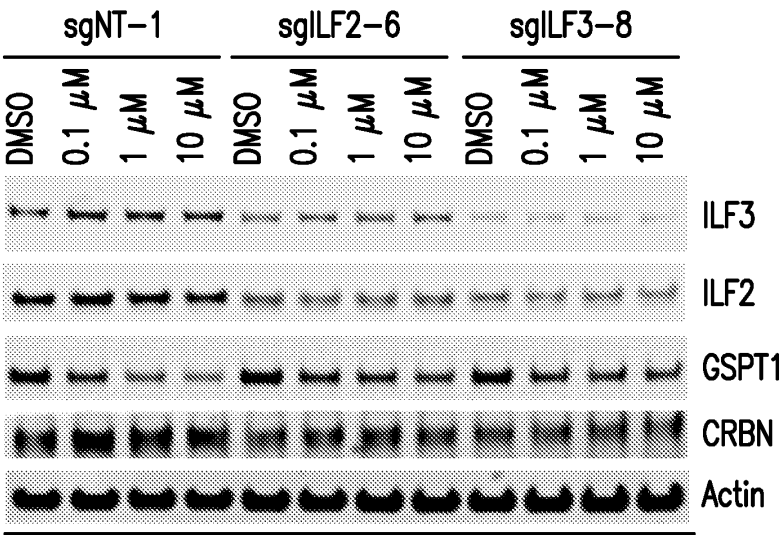


FIG. 10B



U937 Cas9
6 hours of DMSO/ Cmp D treatment

FIG. 10C

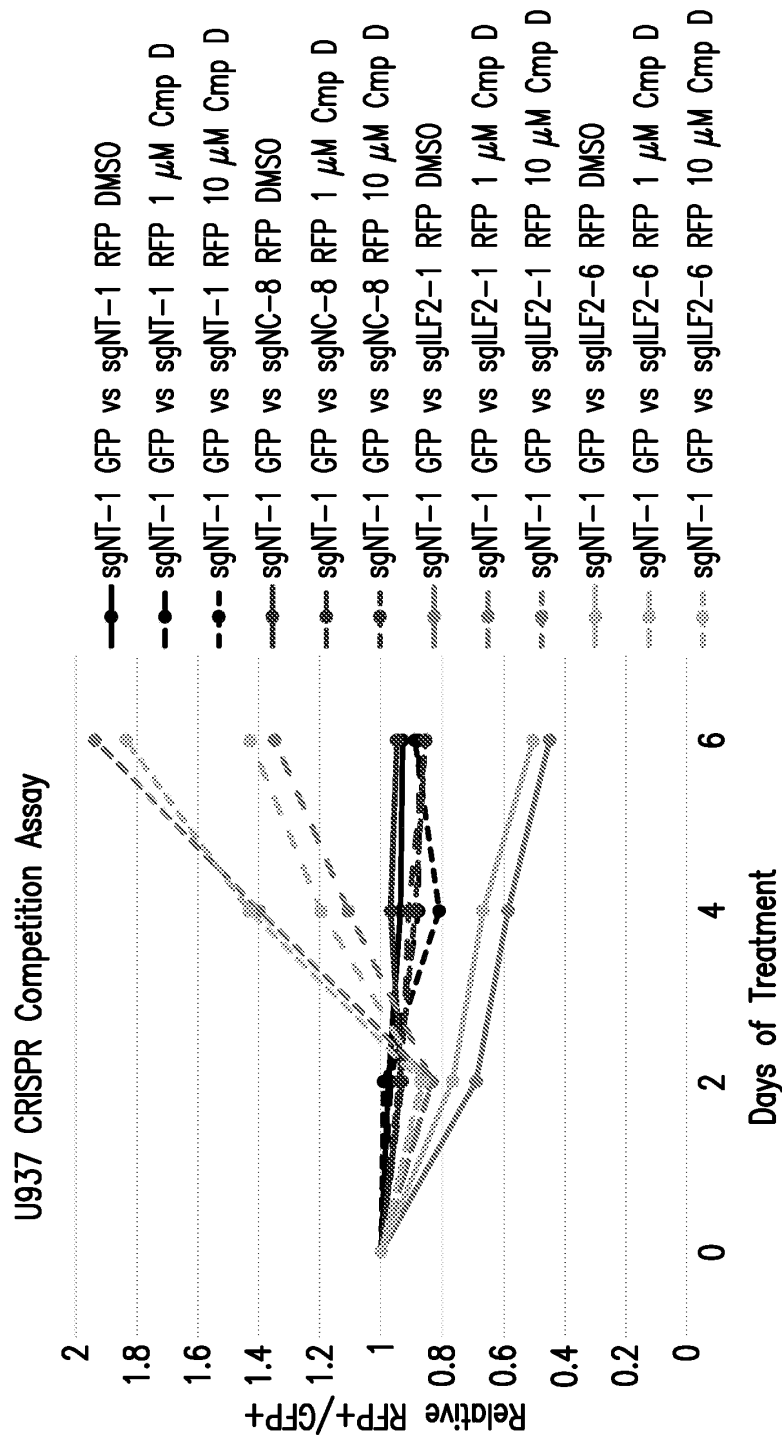


FIG. 10D

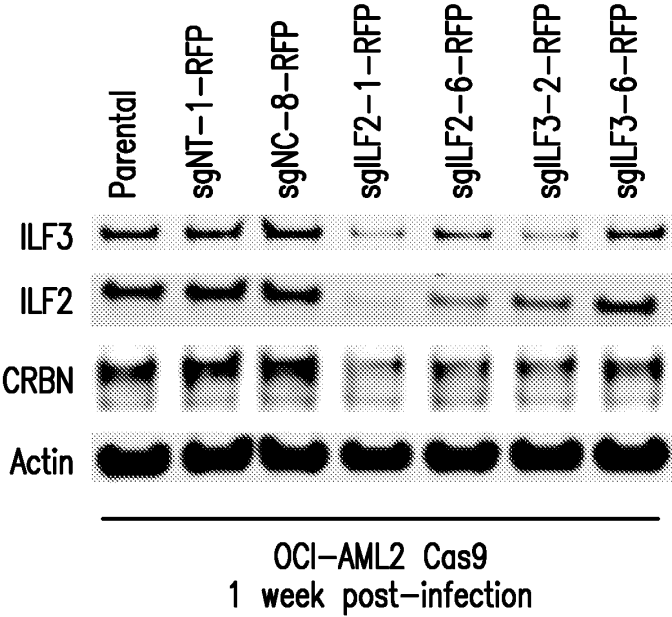


FIG. 10E

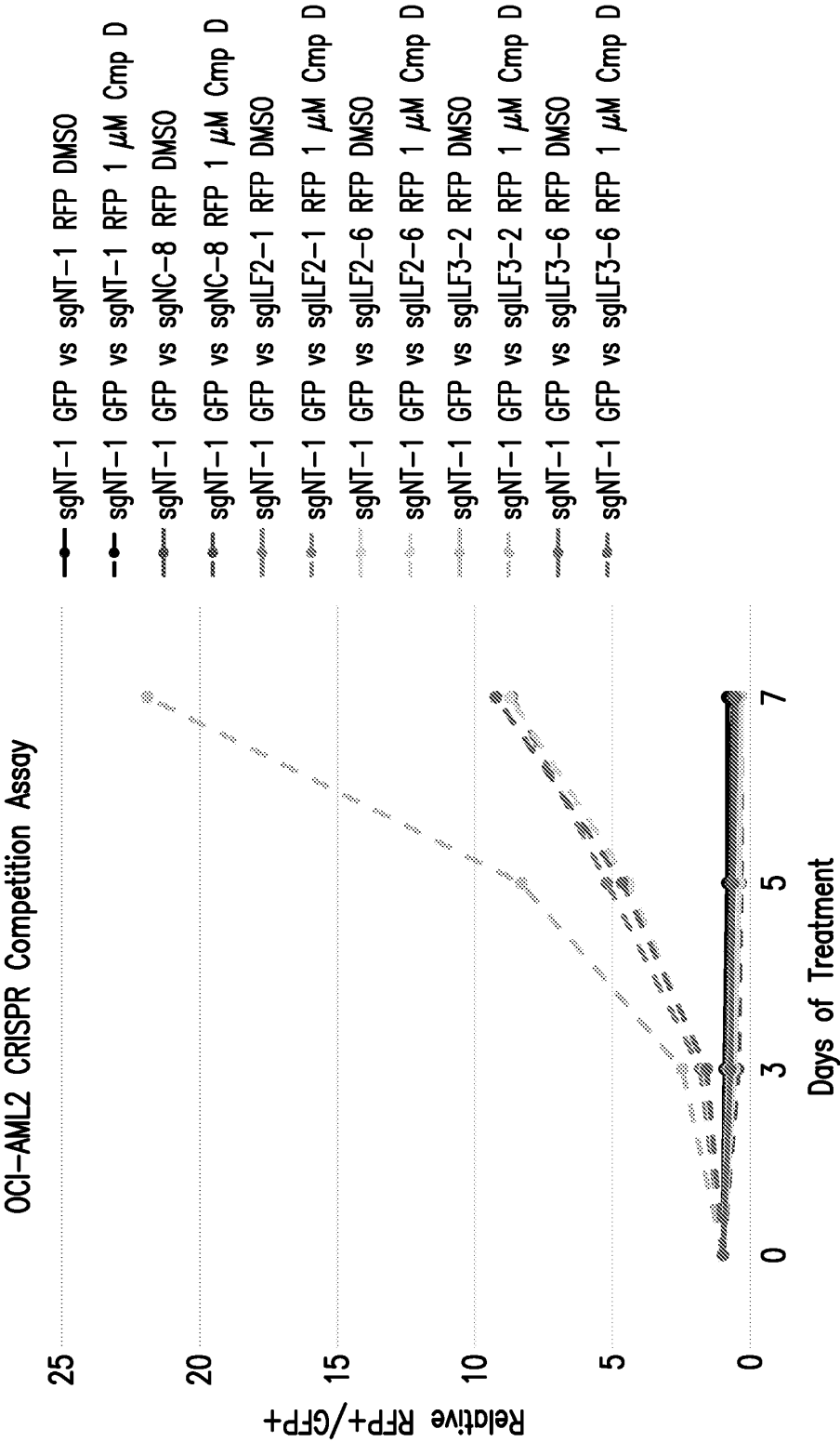


FIG. 10F

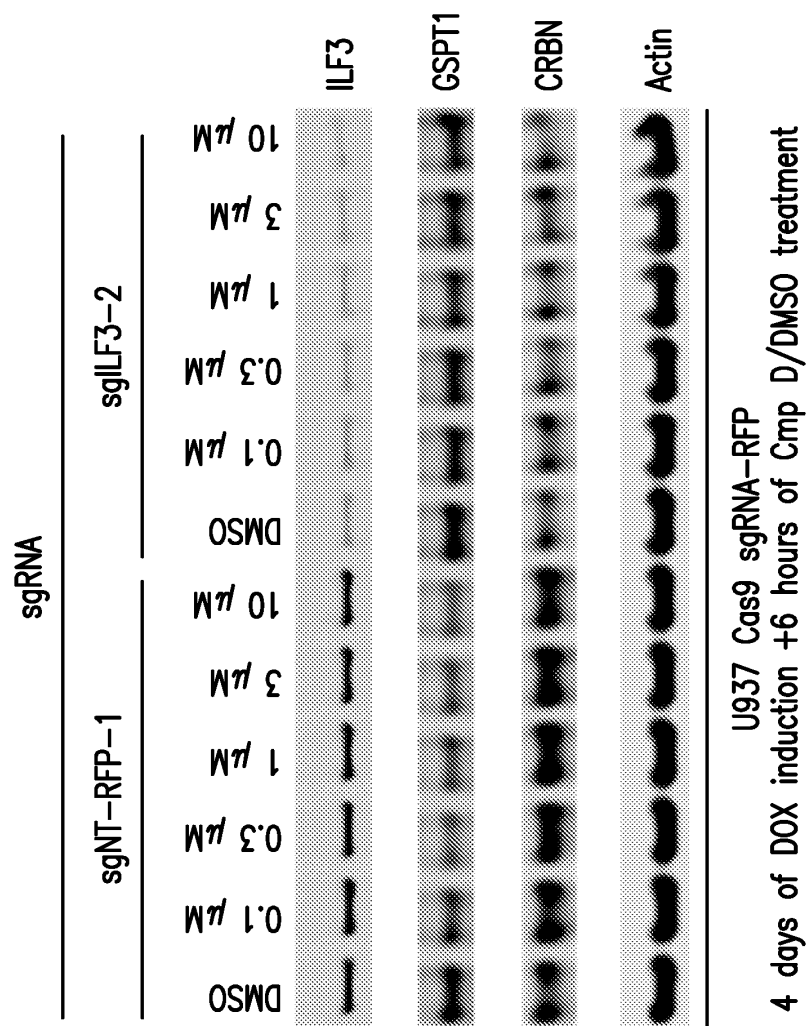


FIG. 10G

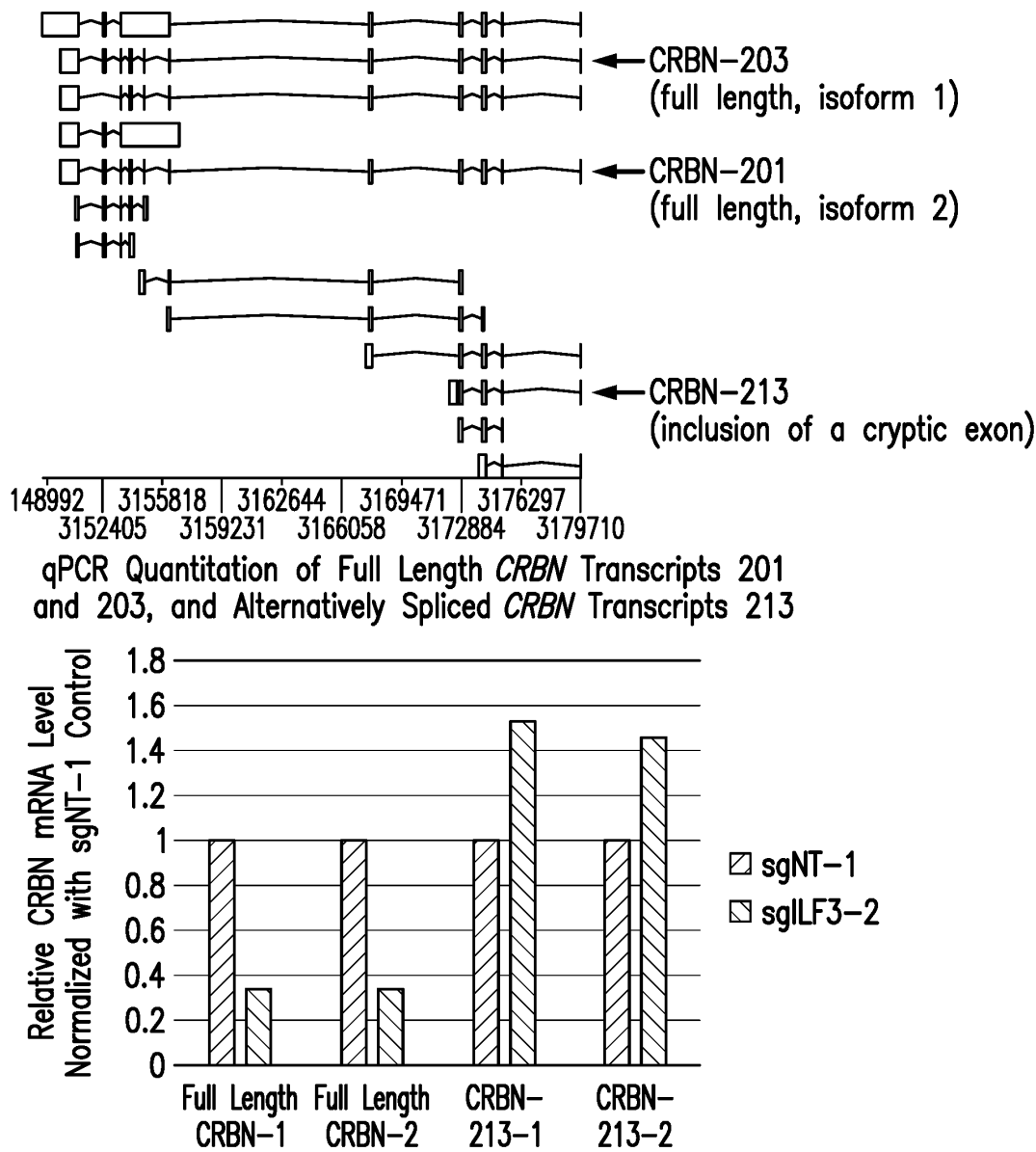


FIG. 10H

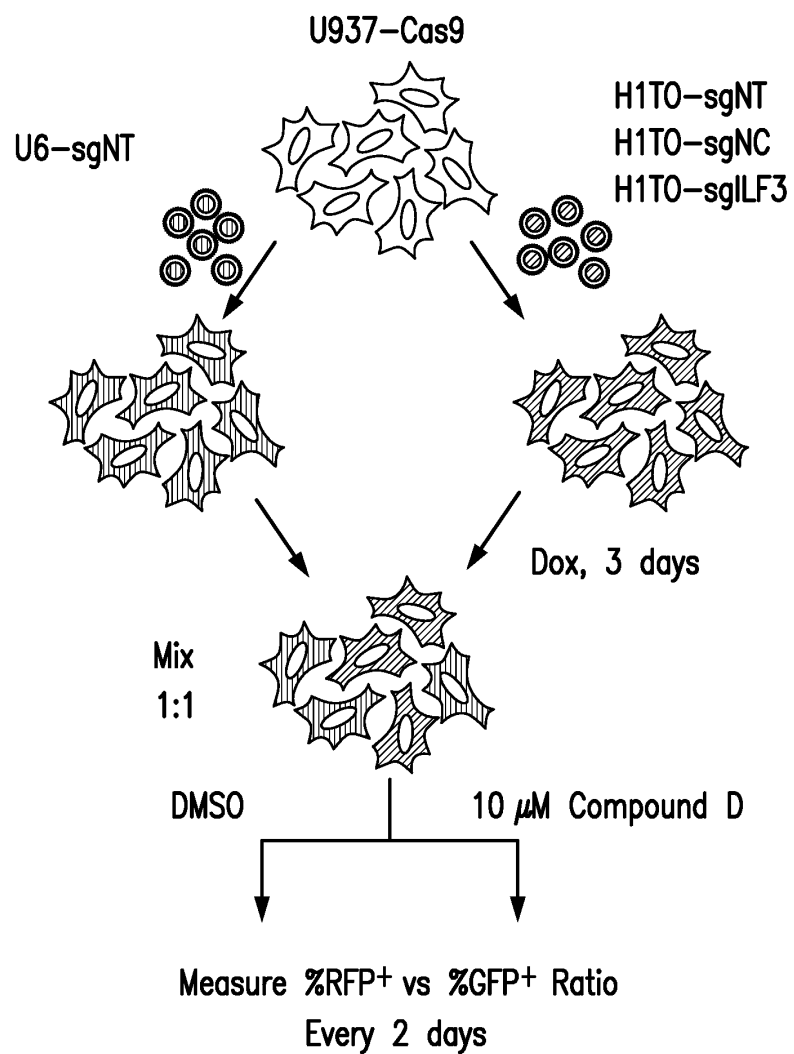


FIG. 10I

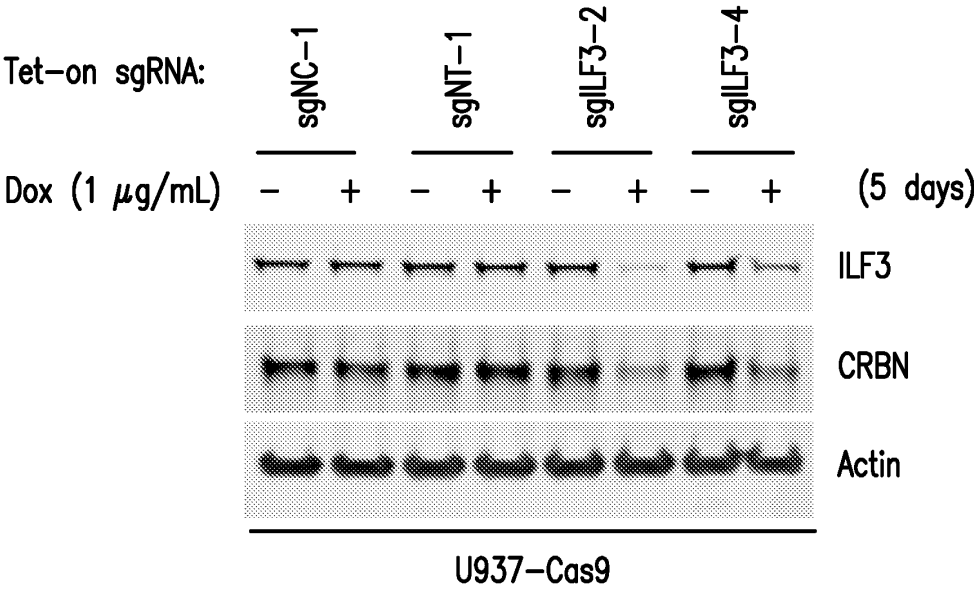


FIG. 10J

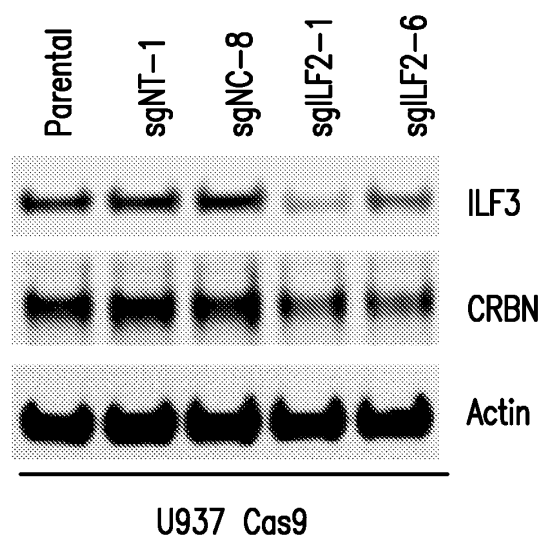


FIG. 10K

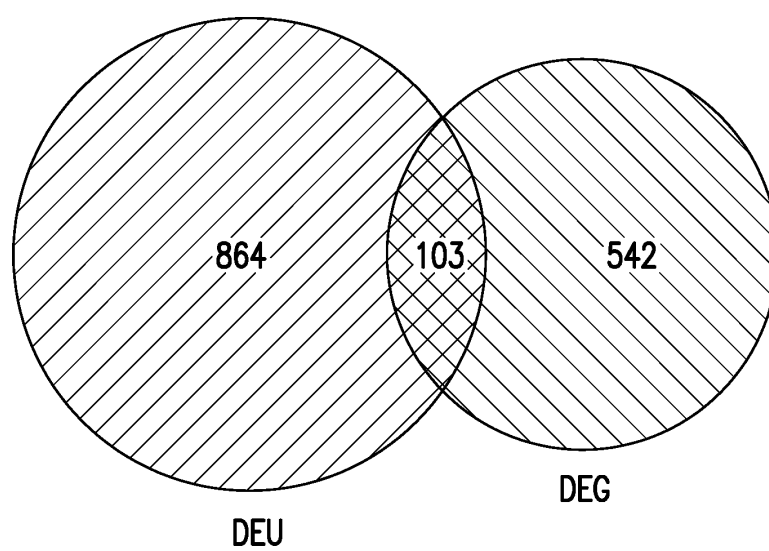


FIG. 11A

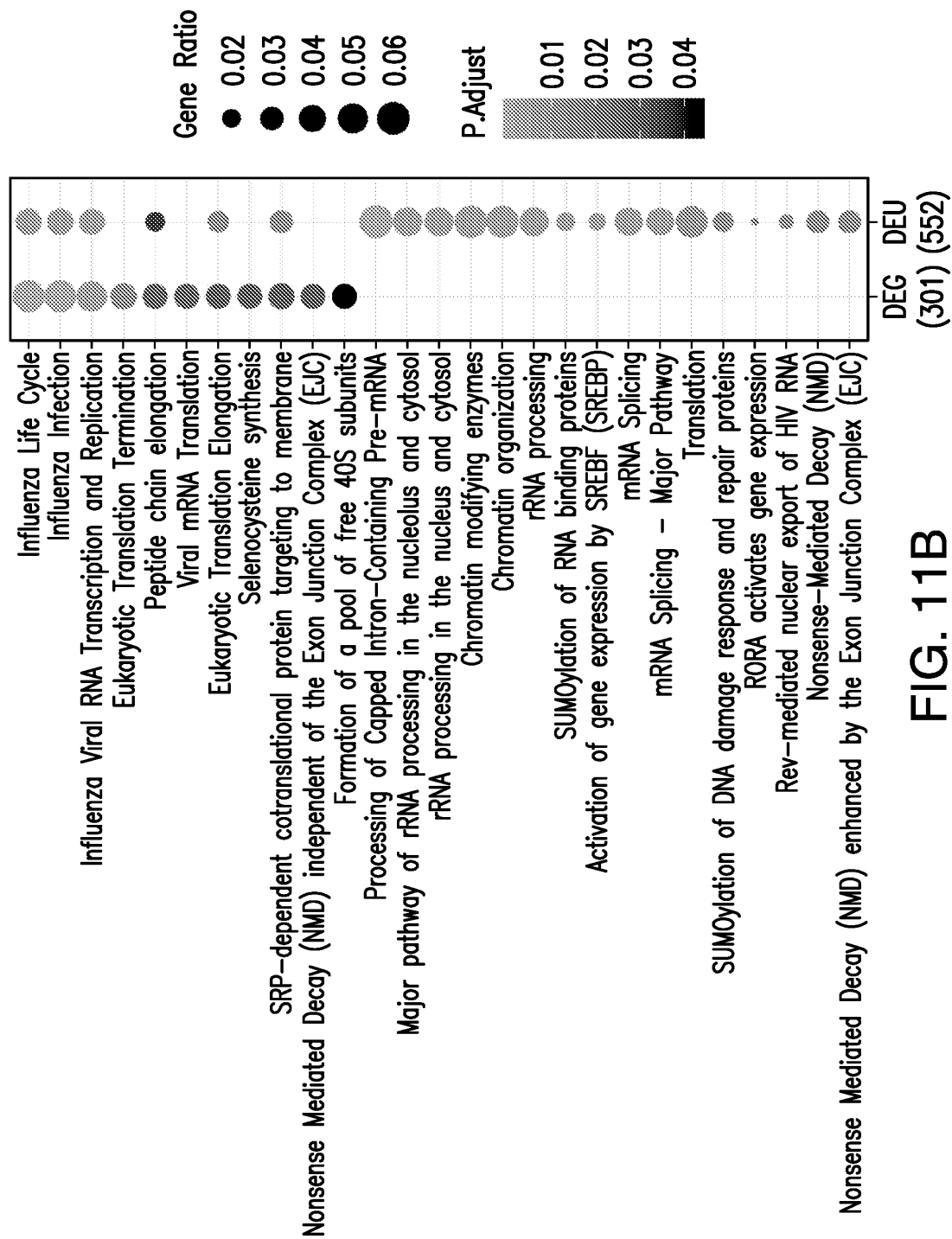


FIG. 11B

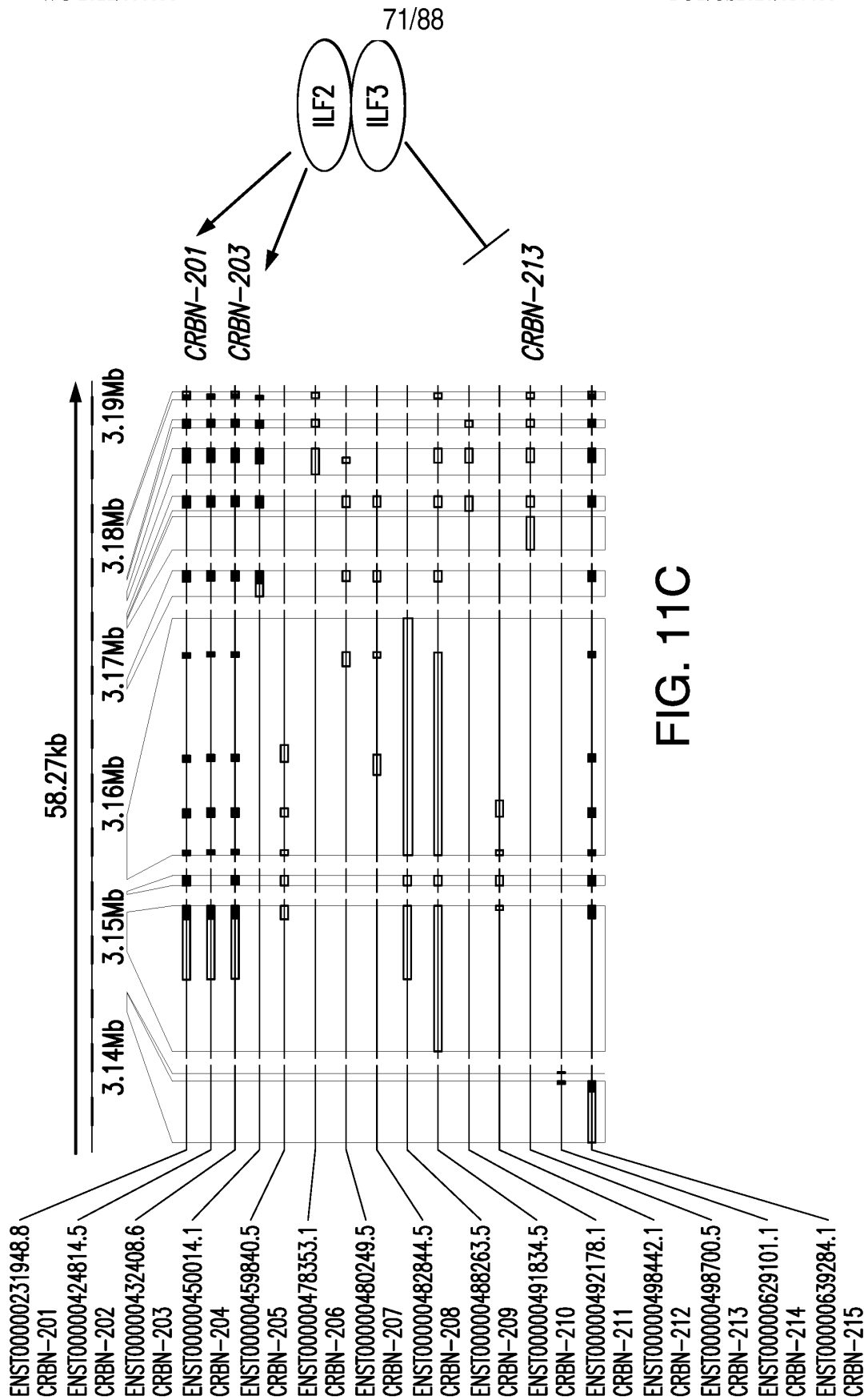


FIG. 11C

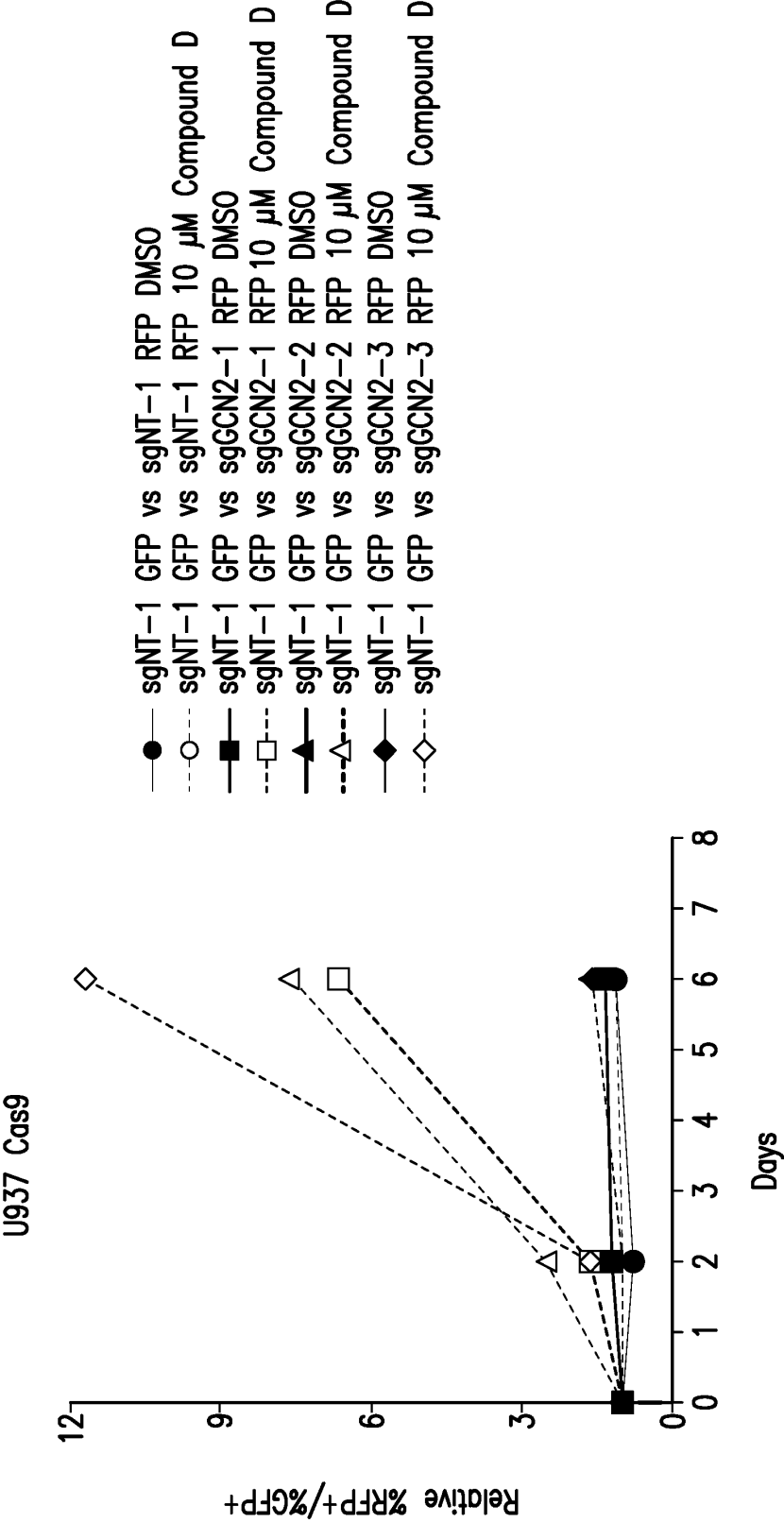


FIG. 12A

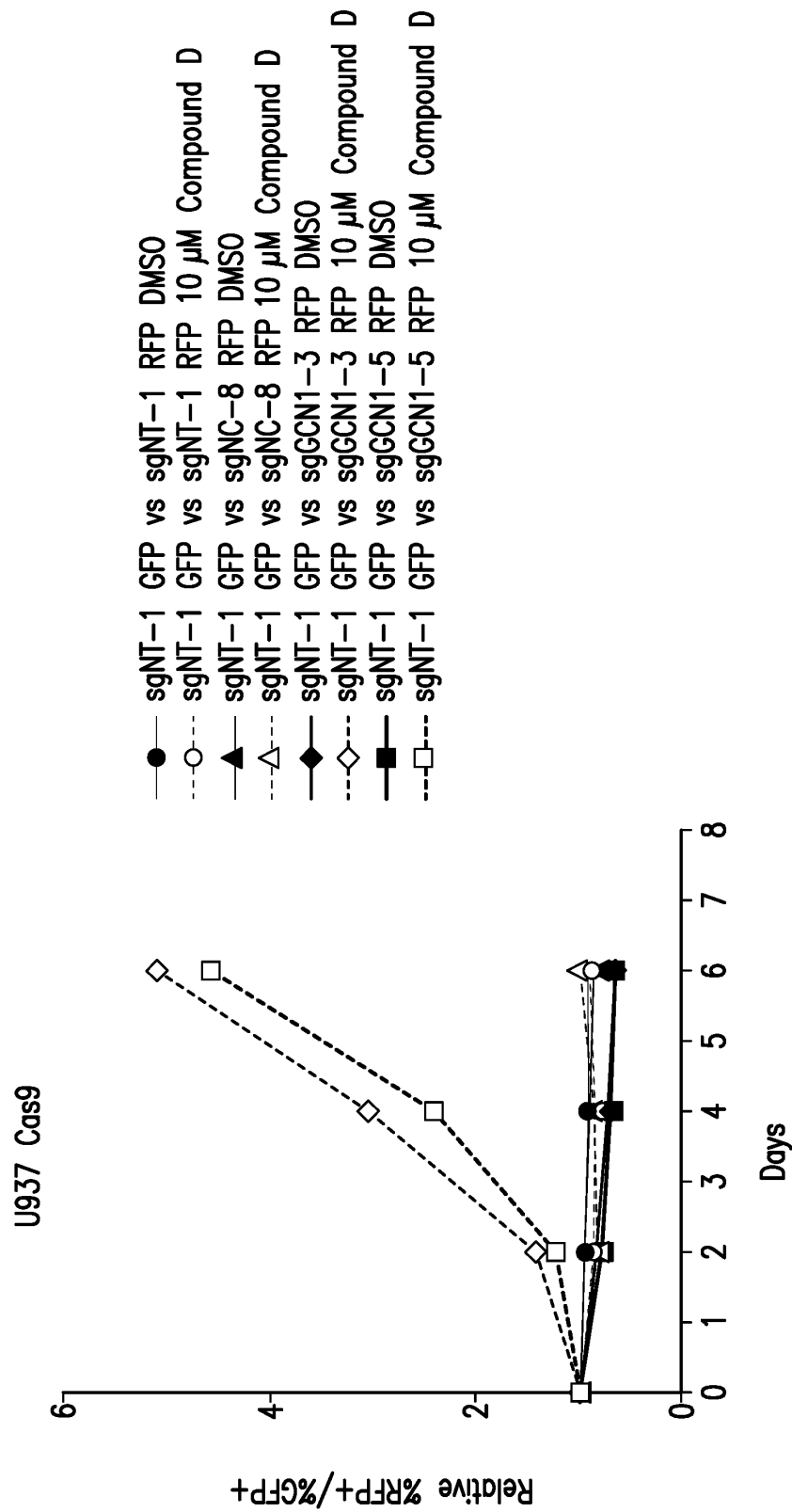


FIG. 12B

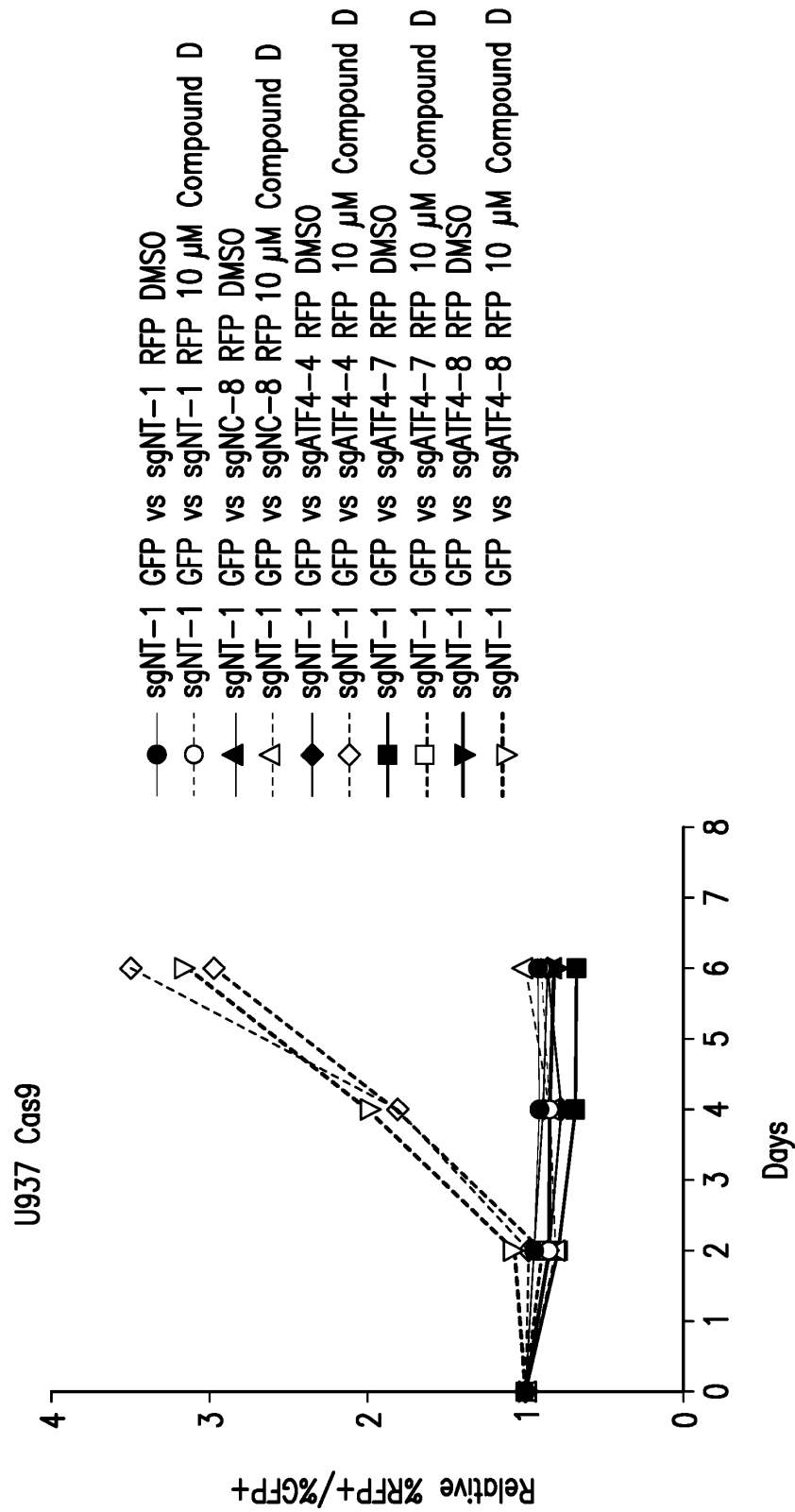


FIG. 12C

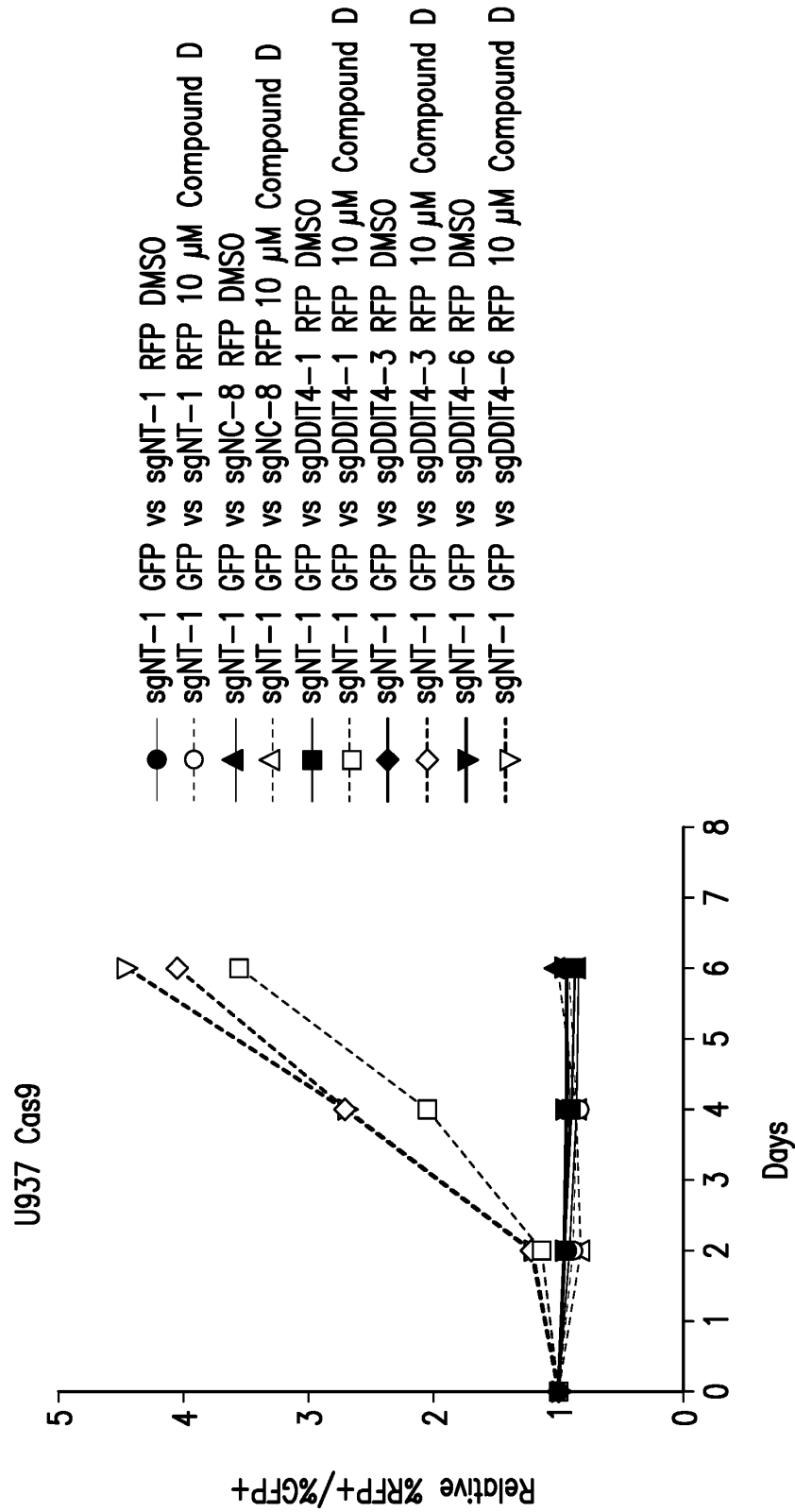


FIG. 12D

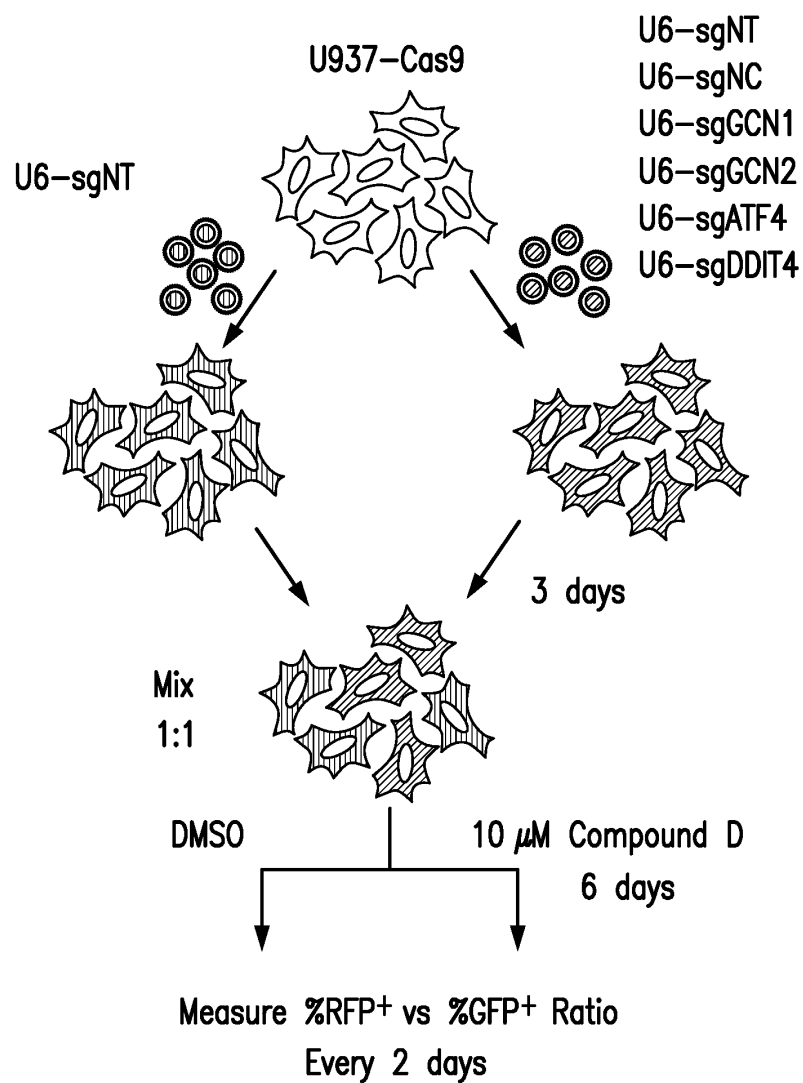


FIG. 12E

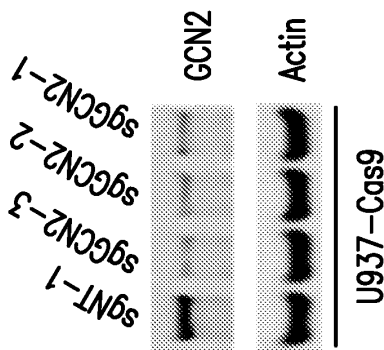
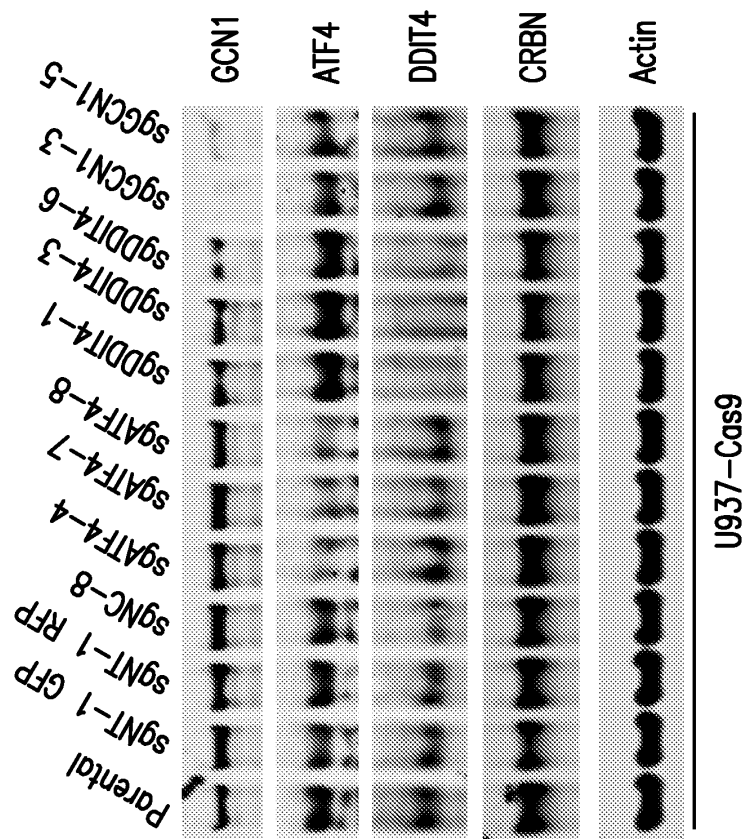


FIG. 12F

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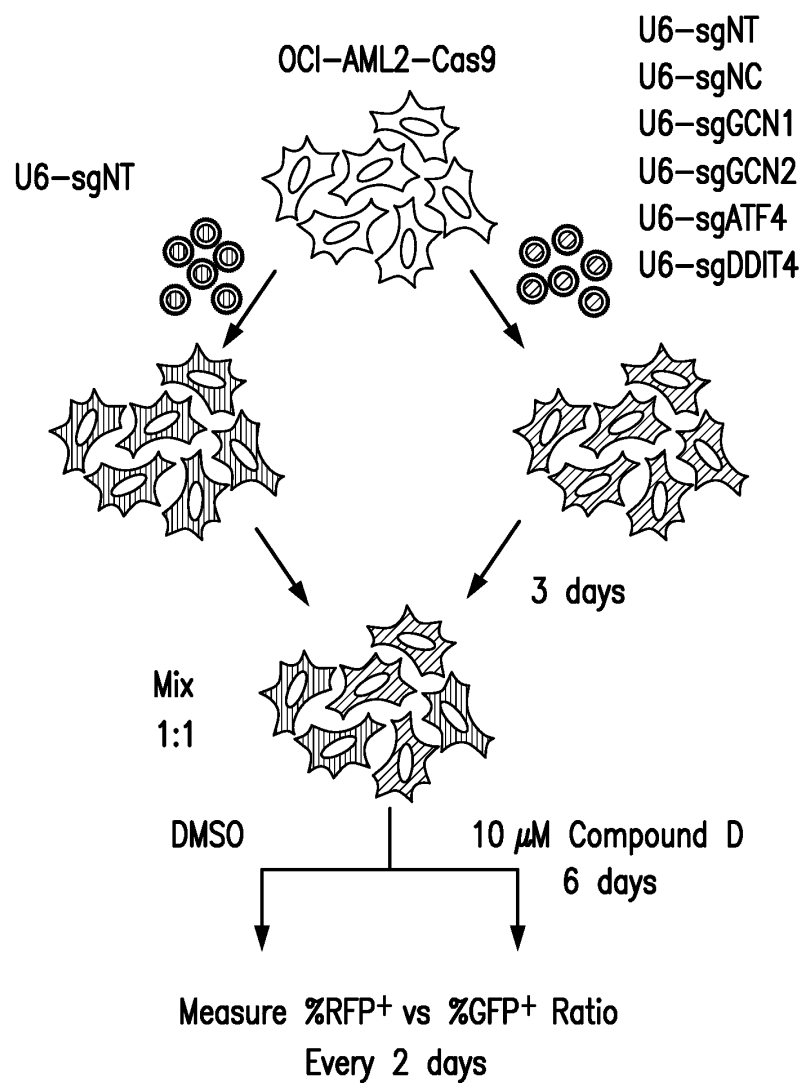


FIG. 12G

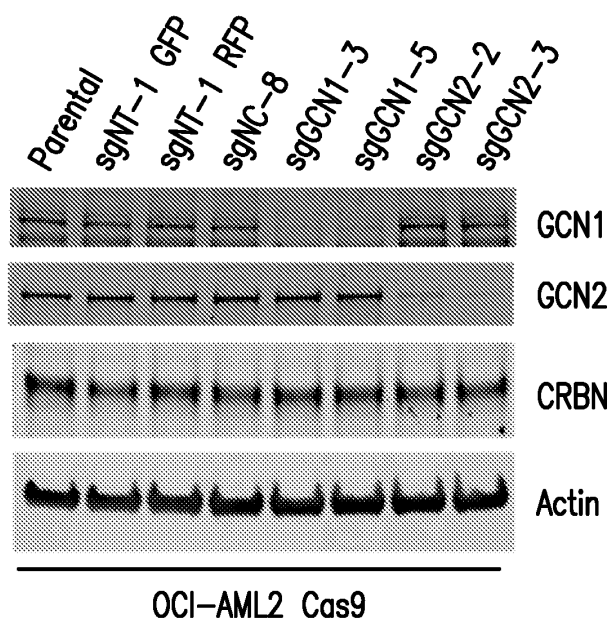


FIG. 12H

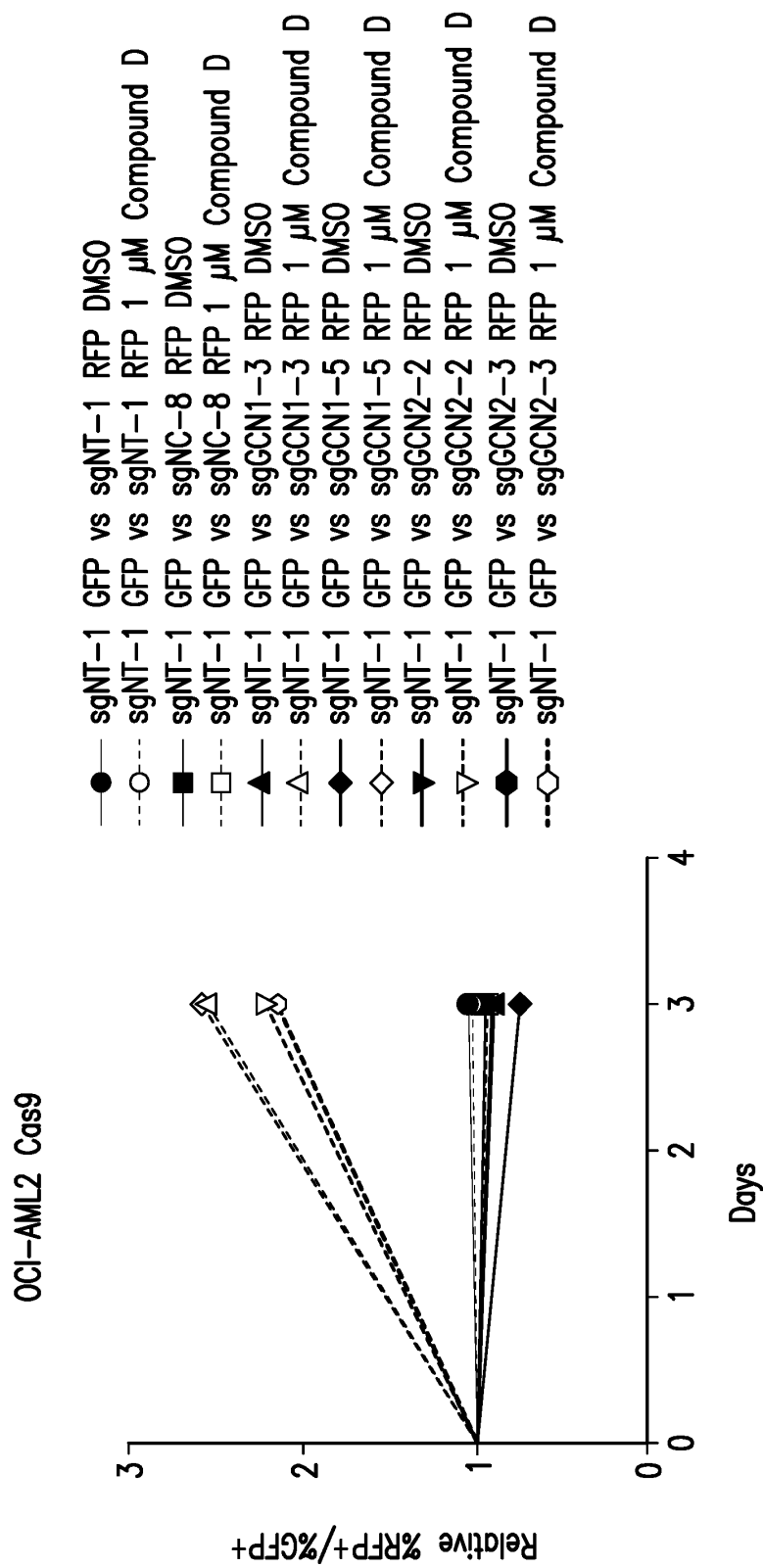


FIG. 12I

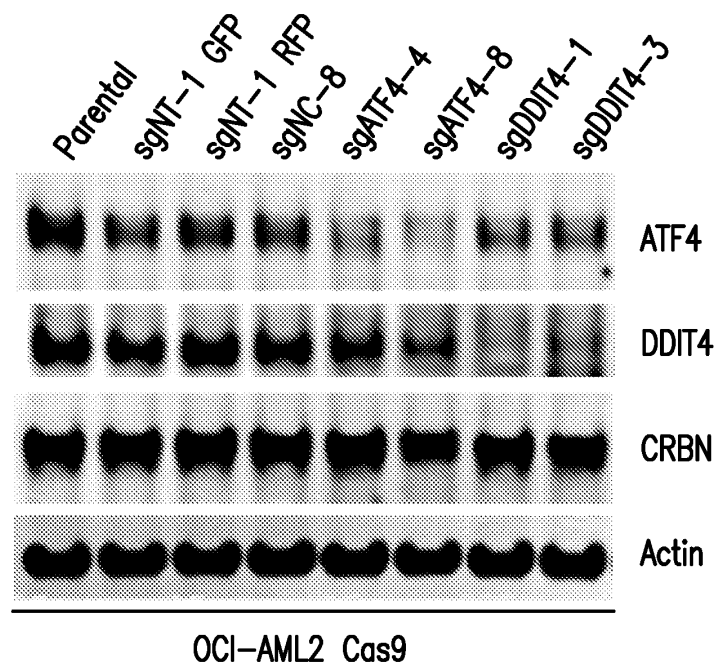


FIG. 12J

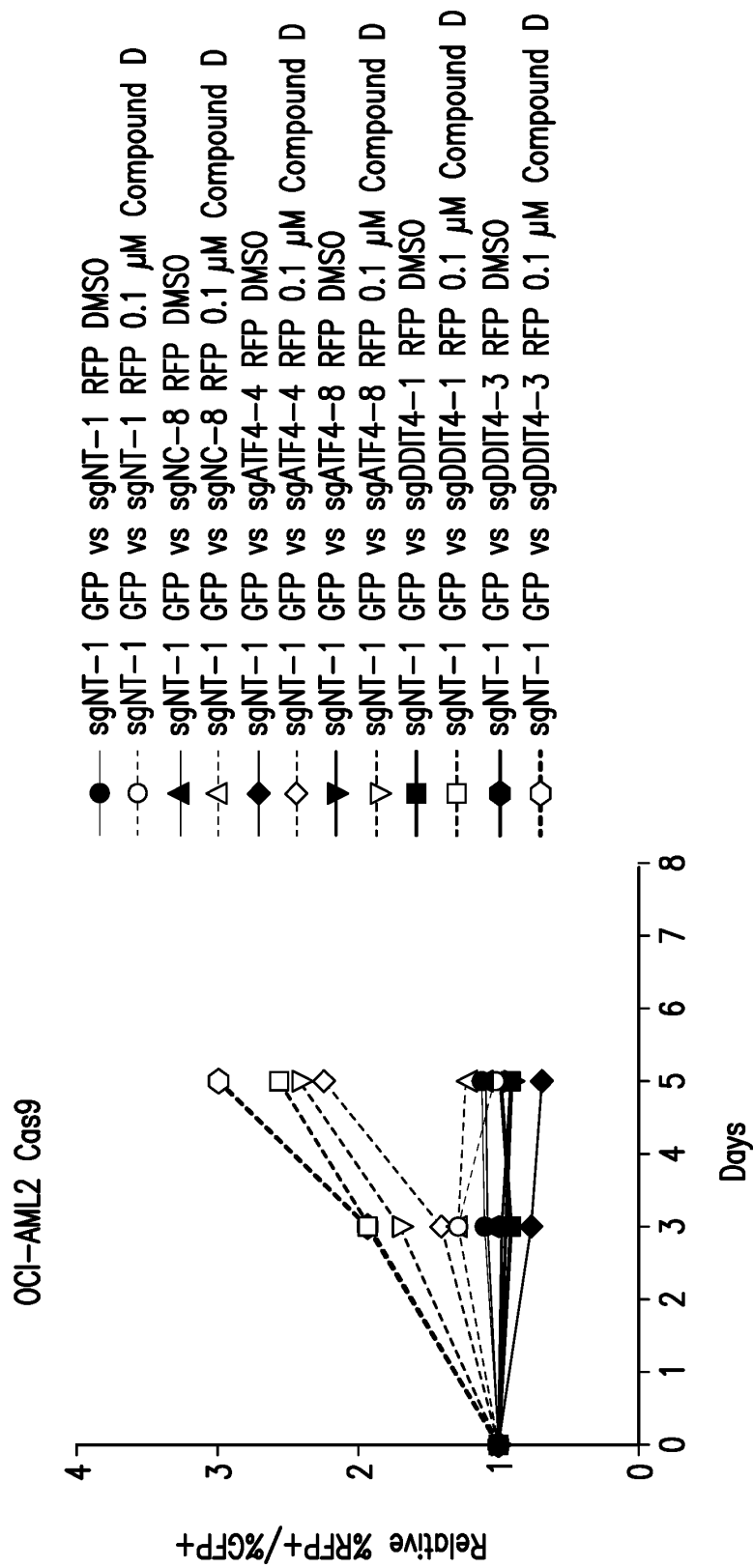


FIG. 12K

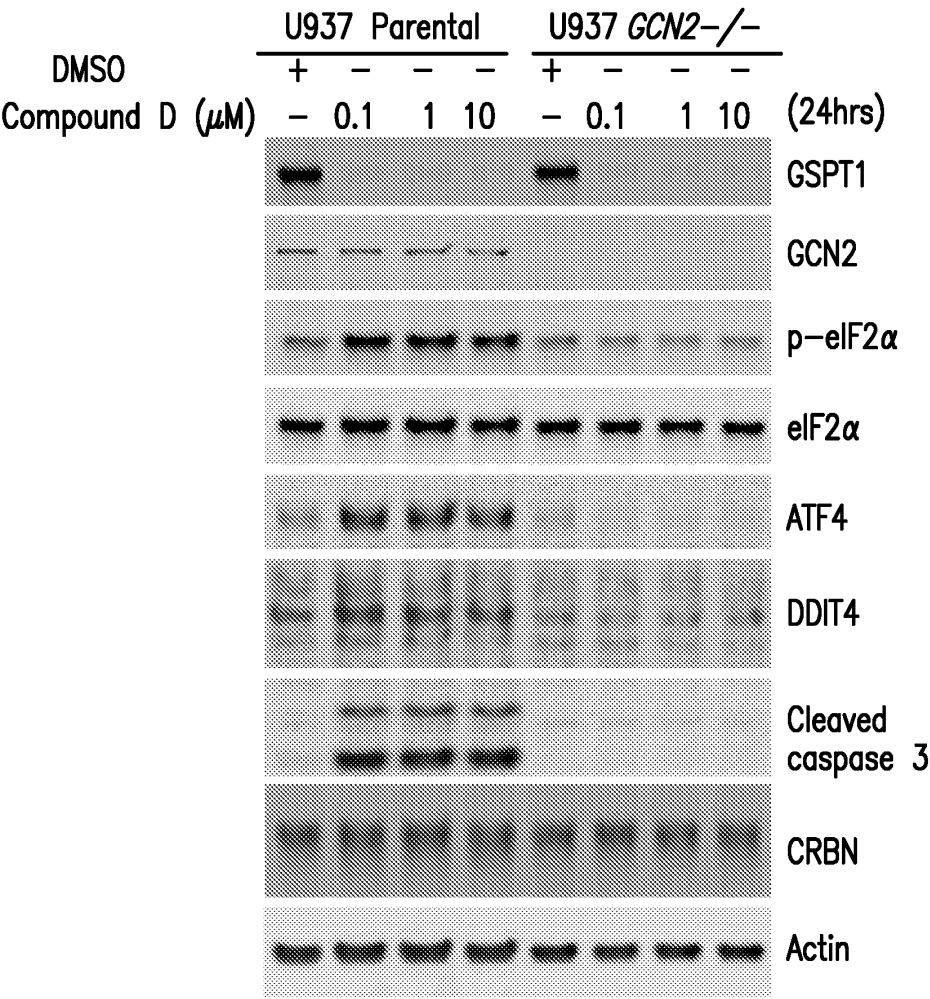


FIG. 13A

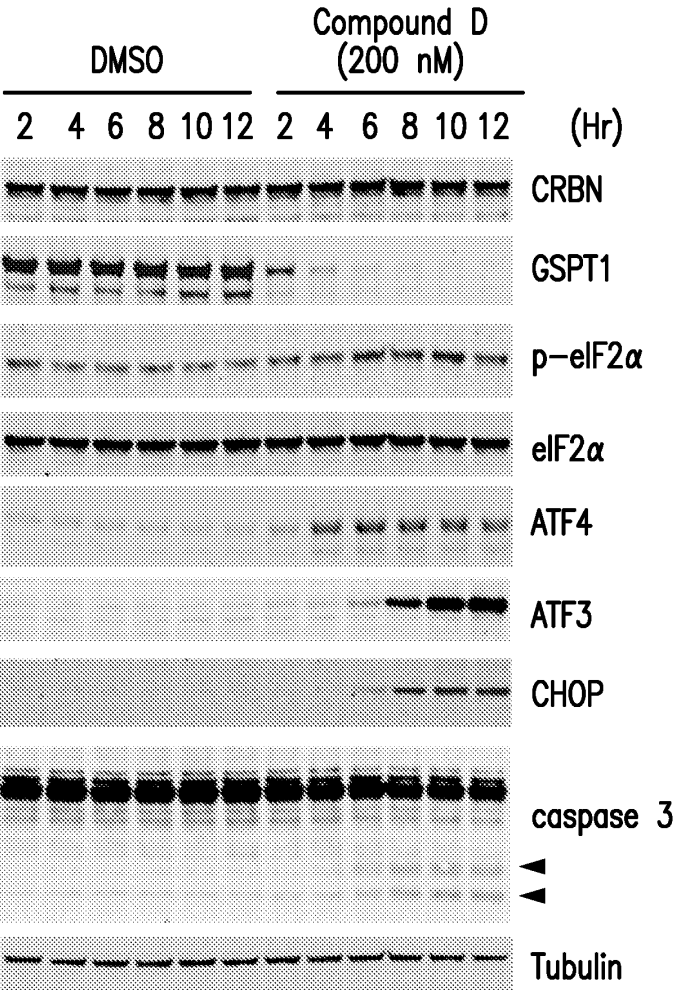


FIG. 13B

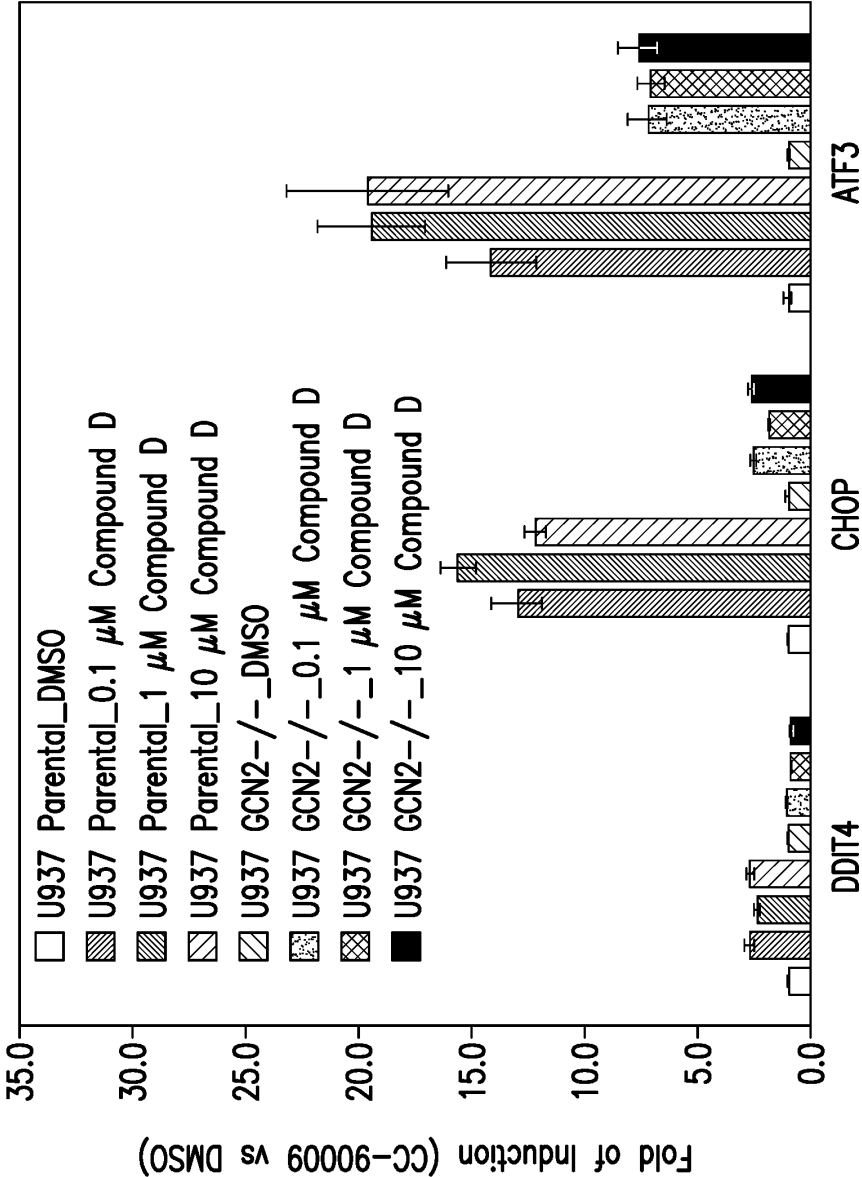


FIG. 13C

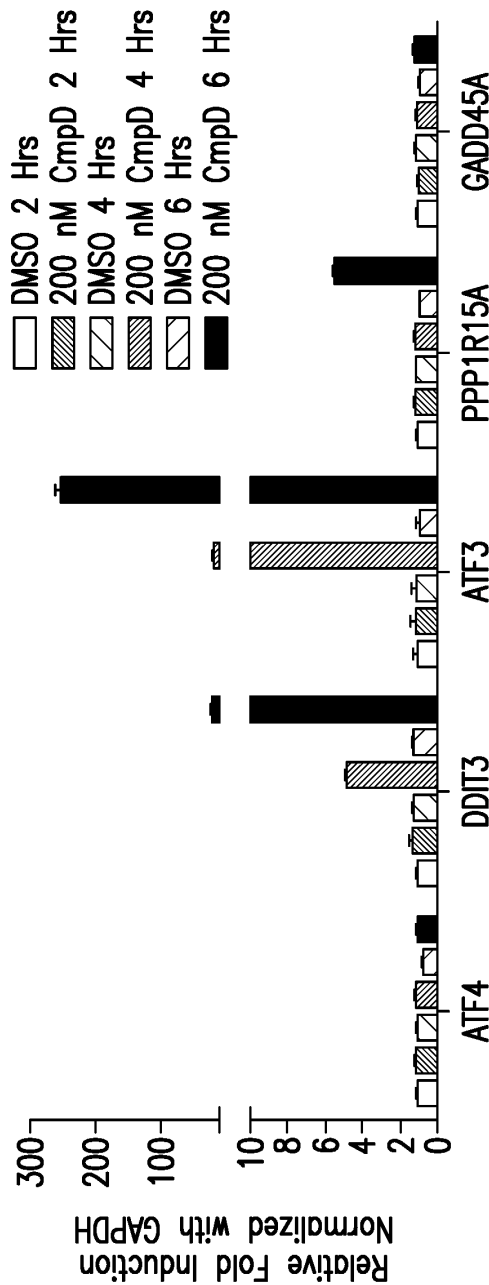


FIG. 13D

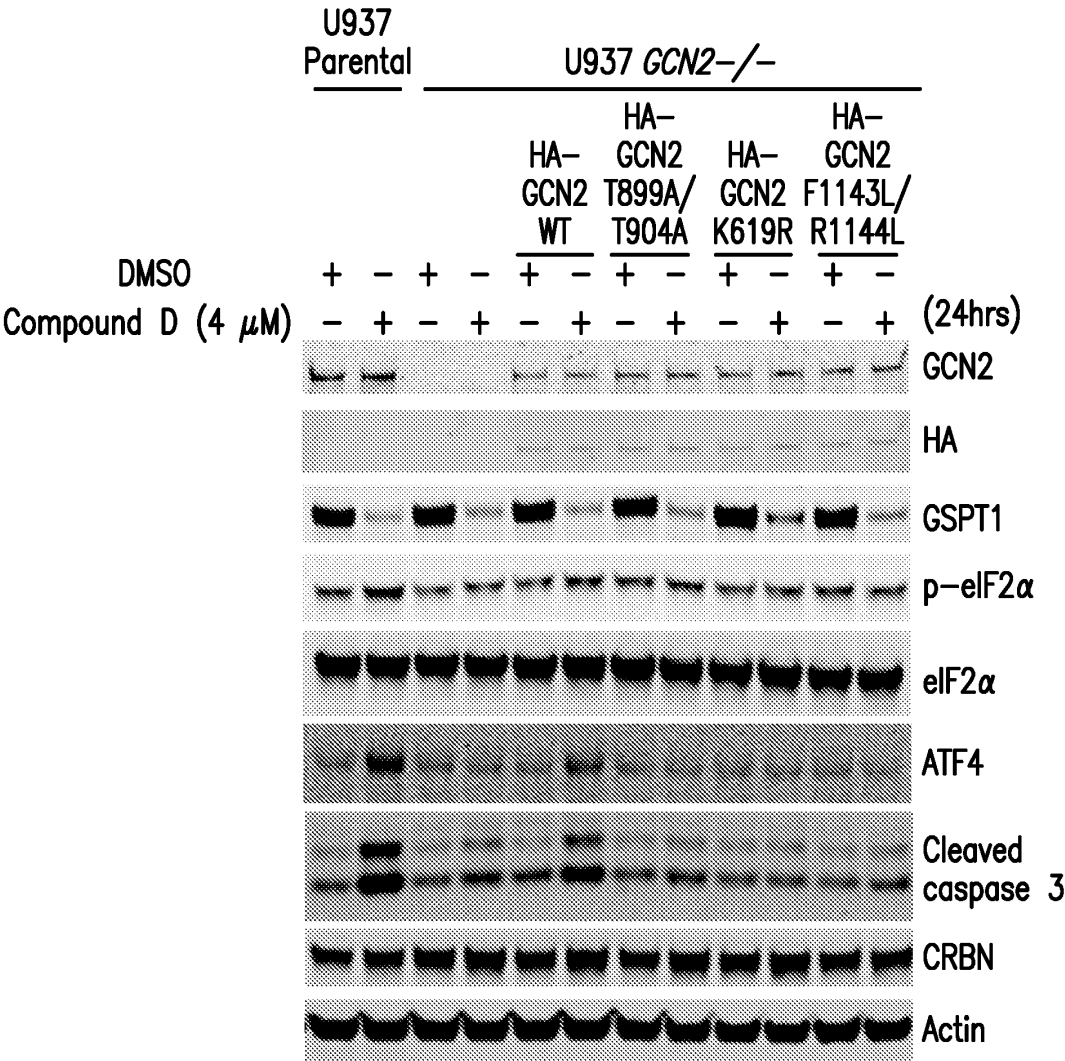


FIG. 13E

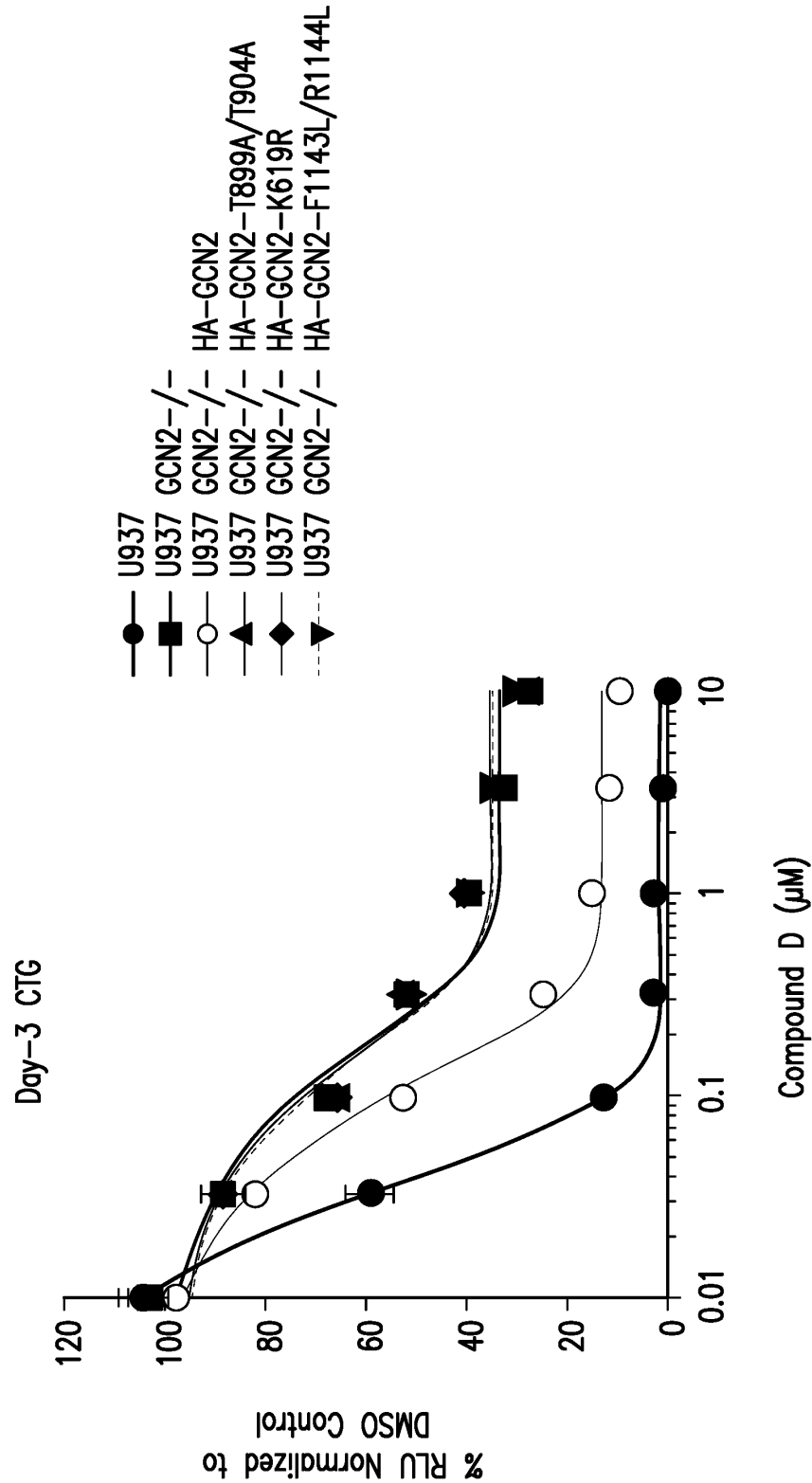


FIG. 13F