

1/100

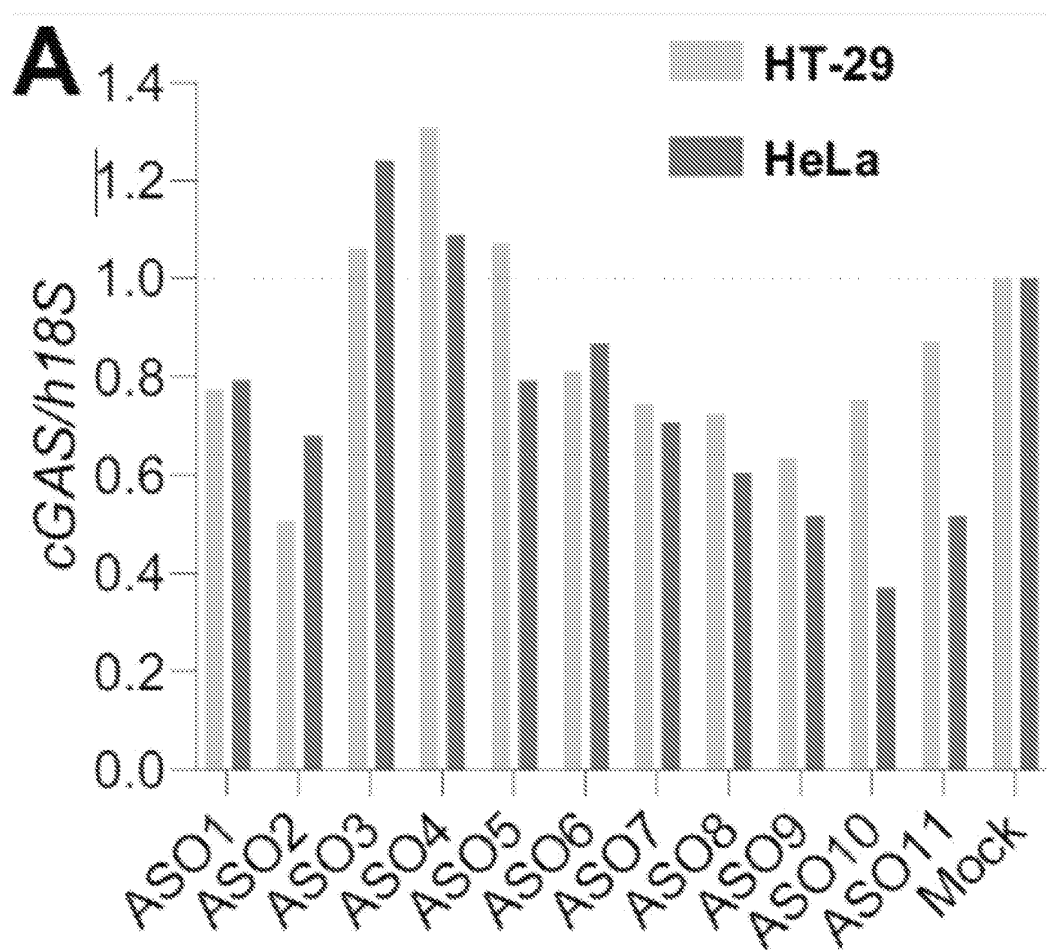
**FIGURE 1A**

FIGURE 1B

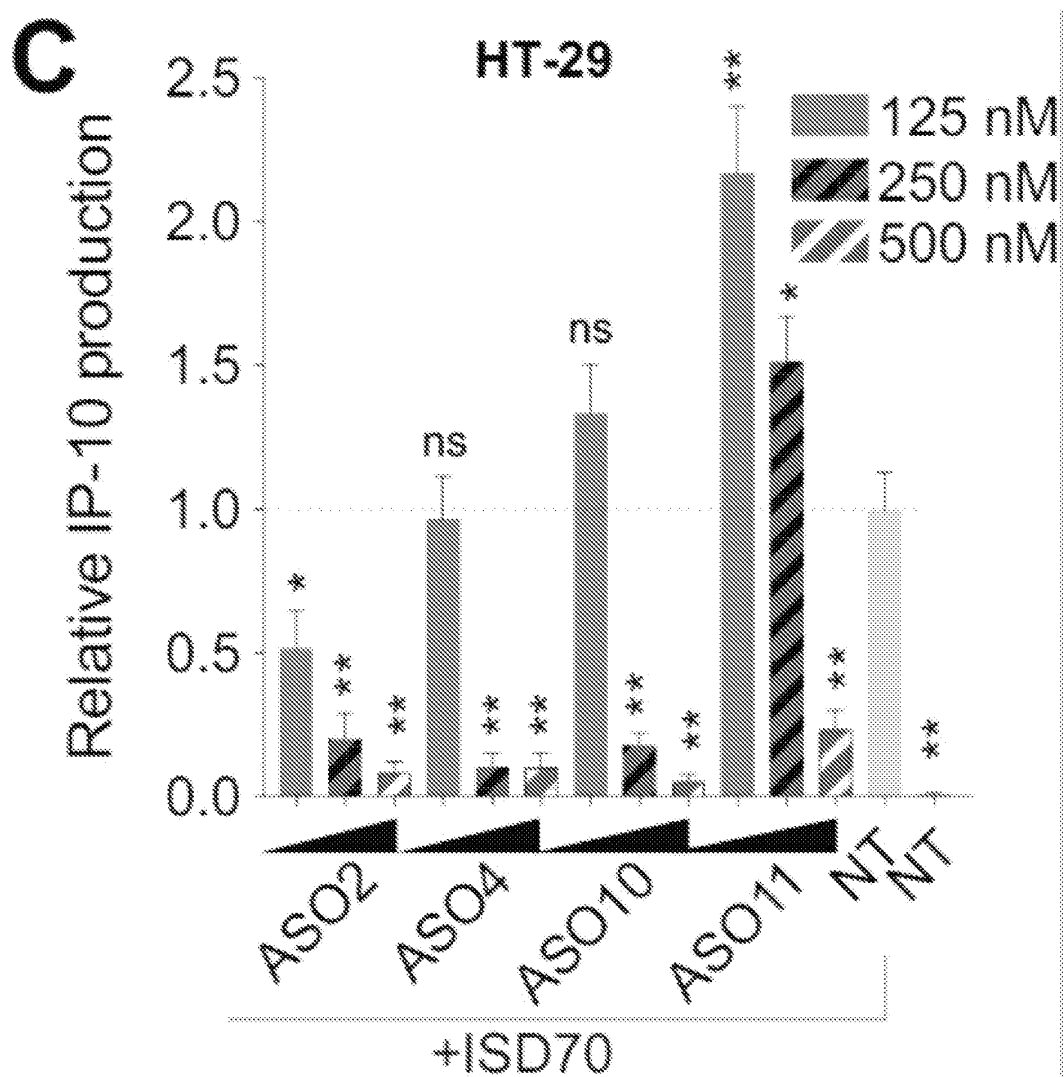


FIGURE 1C

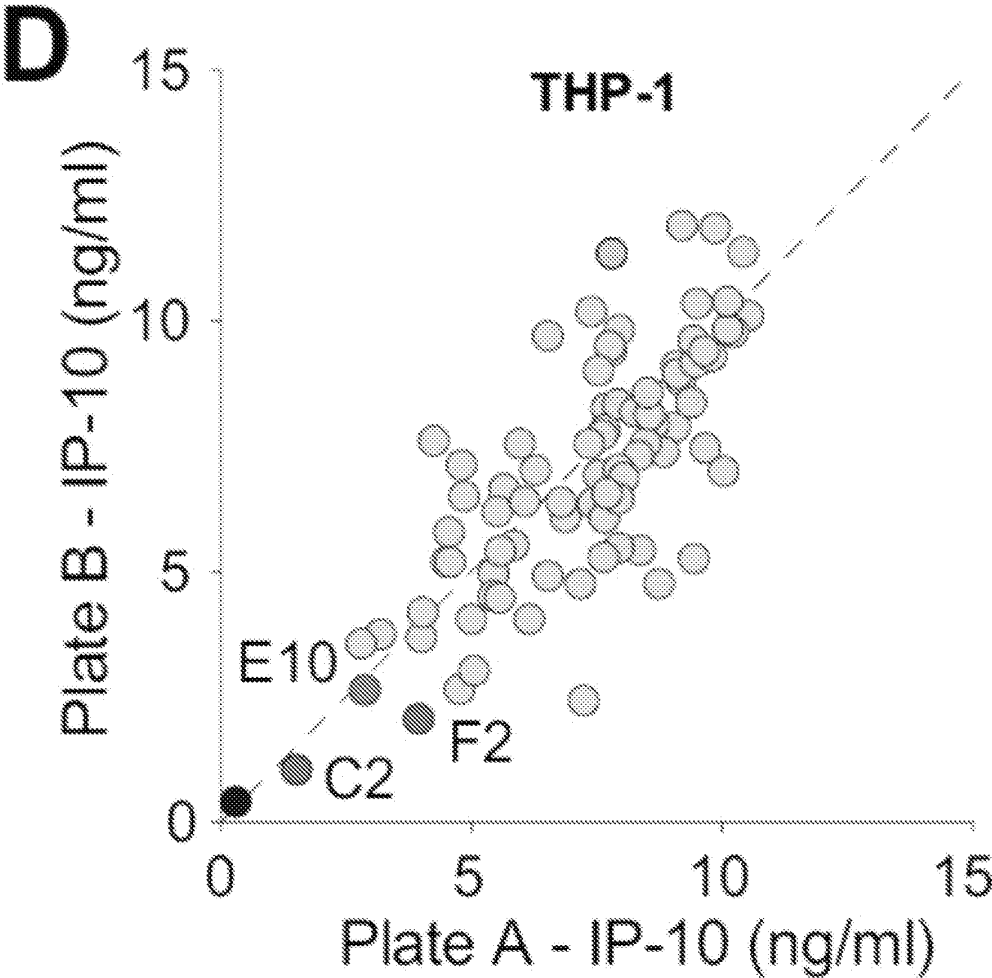
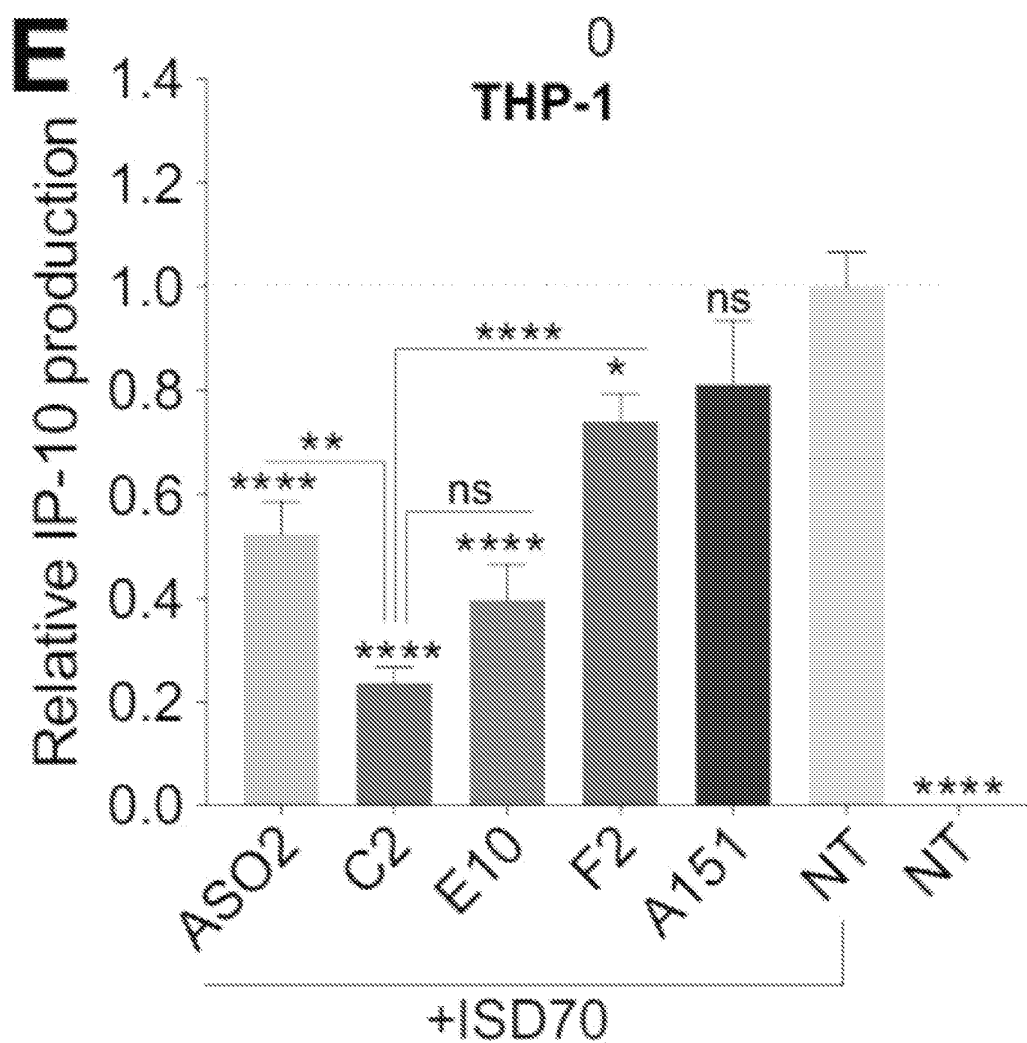
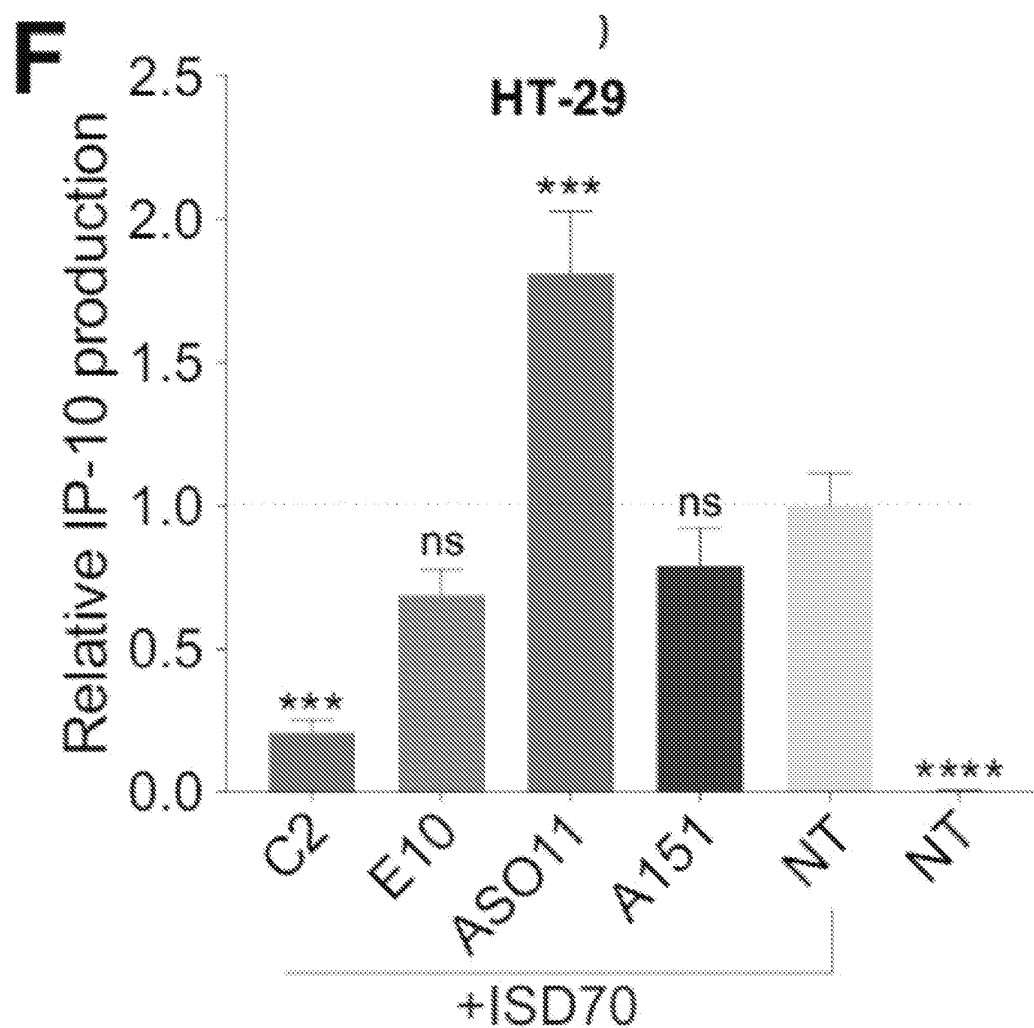


FIGURE 1D

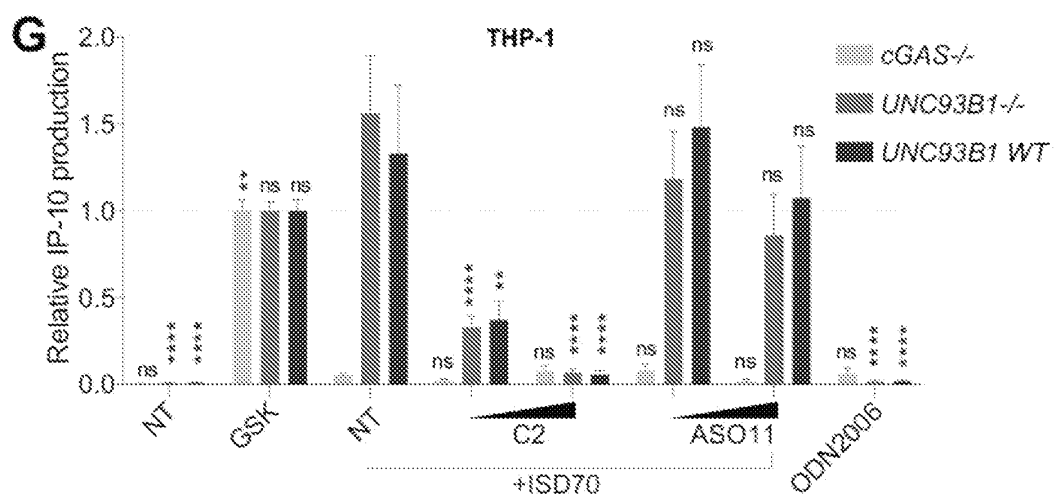
5/100

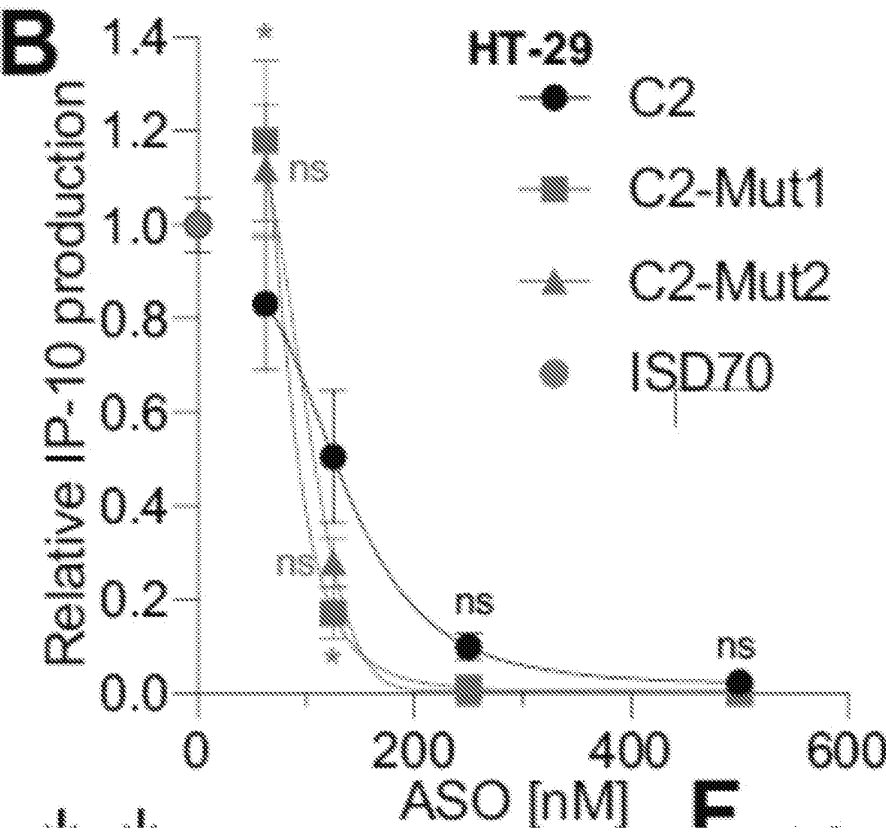
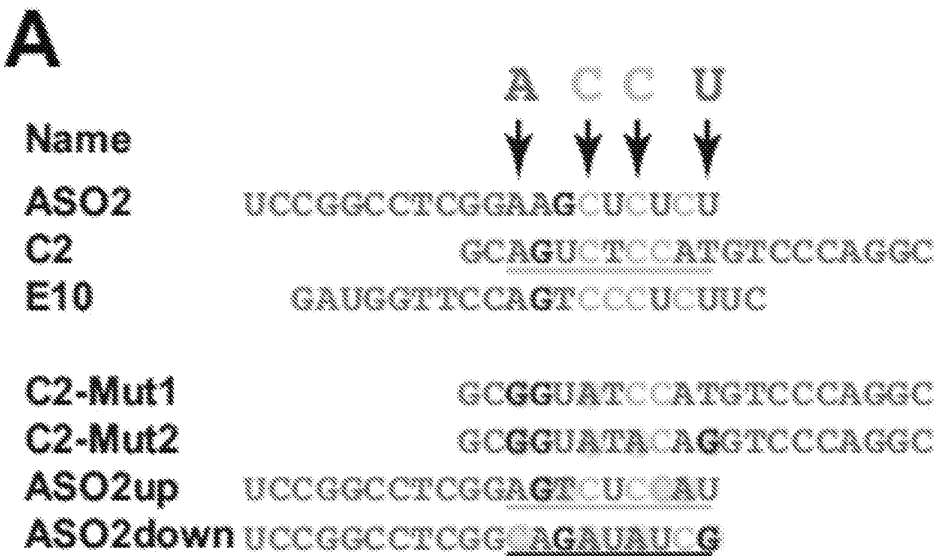
**FIGURE 1E**

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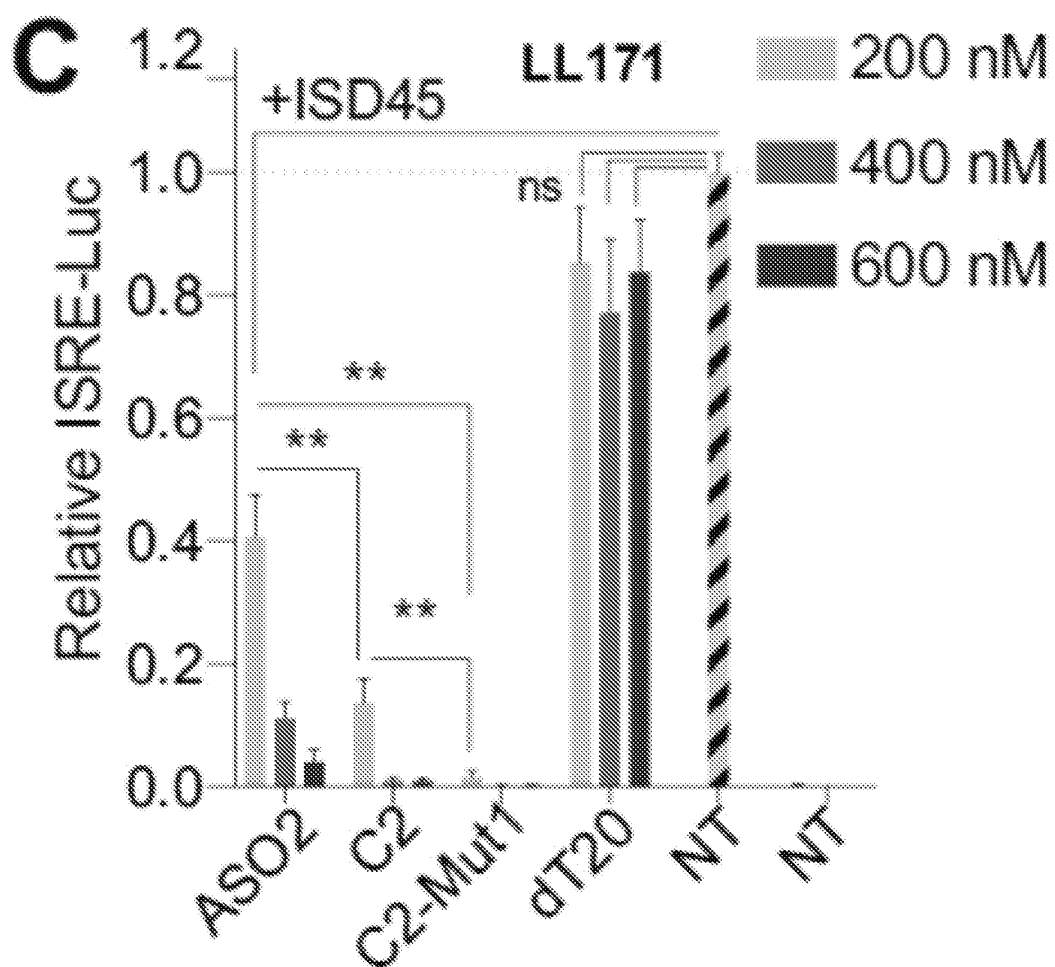
**FIGURE 1F**

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**FIGURE 1G**



FIGURES 2A & 2B

**FIGURE 2C**

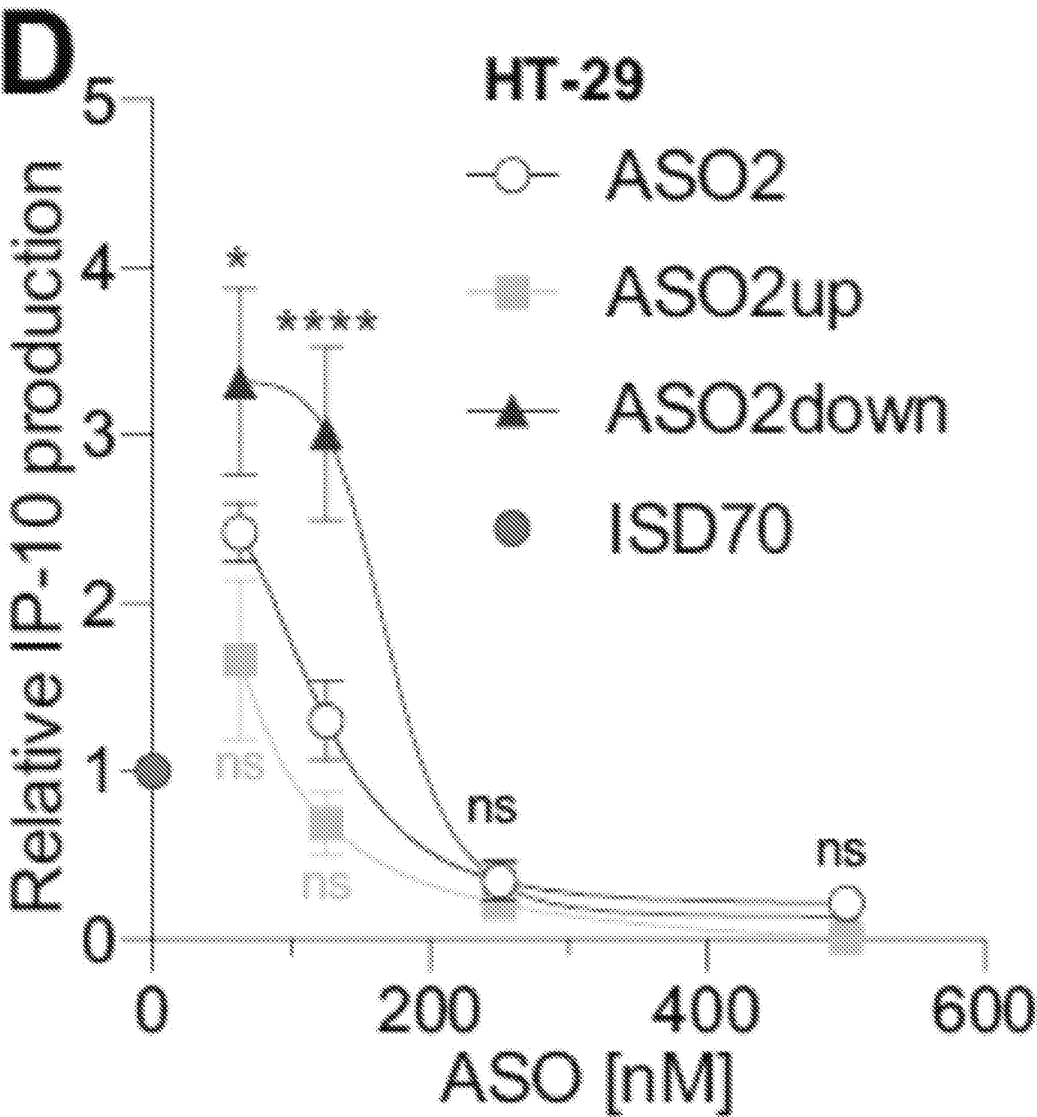


FIGURE 2D

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E	Name	↓ ↓
	C2	GCAGUCTCCATGTCCCAGGC
	C2-Mut1	GCGGUATCCATGTCCCAGGC
	C2-Mut1v1	GCUGUTTCATGTCCCAGGC
	C2-Mut1v2	GCUGUGTCCATGTCCCAGGC
	C2-Mut1v3	GCUGUTTCATGTCCCAGGC
	C2-Mut1v4	GCUGUGTCCATGTCCCAGGC
	C2-ASO2-A	GCGGUATCCATAGT <u>UCCAU</u>
	C2-ASO2-B	GCGGUATCCAT <u>AGAUAU</u> CG
	Mut1-dC	<u>GGUAT</u> CCCCCCCCCCCCCCCC
	Mut1-v3-dC	<u>CGUT</u> CCCCCCCCCCCCCCCC
	dC20	CCCCCCCCCCCCCCCCCCCC

FIGURE 2E

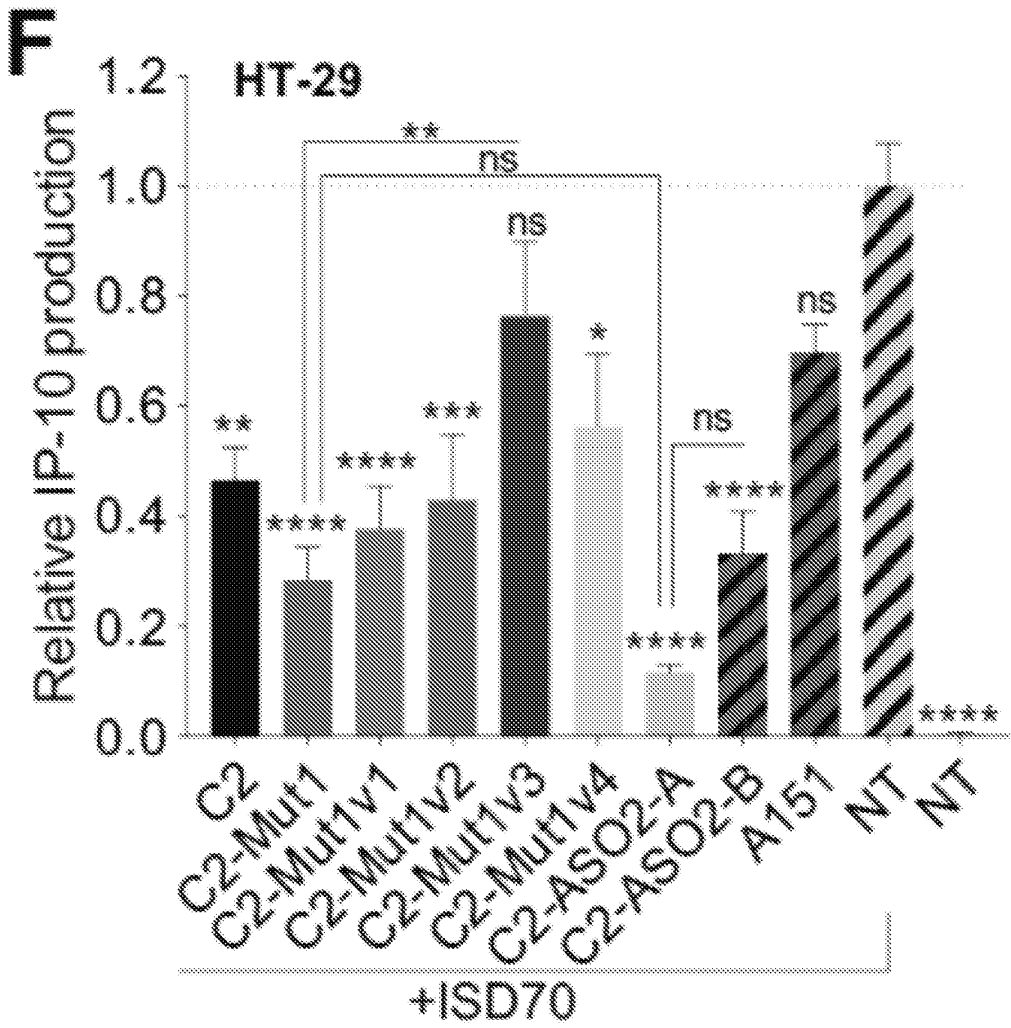


FIGURE 2F

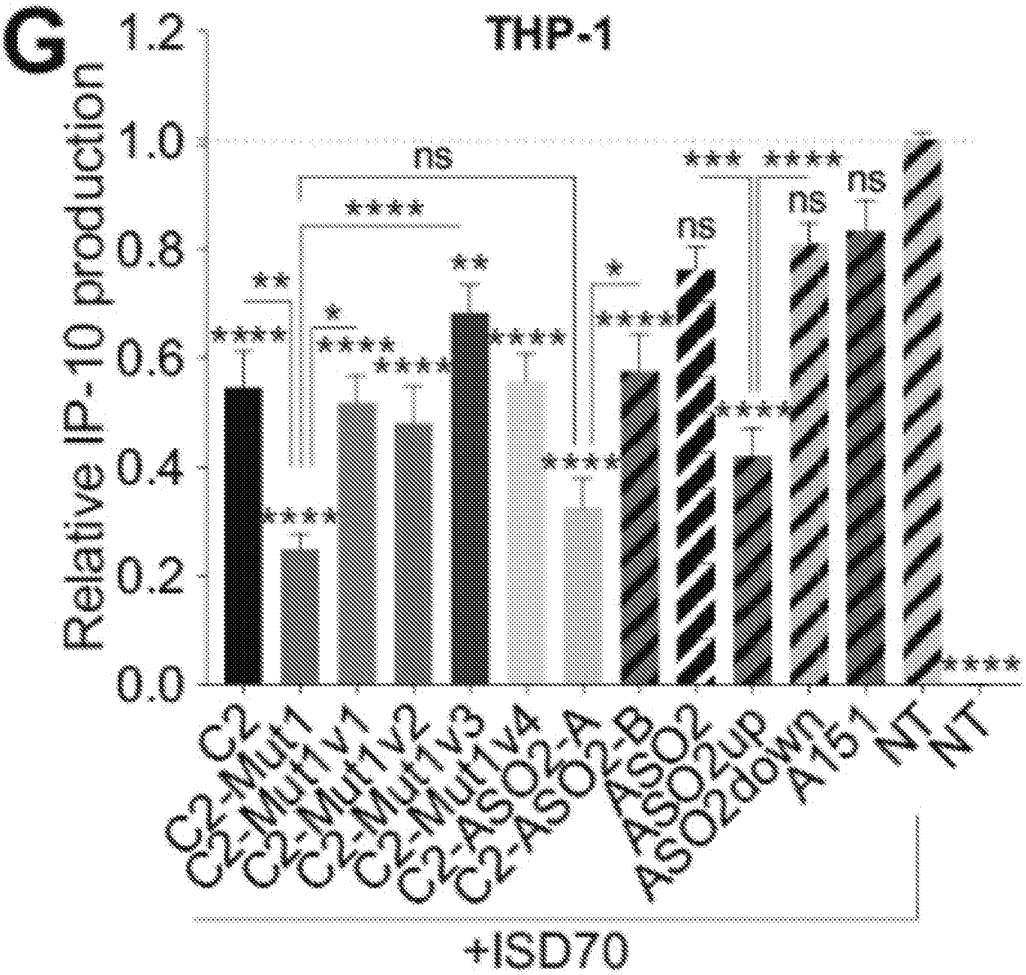
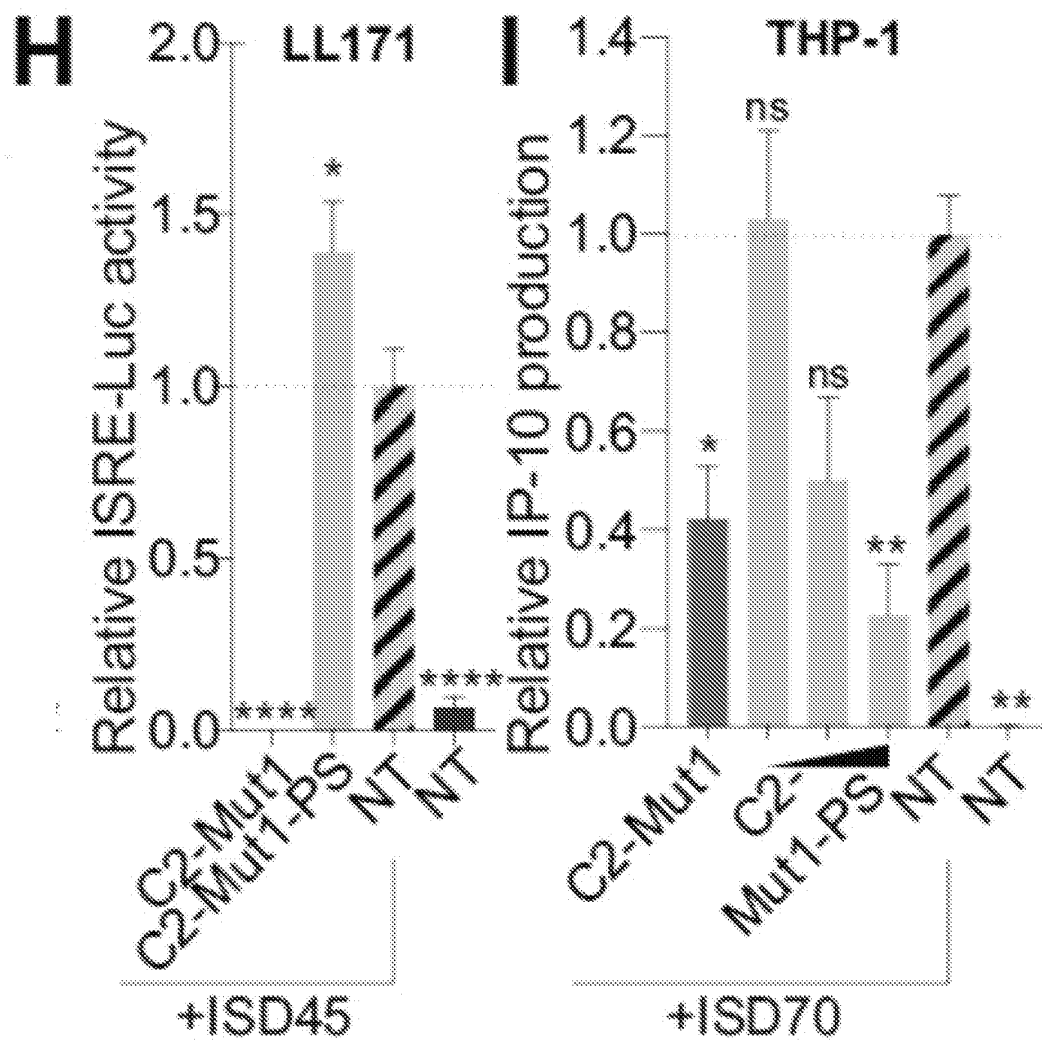


FIGURE 2G

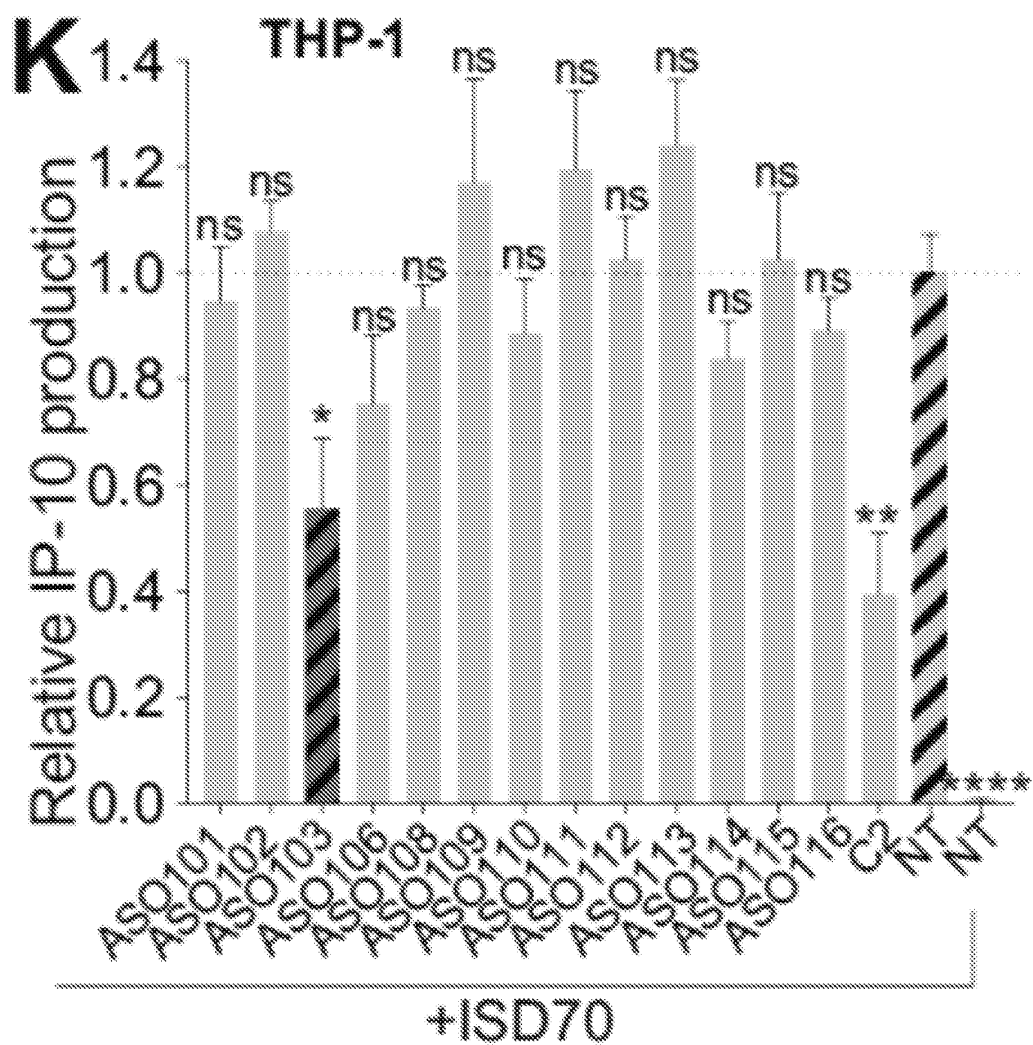
**FIGURES 2H & 2I**

J

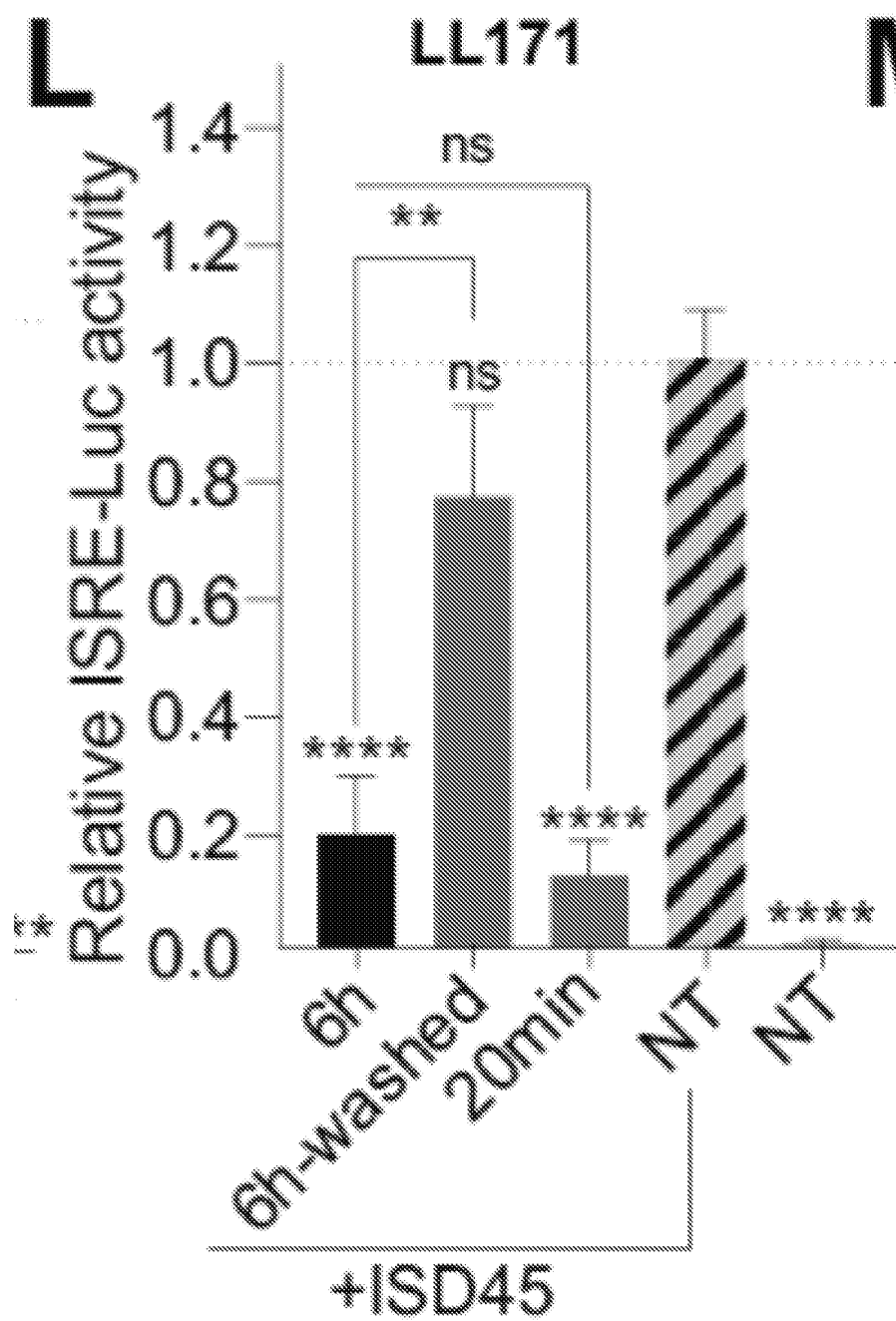
ASO101	UCCCATCCCTTCTGCUGCCA
ASO102	GUCCCATCCCTTCTGCUGCC
ASO103	<u>GGUCCCATCCCTTCTGCUGC</u>
ASO106	UCUGGTCCCATCCCTUCUGC
ASO108	UCUCUGGTCCCATCCCUUCU
ASO109	CUCUCTGGTCCCATCCCUUC
ASO110	UCUCUCTGGTCCCATCCCUU
ASO111	UUCUCTCTGGTCCCAUCCCU
ASO112	CUUCUCTCTGGTCCCAUCCC
ASO113	CCUUCTCTCTGGTCCCAUCC
ASO114	CCCUUCTCTCTGGTCCCAUC
ASO115	ACCCUTCTCTCTGGTCCCAU
ASO116	CACCCTTCTCTCTGGUCCCA

FIGURE 2J

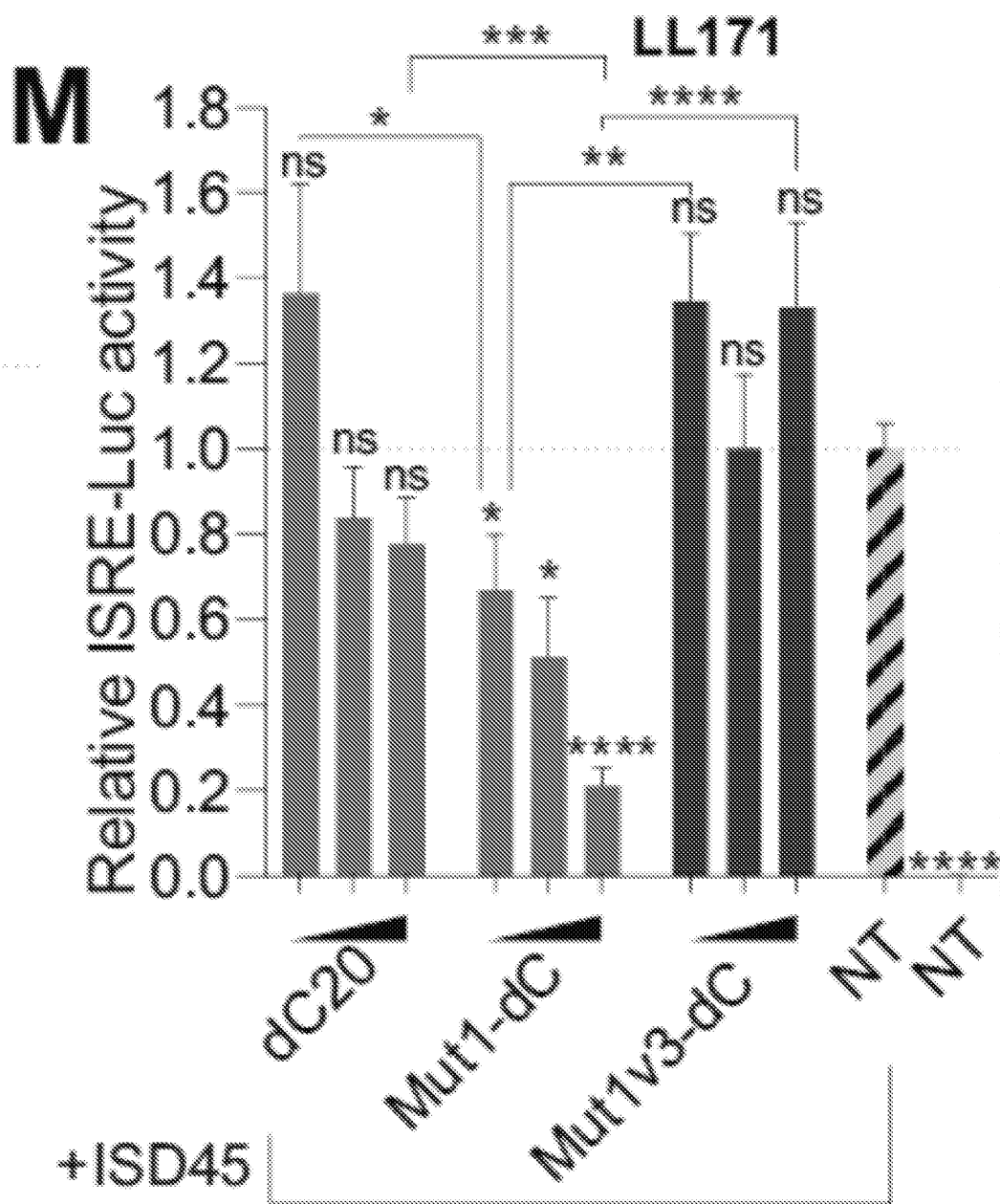
16/100

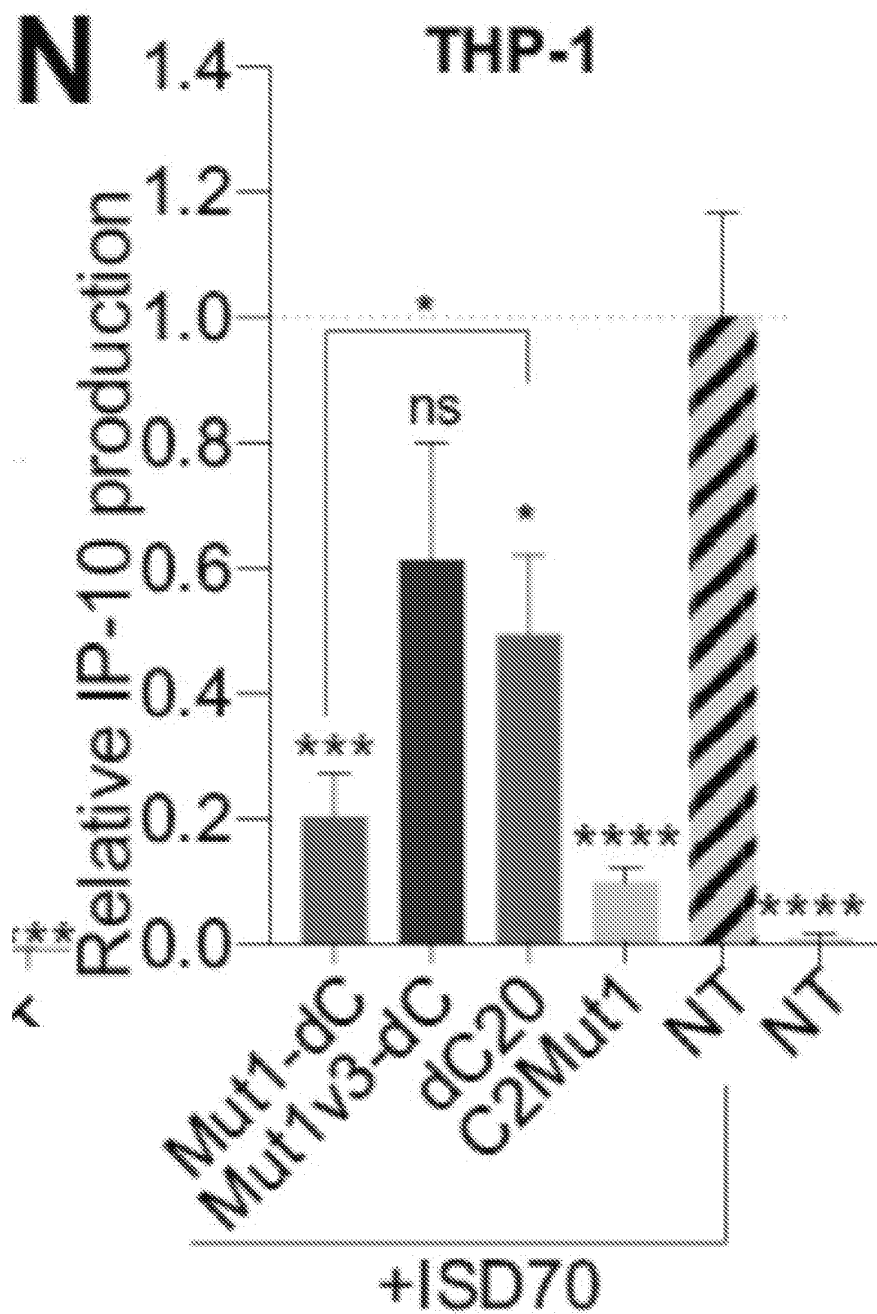
**FIGURE 2K**

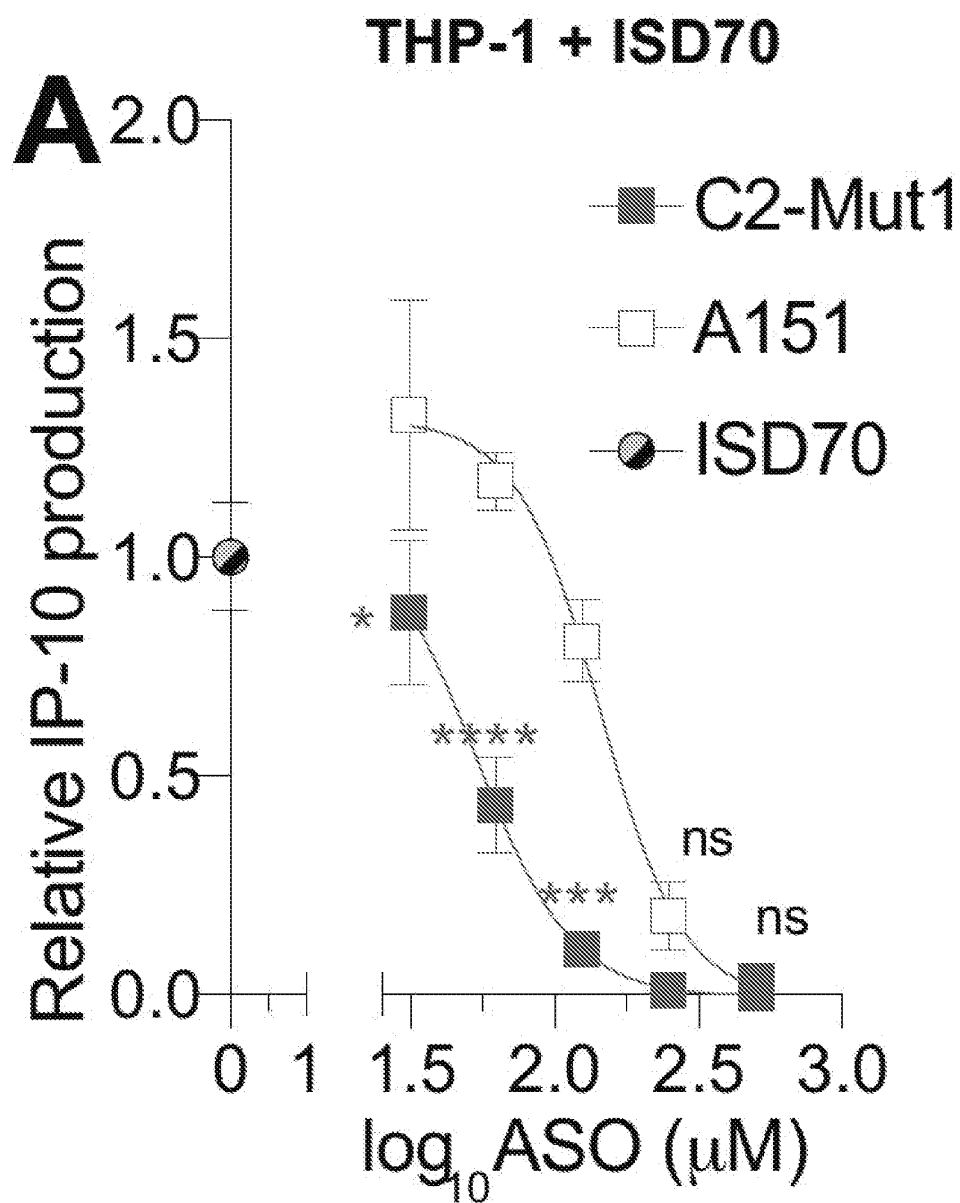
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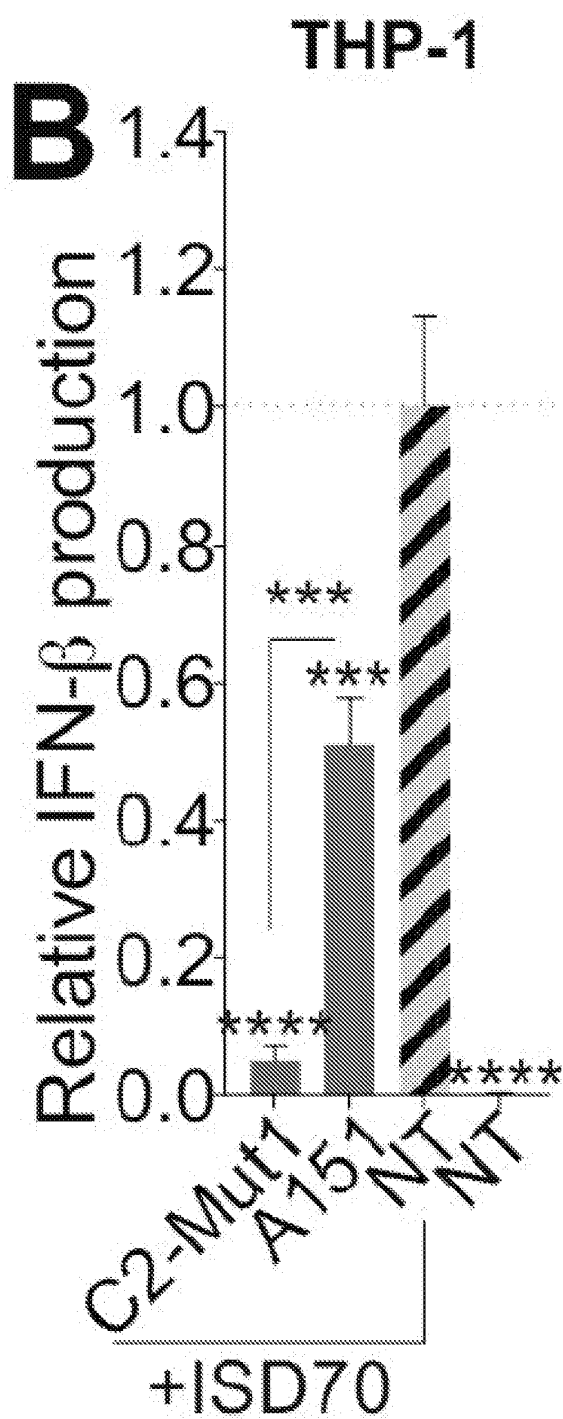
**FIGURE 2L**

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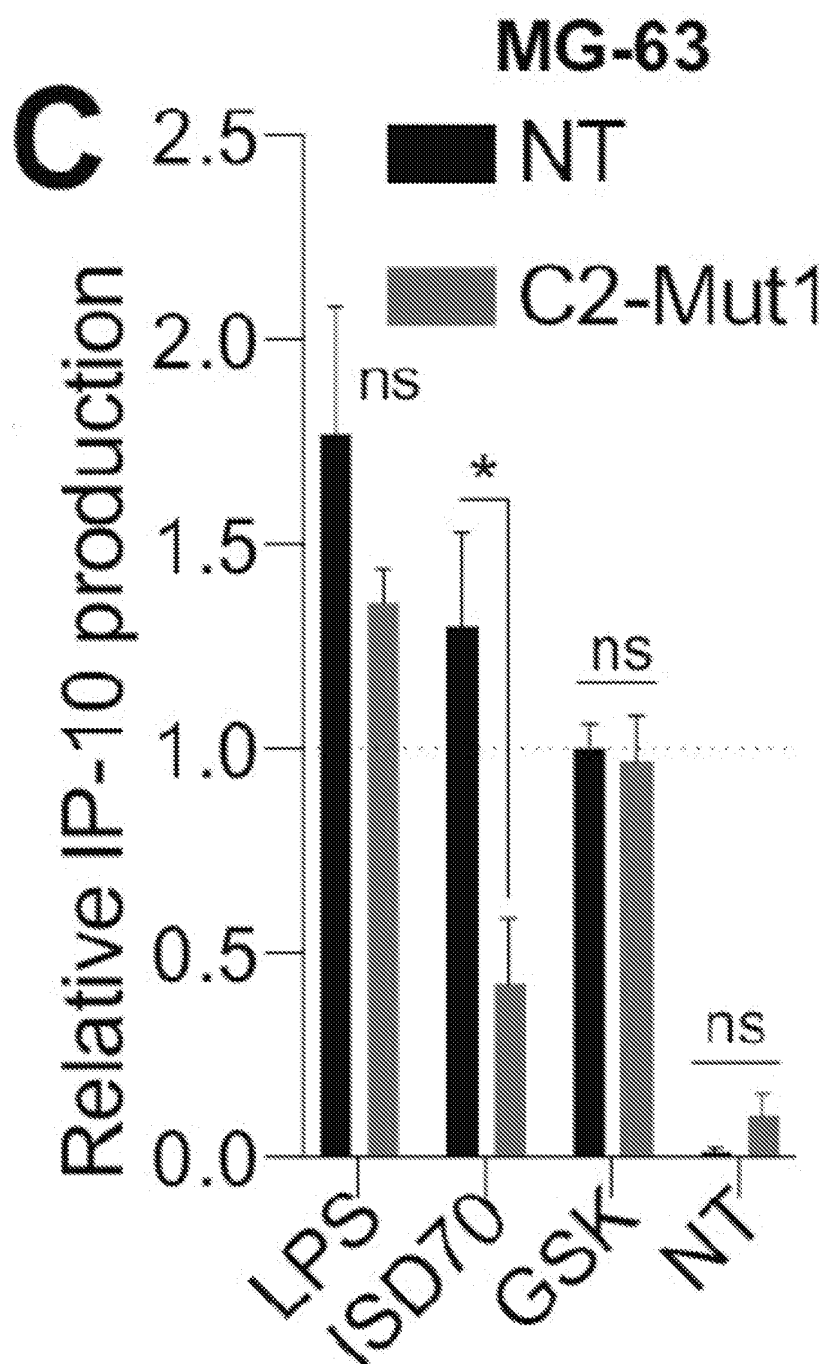
**FIGURE 2M**

**FIGURE 2N**

**FIGURE 3A**

**FIGURE 3B**

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**FIGURE 3C**

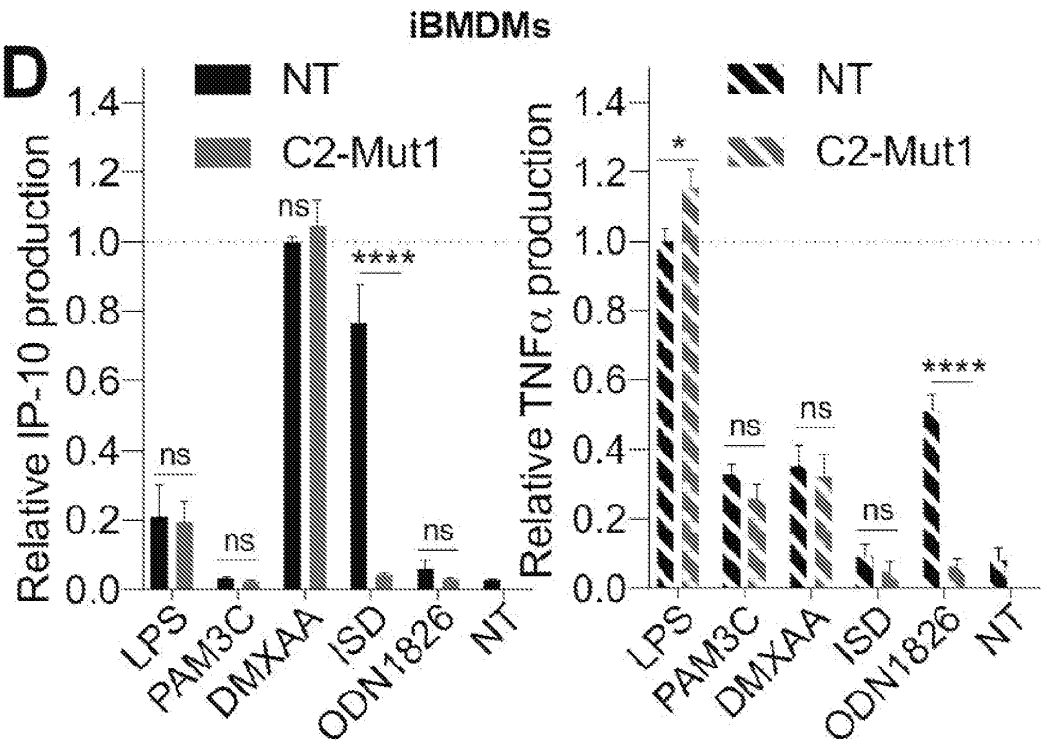
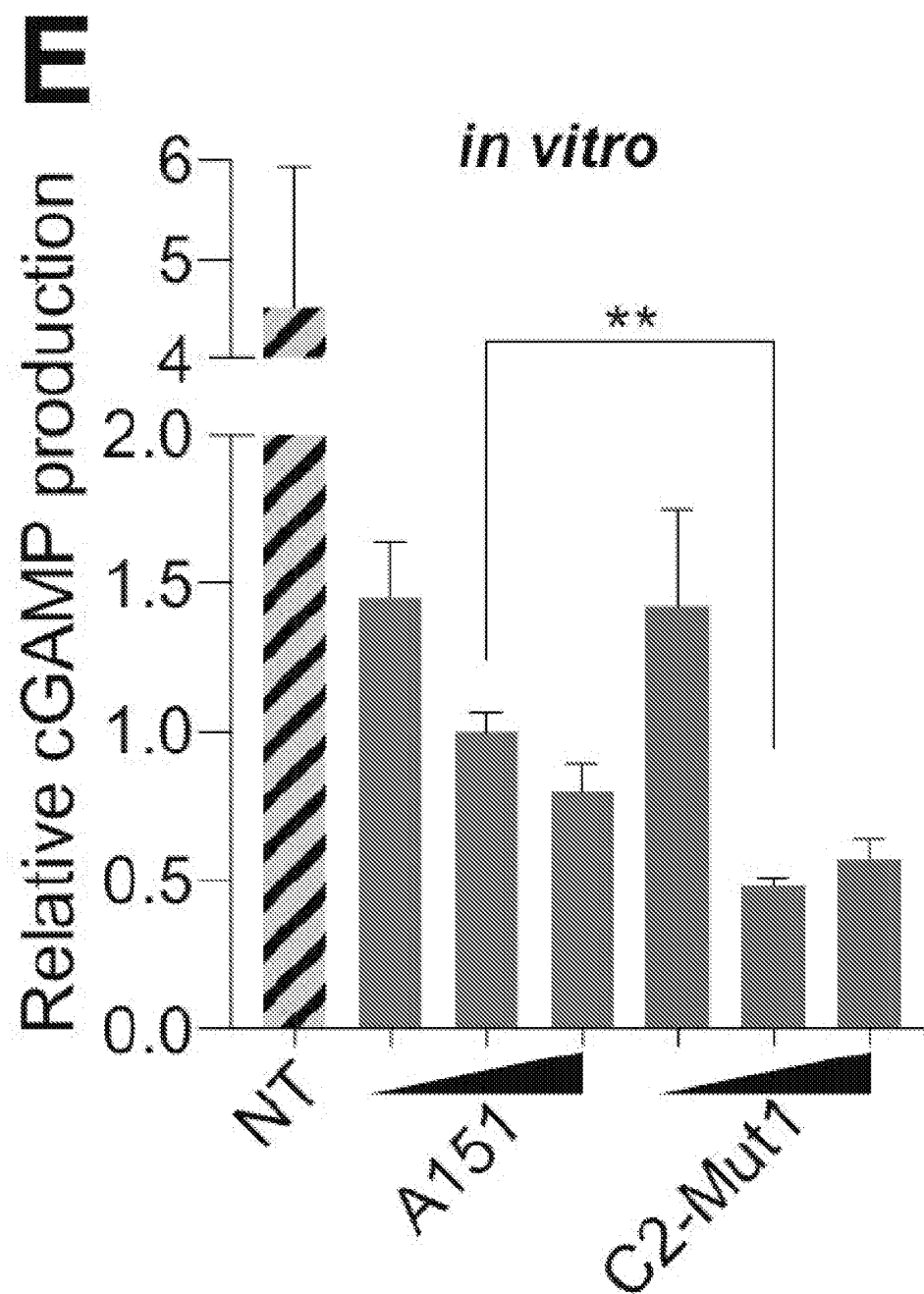


FIGURE 3D

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**FIGURE 3E**

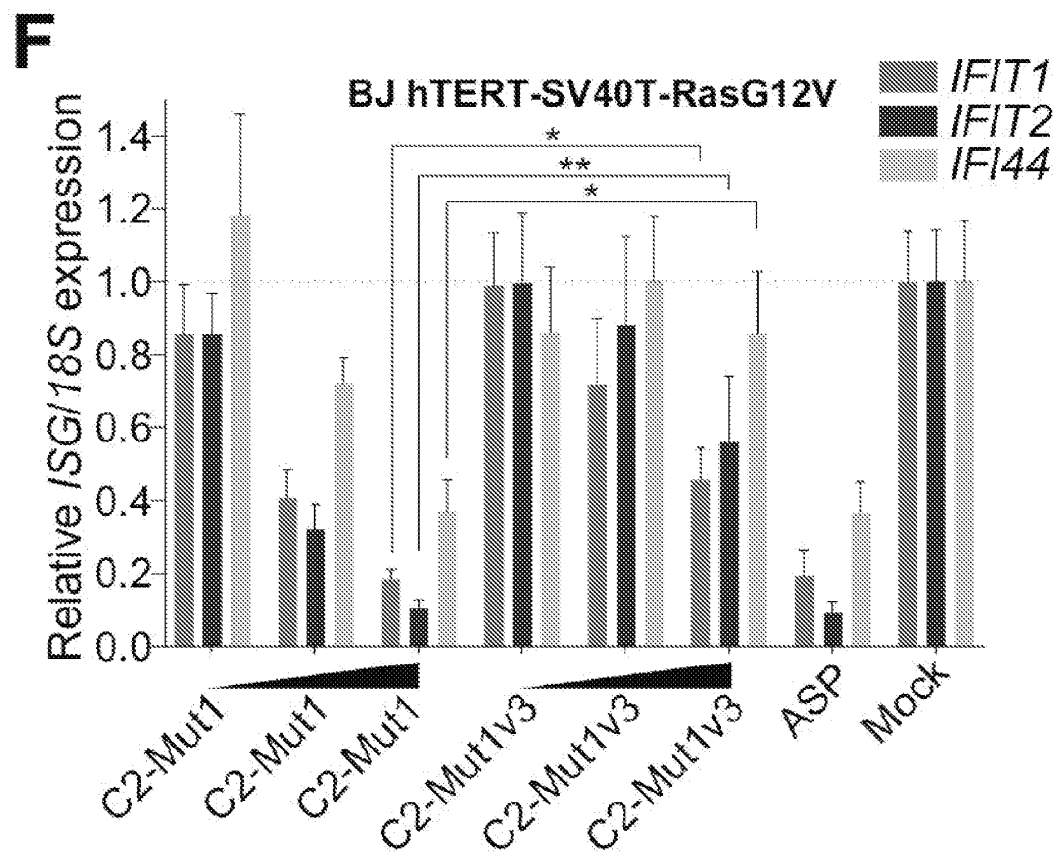
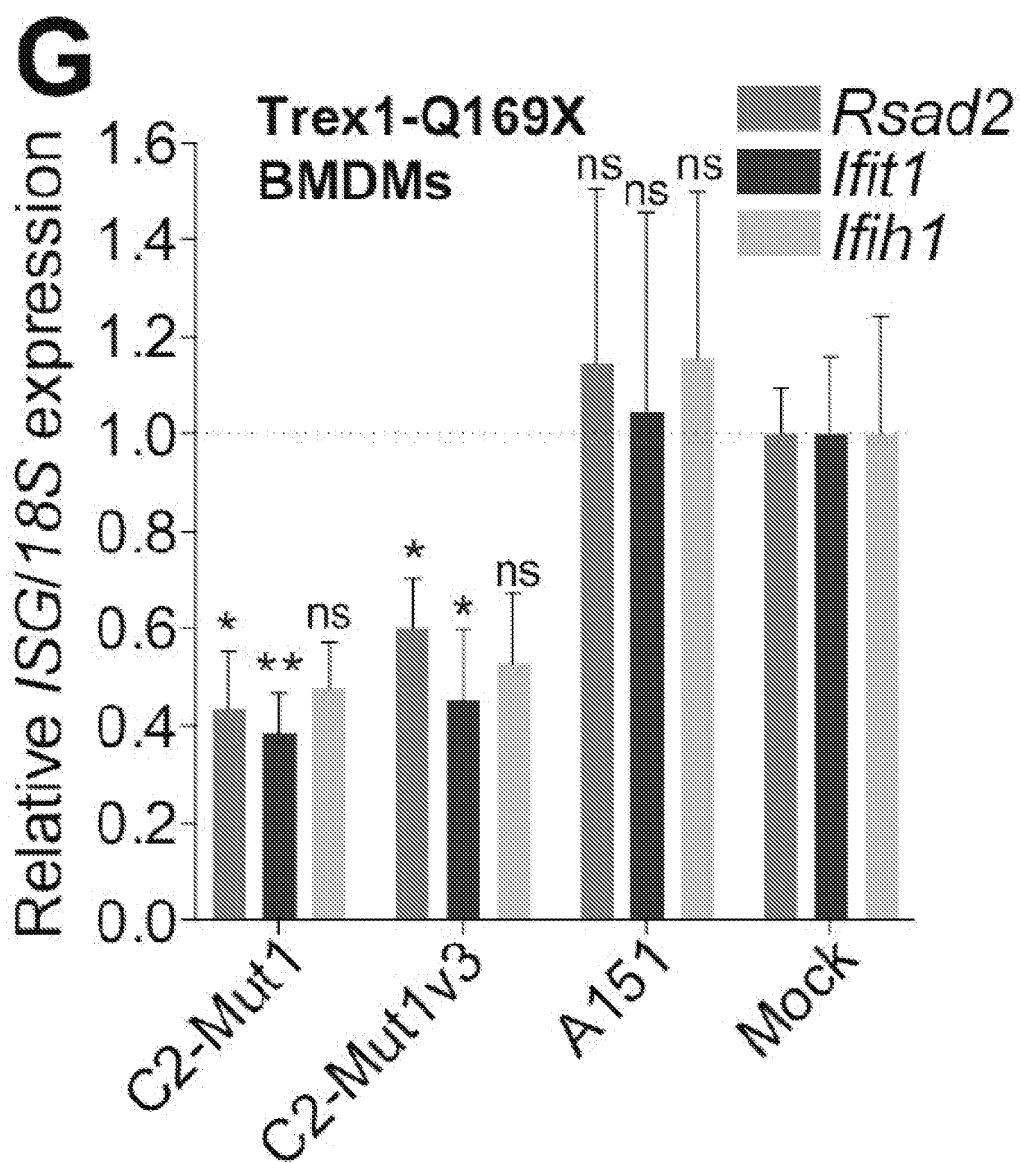
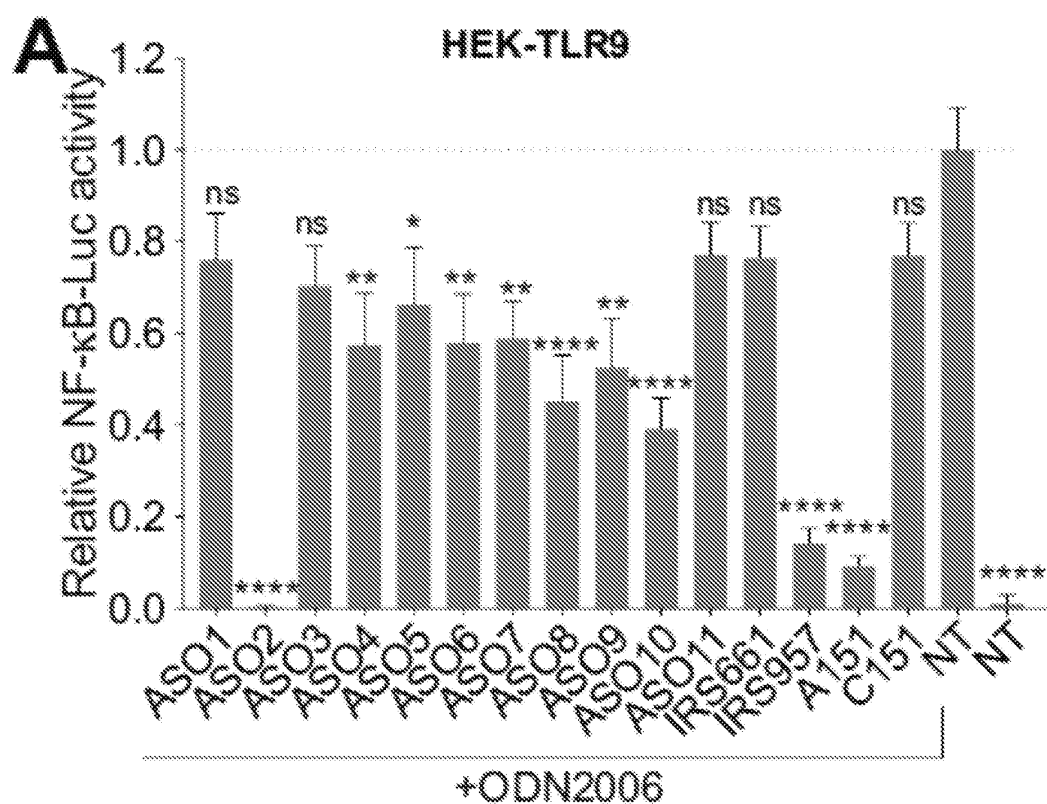


FIGURE 3F

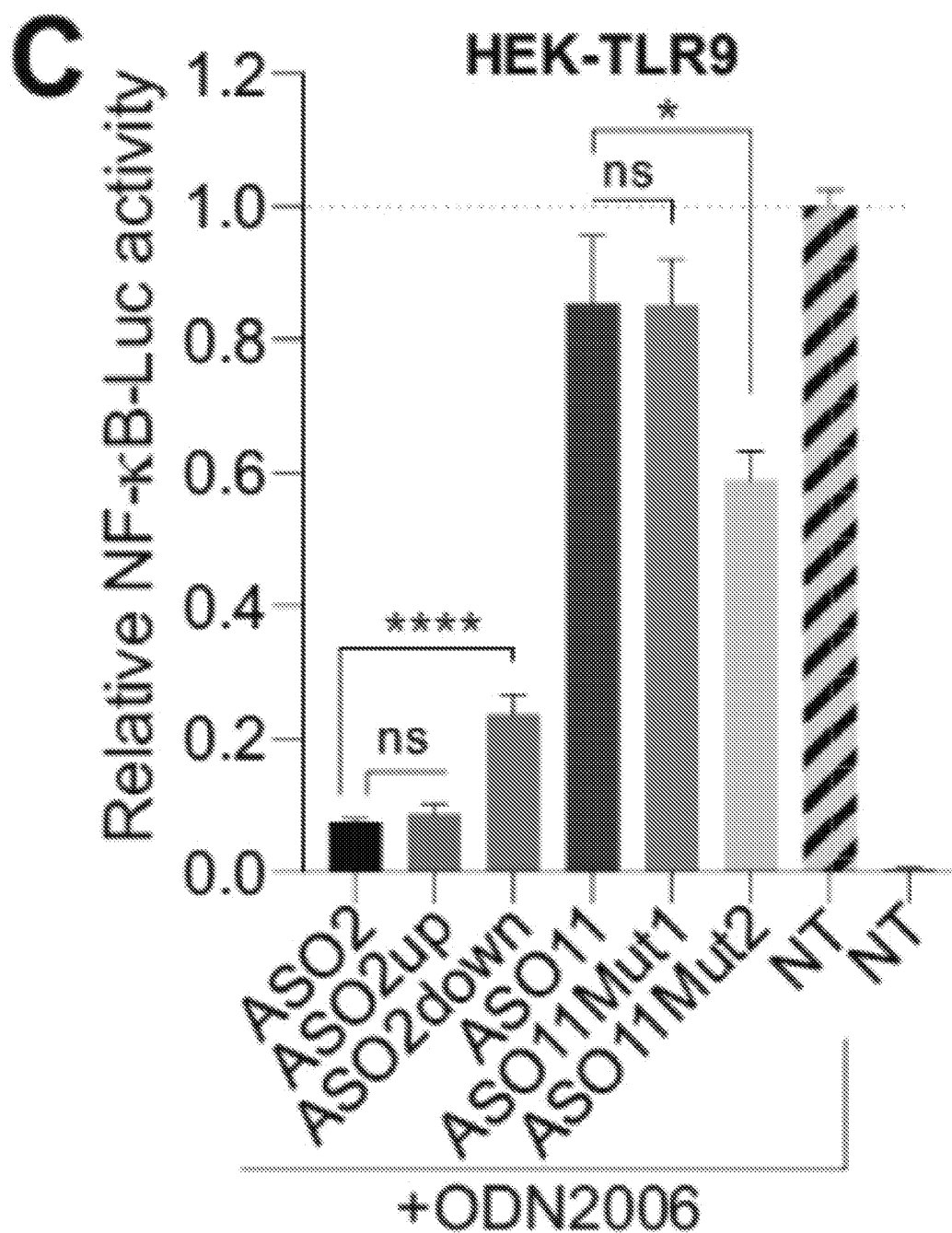
**FIGURE 3G**

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**B**

ASO2	<u>UCCGGCCTCGGAAGCUCUCU</u>
ASO2up	UCCGGCCTCGGAGTCUCCA
ASO2down	UCCGGCCTCGGAGAUUAUCG
ASO11	CUUUAGTCGTAGTTGCUUCC
ASO11Mut1	CUUUAGTCGTAGTTG <u>UCUCU</u>
ASO11Mut2	<u>UCCGGGTCGTAGTTGCUUCC</u>

FIGURES 4A & 4B

**FIGURE 4C**

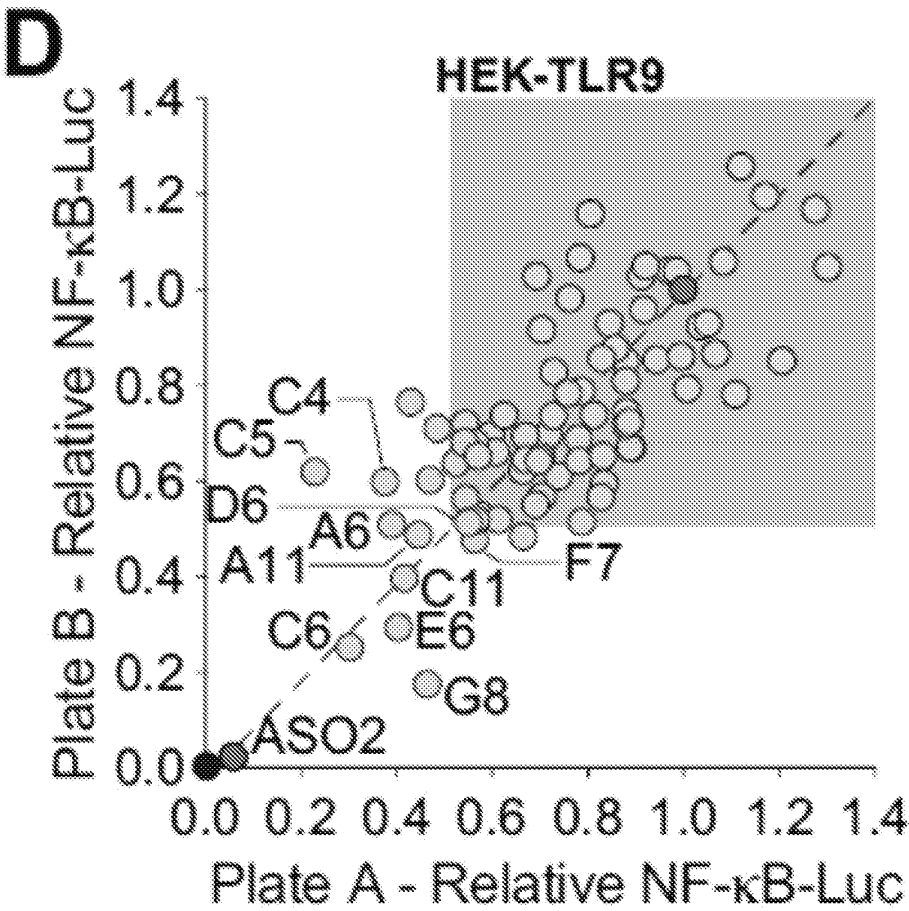


FIGURE 4D

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E

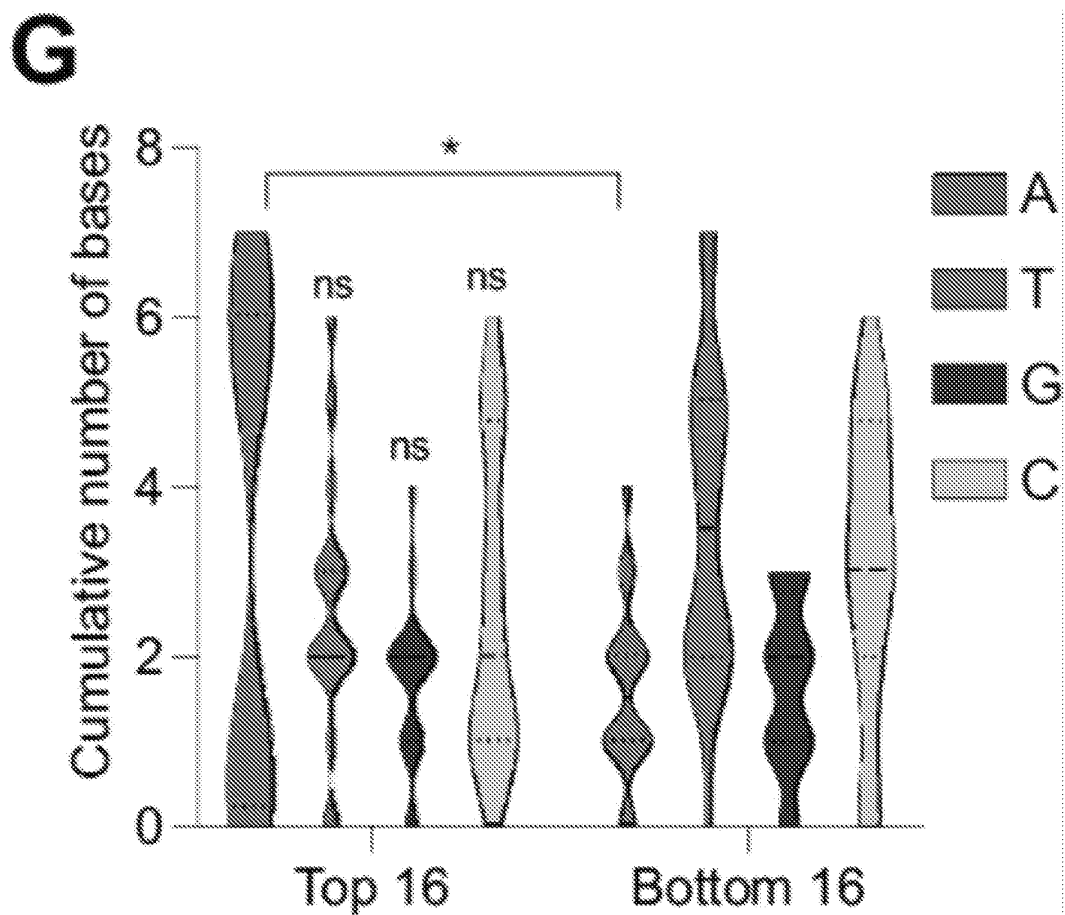
A6 GAU UAAAACAGATTA AUACA
C6 GGAU UAAAACAGATTA AUAC
E6 CUU GUGAAAAGATTA UCUUC
C5 CC UAGAAAGAAGCA AAGAUU
D6 AA UUUAAAGCATGA AUAUUA

**F**

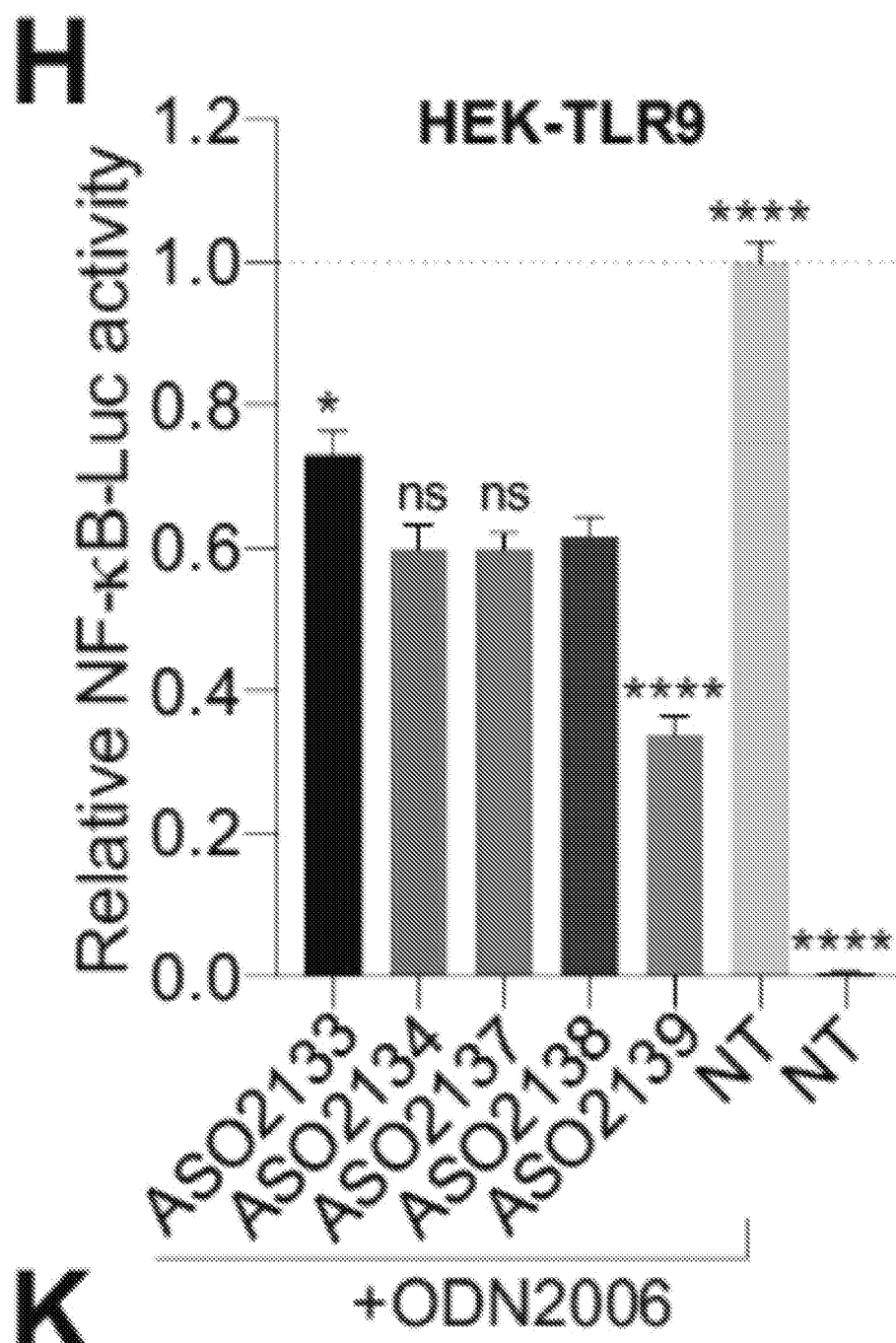
ASO2 TCC GGCCTC GGAAGCTCTC
C4 CCATGTCCCA GGCCTC CAGT
C11 TT GGCCTG TGGATGCTTT
A11 AAATGTCCTG GCCCTC ACTG

FIGURES 4E & 4F

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**FIGURE 4G**

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**FIGURE 4H**

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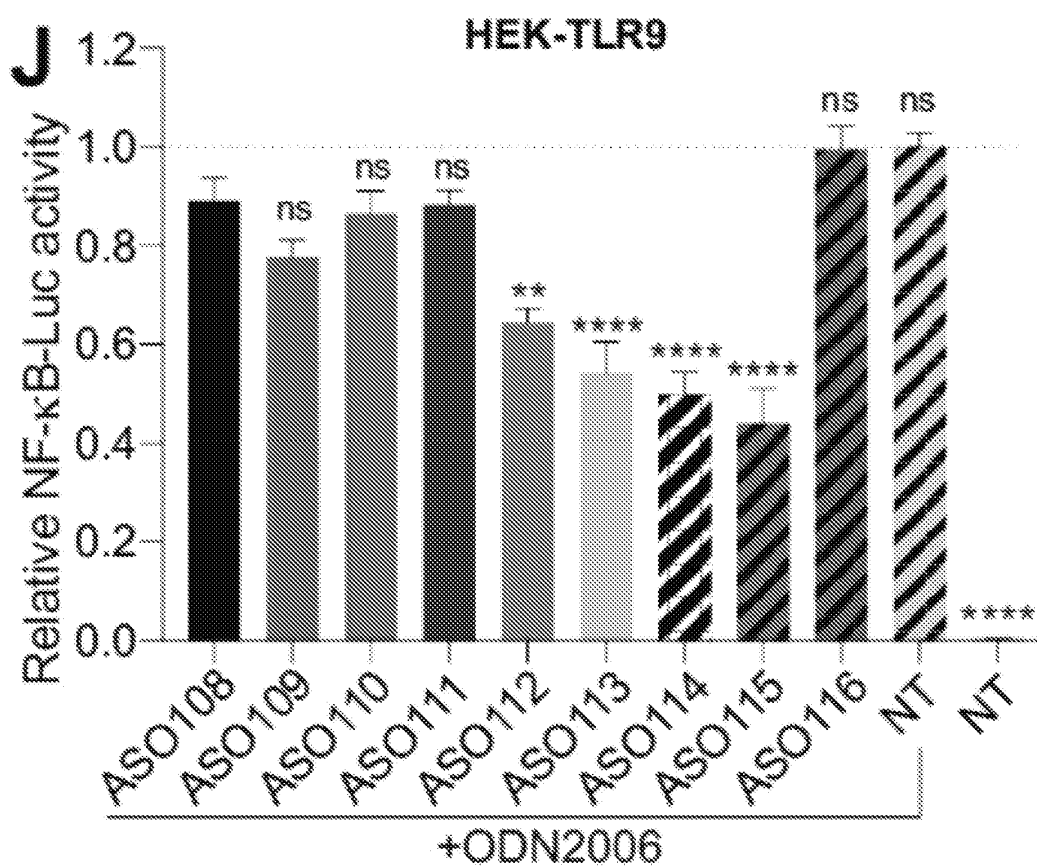
I

ASO2133 AAAAGATTATCTTCTUUUAA
ASO2134 GAAAAGATTATCTTUUUUA
ASO2137 UGUGAAAAGATTATCUUCUU
ASO2138 UUGUGAAAAGATTATCUUCU
ASO2139 CUUGUGAAAAGATTACUUC

ASO108 UCUCUGGTCCCATCCCUUCU
ASO109 CUCUCTGGTCCCATCCCUUC
ASO110 UCUCUCTGGTCCCATCCCUU
ASO111 UUCUCTCTGGTCCCAUCCCU
ASO112 CUUCUCTCTGGTCCCAUCCC
ASO113 CCUUCTCTCTGGTCCCAUCC
* ASO114 CCCUUCTCTCTGGTCCCAUC
ASO115 ACCCUTCTCTCTGGTCCCAU
ASO116 CACCCTTCTCTCTGGUCCCA

FIGURE 4I

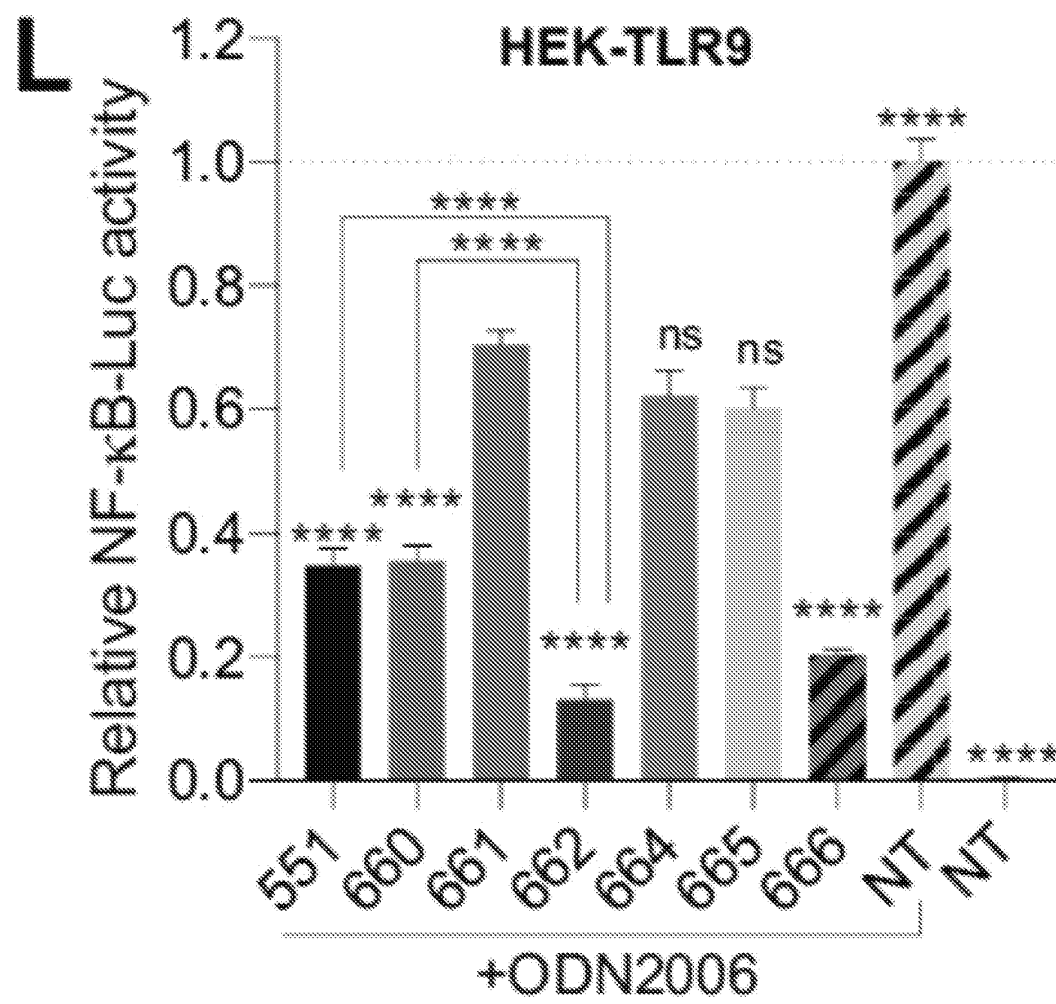
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**K**

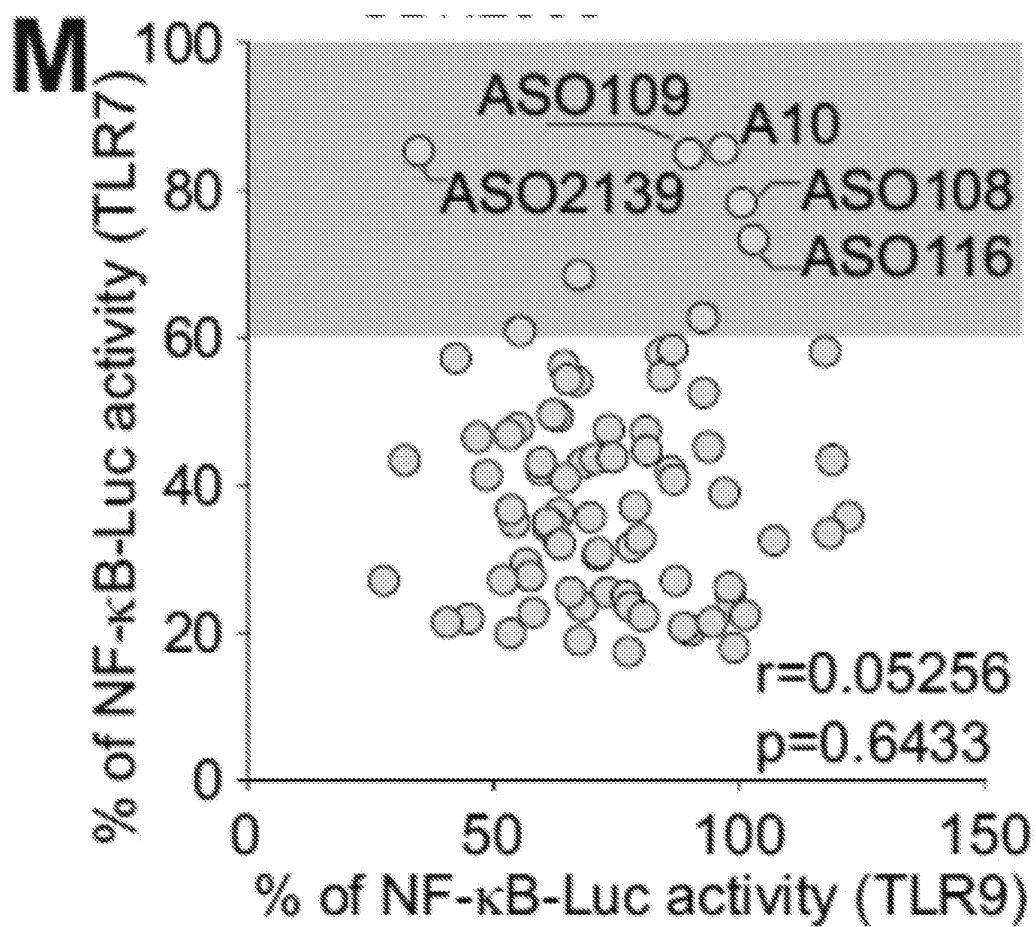
HPRT551	CUUCCACAATCAAGACAUUC
HPRT660	CUUCGTGGGGGTCCTTUUCAC
HPRT661	ACUUCGTGGGGGTCCTFUUCA
HPRT662	CACUUCGTGGGGGTCUUUUC
HPRT664	AACACTTCGTGGGGGTCUUU
HPRT665	CAACACTTCGTGGGGGUCCU
HPRT666	CCAACACTTCGTGGGGGUCCU

FIGURES 4J & 4K

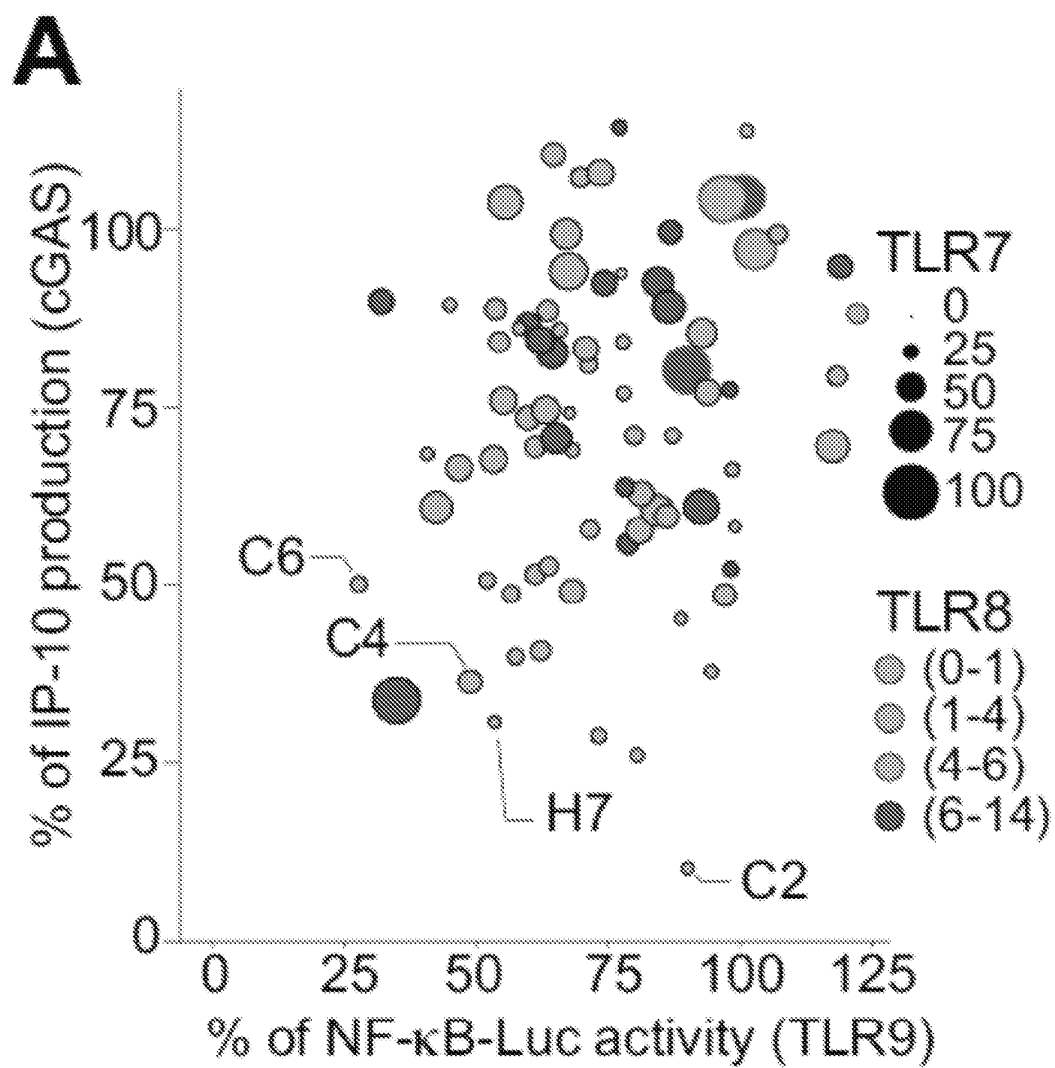
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**FIGURE 4L**

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**FIGURE 4M**

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**FIGURE 5A**

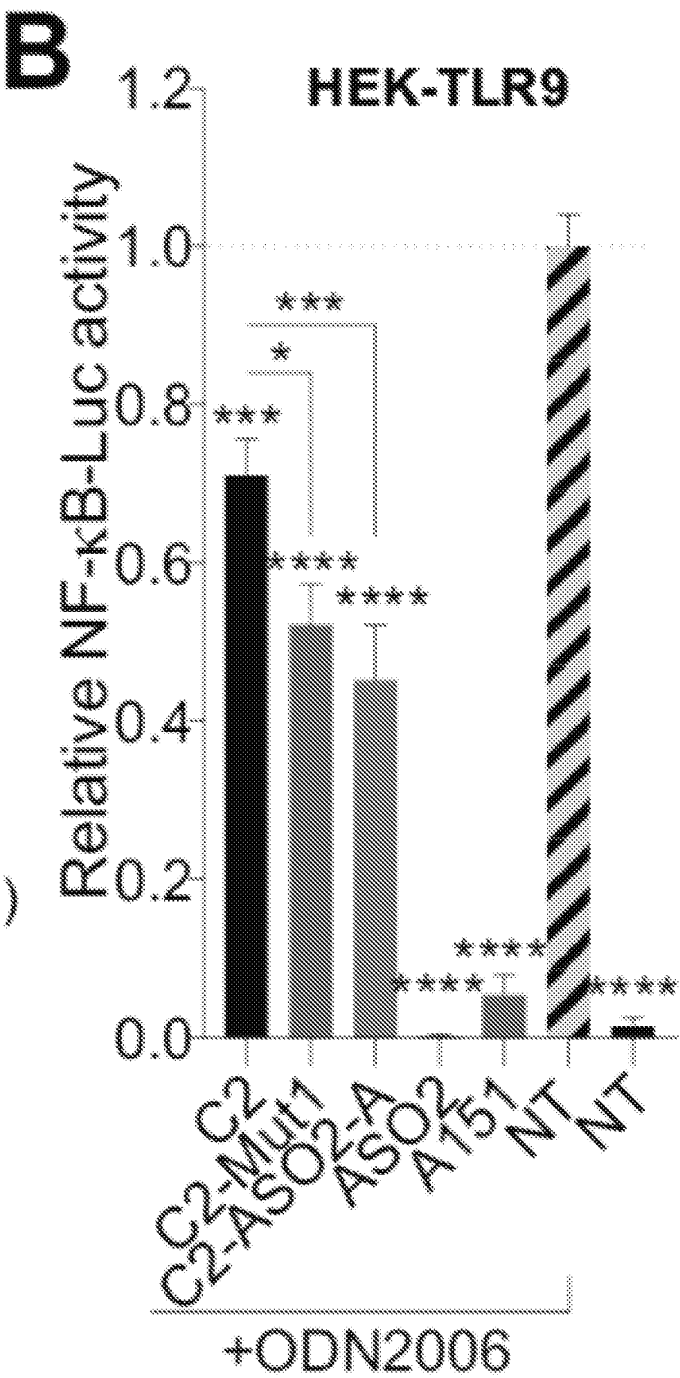
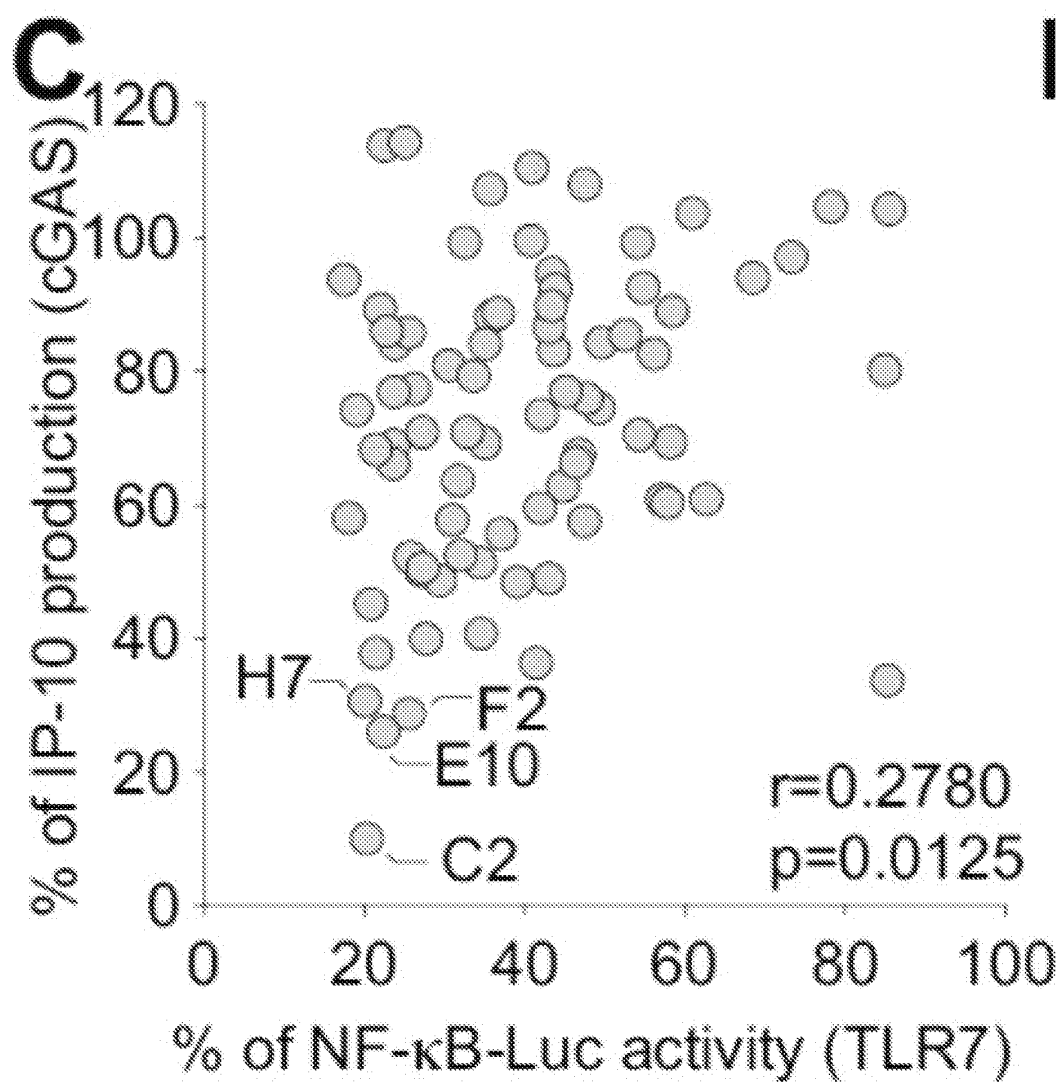
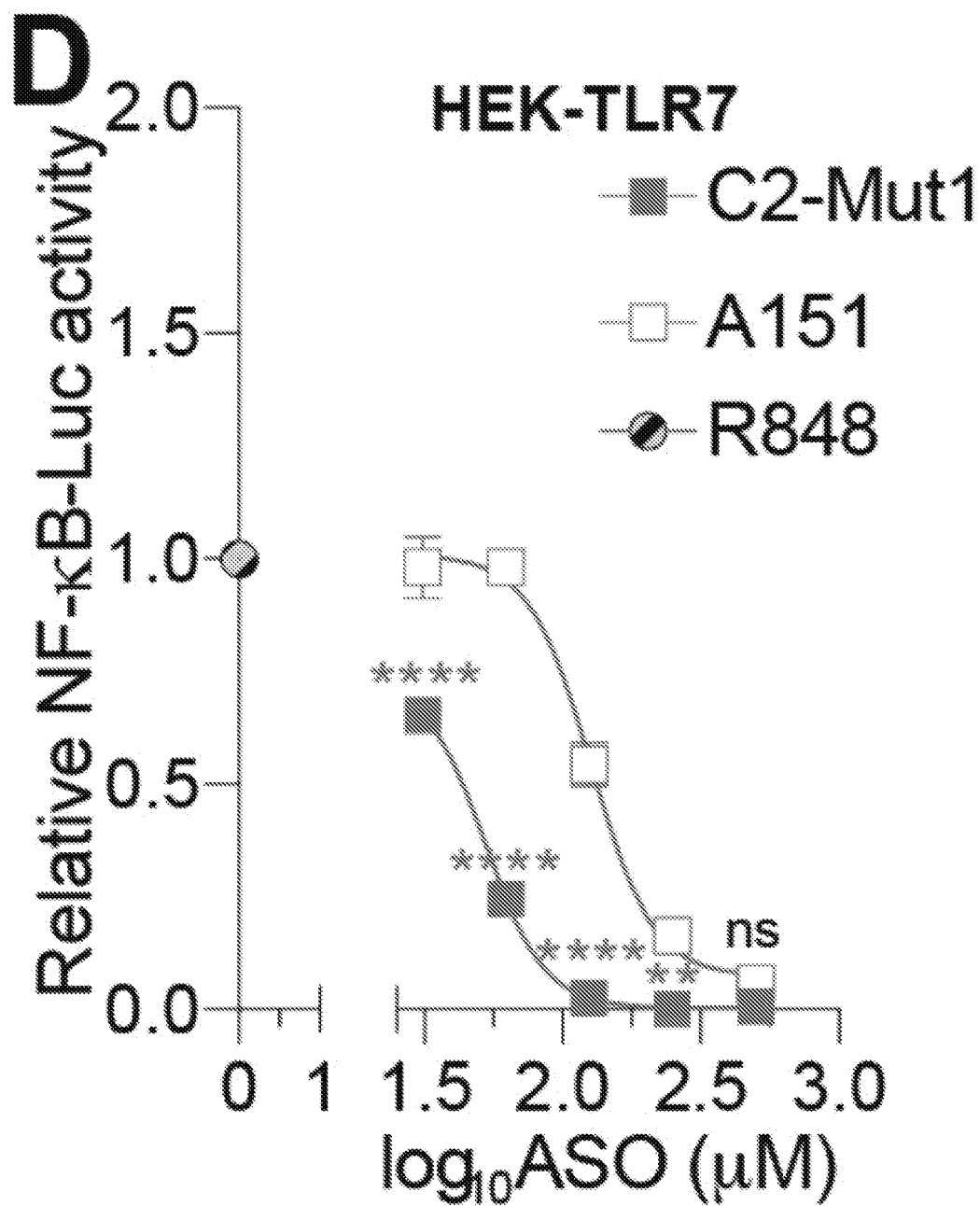


FIGURE 5B

**FIGURE 5C**

**FIGURE 5D**

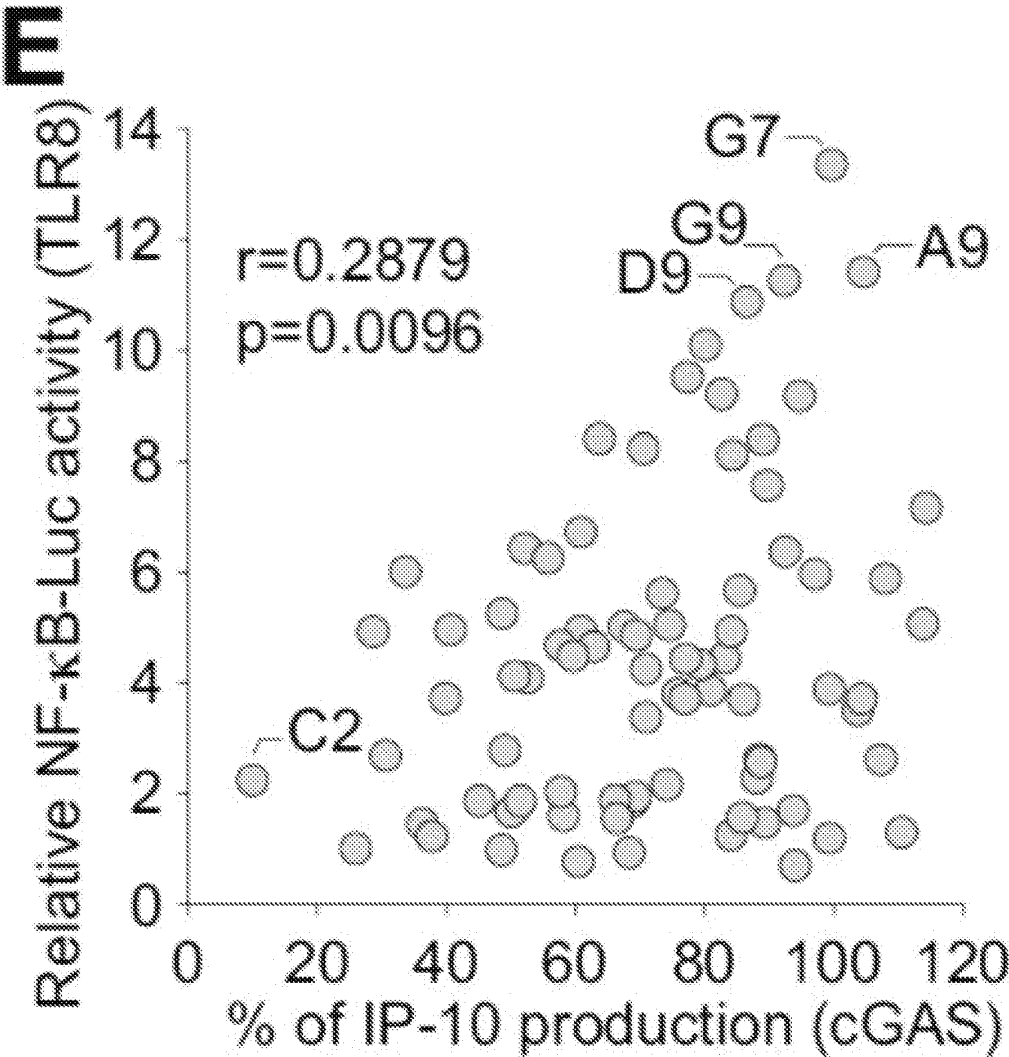
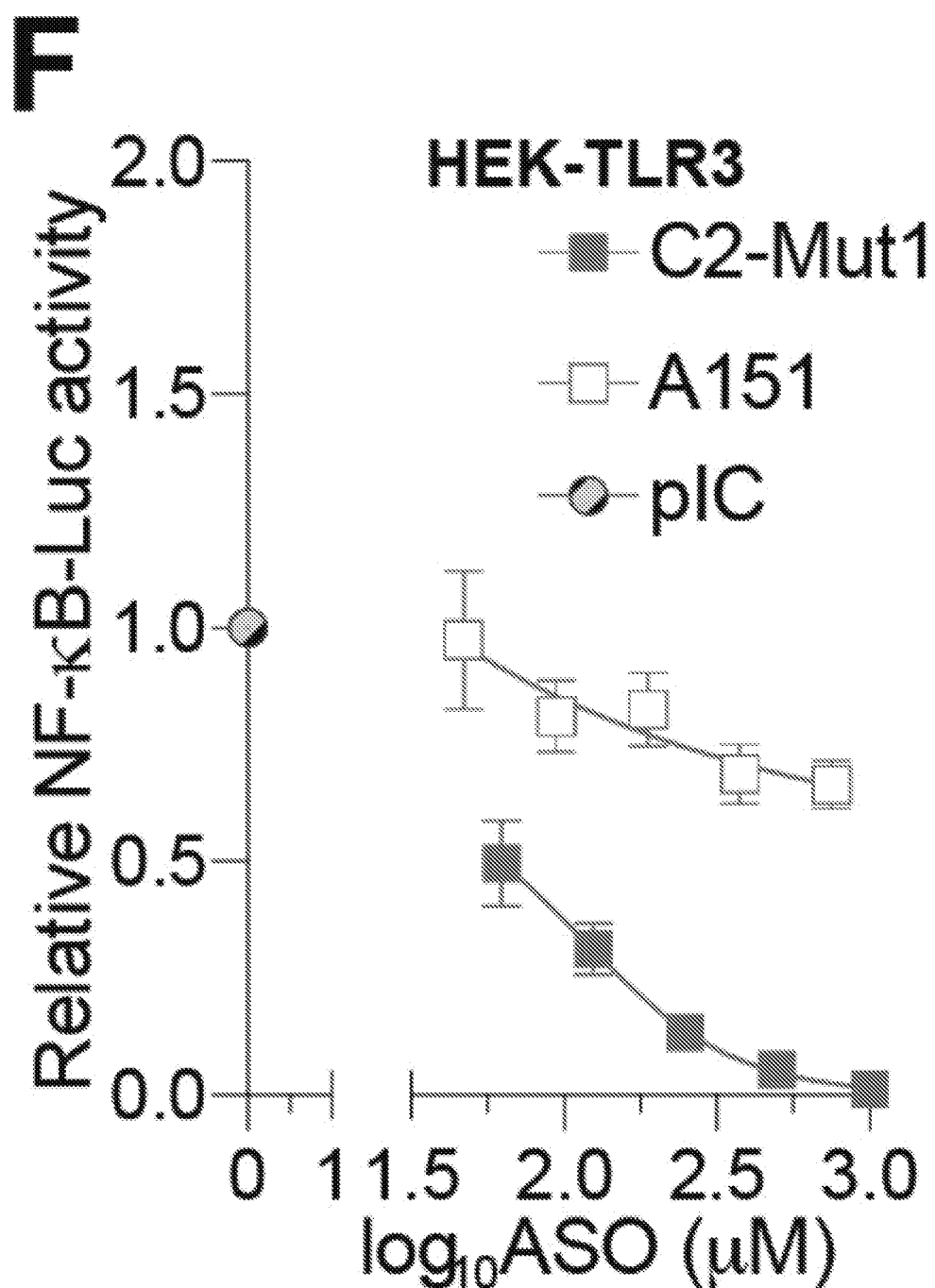
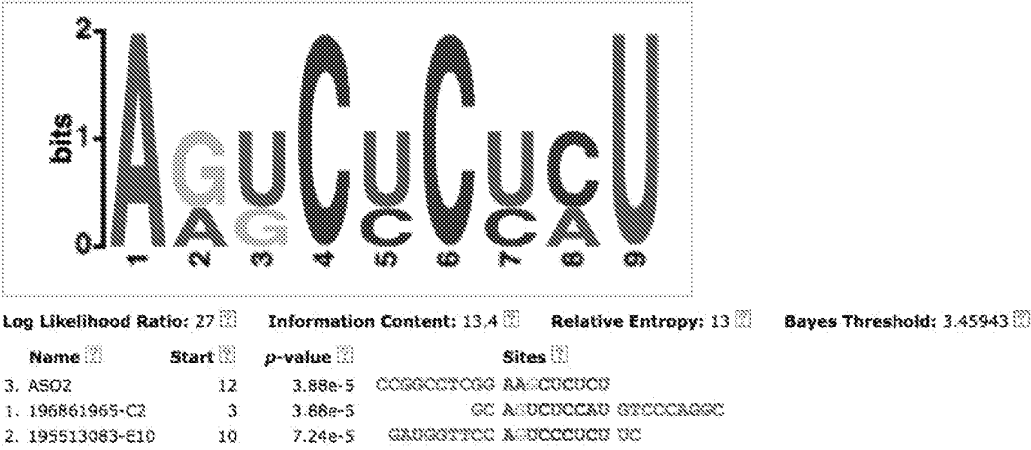


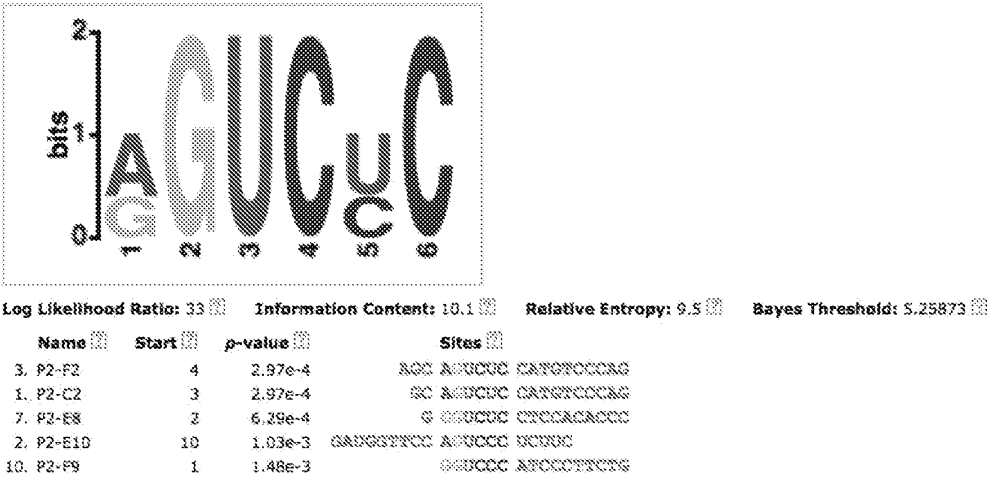
FIGURE 5E

**FIGURE 5F**

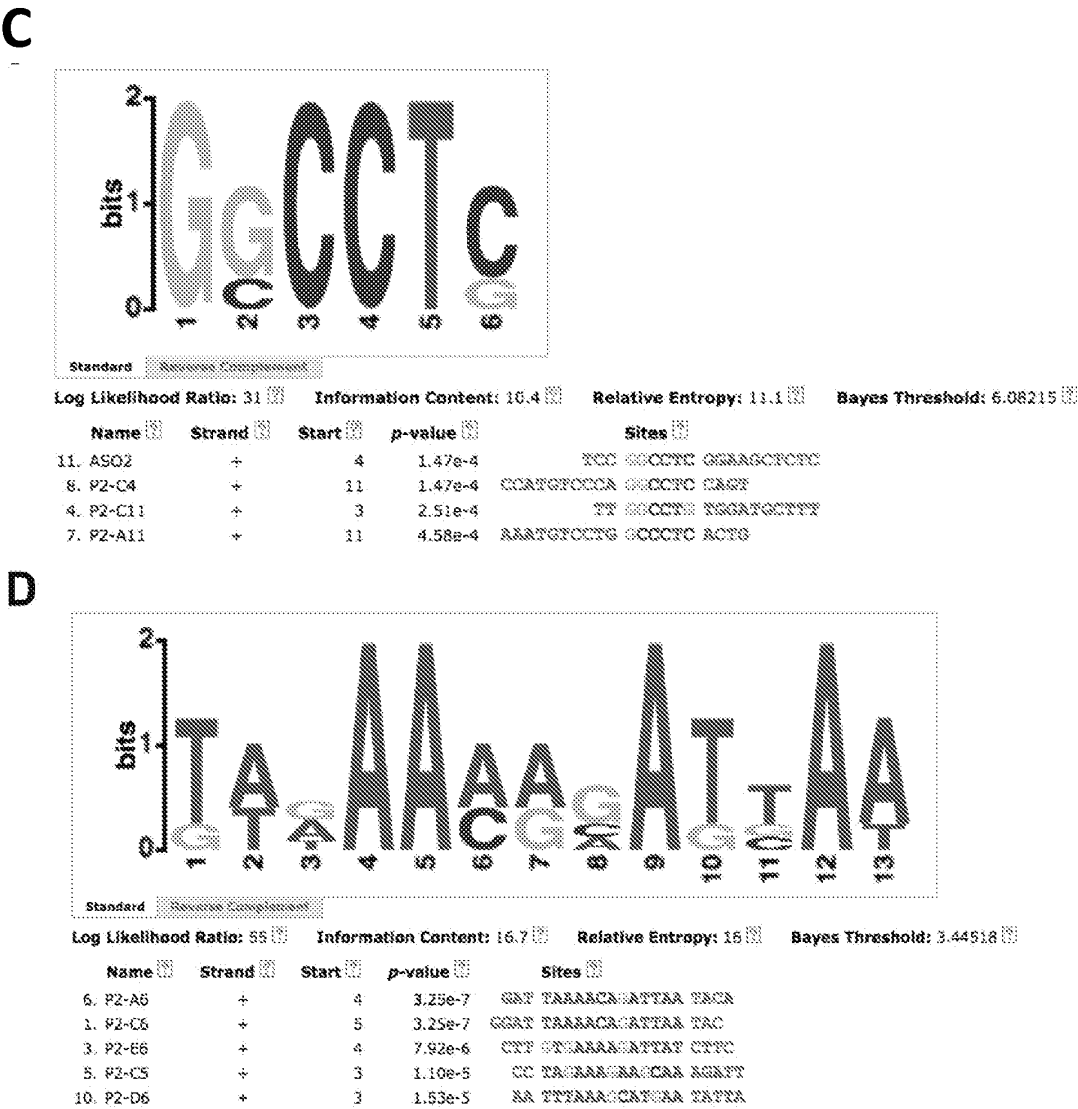
A



B



FIGURES 6A & 6B



FIGURES 6C & 6D

E

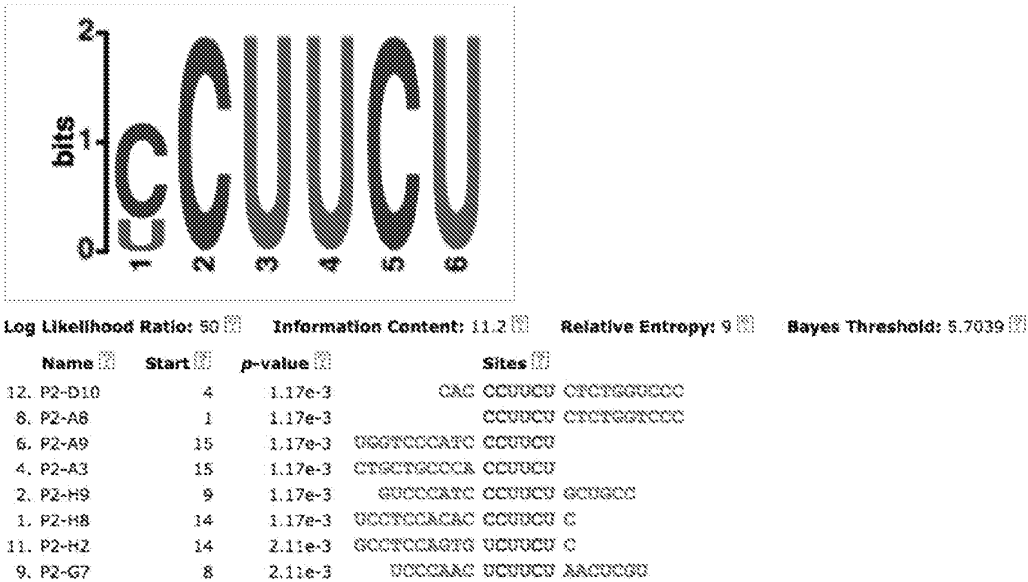
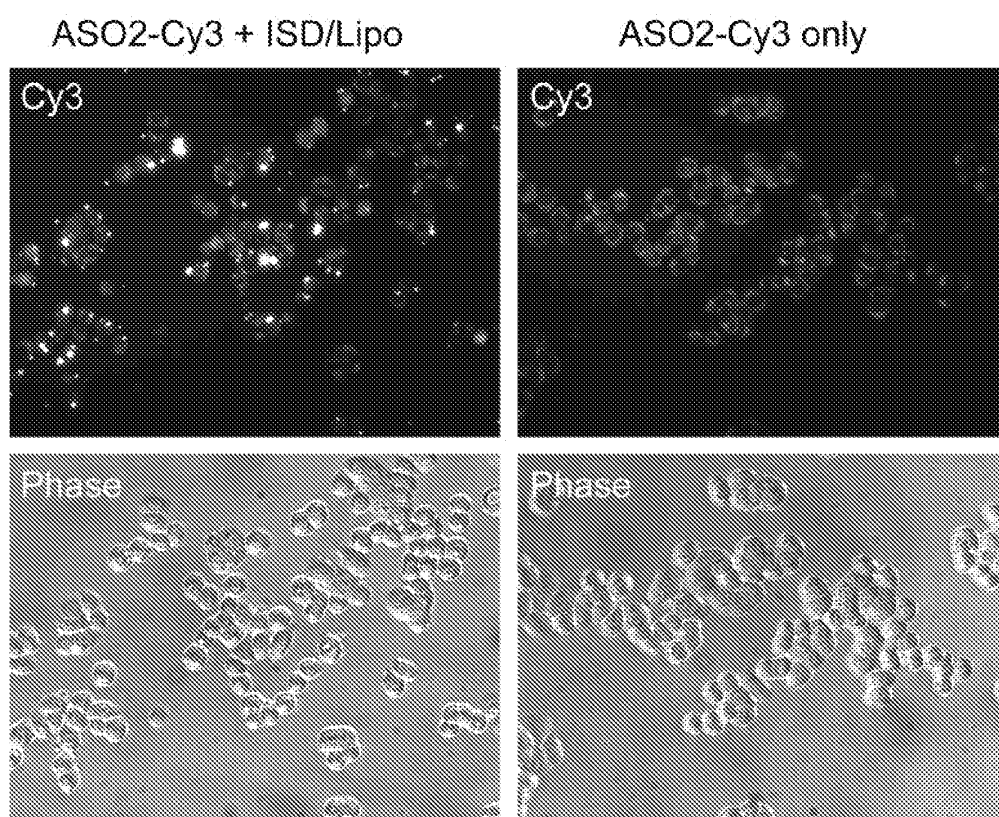
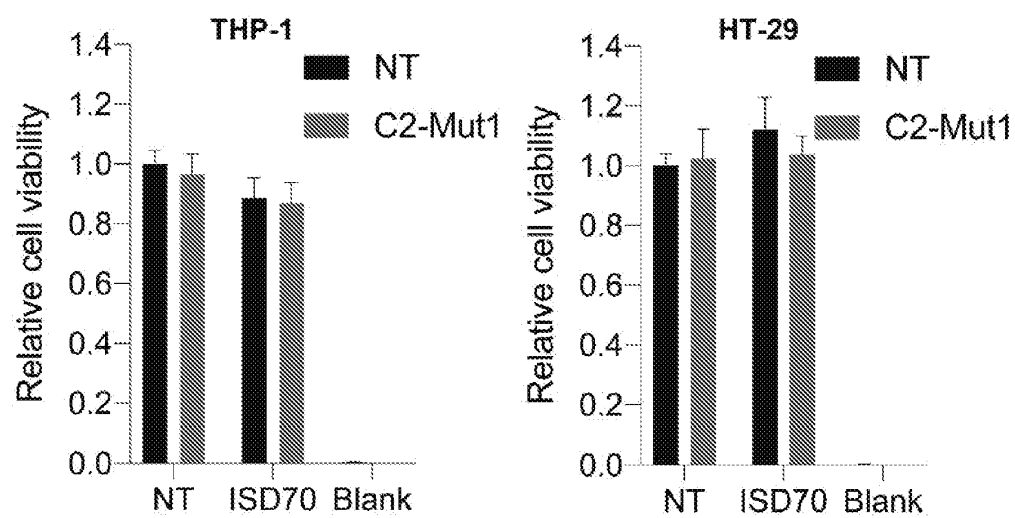


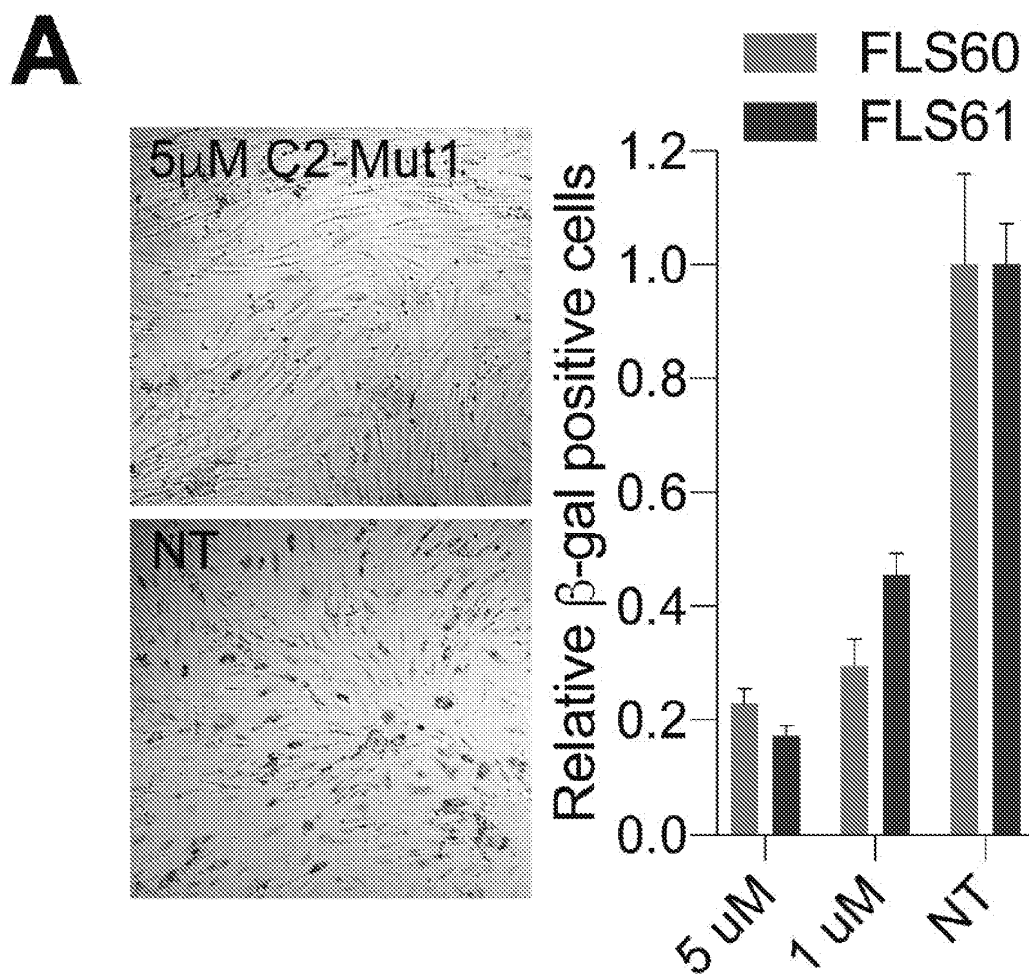
FIGURE 6E

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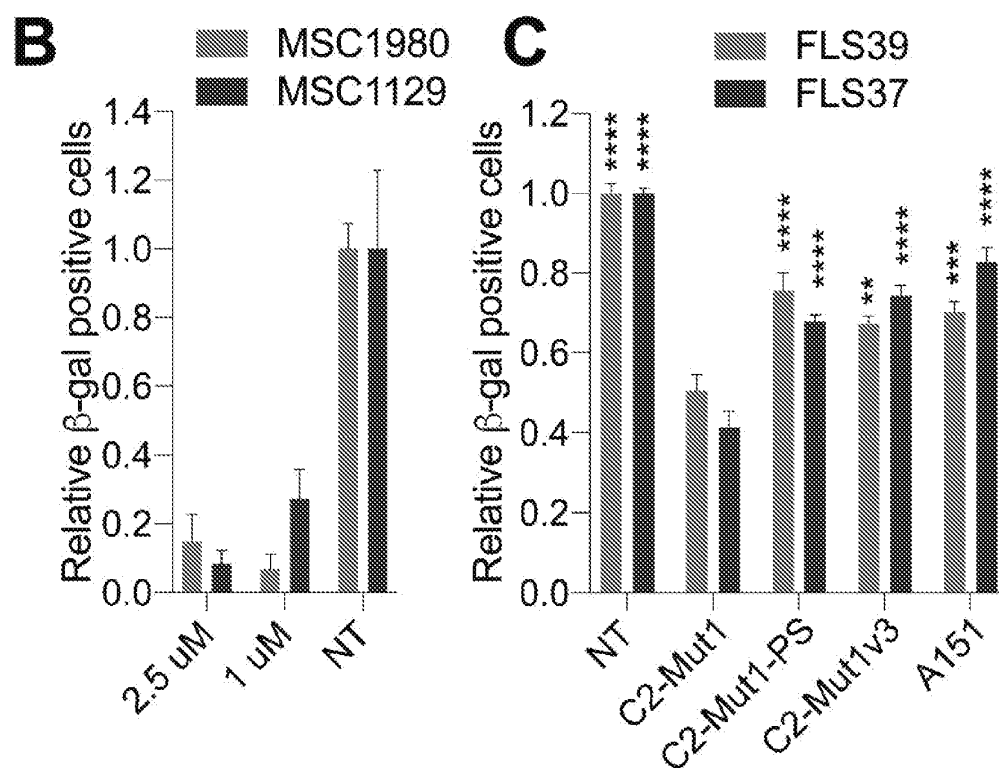
**FIGURE 7**

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**FIGURE 8**

**FIGURE 9A**

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**FIGURES 9B & 9C**

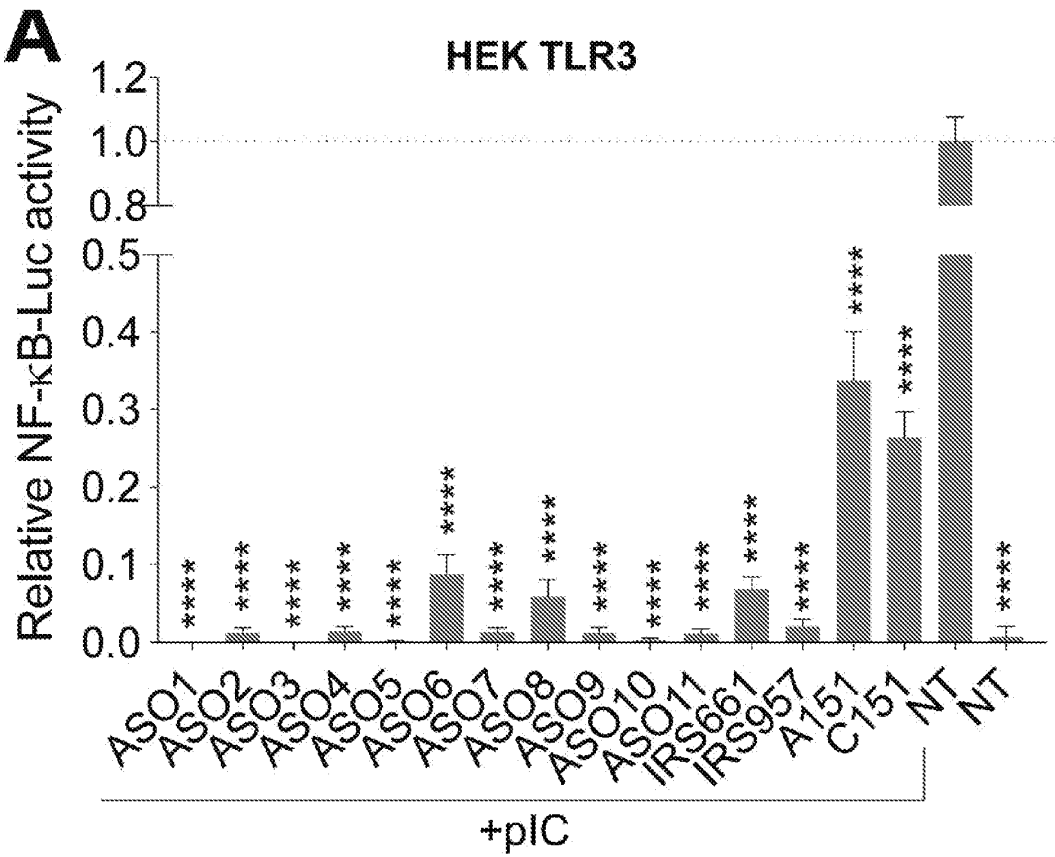
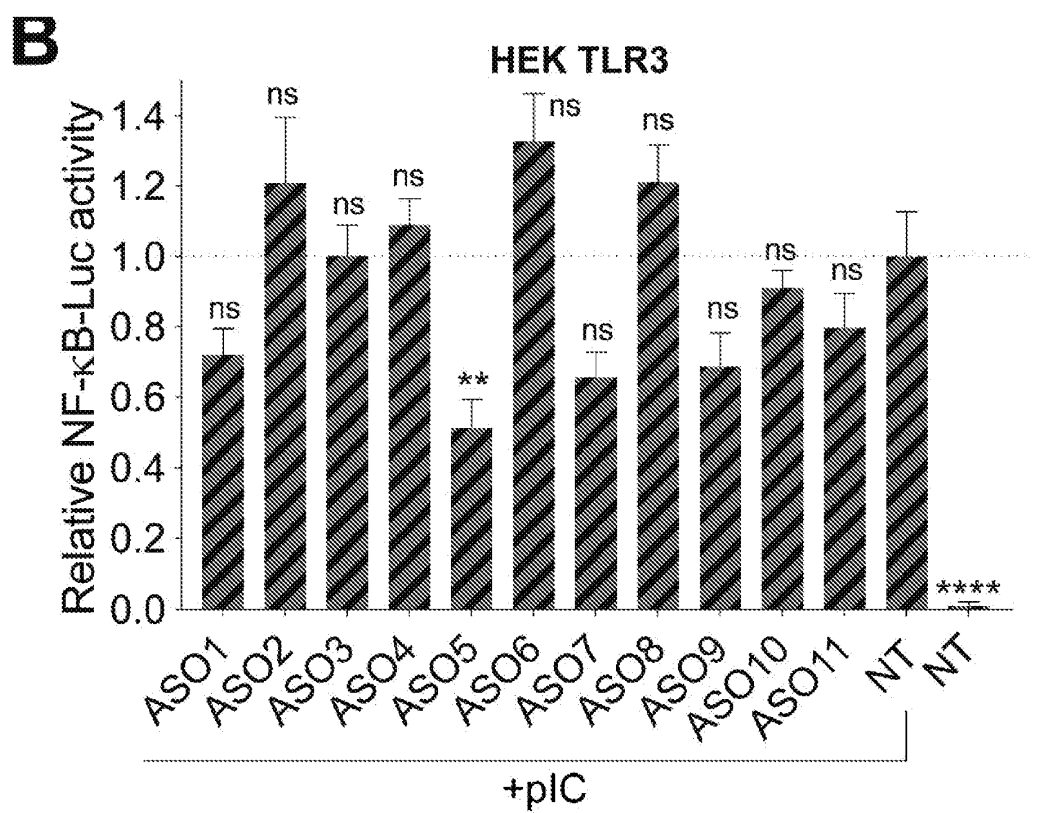
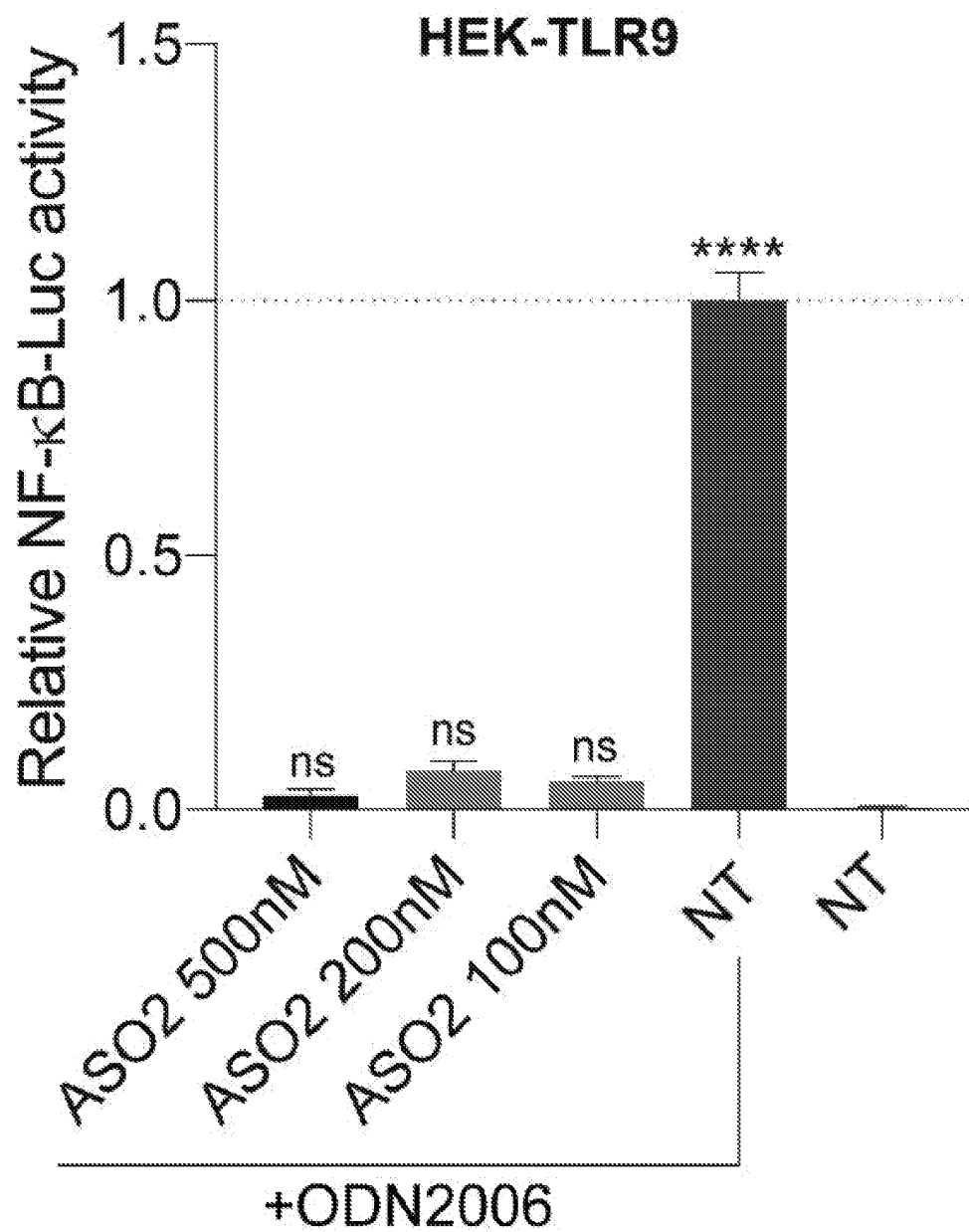


FIGURE 10A

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**FIGURE 10B**

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**FIGURE 11**

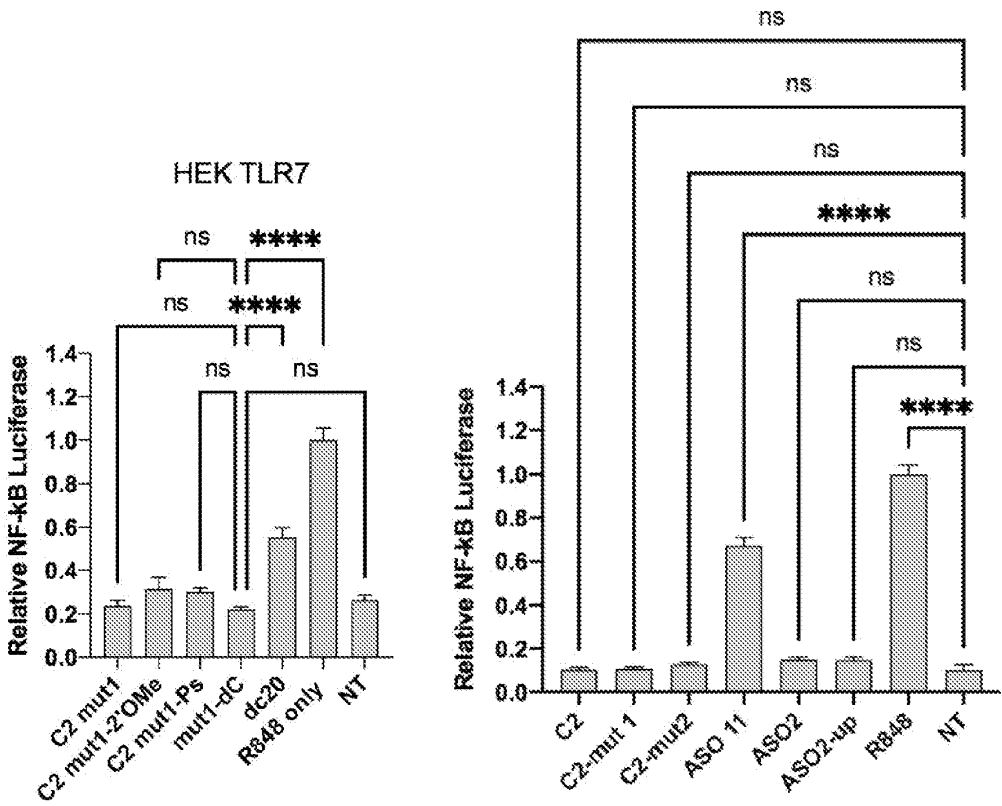
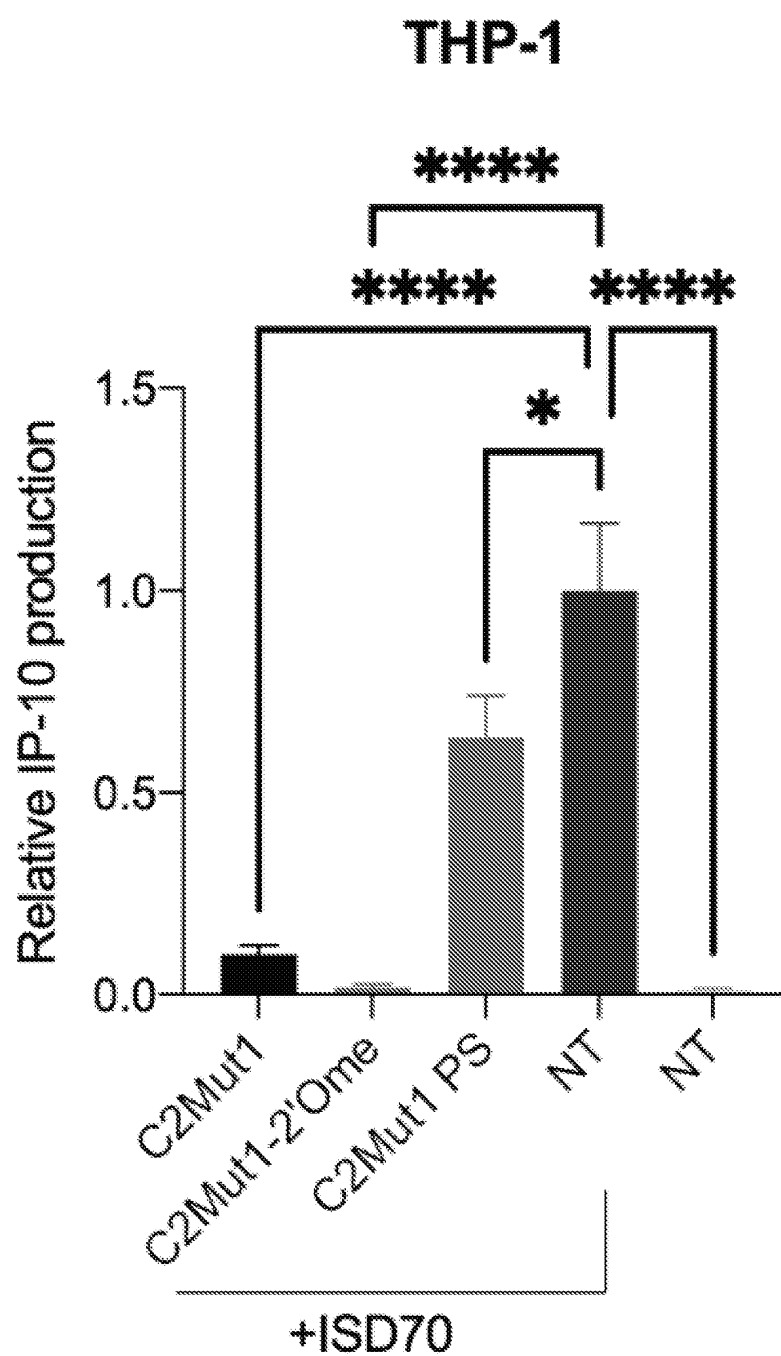
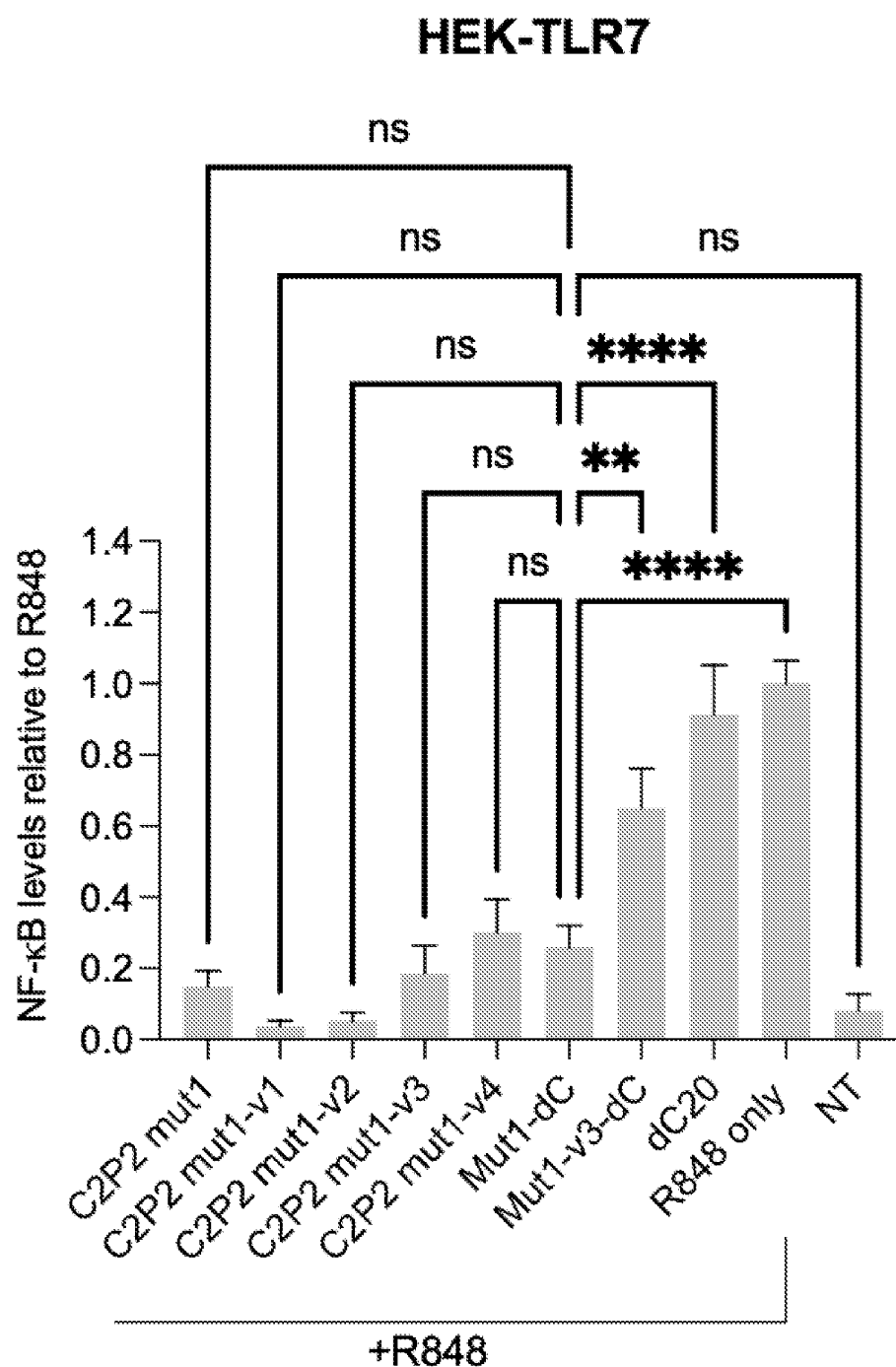


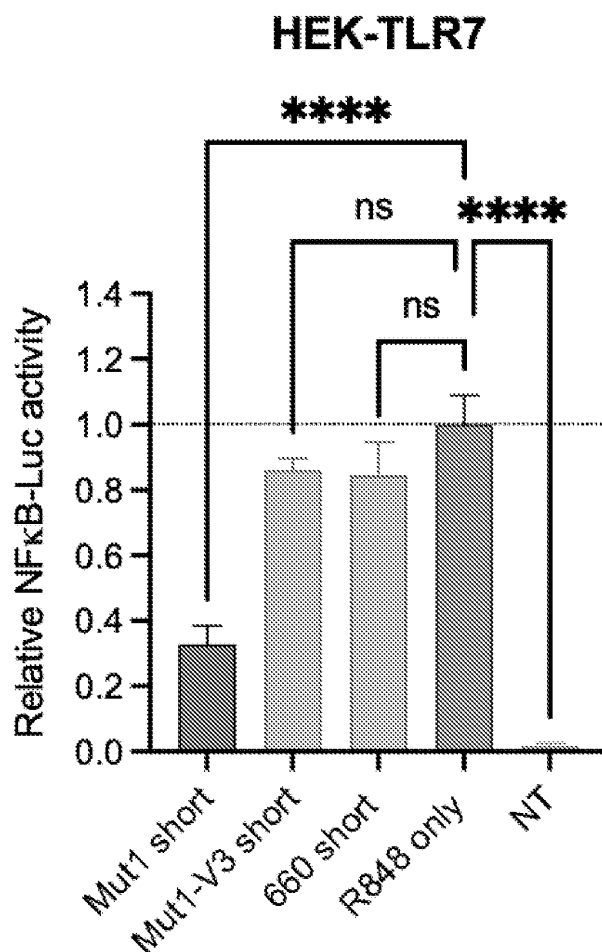
FIGURE 12

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**FIGURE 13**

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A**FIGURE 14A**

B

ShortMut1: mG*mG*mU*mA*mU

ShortMut1v3: mC*mG*mU*mU*mU

Short660v1: mC*mU*mU*mC*mG

FIGURE 14B

C **Primary BMDMs WT mice**

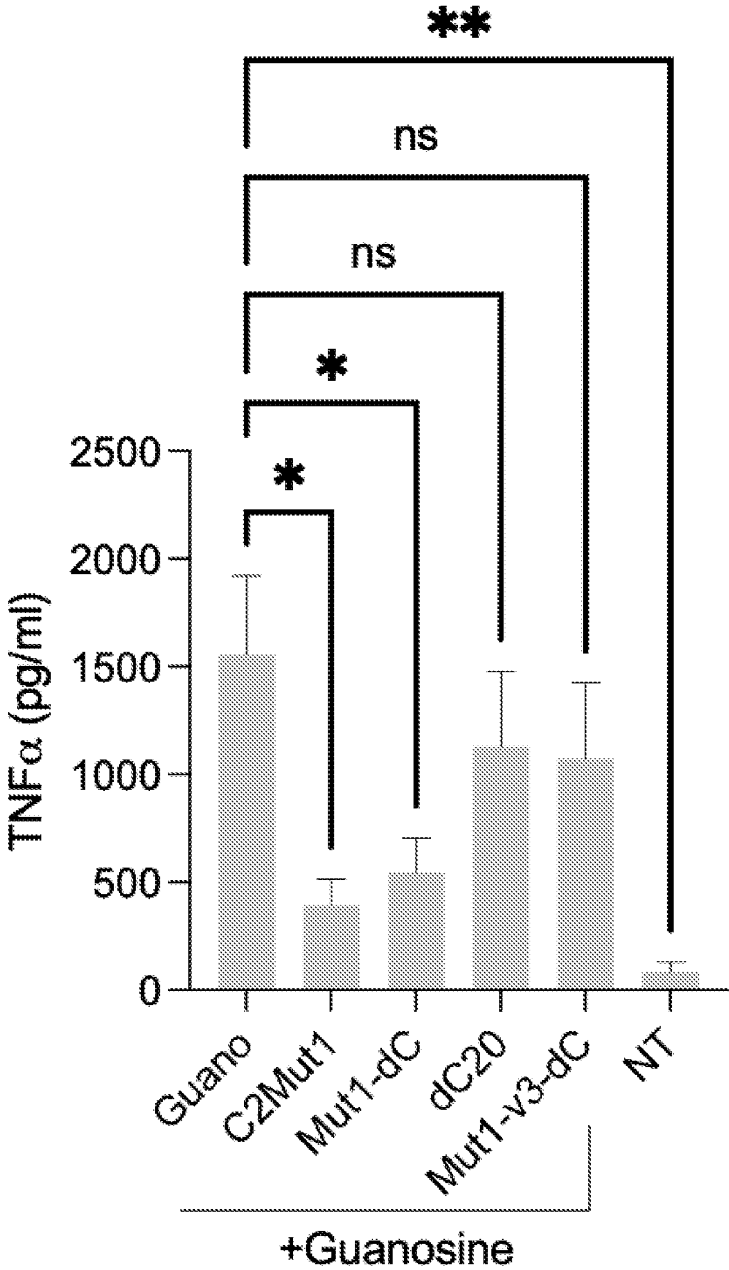
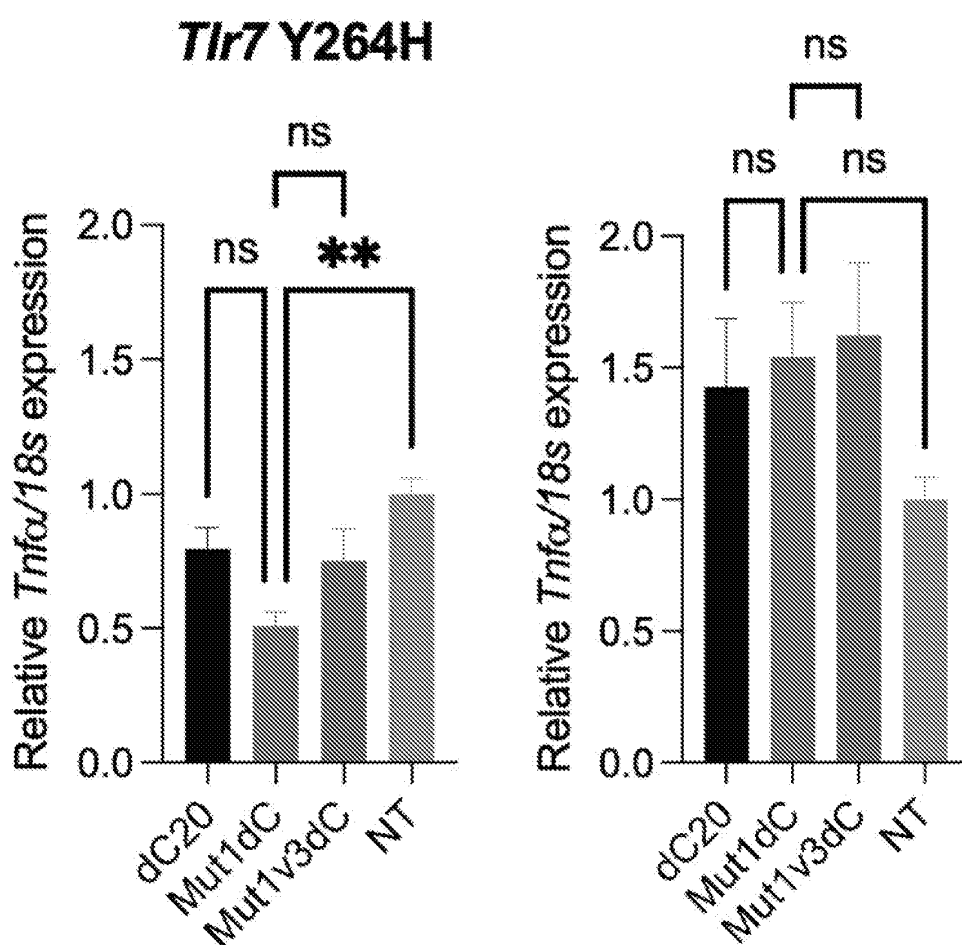
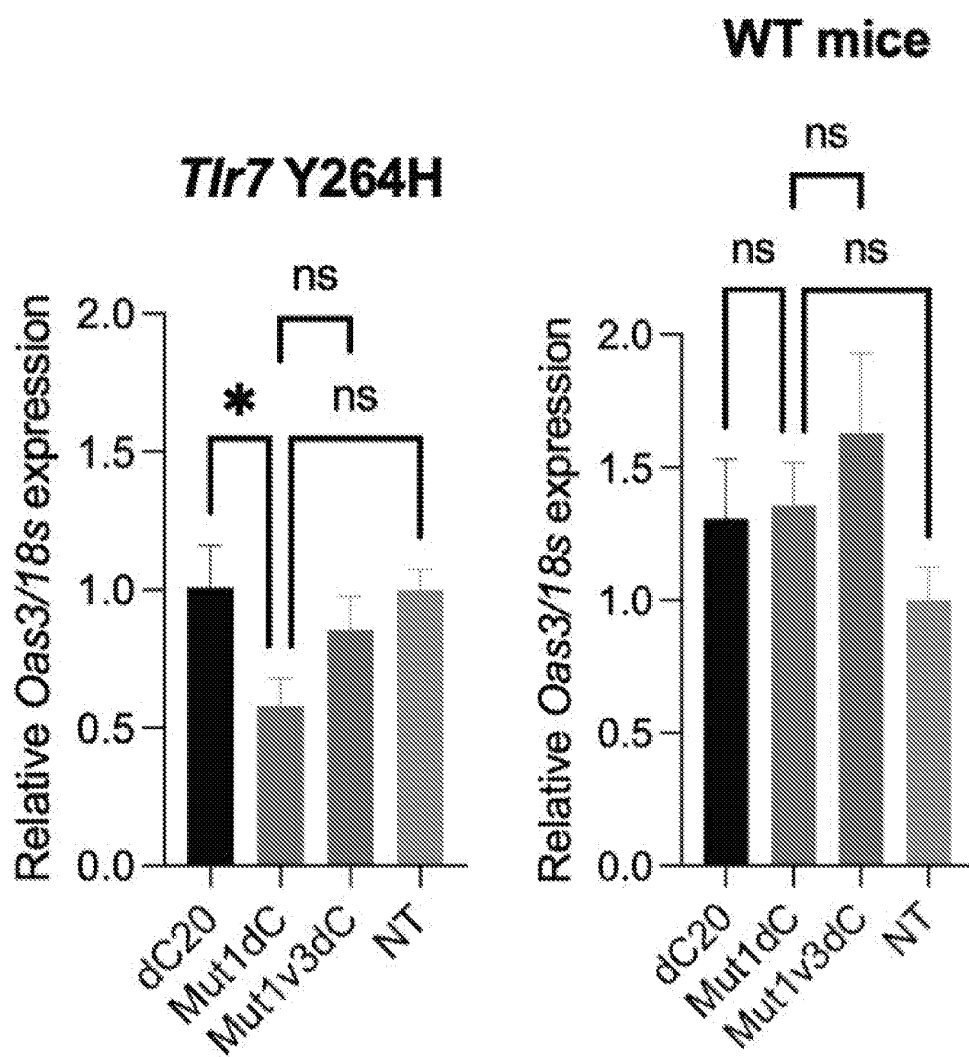


FIGURE 14C

**FIGURE 15**

**FIGURE 15 continued**

Name	Strand	Start	p-value	Sites
3. G5	+	1	2.51e-4	GGCATC CACCACGTCG
4. E6	+	13	1.17e-3	CCTTGACAGT GGCTTC GT
1. F5	+	14	1.17e-3	CCTTGACAGT GGCTTC G
10. E5	+	15	1.48e-3	ATTTCAGAGC AGCTTC
2. F4	+	7	1.48e-3	TTCTGC AGCTTC CTTGTCCCT
5. D5	+	7	2.46e-3	TGGGCT GGAATC CGAGTTAT
8. G8	+	4	2.77e-3	GTC CACATC CTGTGGCTCG
9. E2	+	7	5.29e-3	TGTGAT GGCTTC CCATCTCC
6. C8	+	7	5.29e-3	TTTGCA CACTTC GTACCCAA
7. D3	+	5	6.22e-3	GTCC AAGATC AGCAGTCTCA

>F5 TGTCCTTGCACGTGGCTTCG
>F5-Mut TGTCCTTGCACGTGCCTAAG

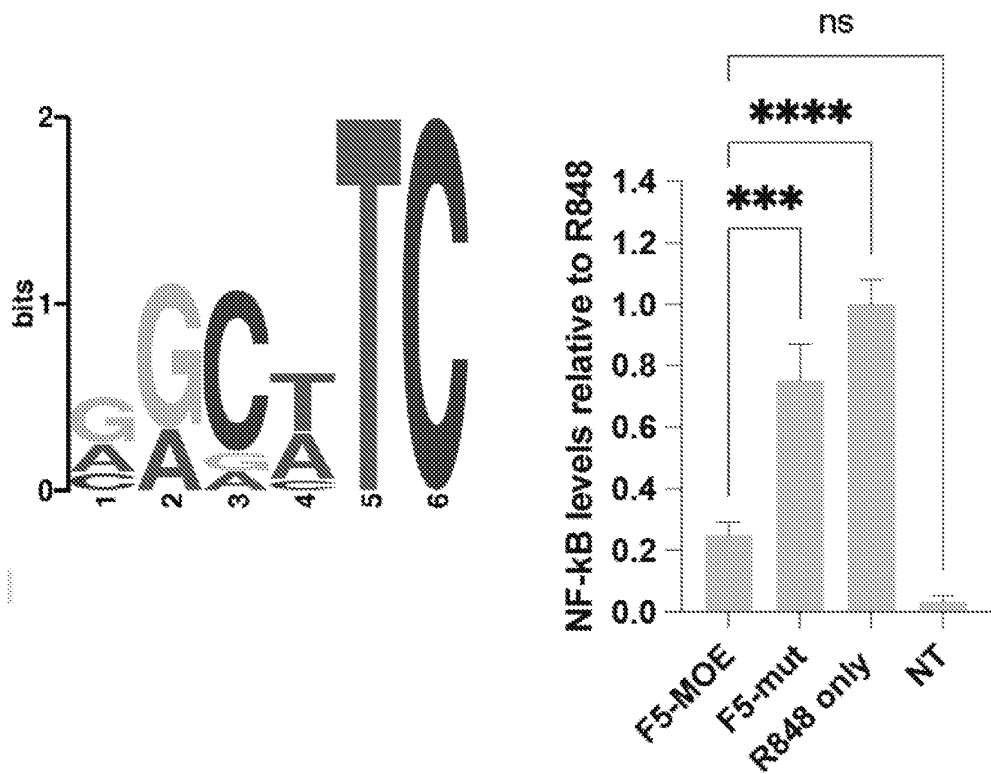
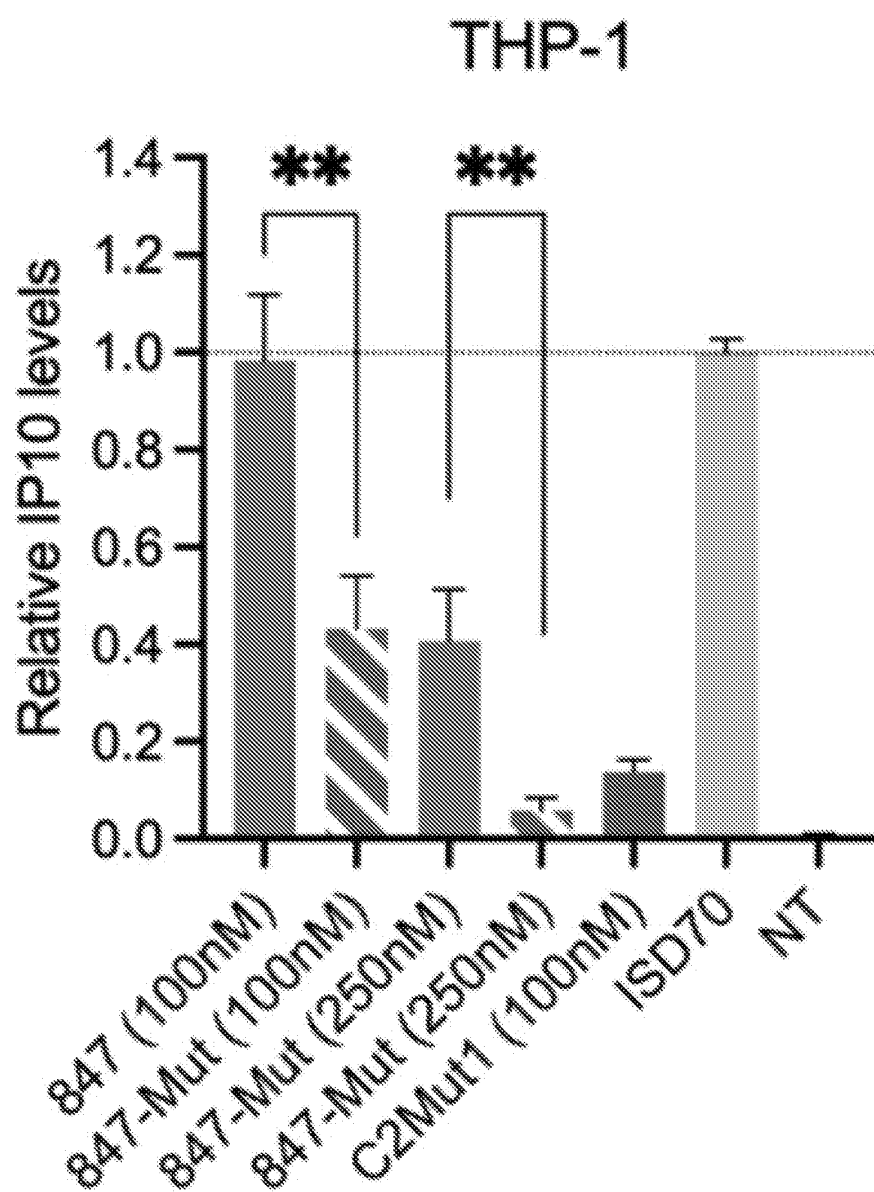
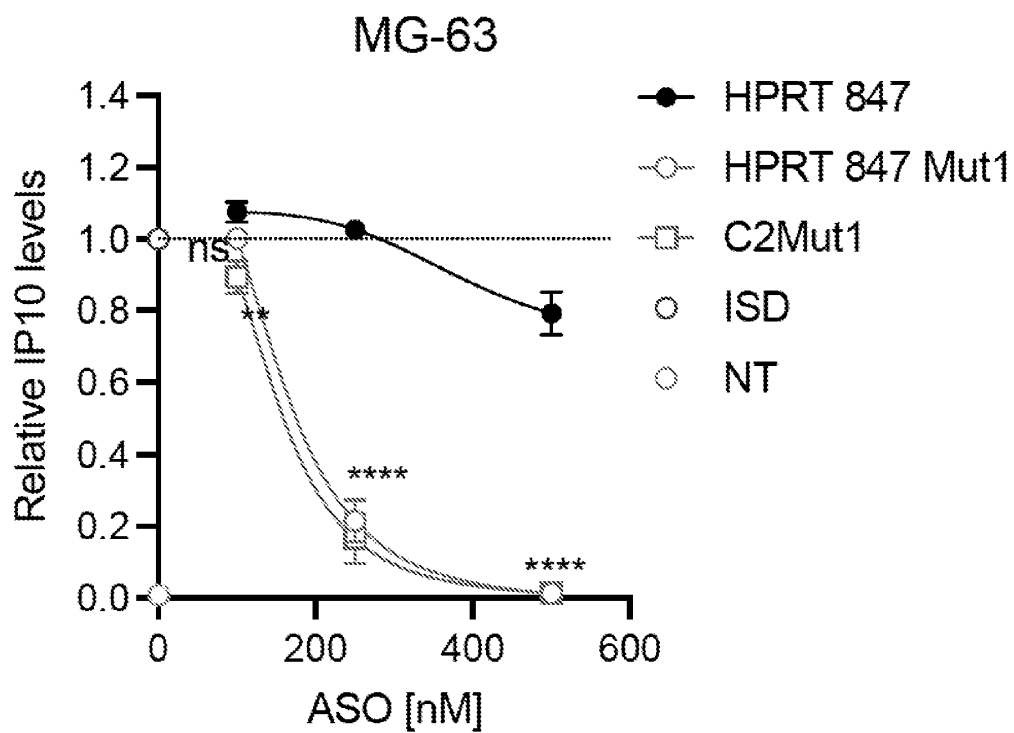


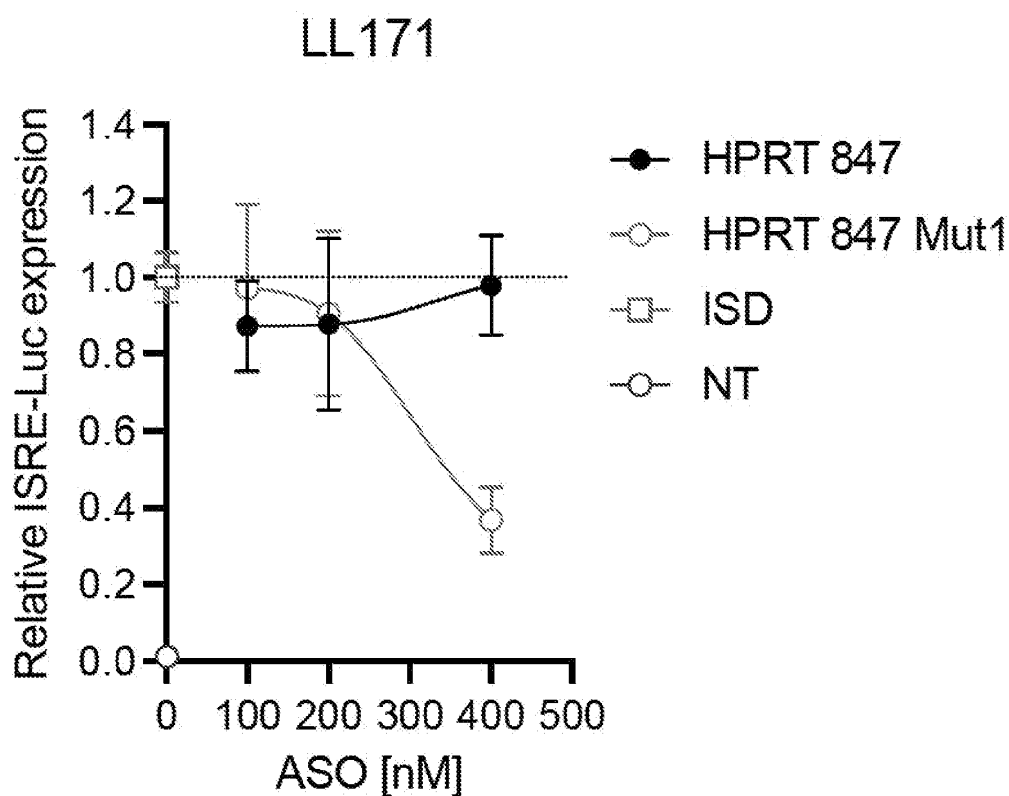
FIGURE 16

**FIGURE 17**

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**FIGURE 17 continued**

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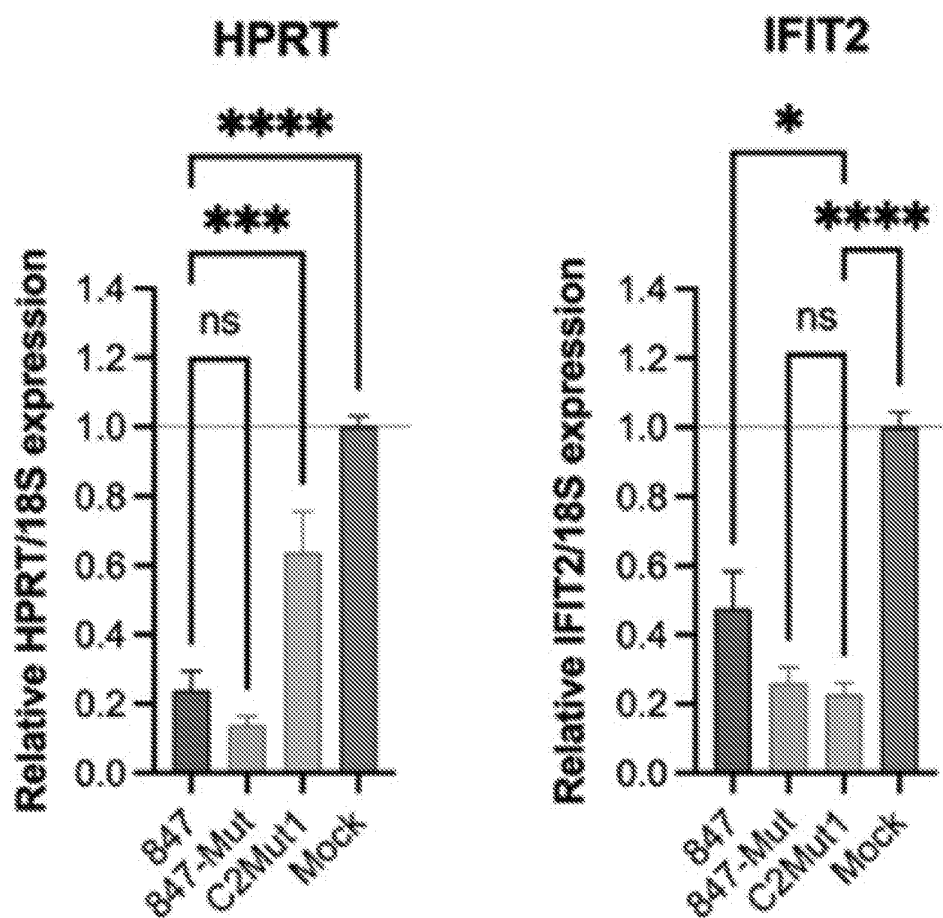
HPRT-2OMe-847:

mA*mU*mA*mG*mG*A*C*T*C*C*A*G*A*T*G*mU*mU*mU*mC*mC

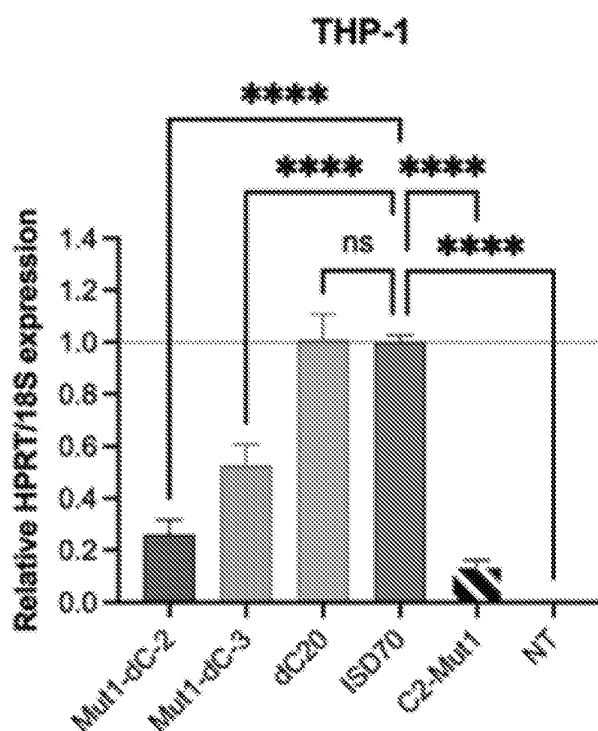
HPRT-2OMe-847-Mut1:

mG*mG*mU*mA*mU*mA*mG*mG*A*C*T*C*C*A*G*A*T*G*mU*mU*mU*mC*mC

FIGURE 17 continued

**FIGURE 18**

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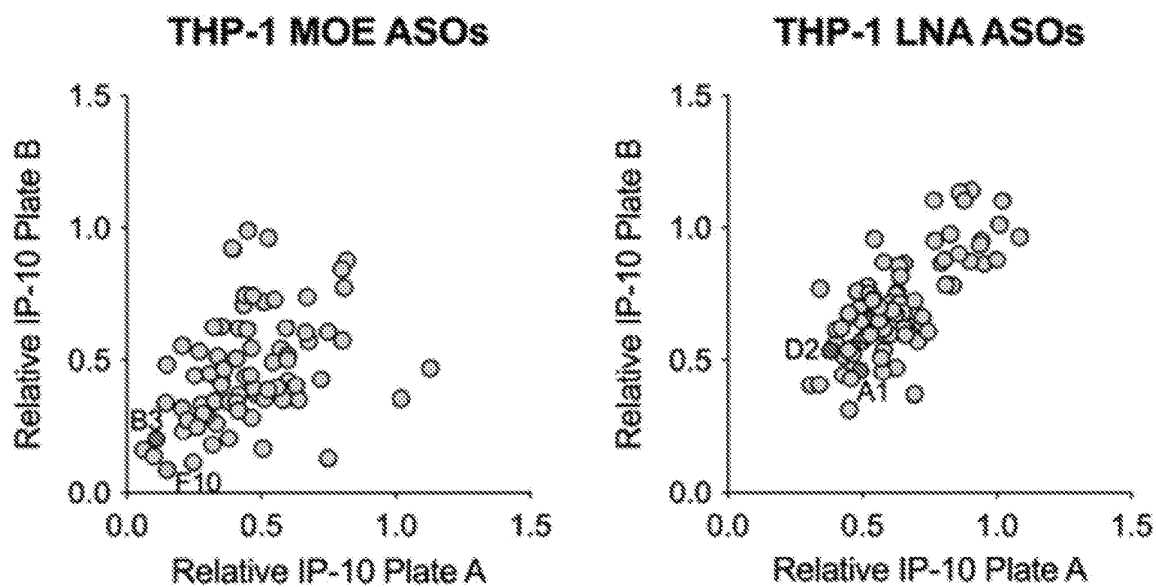
C2Mut1-dC-2:

mG*mG*mU*A*C*C*C*C*C*C*C*C*C*C*C*C*C*C*C*C*C

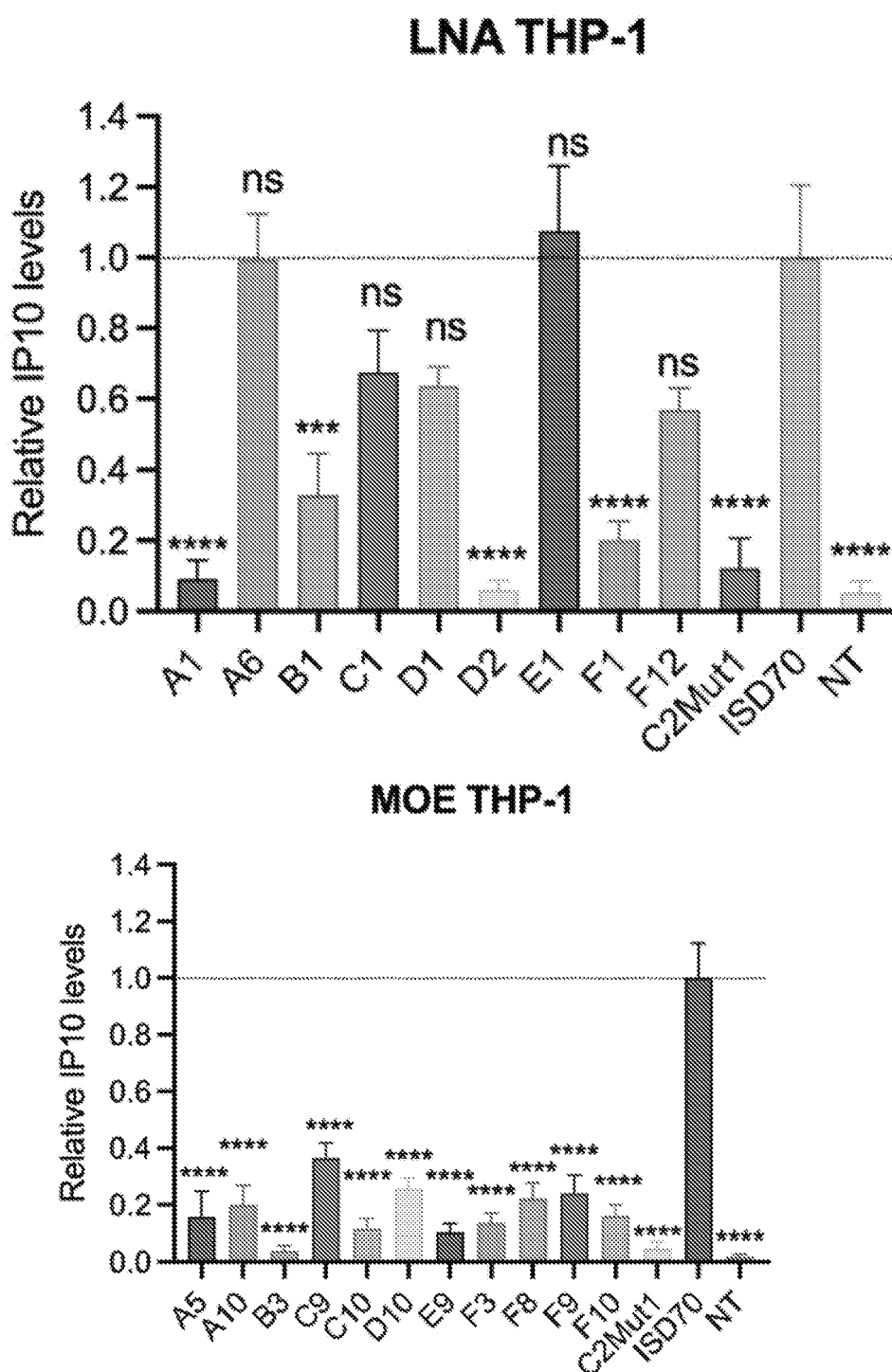
C2Mut1-dC-3:

mG*mG*mU*C*C*C*C*C*C*C*C*C*C*C*C*C*C*C*C*C

FIGURE 19

**FIGURE 20**

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**FIGURE 21**

SUBSTITUTE SHEET (RULE 26)

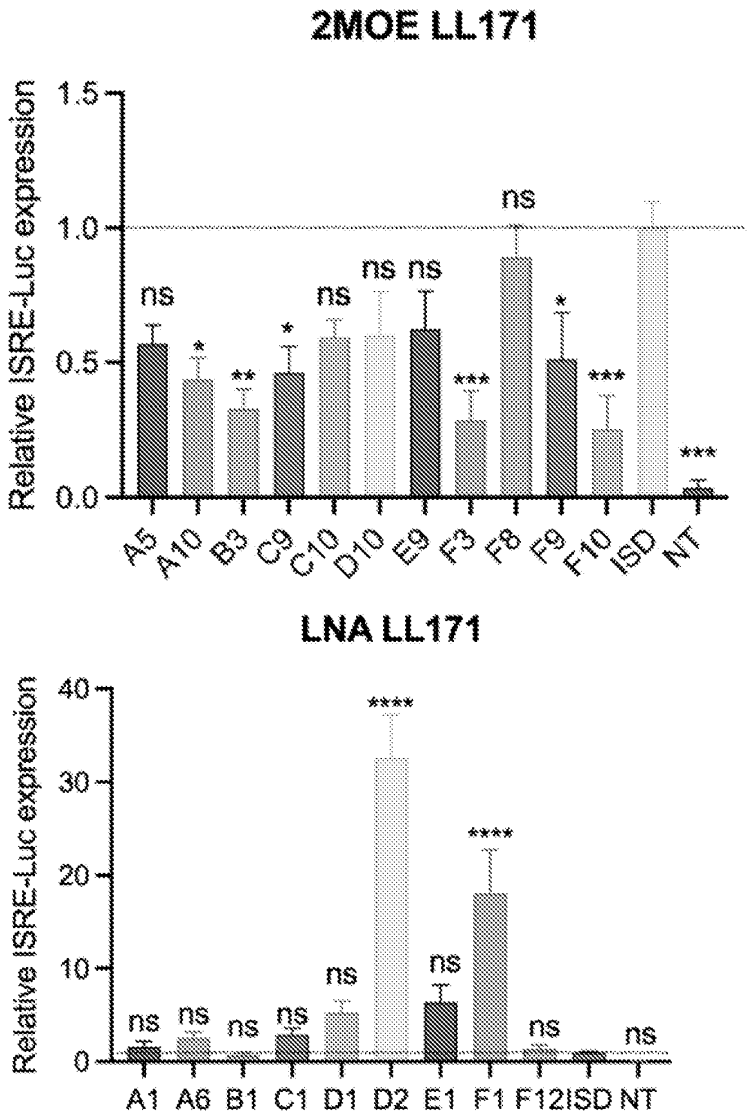
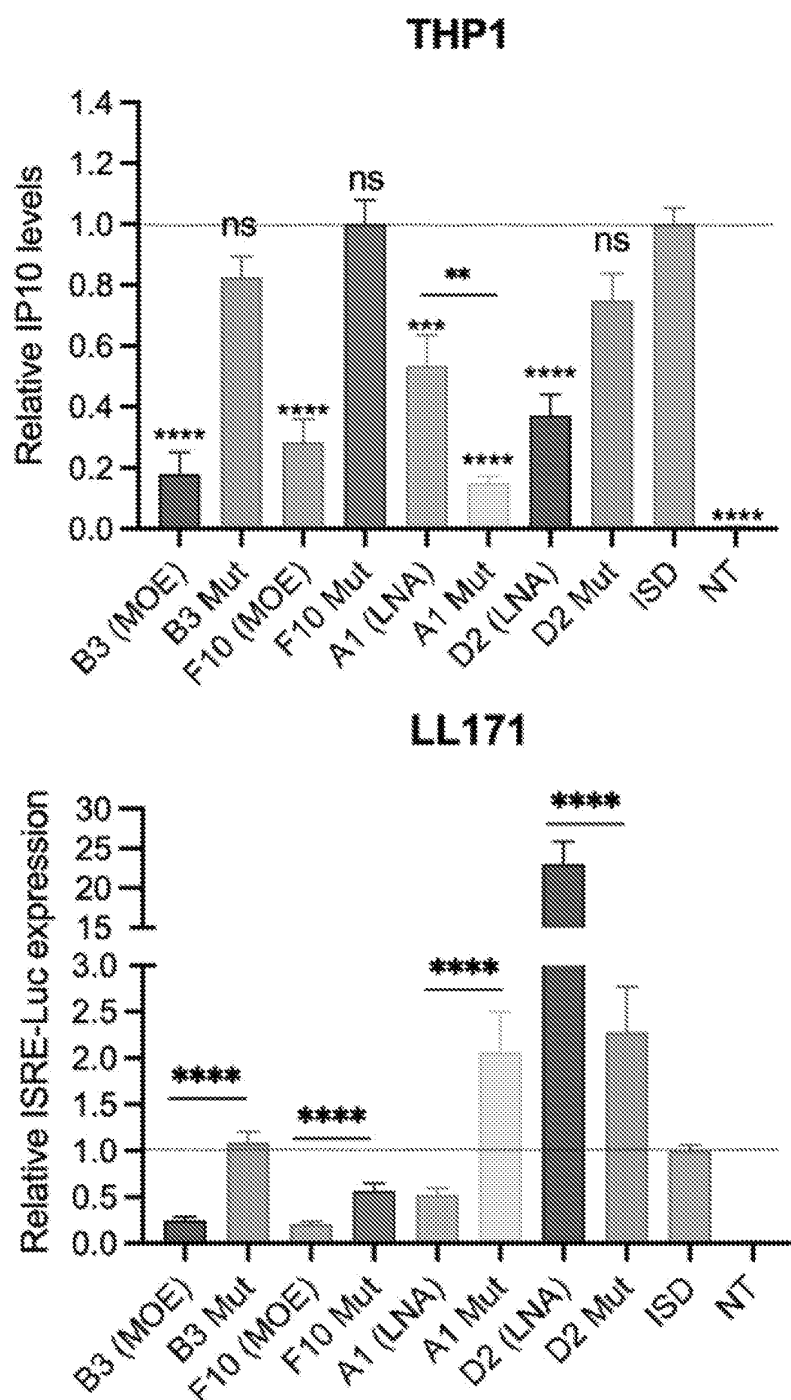


FIGURE 22

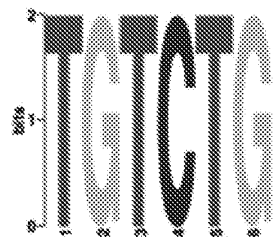
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**FIGURE 23**

SUBSTITUTE SHEET (RULE 26)

LNA Motif 1

Name	Strand	Start	p-value	Sites
5. F1	+	2	5.60e-4	G TGTCTG GAAGCTTCC
4. A1	+	9	5.60e-4	CGCTTTTC TGTCTG GT



A1-LNA: +C*+G*+C*T*T*T*T*C*T*G*T*C*T*+G*+G*+T
A1-Mut-LNA: +C*+G*+C*T*T*T*T*C*T*C*T*C*C*+G*+G*+T

LNA Motif 2

Name	Strand	Start	p-value	Sites
2. B1	+	2	4.88e-5	G AAAGCTTA TGCAAGG
5. F1	+	8	6.12e-5	GTGTCTG <u>GAAGCTTC</u> C
1. D2	+	1	2.01e-4	<u>GAAGCTC</u> AGTGATGT

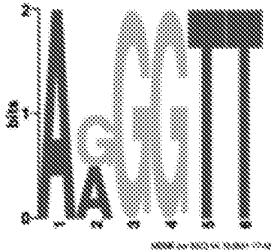


D2-LNA: +G*+C*+A*G*G*C*T*C*A*G*T*G*A*+T*+G*+T
D2-Mut-LNA: +G*+C*+C*G*C*T*C*A*G*T*G*A*+T*+G*+T

FIGURE 23 continued

MOE Motif 1

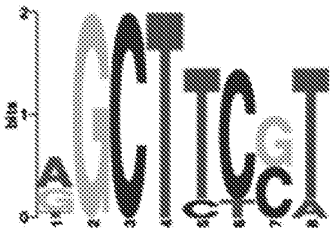
Name	Strand	Start	p-value	Sites
3. B3	+	5	1.72e-4	GGGA AAGGTT ATGCAAGGTC
6. E9	+	14	4.01e-4	GACTGTCTTG AAGGTT C



B3-MOE: /G*/G*/G*/A*/A*A*G*G*T*T*A*T*G*C*A*/A*/G*/G*/T*/C
B3-Mut-MOE: /G*/G*/G*/A*/A*A*C*G*C*T*A*T*G*C*A*/A*/G*/G*/T*/C

MOE Motif 2

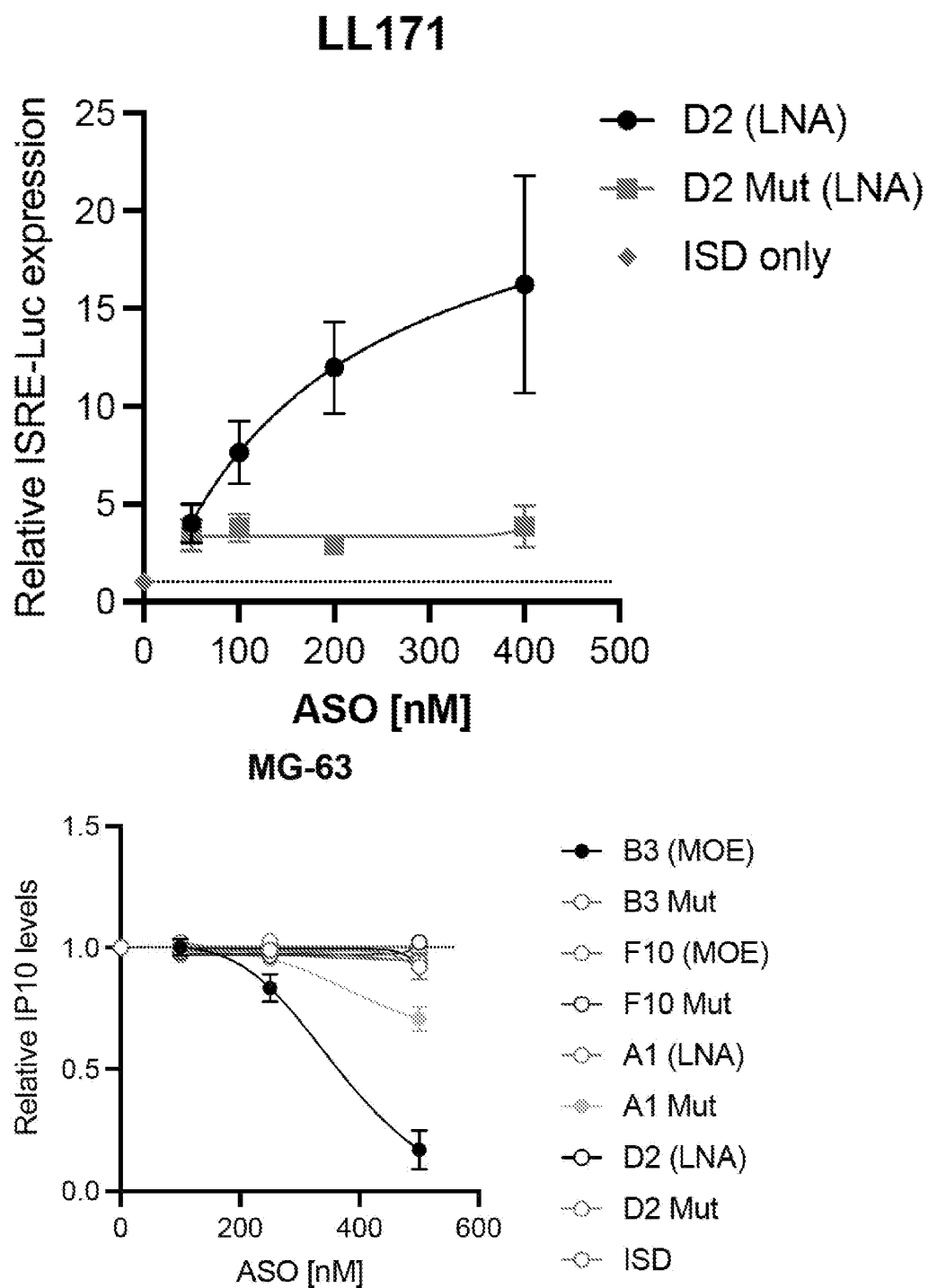
Name	Strand	Start	p-value	Sites
2. F3	+	12	1.63e-5	CGTGTCTGGA AGCTTCCT T
1. F8	+	11	1.63e-5	GAGTGTCTGG AGCTTCCT CT
11. F10	+	3	9.50e-5	GG AGCTTCGA GGGCCAGGC
10. A10	+	11	1.47e-4	CGGAGGTCCT GCTTCCT GG
9. C10	+	8	1.47e-4	AGGTCTT GCTTCCT GGAGC
8. F9	+	7	1.47e-4	GCTCTT GCTTCCT GGAGCA
5. C9	+	10	2.33e-4	AGTCGTAGT TCTTCCT AAC
7. D10	+	13	6.24e-4	CGGCTCGGA AGCTCTCT



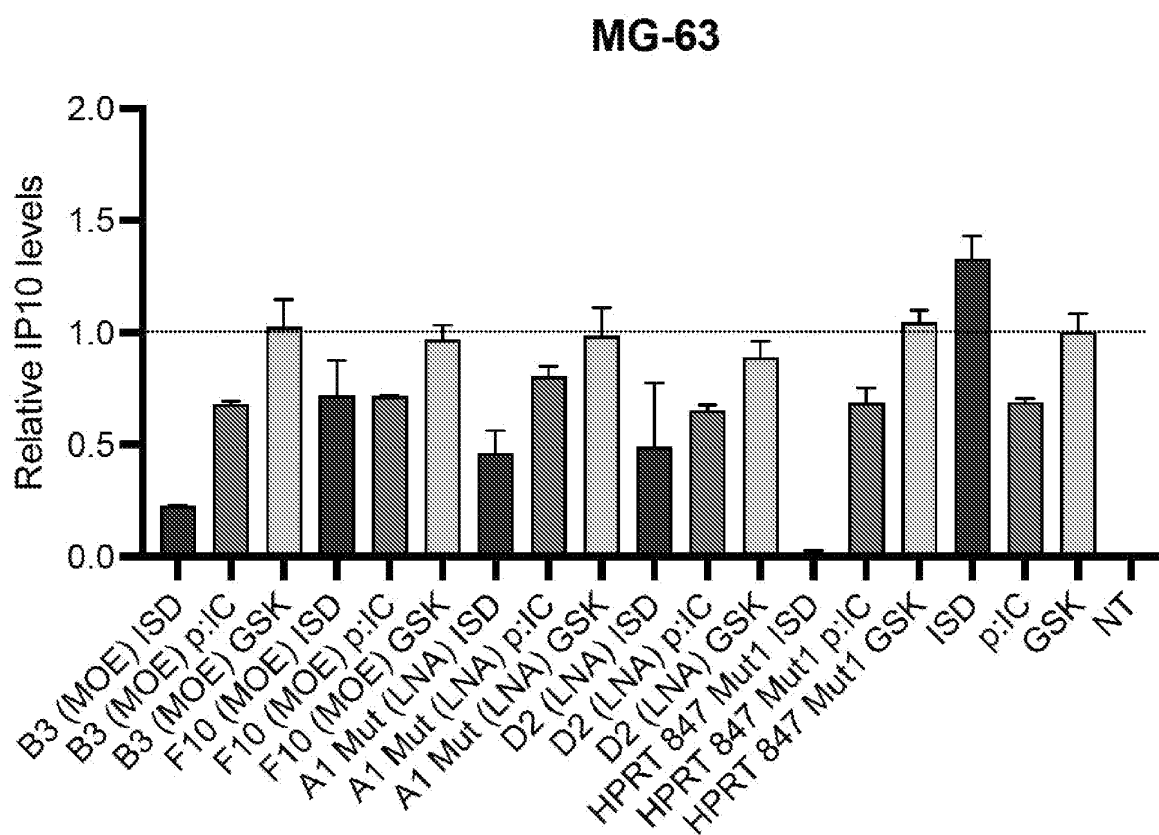
F10-MOE: /G*/G*/A*/G*/C*T*T*C*G*A*G*G*C*C*C*/C*/A*/G*/G*/C
F10-Mut-MOE: /G*/G*/A*/C*/C*C*T*C*G*A*G*G*C*C*C*/C*/A*/G*/G*/C

FIGURE 23 continued

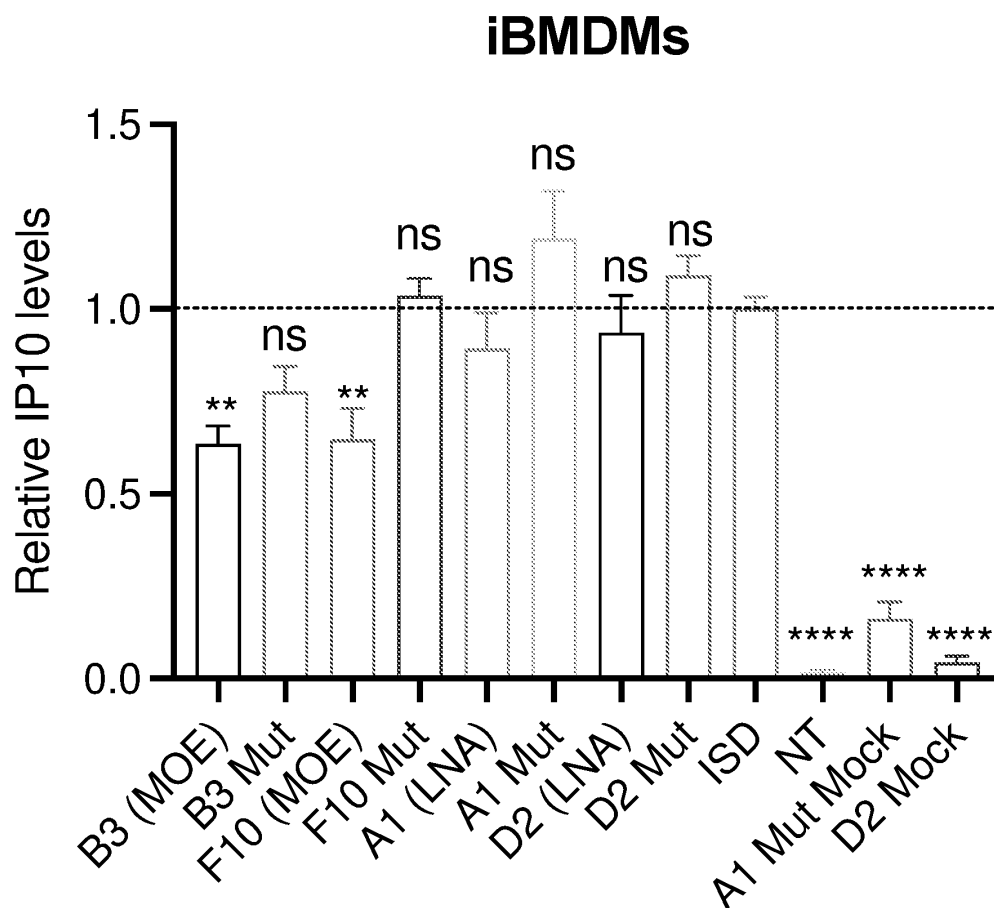
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**FIGURE 24**

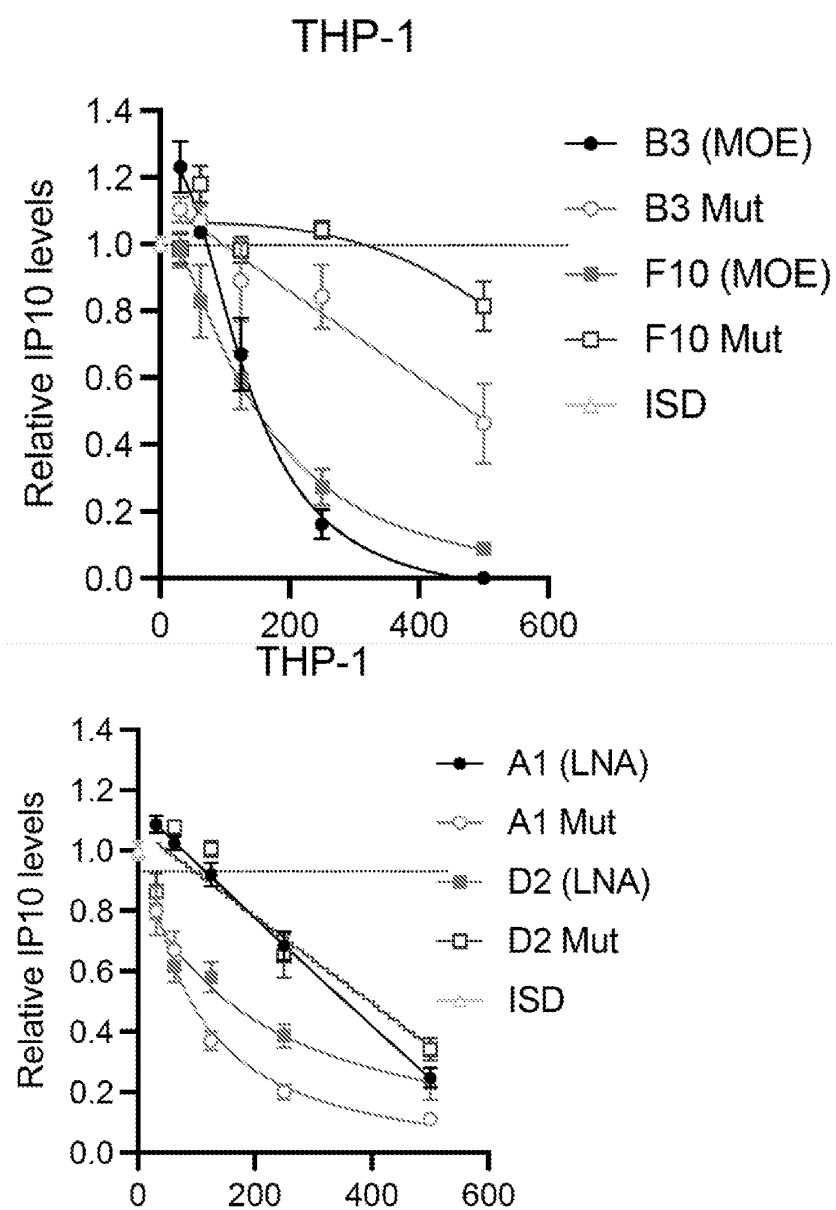
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**FIGURE 25**

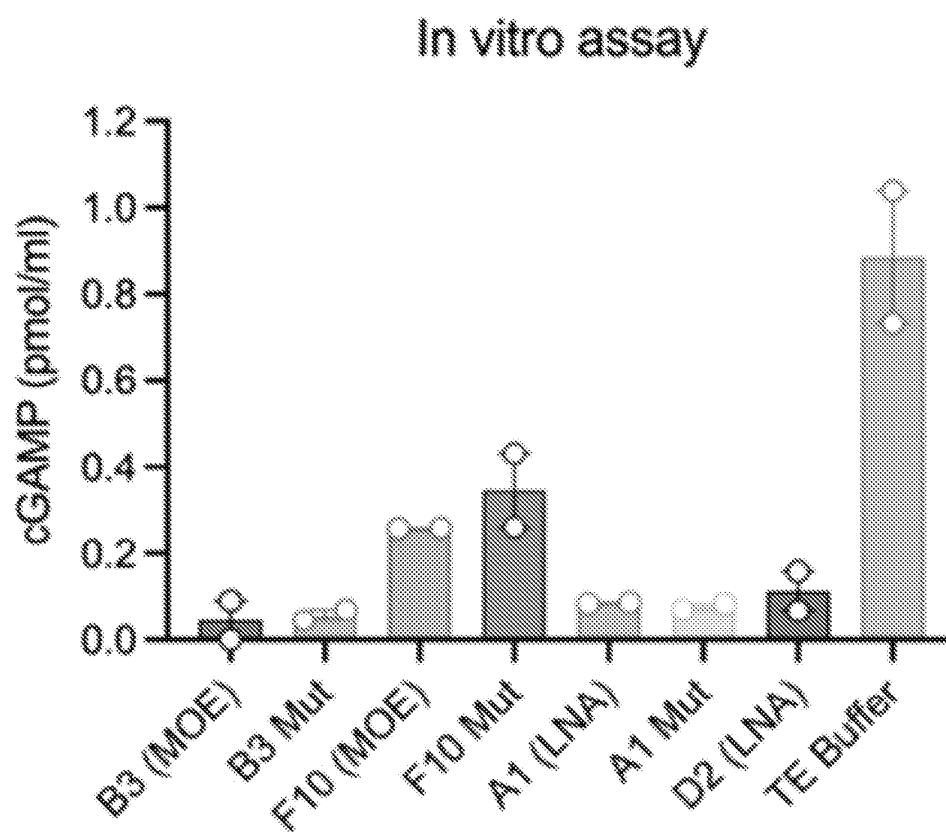
74/100

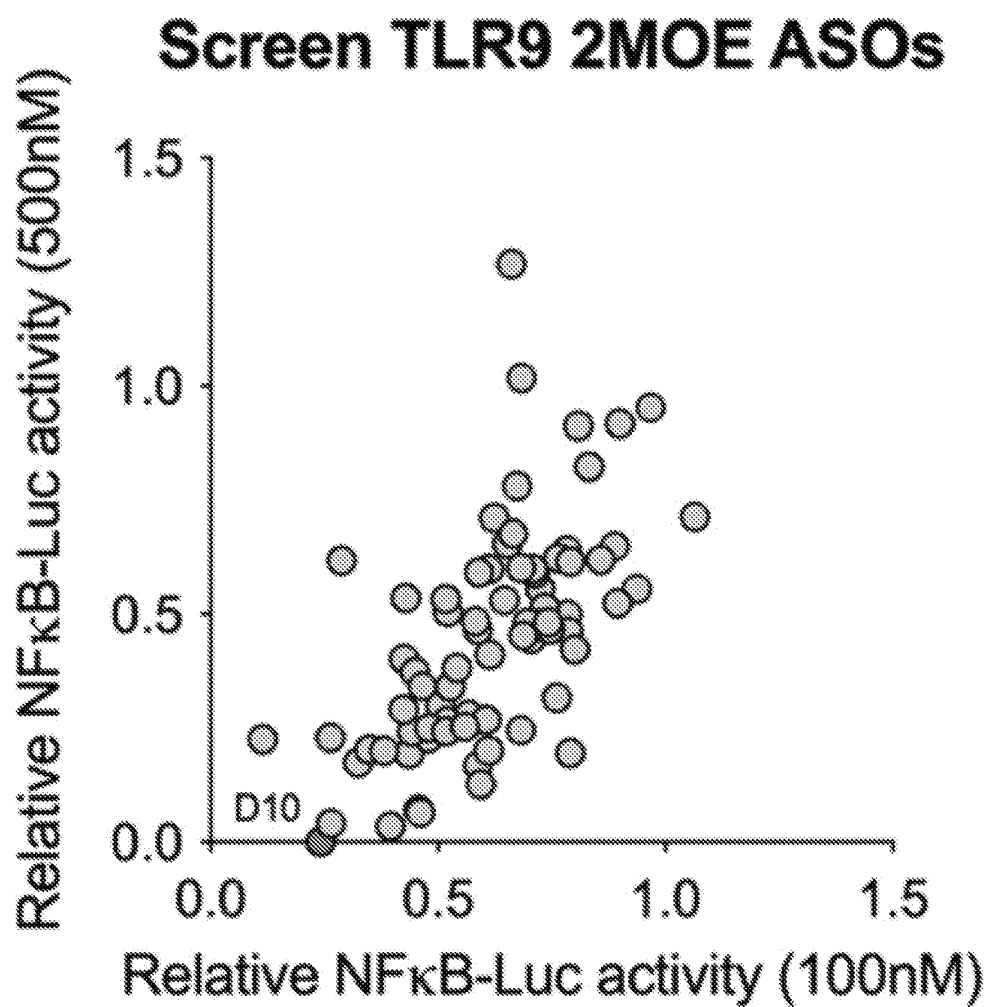
**FIGURE 26**

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**FIGURE 27**

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**FIGURE 28**

**FIGURE 29**

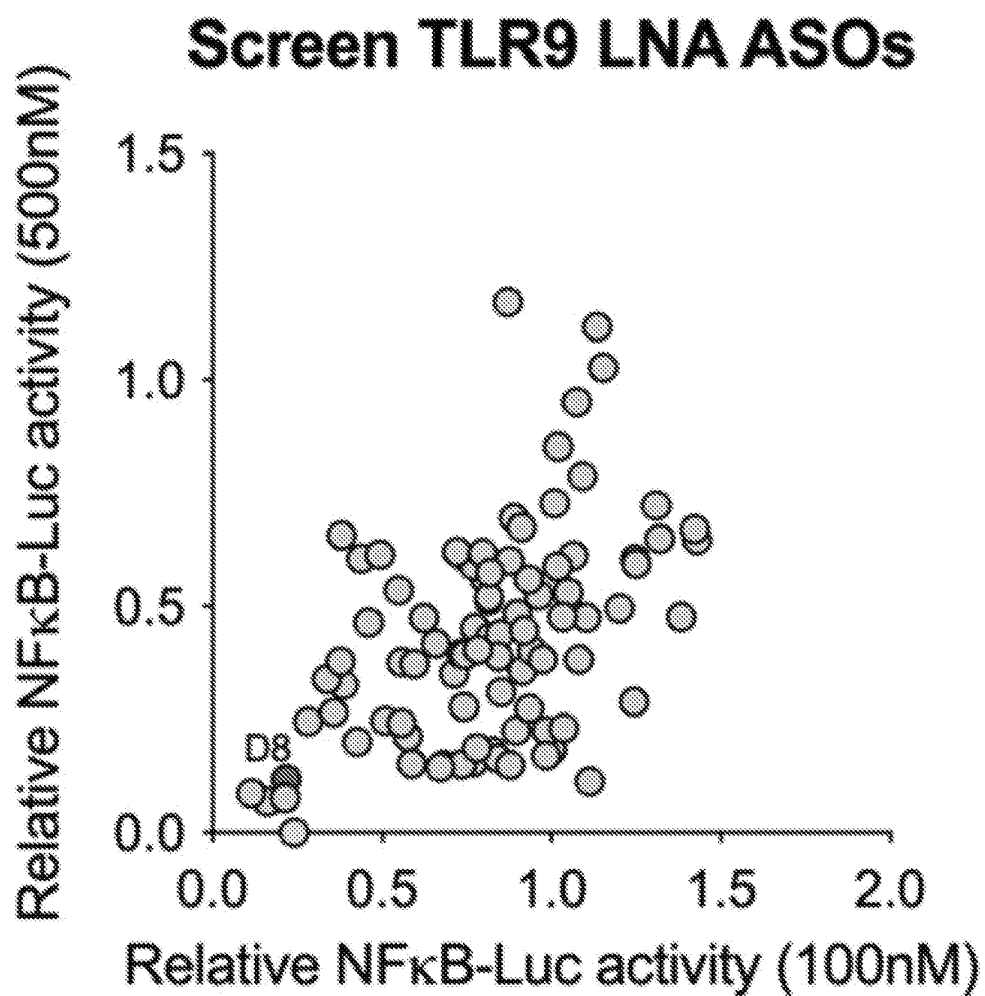
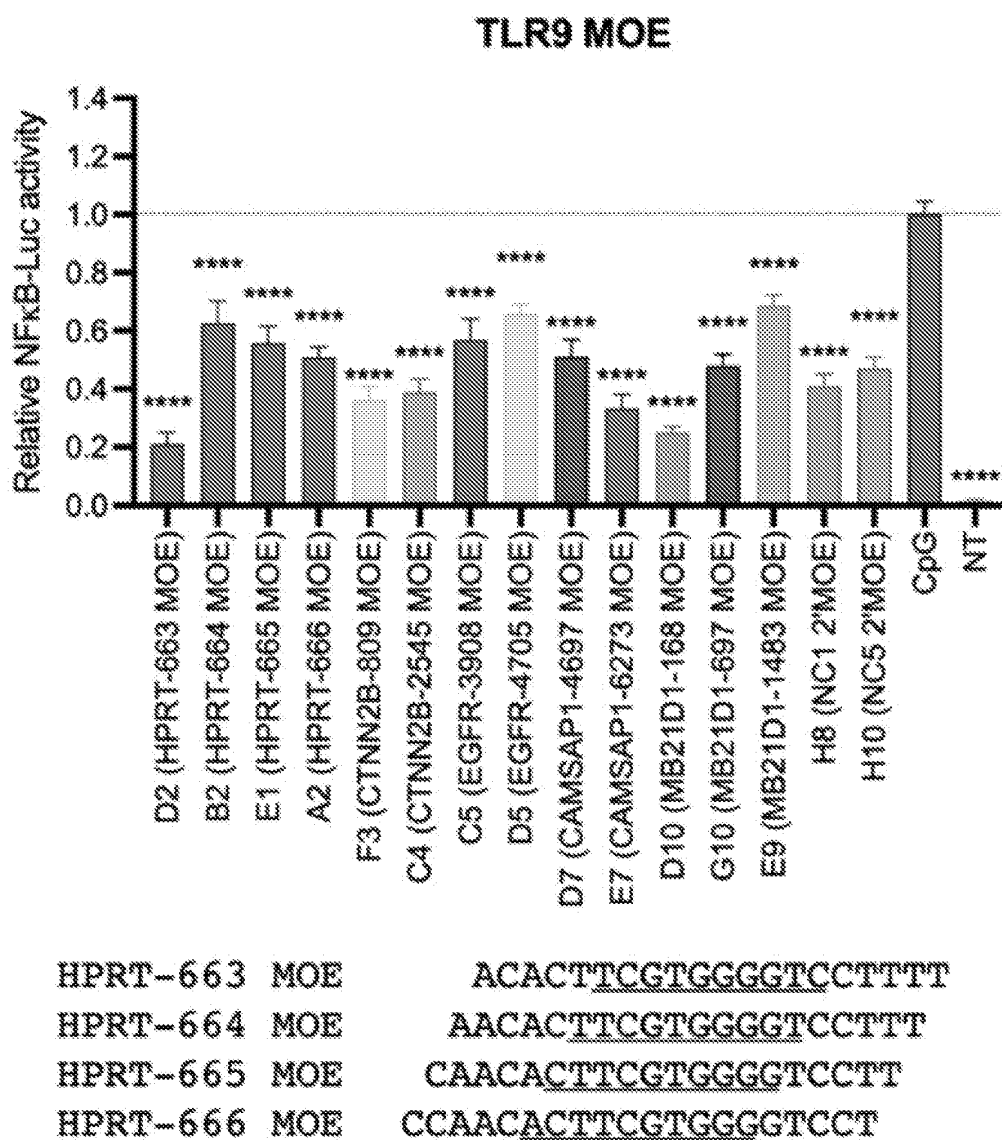
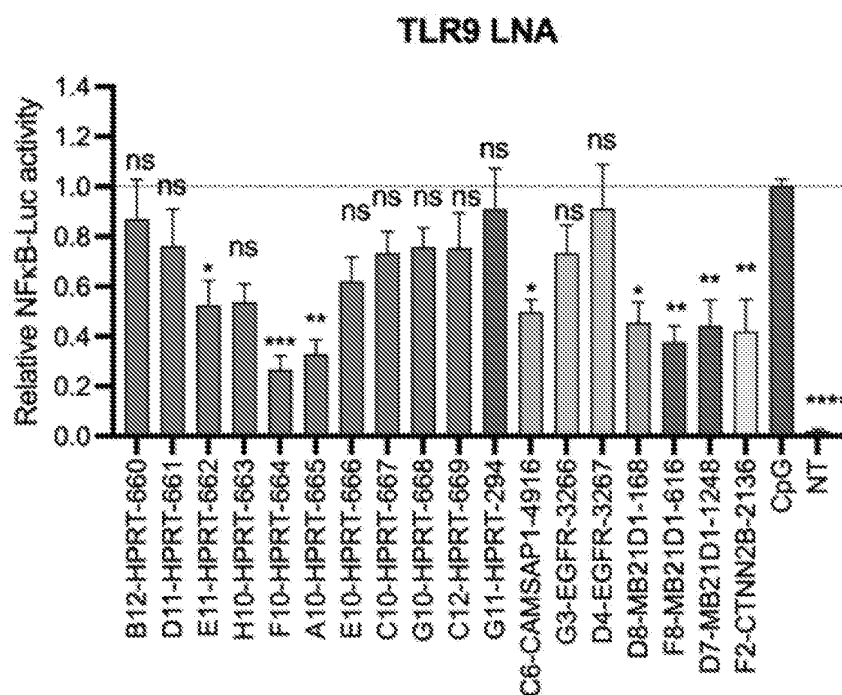


FIGURE 29 continued

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**FIGURE 30**

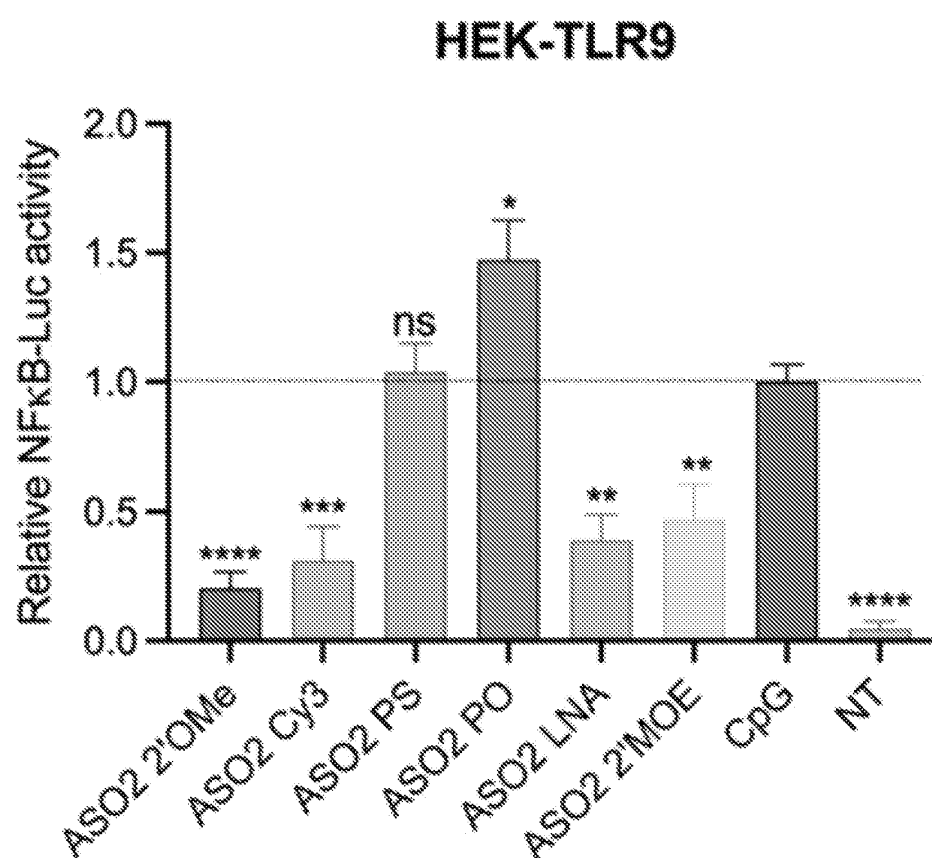
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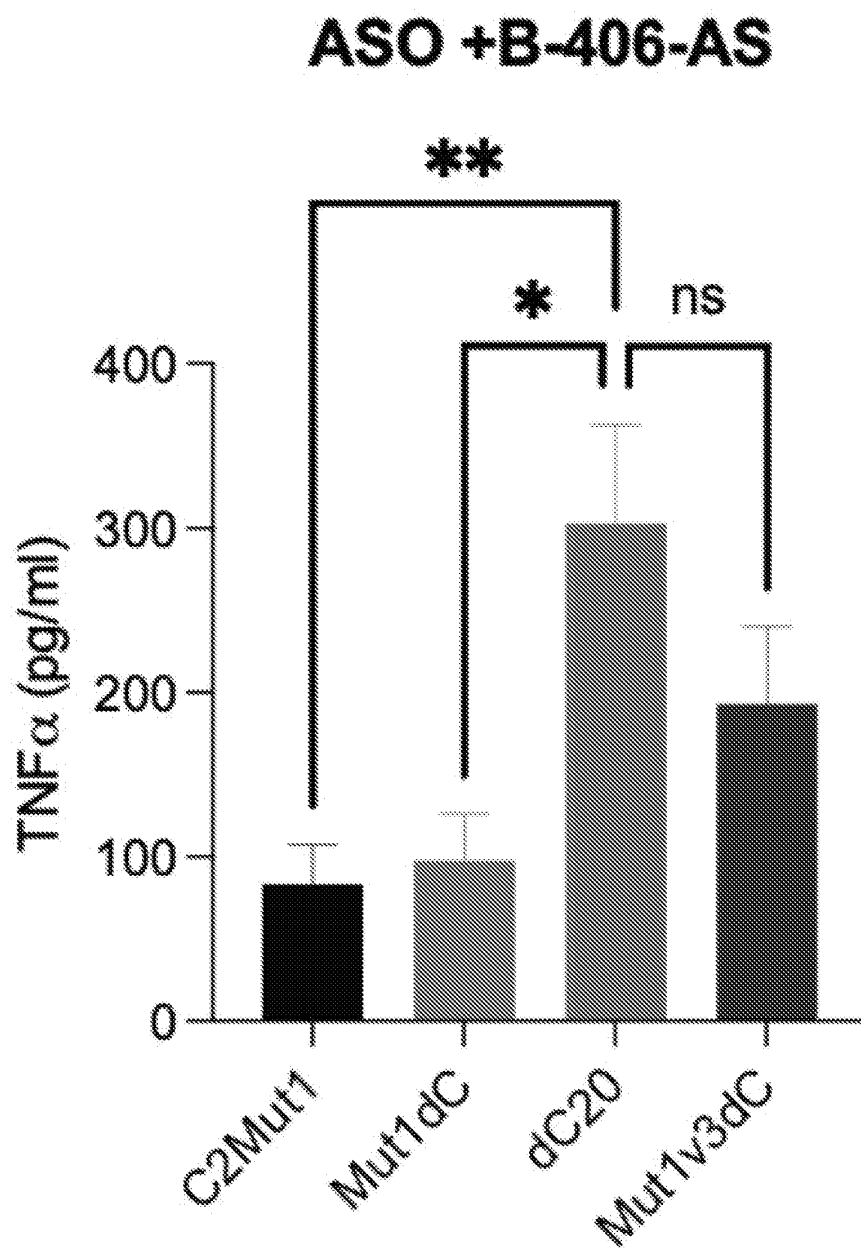
660 TCGTGGGGTCCTTTTC
 661 TTCGTGGGGTCCTTTT
 662 CTTCGTGGGGTCCTTT
 663 ACTTCGTGGGGTCCTT
 664 CACTTCGTGGGGTCCT
 665 ACACTTCGTGGGGTCC
 666 AACACTTCGTGGGGTC
 667 CAACACTTCGTGGGGT
 668 CCAACACTTCGTGGGG
 669 TCCAACACTTCGTGGG

FIGURE 30 continued

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**FIGURE 31**

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**FIGURE 32**

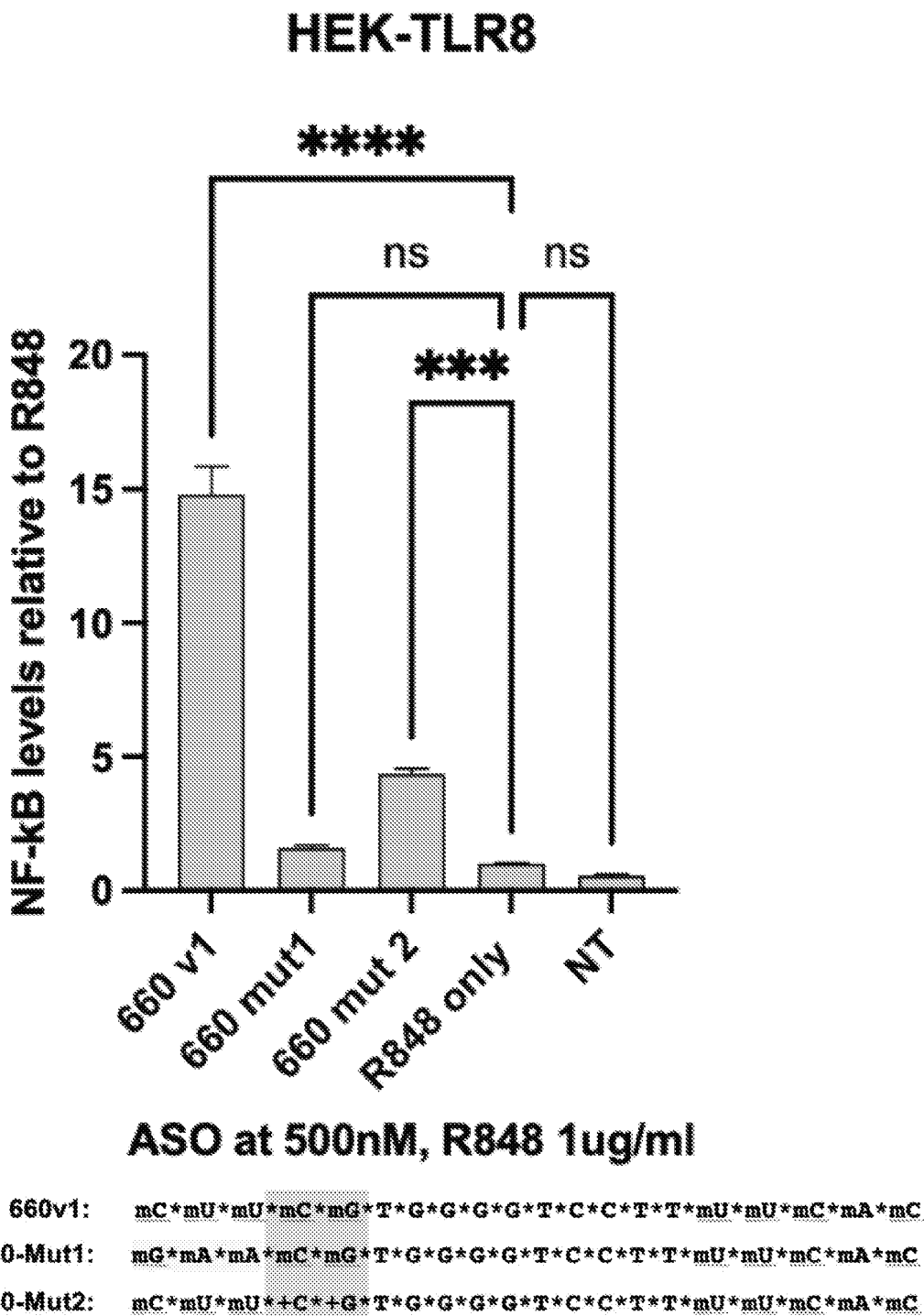
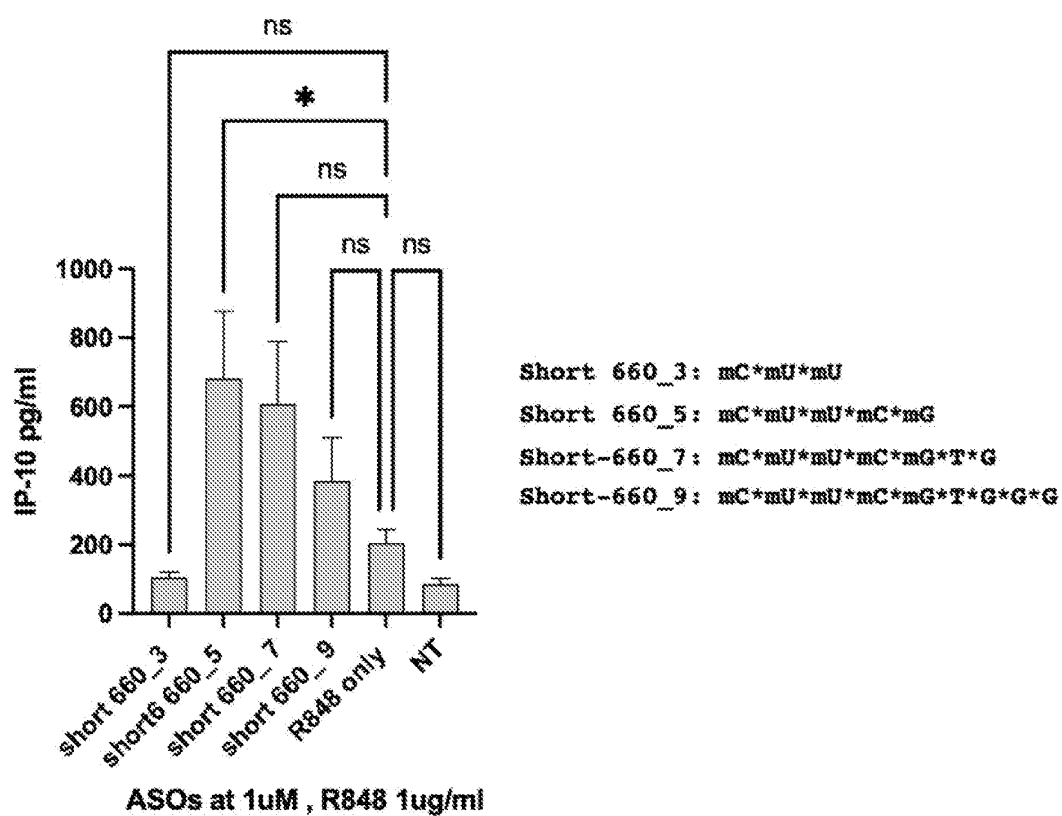
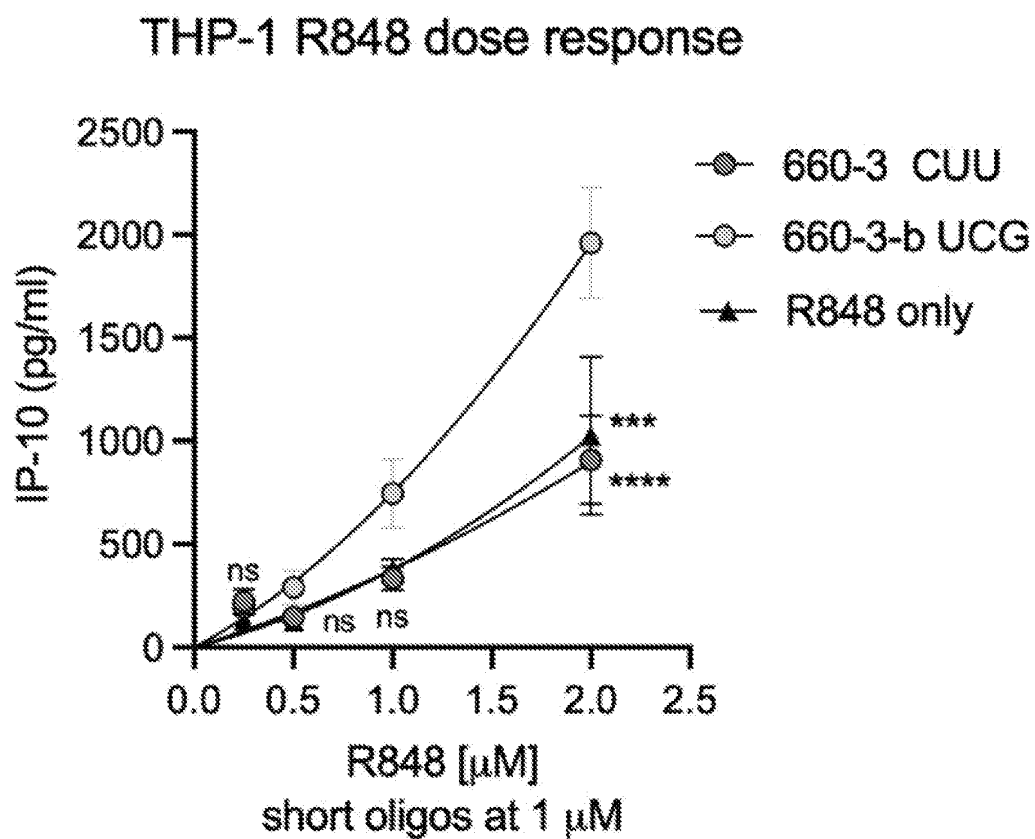


FIGURE 33

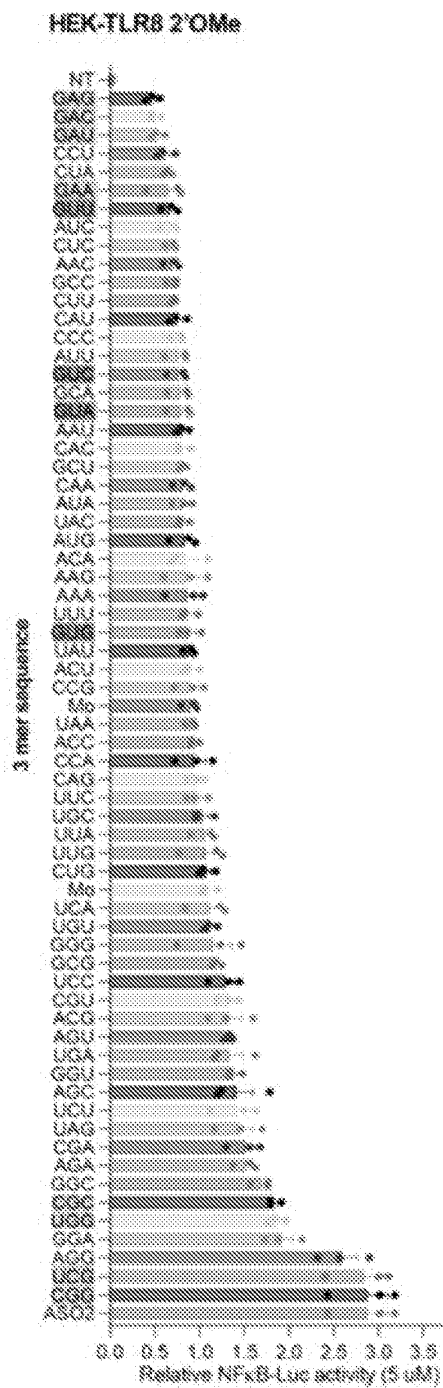
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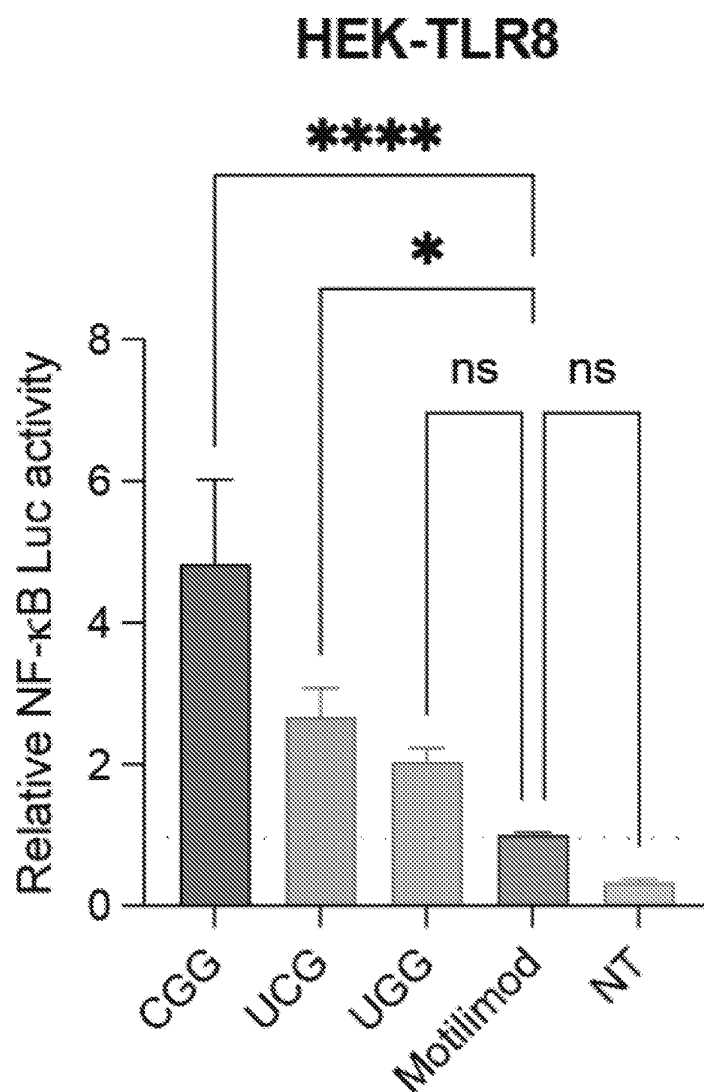
**FIGURE 34**

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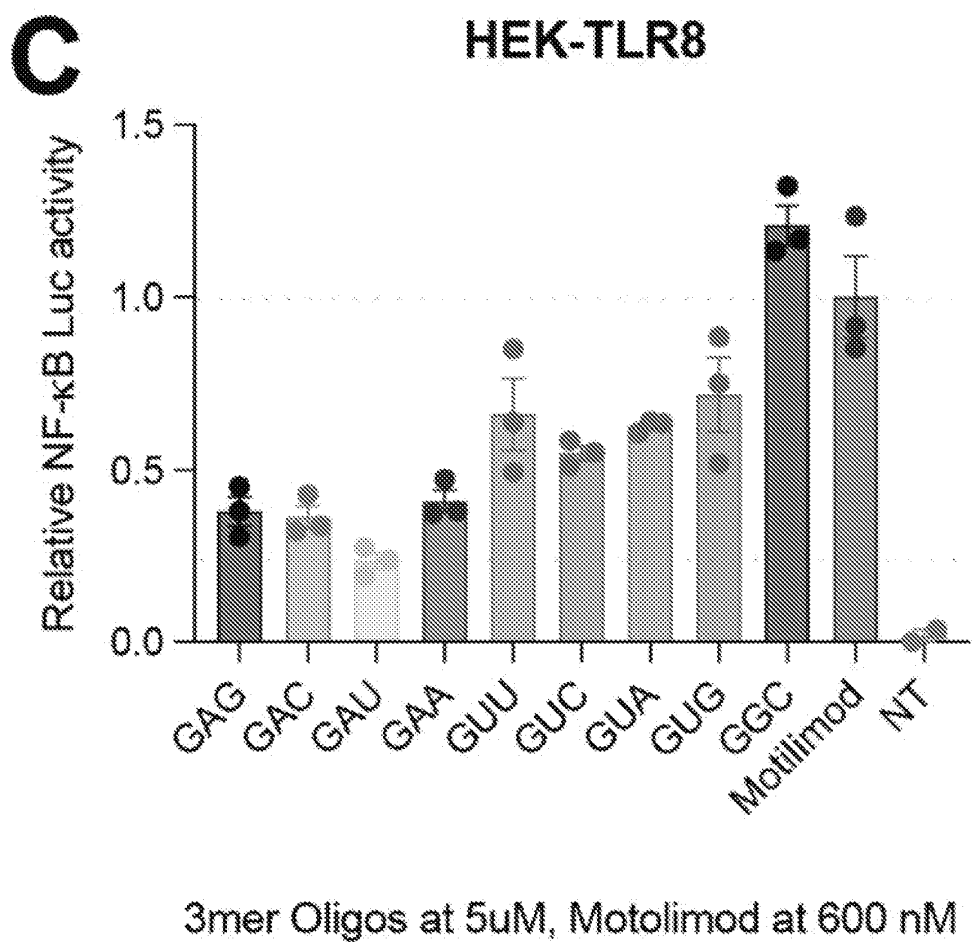
**FIGURE 35**

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**FIGURE 36A**

B**FIGURE 36B**

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**FIGURE 36C**

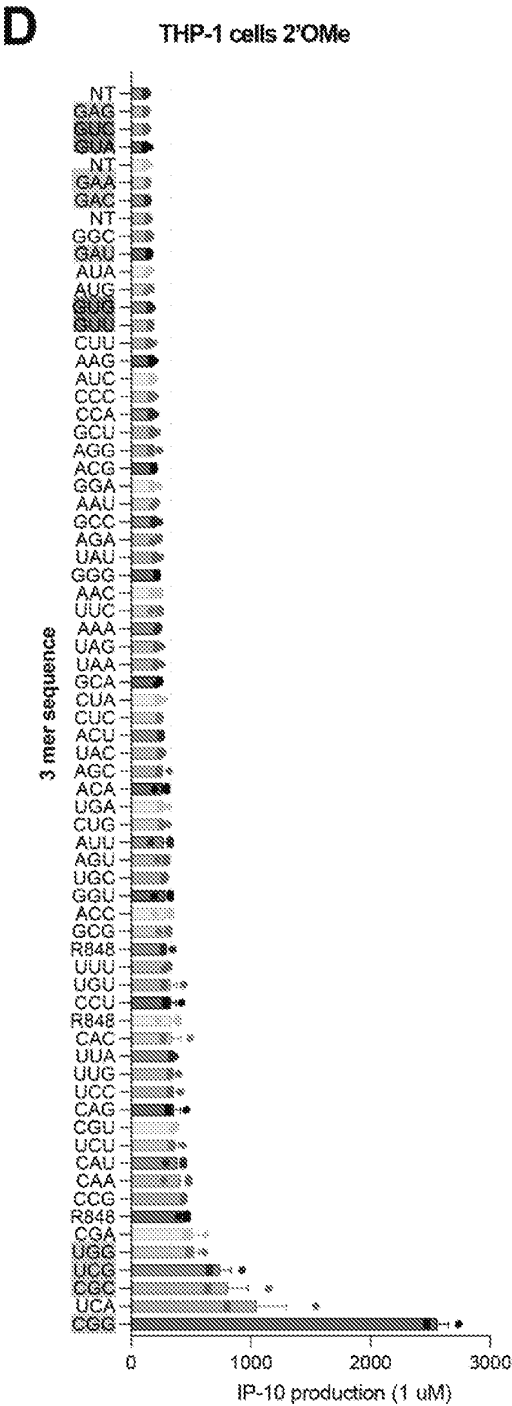


FIGURE 36D

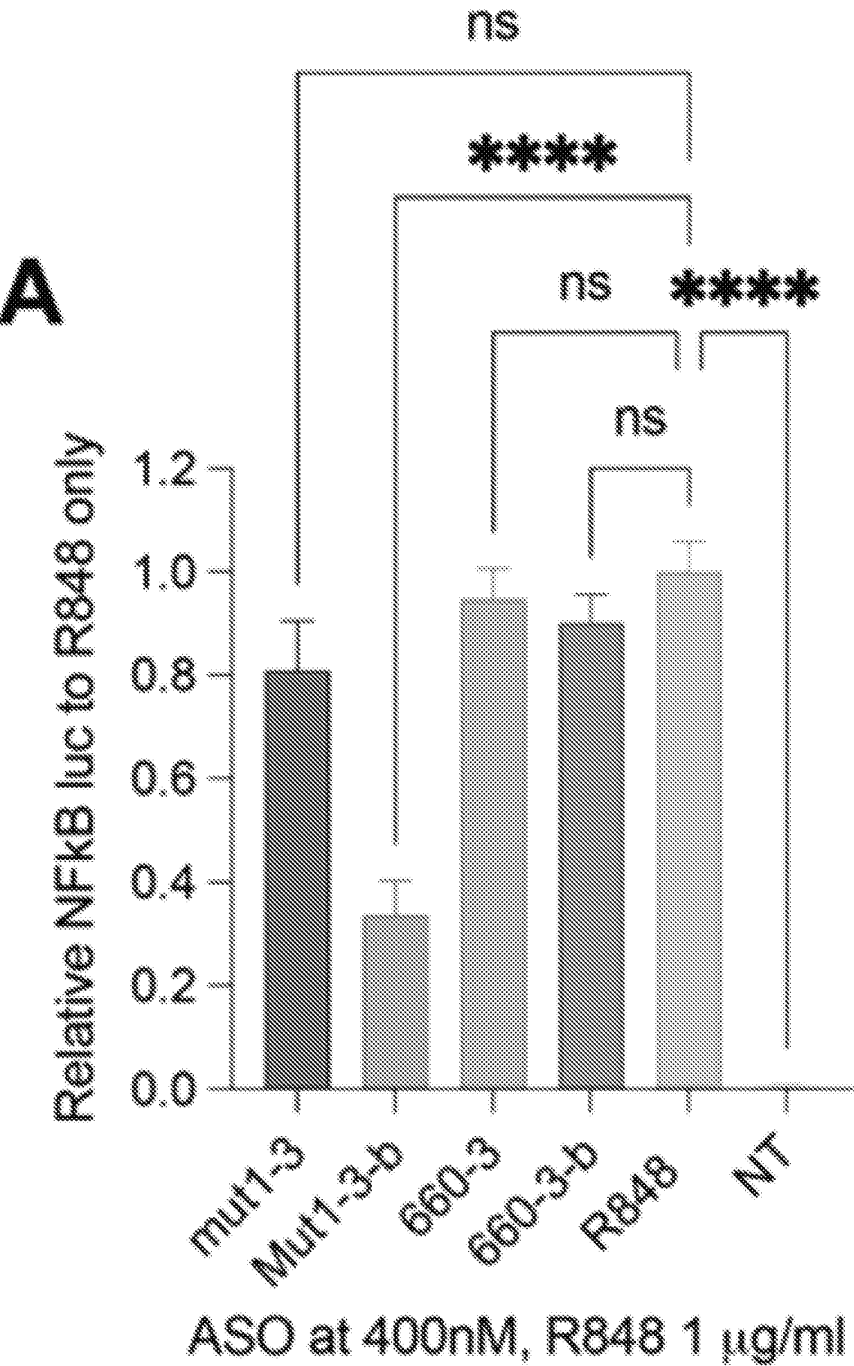


FIGURE 37A

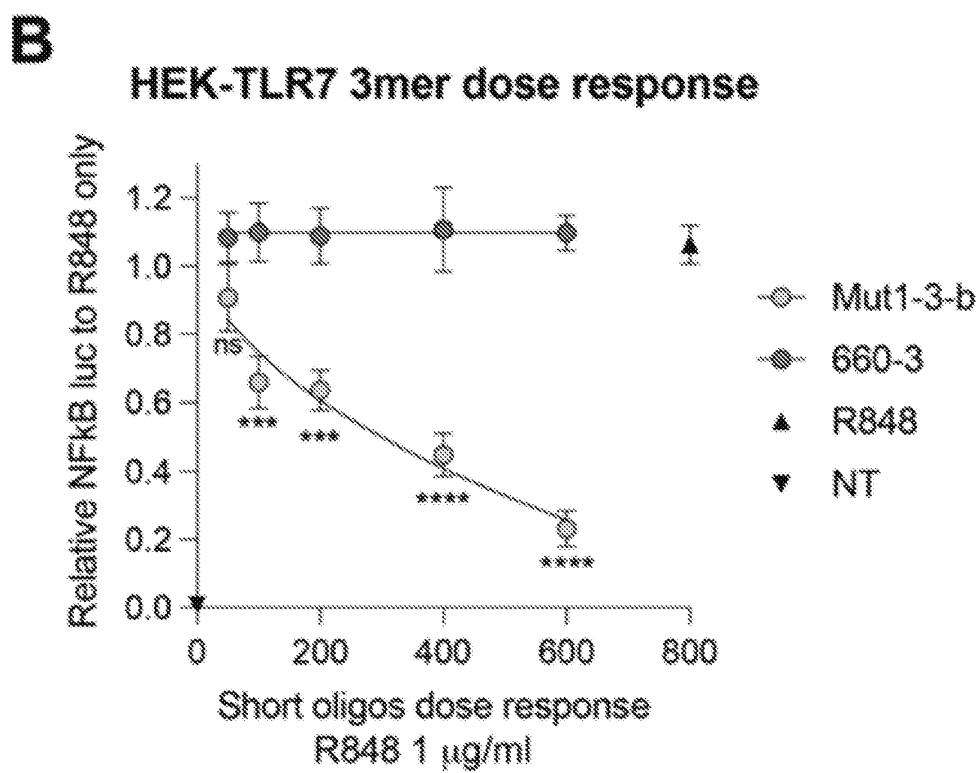


FIGURE 37B

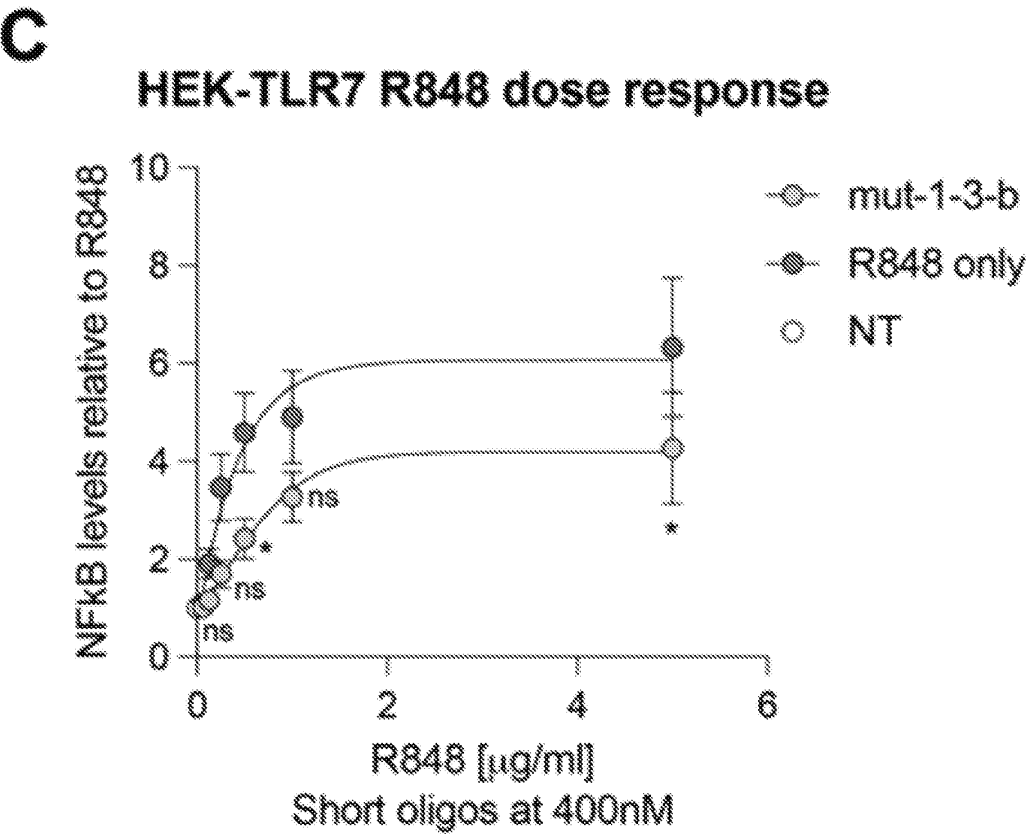


FIGURE 37C

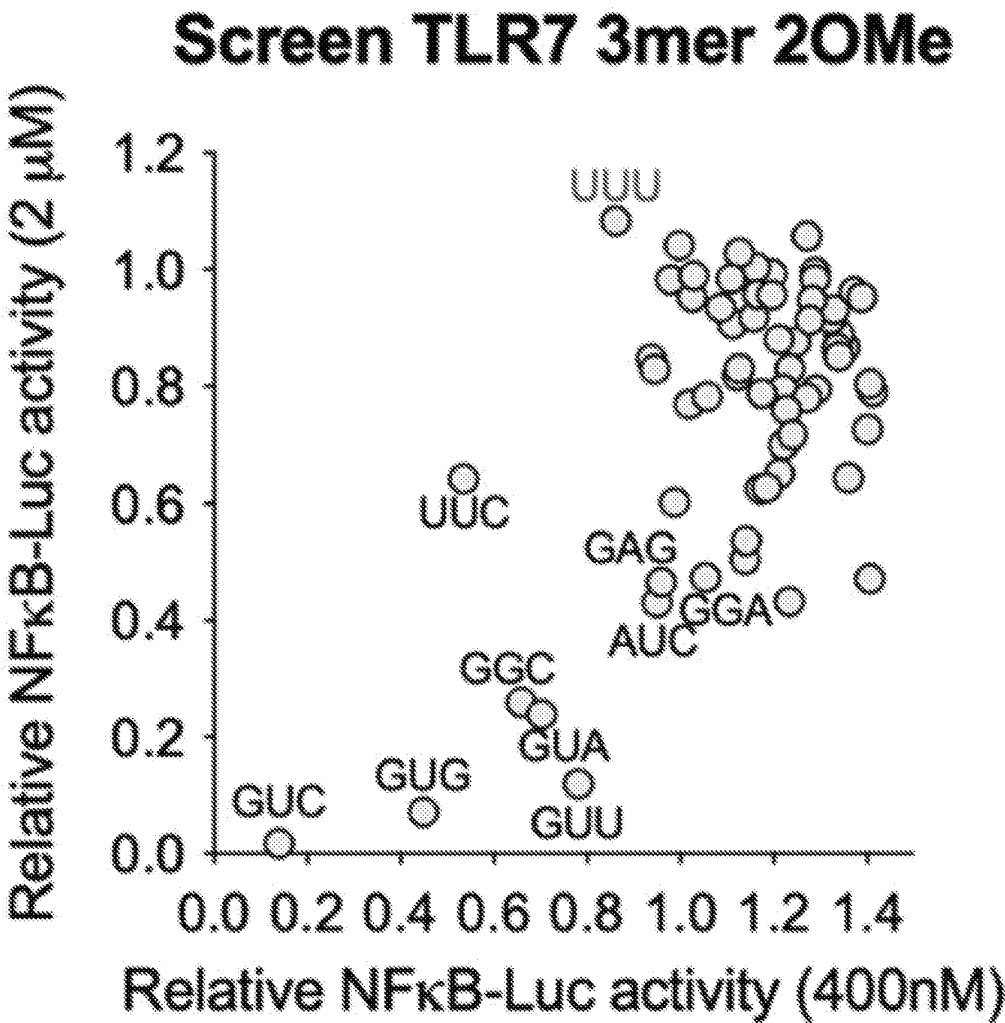
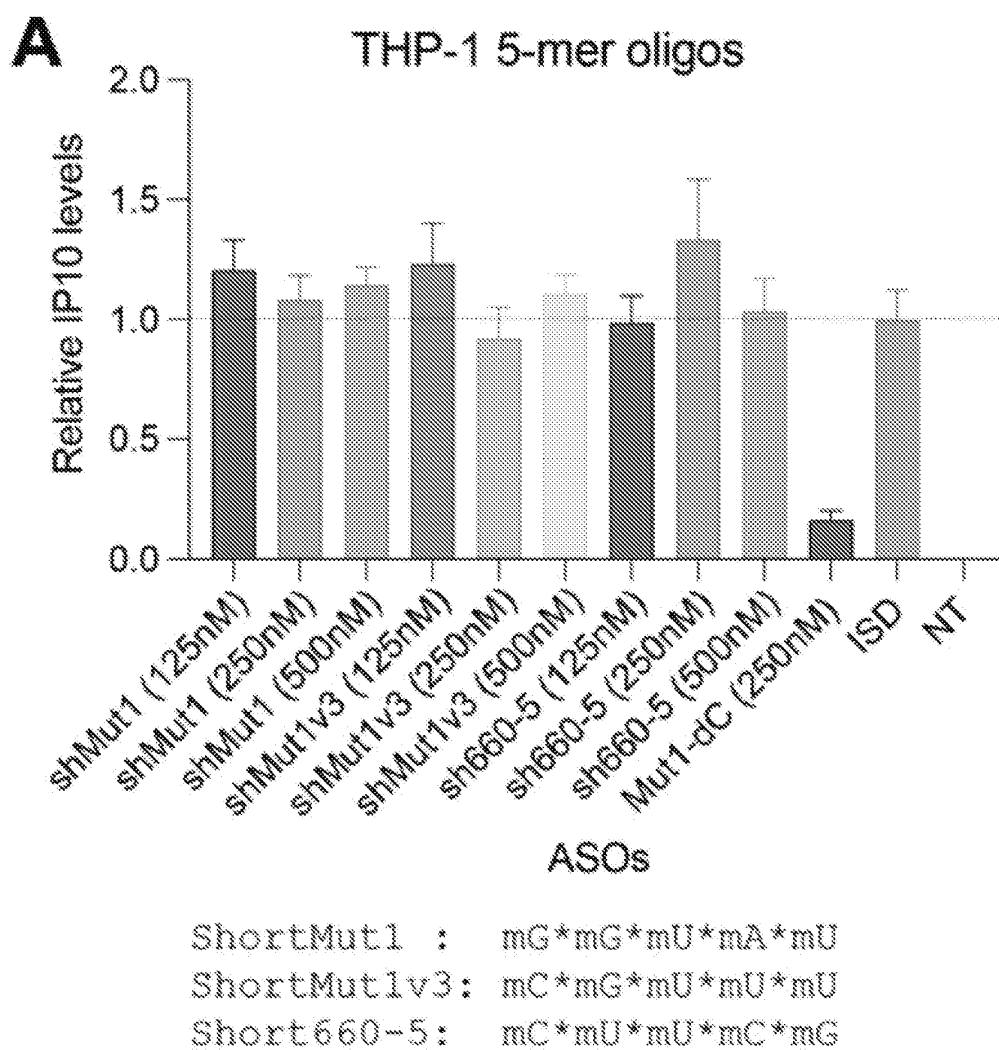
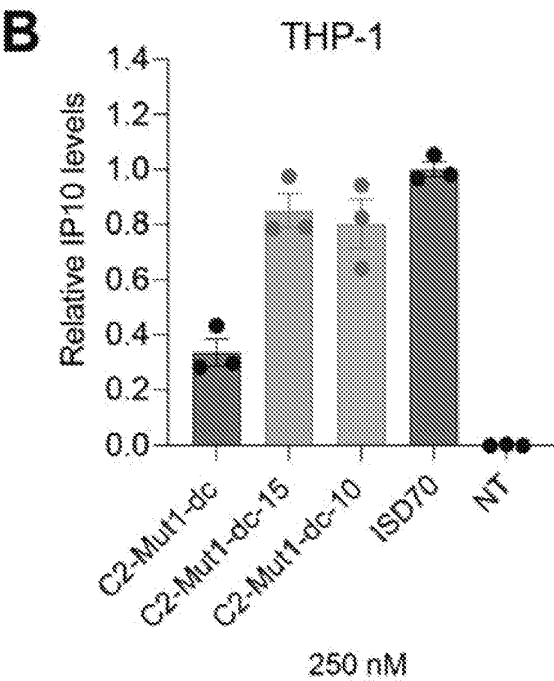


FIGURE 38

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**FIGURE 39A**



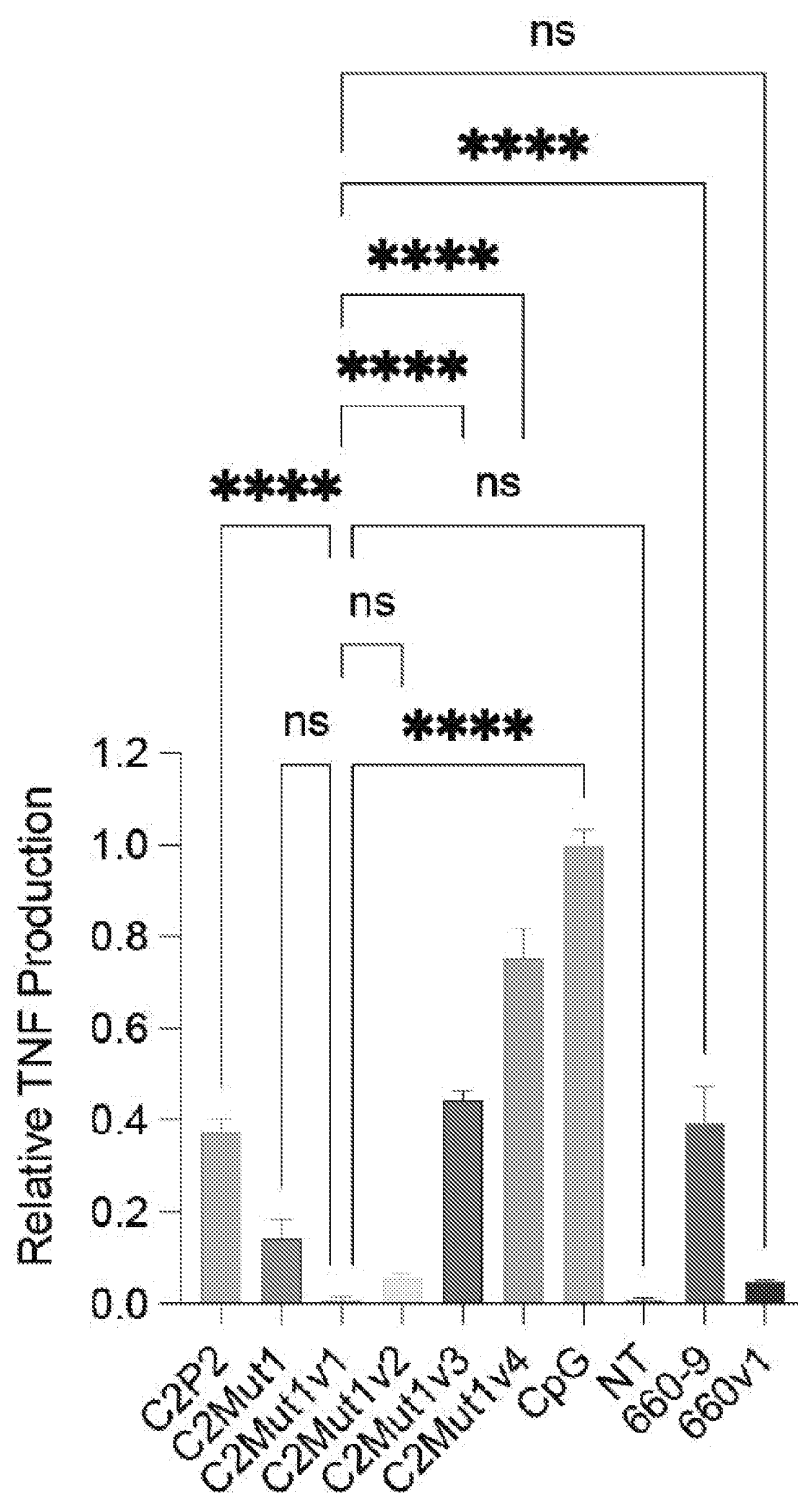
C2Mut1-dC: mG*mG*mU*A*T*C*C*C*C*C*C*C*C*C*C*C*C*C*C

C2Mut1-dC-15: mG*mG*mU*A*T*C*C*C*C*C*C*C*C*C*C*C

C2Mut1-dC-10: mG*mG*mU*A*T*C*C*C*C*C

FIGURE 39B

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**FIGURE 40**

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Name	
C2	GCAGUCTCCATGTCCCAGGC
C2-Mut1	GCGGUATCCATGTCCCAGGC
C2-Mut1v1	GCUGUTTCCATGTCCCAGGC
C2-Mut1v2	GCUGUGTCCATGTCCCAGGC
C2-Mut1v3	GC●GUTTCCATGTCCCAGGC
C2-Mut1v4	GC●GUGTCCATGTCCCAGGC
C2-ASO2-A	GCGGUATCCATAGT●UCCAU
C2-ASO2-B	GCGGUATCCAT●AGAUAU●CG

FIGURE 40 continued



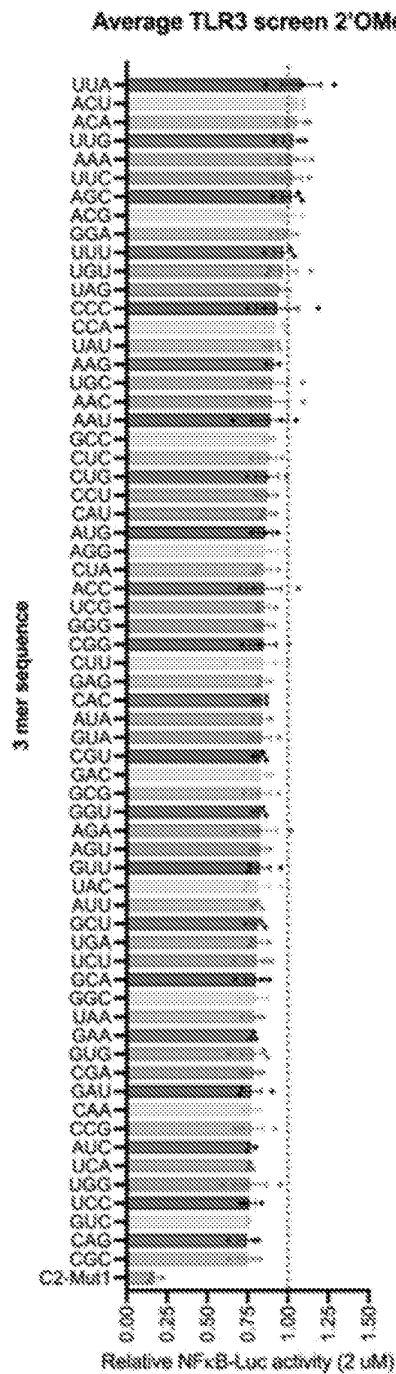


FIGURE 42

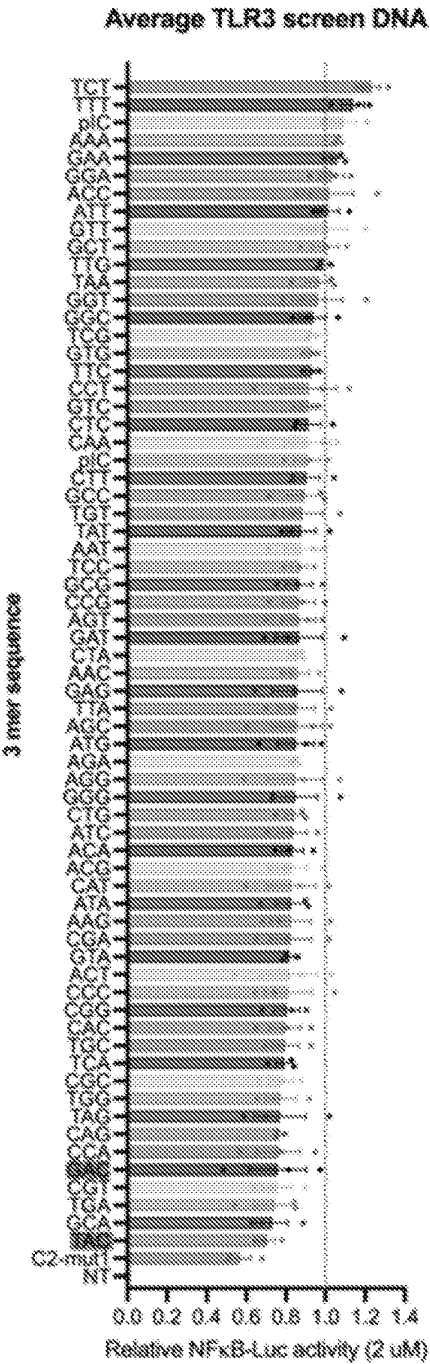


FIGURE 43