

FIG. 1A

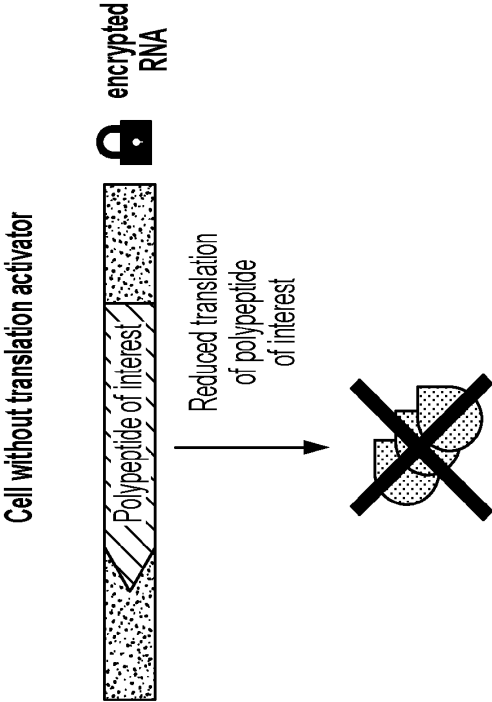


FIG. 1B

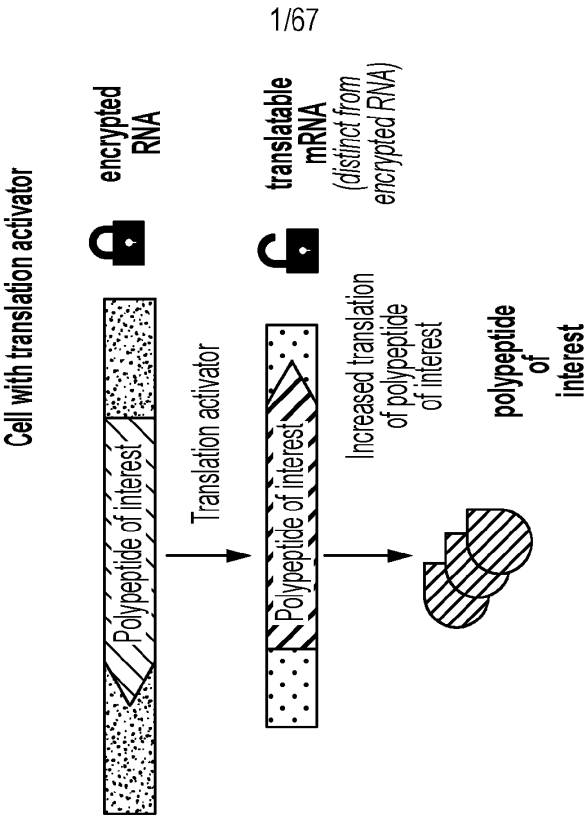


FIG. 2A

mRNA:
Protein production in all cells

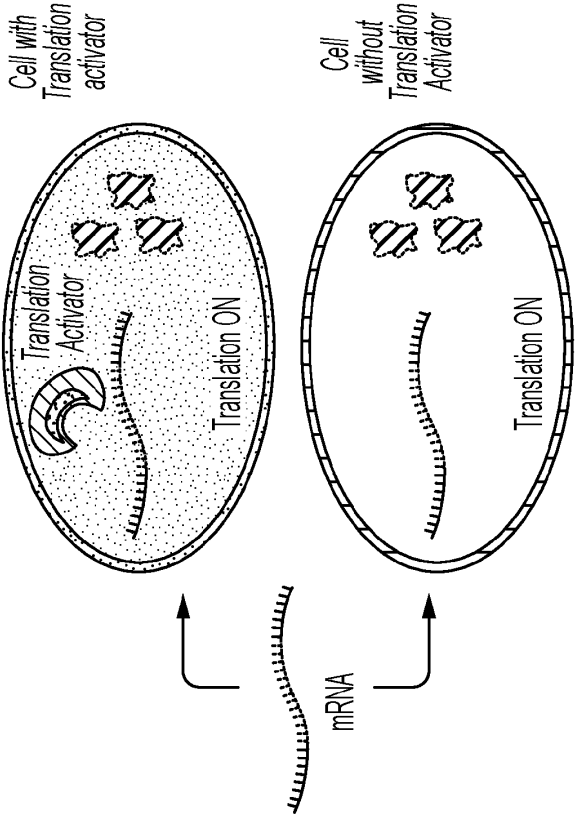


FIG. 2B

Encrypted RNA:
Increased translation of protein of interest in treated cells also provided with translation activator

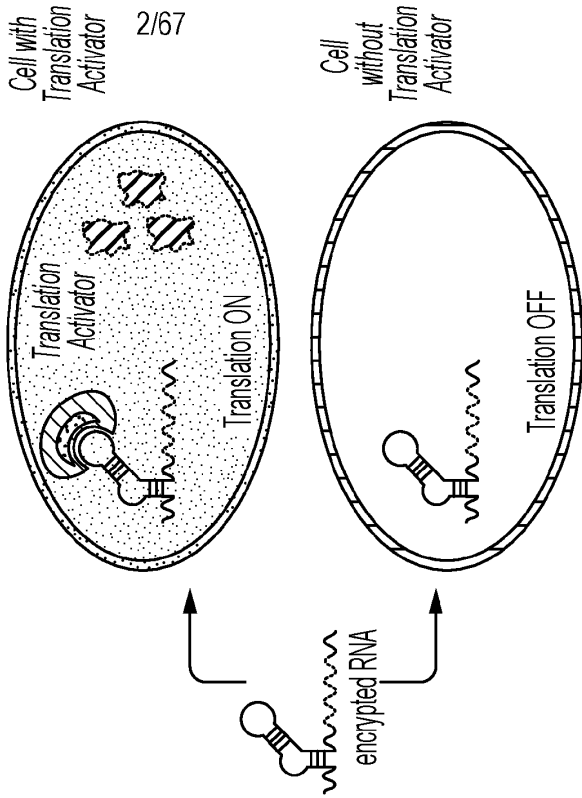


FIG. 3A

Encrypted RNA only

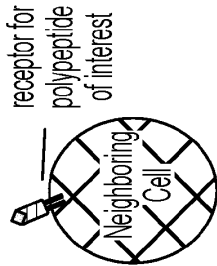
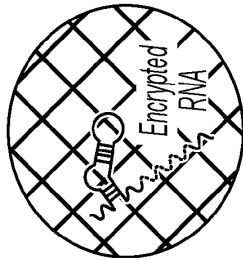


FIG. 3B

Virus Only

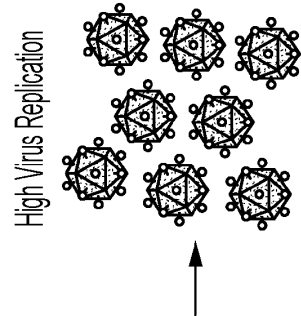
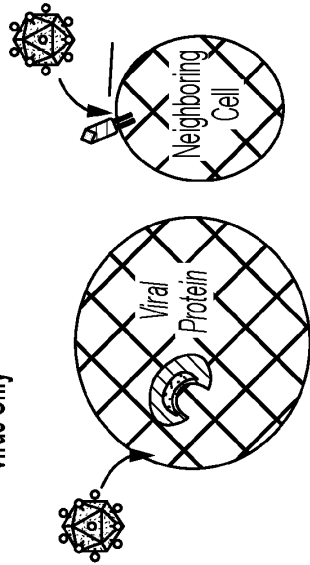


FIG. 3C

Encrypted RNA + Virus

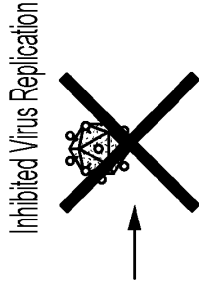
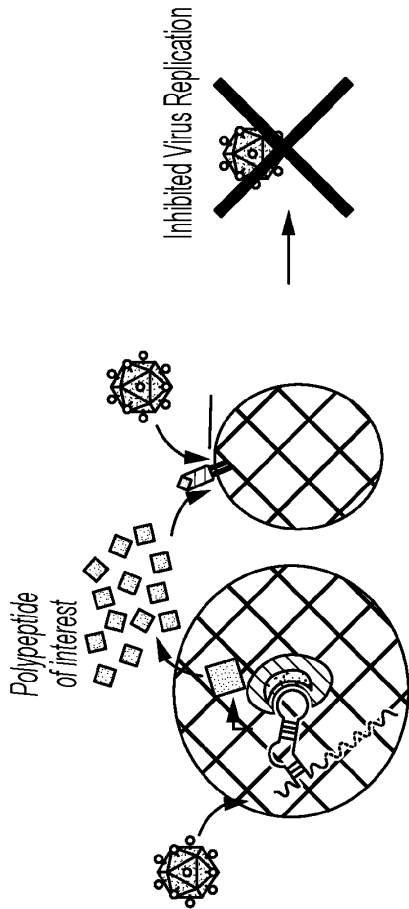


FIG. 4A

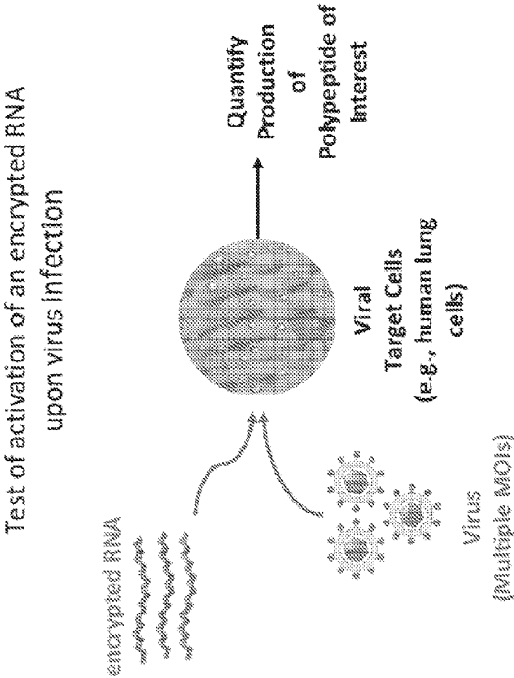


FIG. 4B

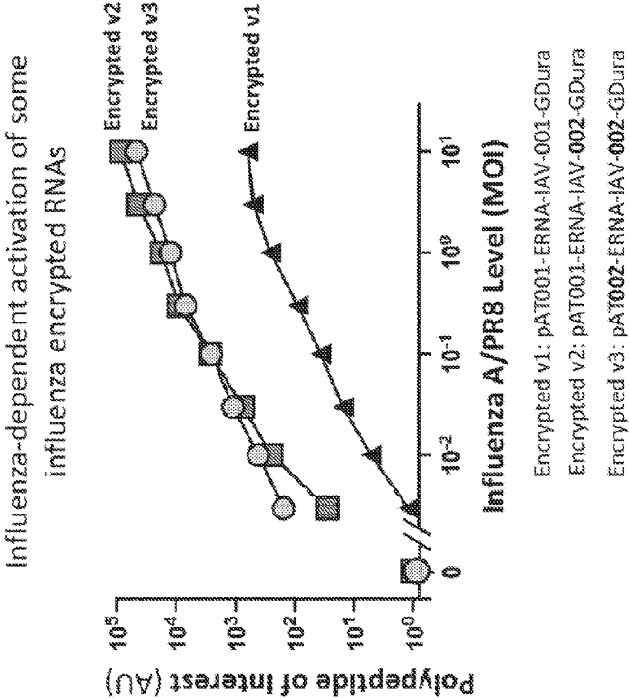


FIG. 5

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Influenza Proteins Provided						Substantially Increased Translation of Polypeptide of Interest?
Pool	PB2	PB1	PA	NP	Encrypted RNA ERNA-IAV-002-GDura	
no TA	-	-	-	-	+	No
Pol _A -PB2	-	+	+	+	+	No
Pol _A -PB1	+	-	+	+	+	No
Pol _A -PA	+	+	-	+	+	No
Pol _A -ERNA	+	+	+	+	-	No
Pol _A	+	+	+	+	+	Yes

↑

↑

↑

↑

↑

↑

FIG. 6

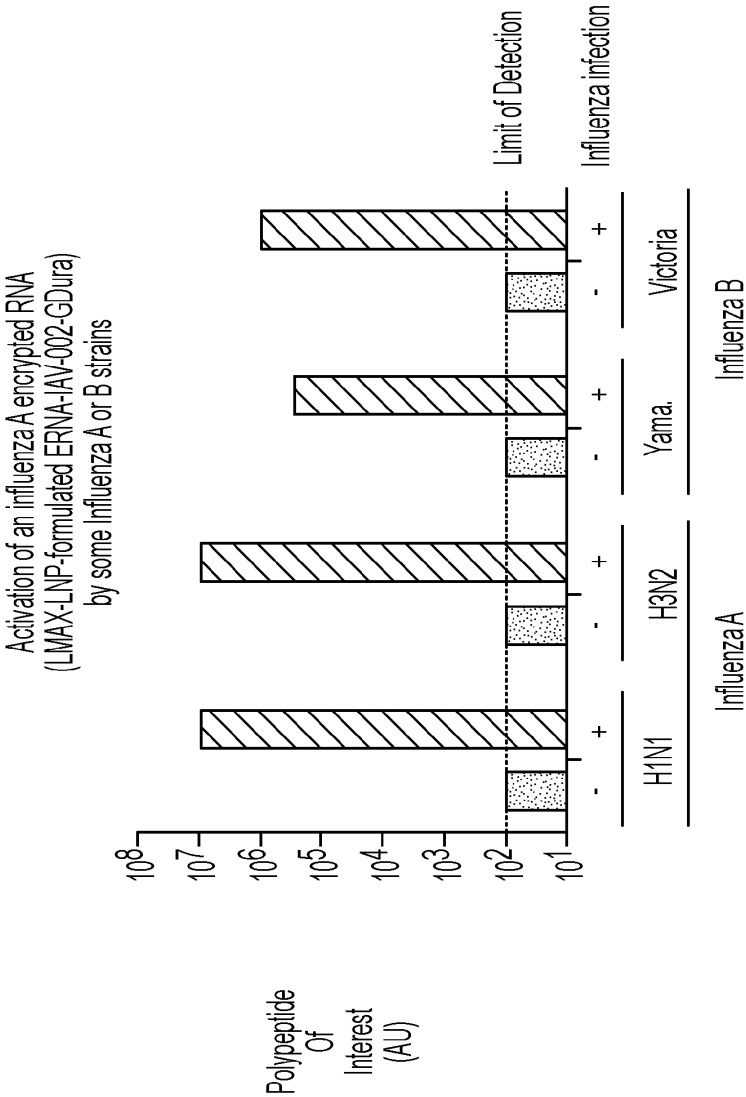


FIG. 7

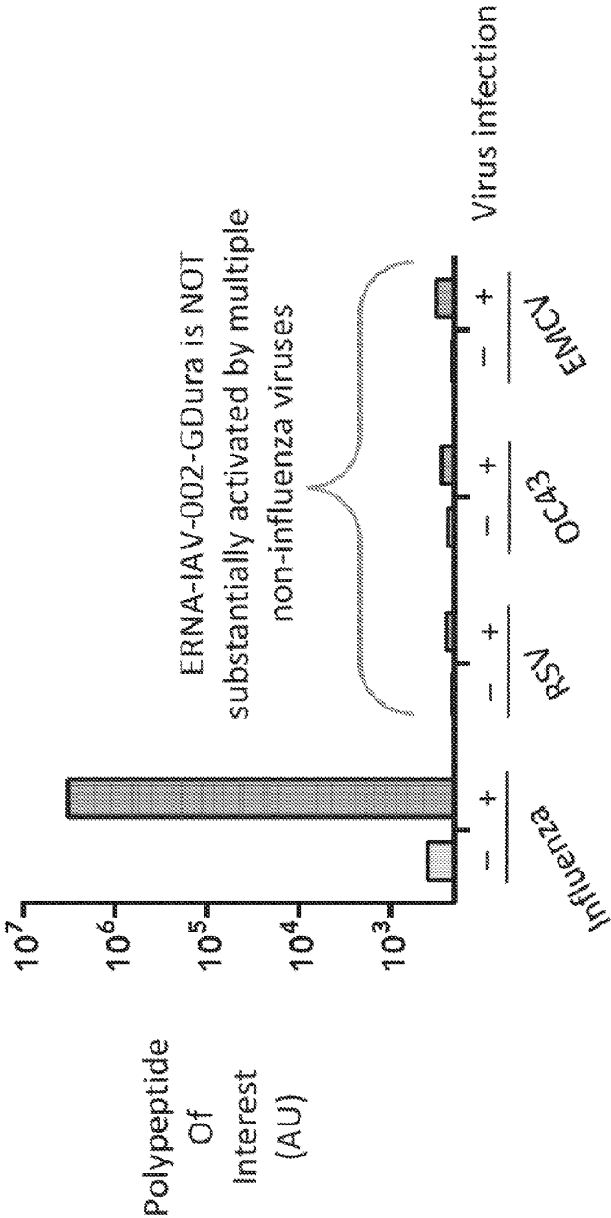


FIG. 8A

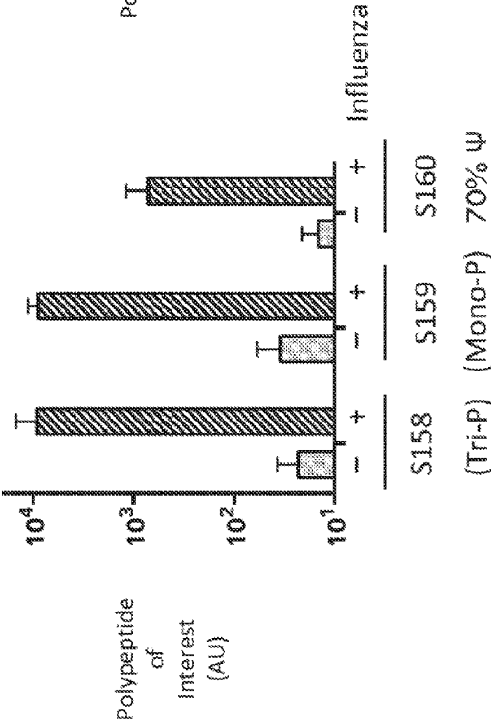


FIG. 8B

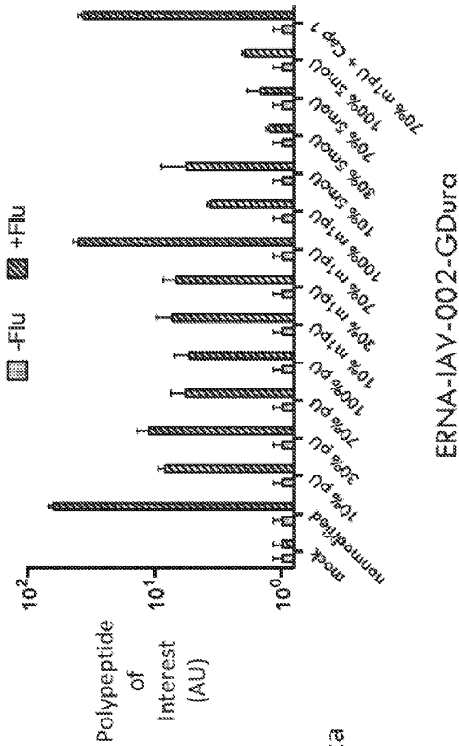


FIG. 9

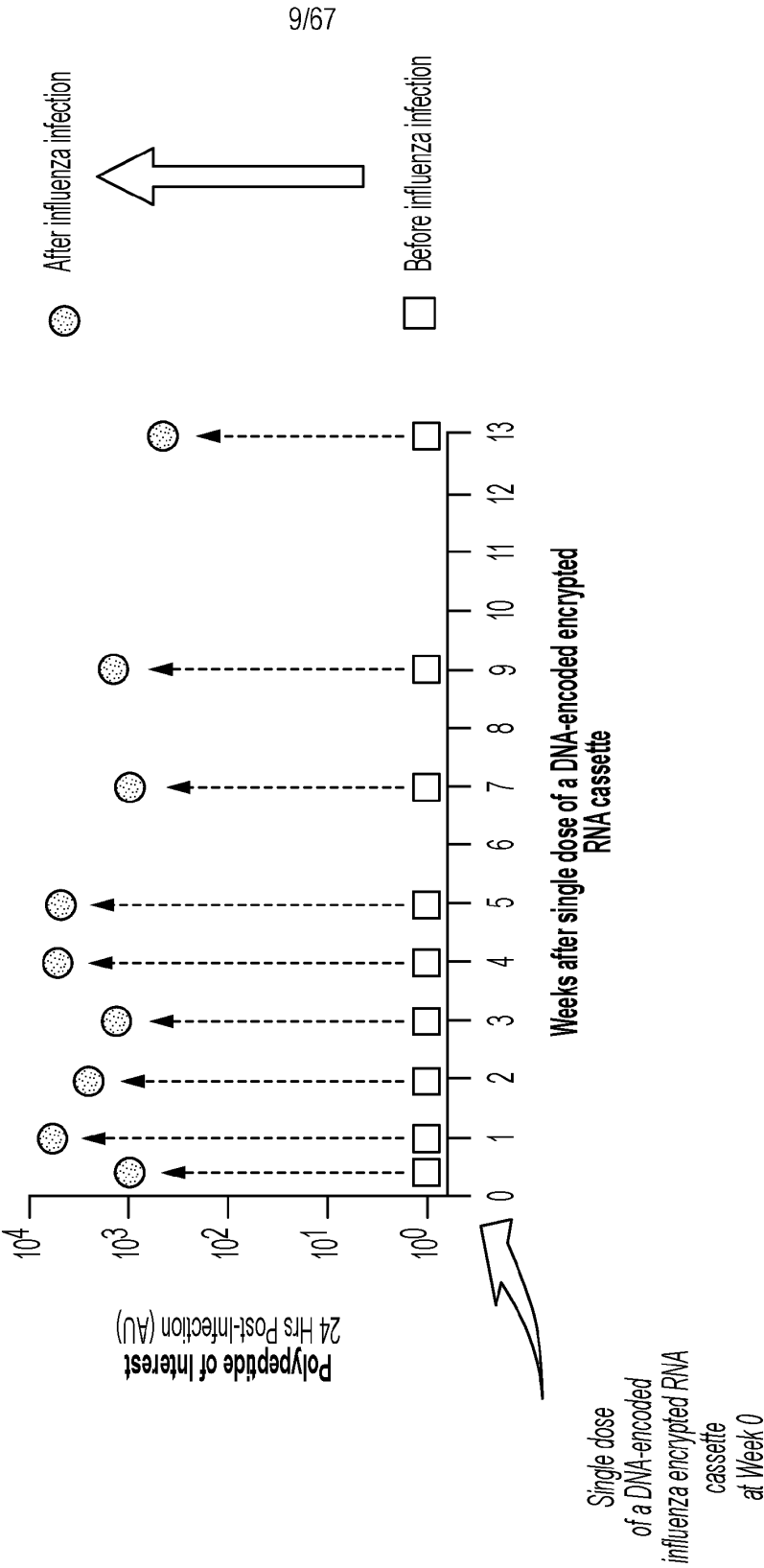


FIG. 10A

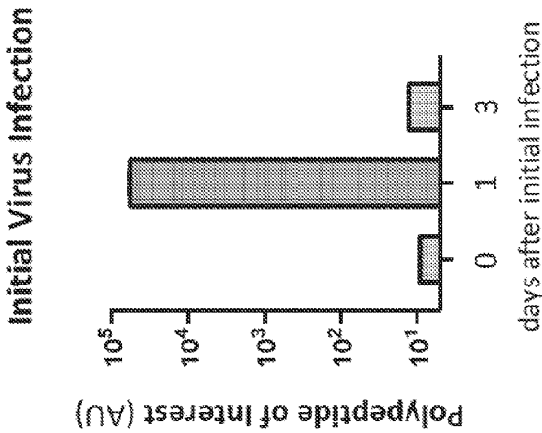


FIG. 10B

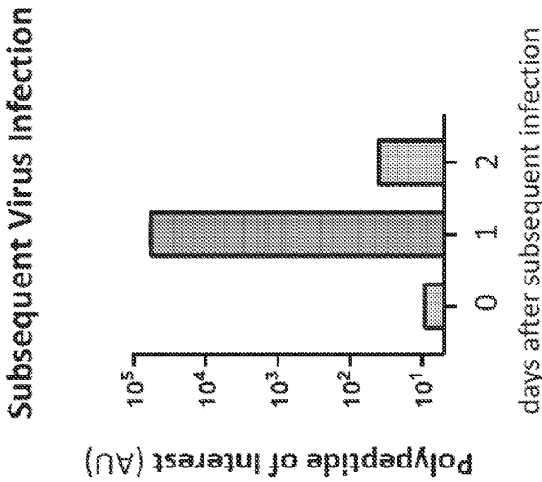
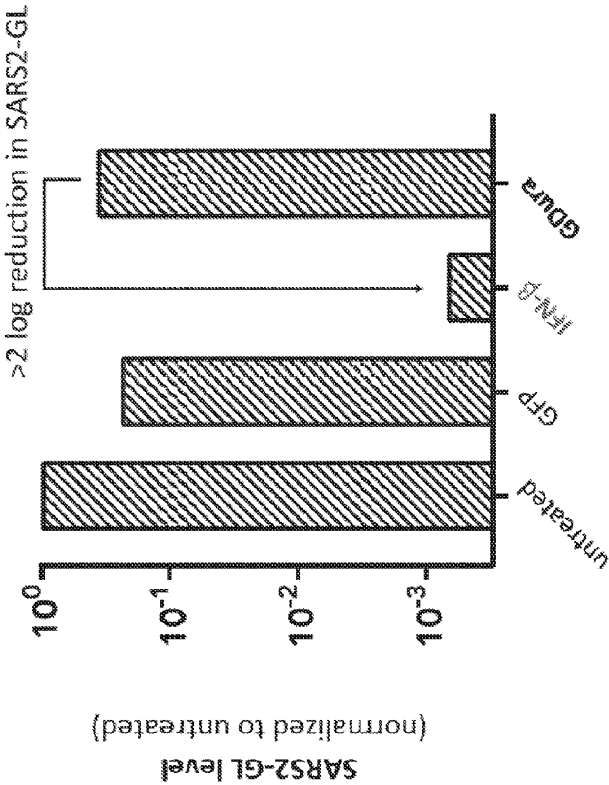
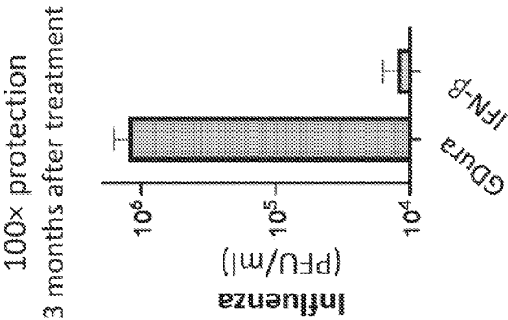


FIG. 11



GDura: LMAX-LNP-formulated uncapped ERNA-SARS2-101-GDura (sarbecovirus encrypted RNA encoding GDura)
IFN-β : LMAX-LNP-formulated uncapped ERNA-SARS2-101-hu__IFNB (sarbecovirus encrypted RNA encoding human IFN-β)
GFP: LMAX-LNP-formulated uncapped mRNA encoding a GFP

FIG. 12



GDura: DNA-encoded influenza encrypted RNA cassette encoding GDura
IFN-β : DNA-encoded influenza encrypted RNA cassette encoding human IFN-β

FIG. 13

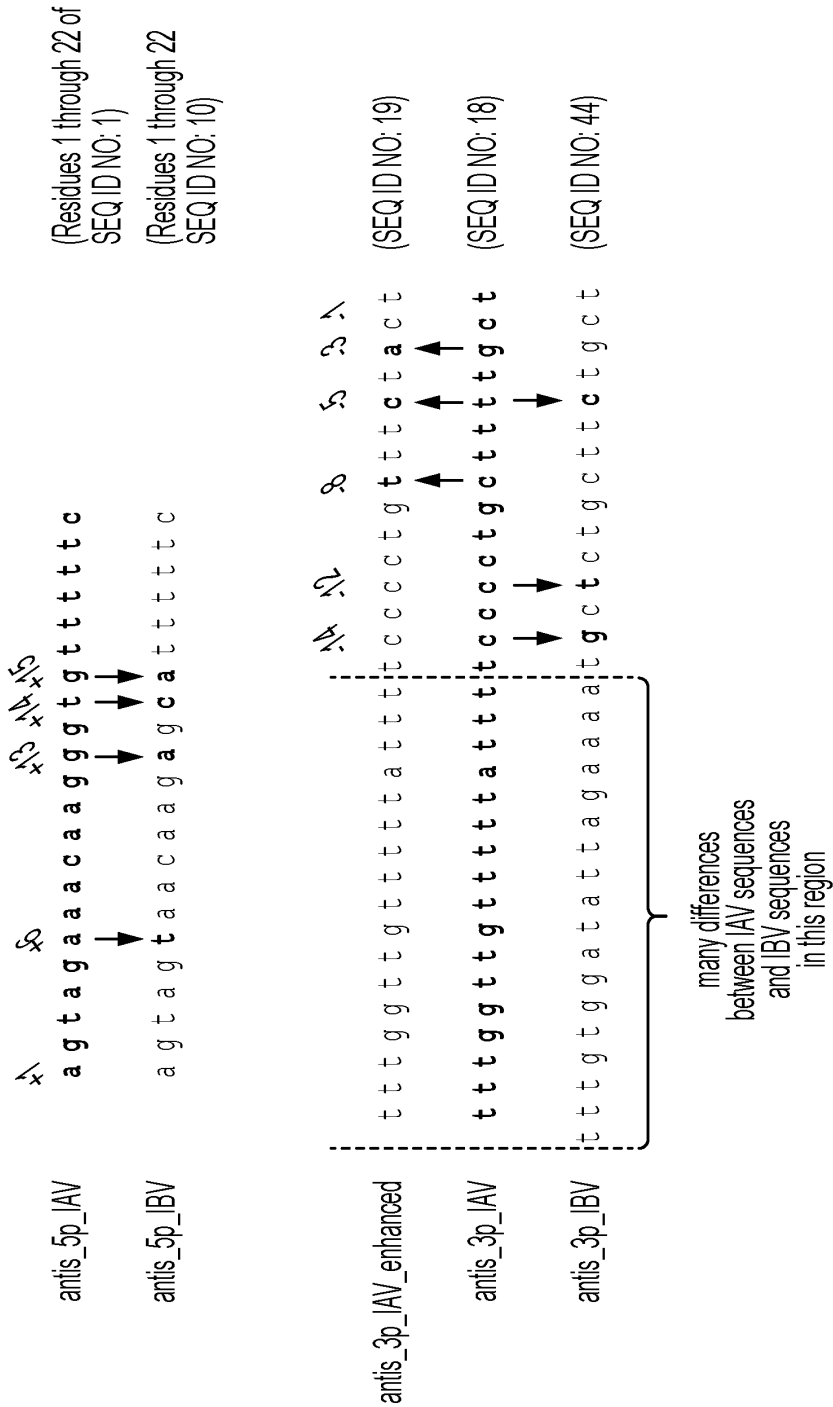


FIG. 14

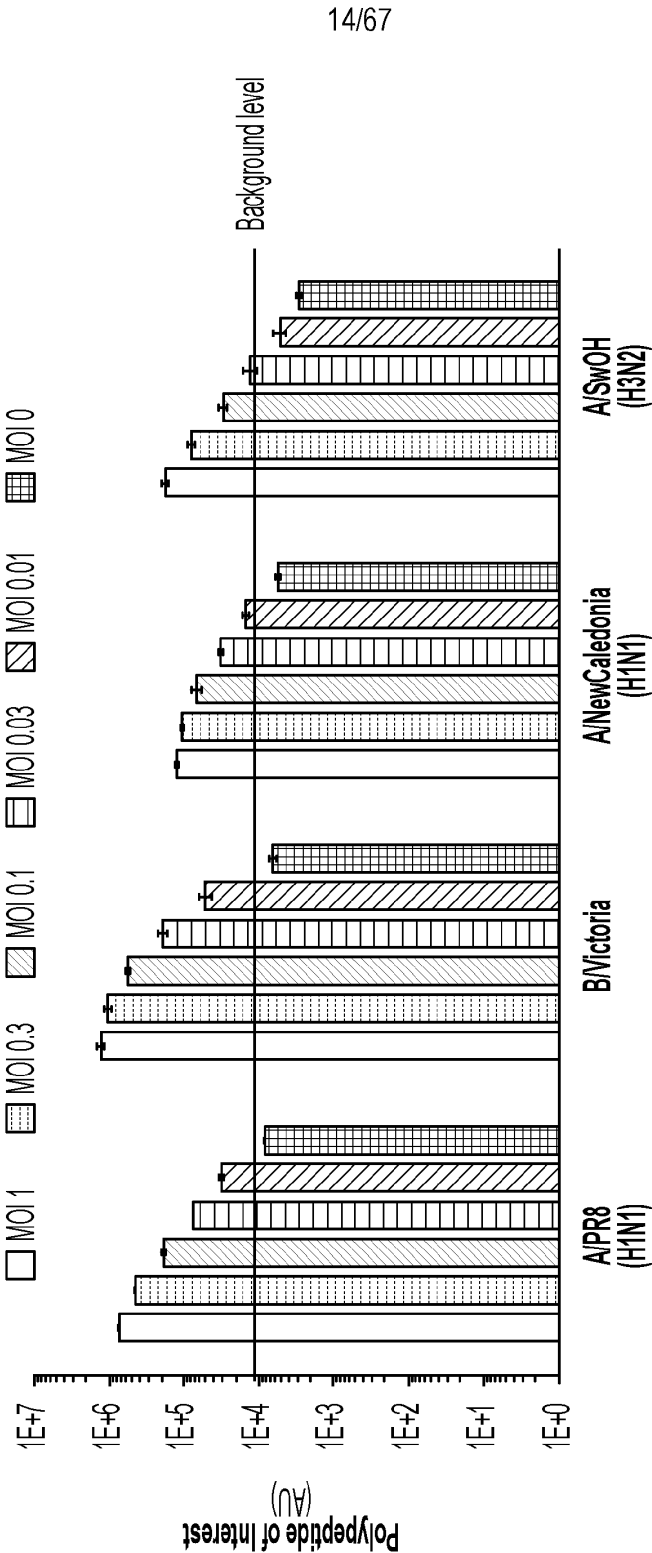
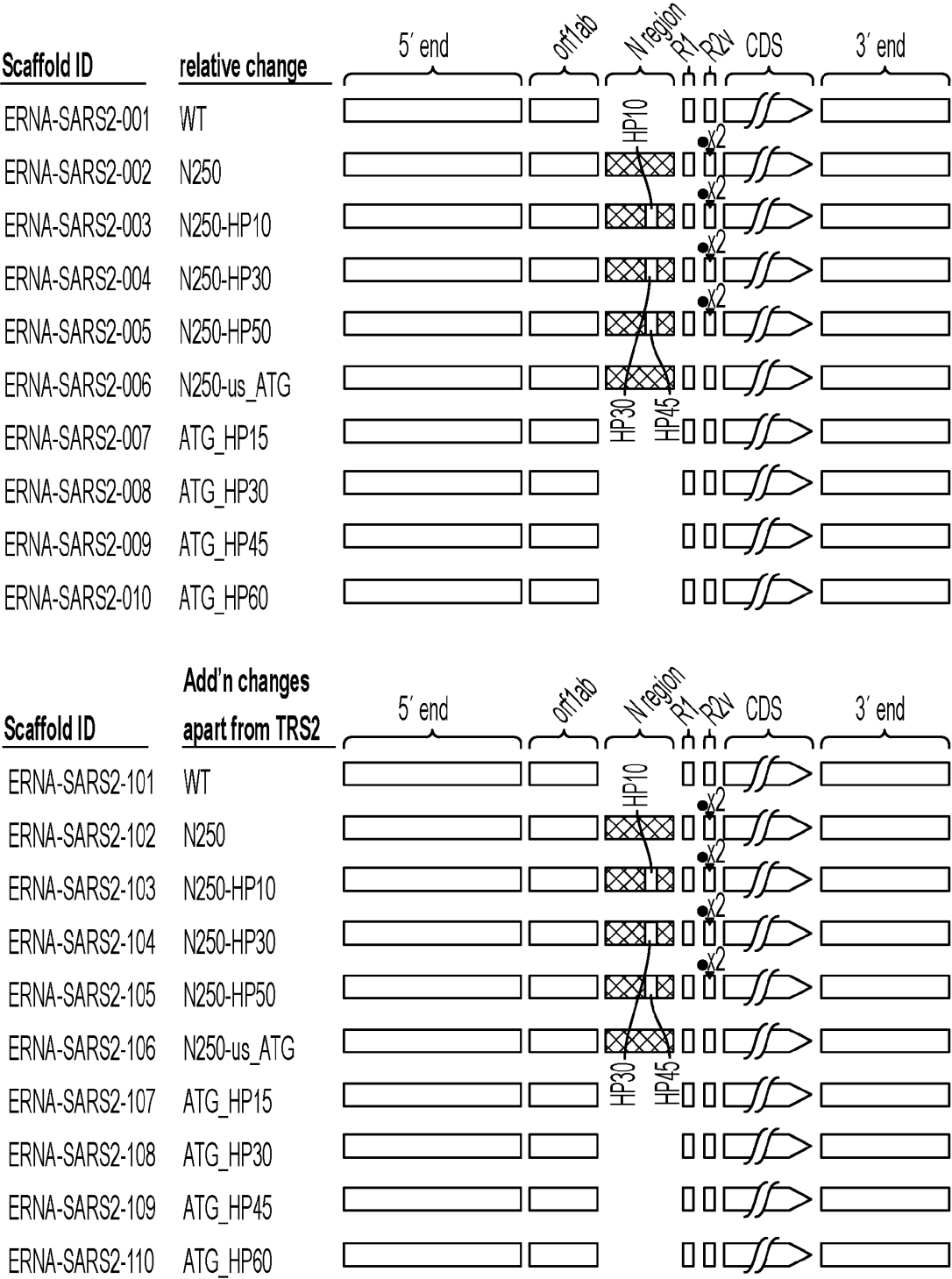


FIG. 15

Representative Sarbecovirus Encrypted RNA Scaffolds
(sense encrypted)



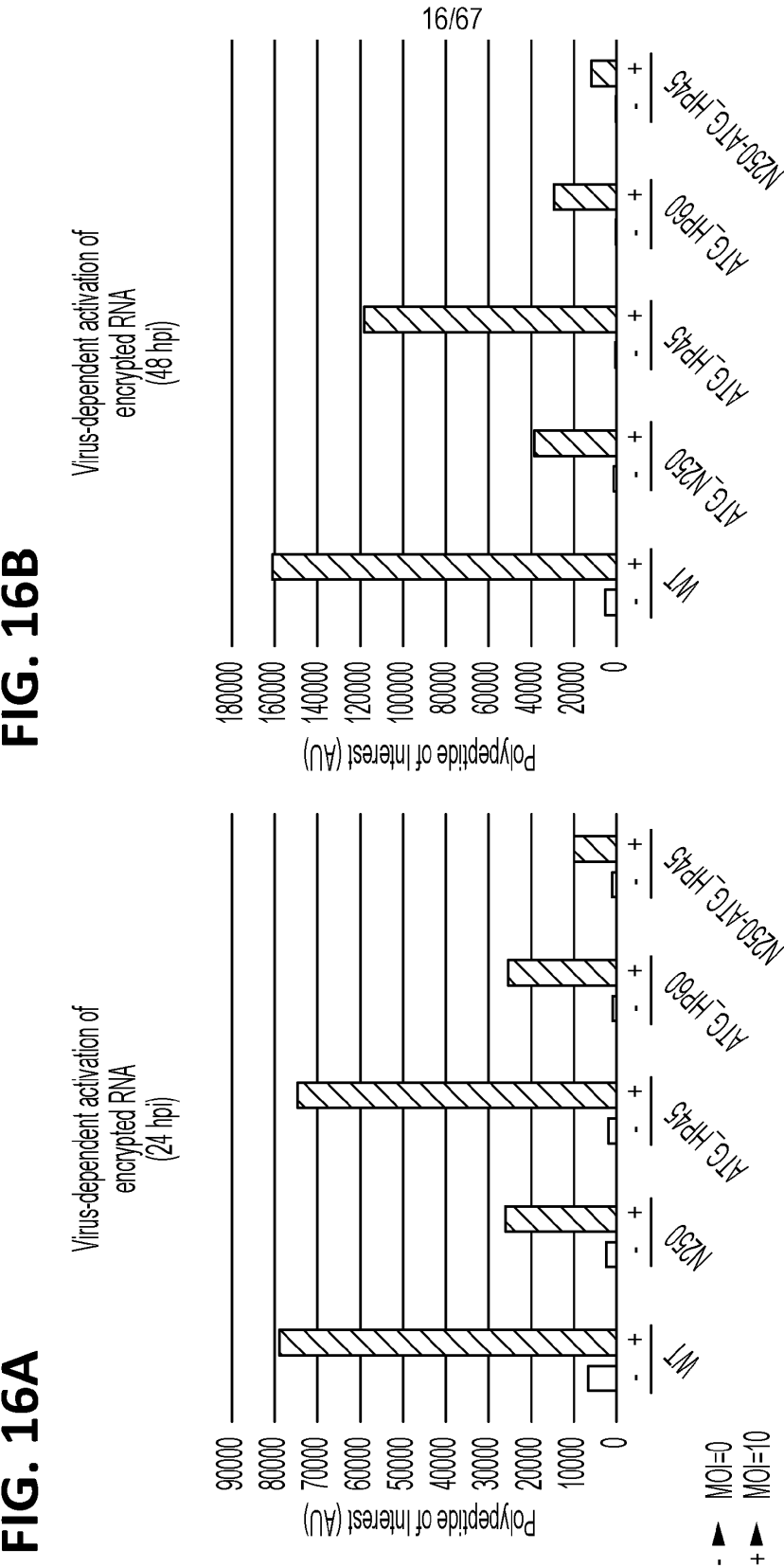


FIG. 17

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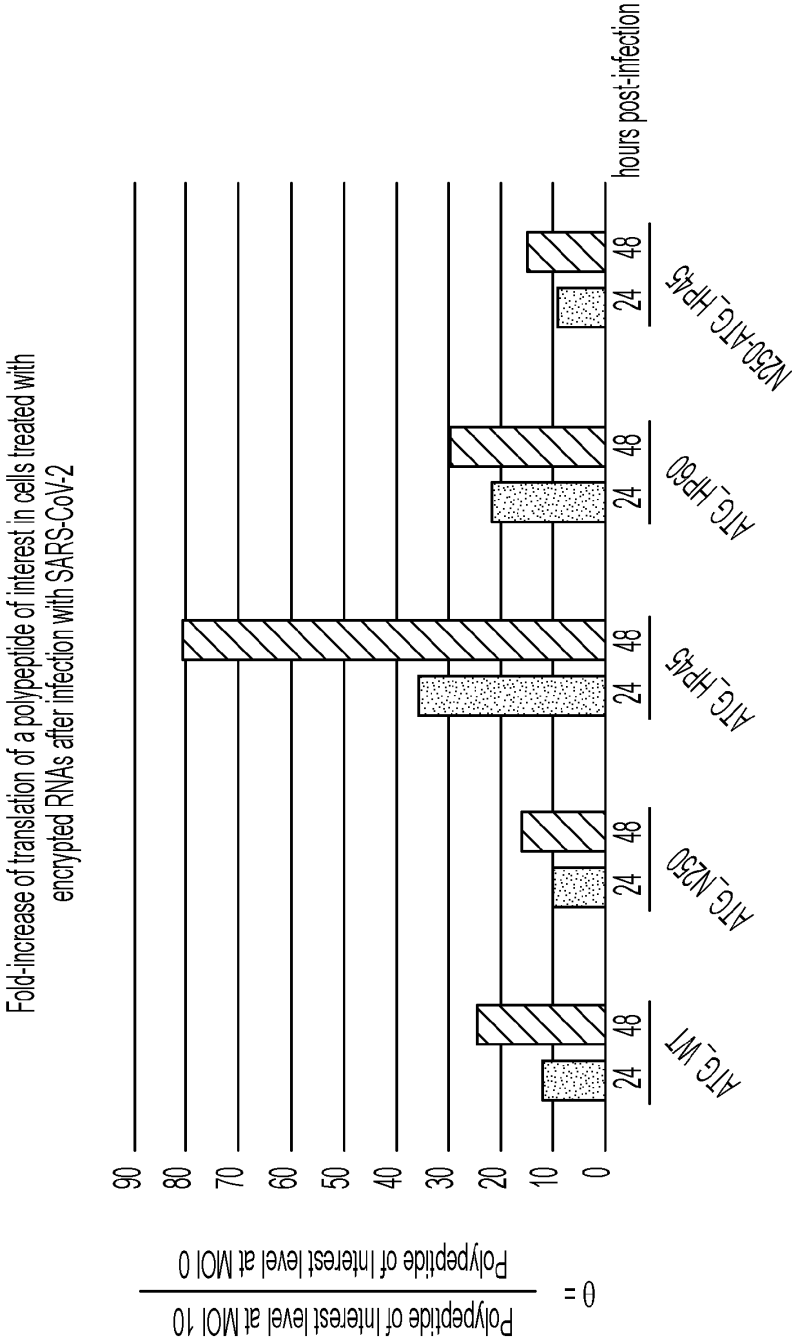


FIG. 18A

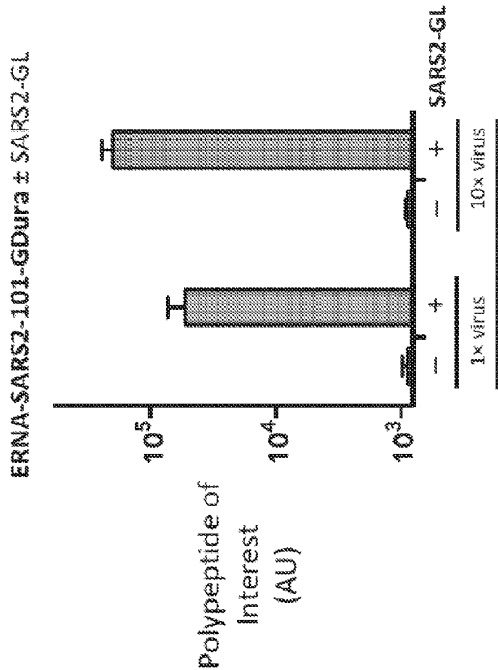


FIG. 18B

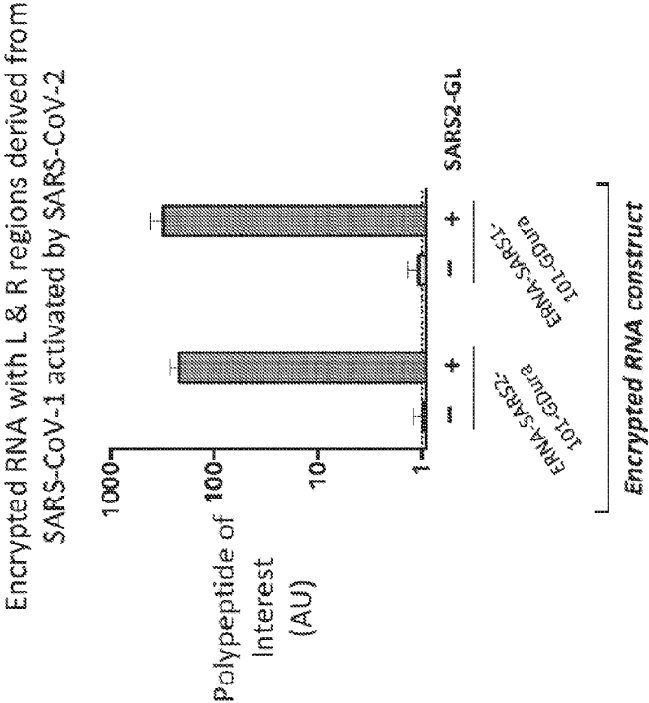


FIG. 19

Representative Sarbecovirus Encrypted RNA Scaffolds
(antisense protein CDS)

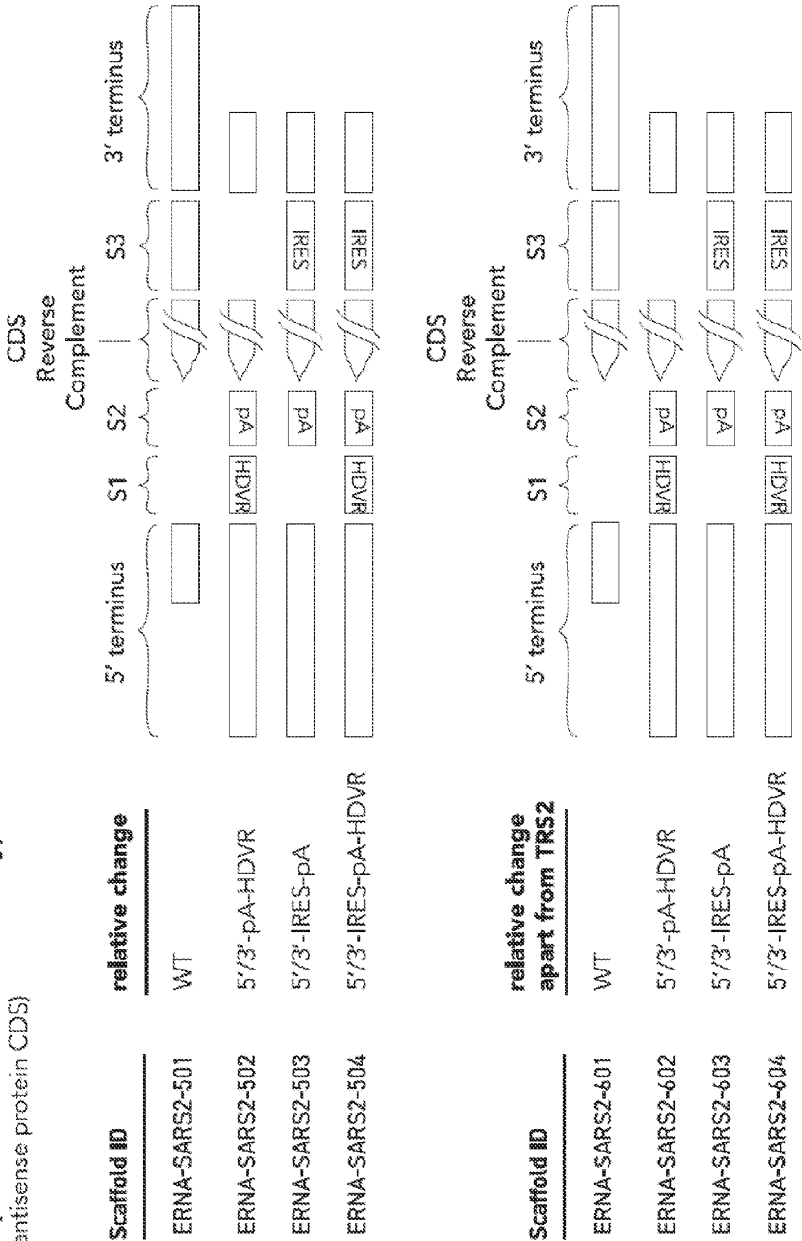


FIG. 20A

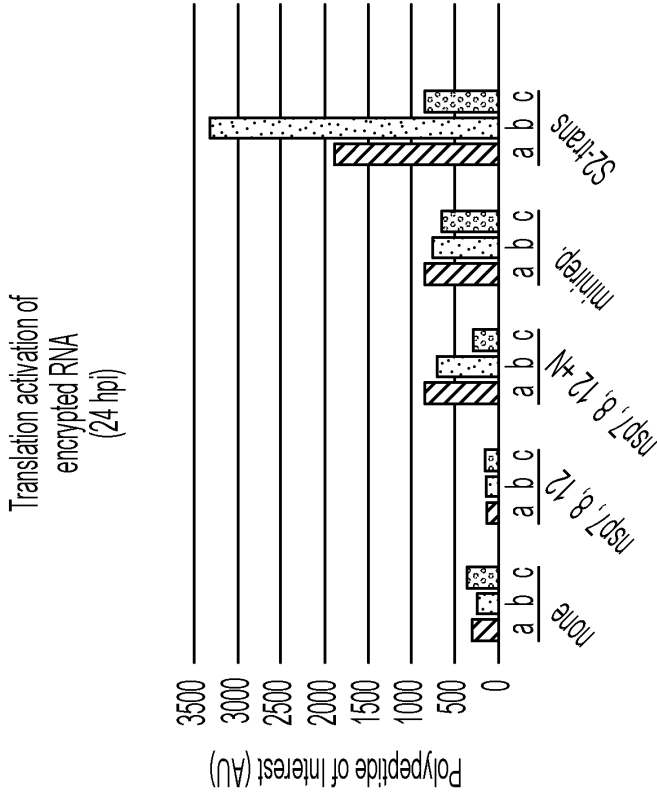
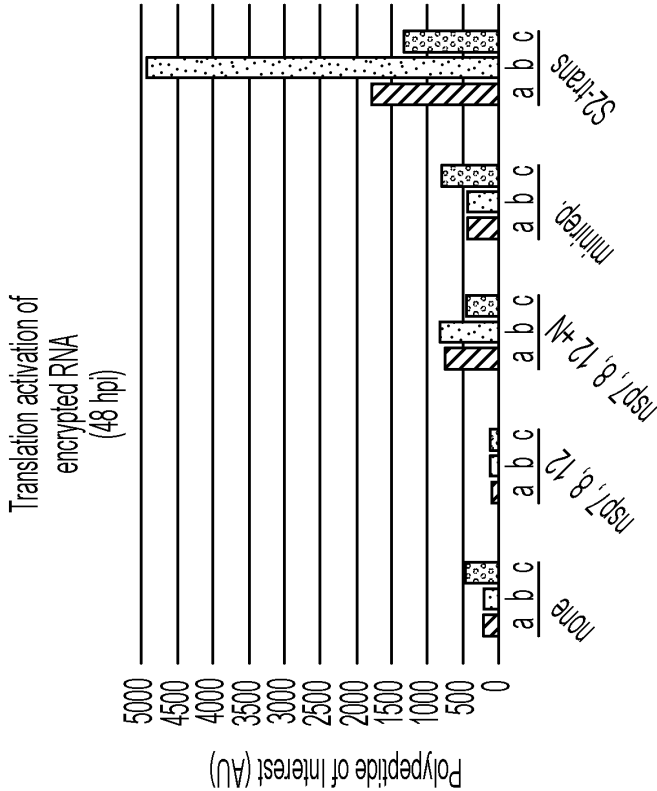


FIG. 20B

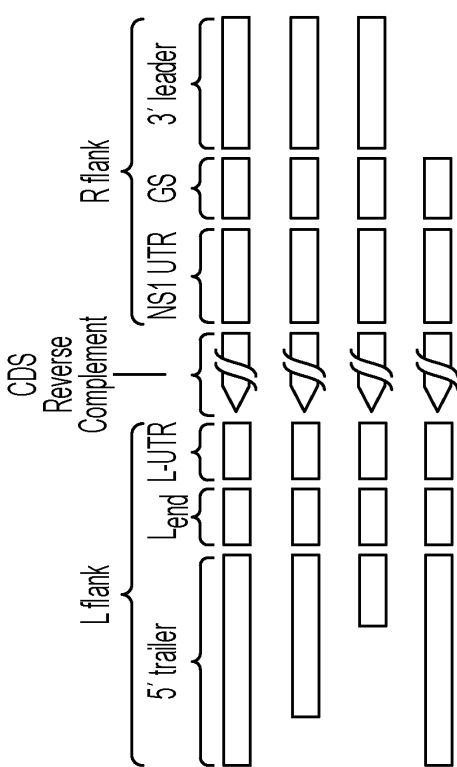


- a pAT401-ERNA-SARS2-601-GDura
- b pAT402-ERNA-SARS2-601-GDura
- c pAT402-ERNA-SARS2-604-GDura

FIG. 21

Representative RSV Encrypted RNA Scaffolds
(antisense protein CDS)

Scaffold ID	relative change
ERNA-RSV-001	WT
ERNA-RSV-002	5p-Δ56
ERNA-RSV-003	5p-Δ115
ERNA-RSV-004	3p-ΔLeader



Representative RSV Encrypted RNA Scaffolds
(sense protein CDS)

Scaffold ID	relative change
ERNA-RSV-101	WT
ERNA-RSV-102	5p-Δ56
ERNA-RSV-103	5p-Δ115
ERNA-RSV-104	3p-ΔLeader

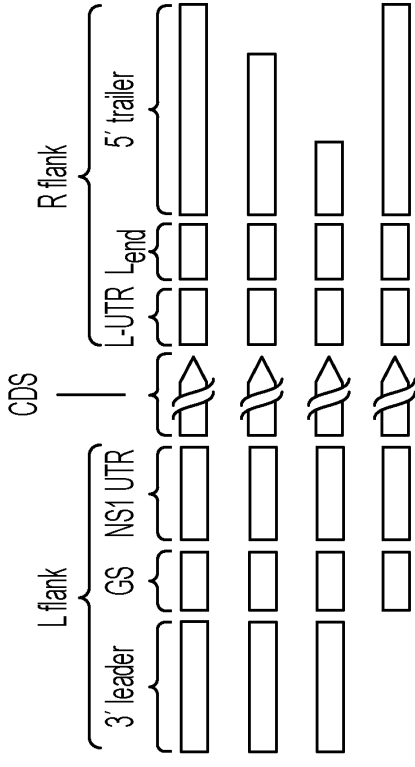


FIG. 22

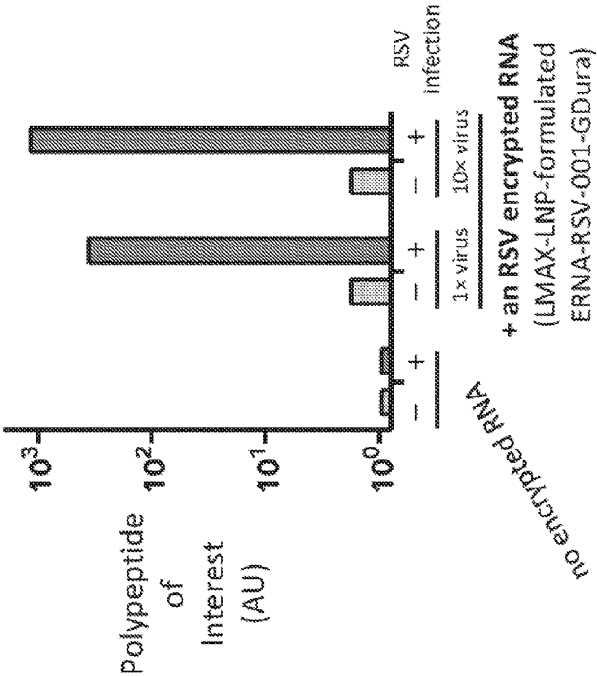
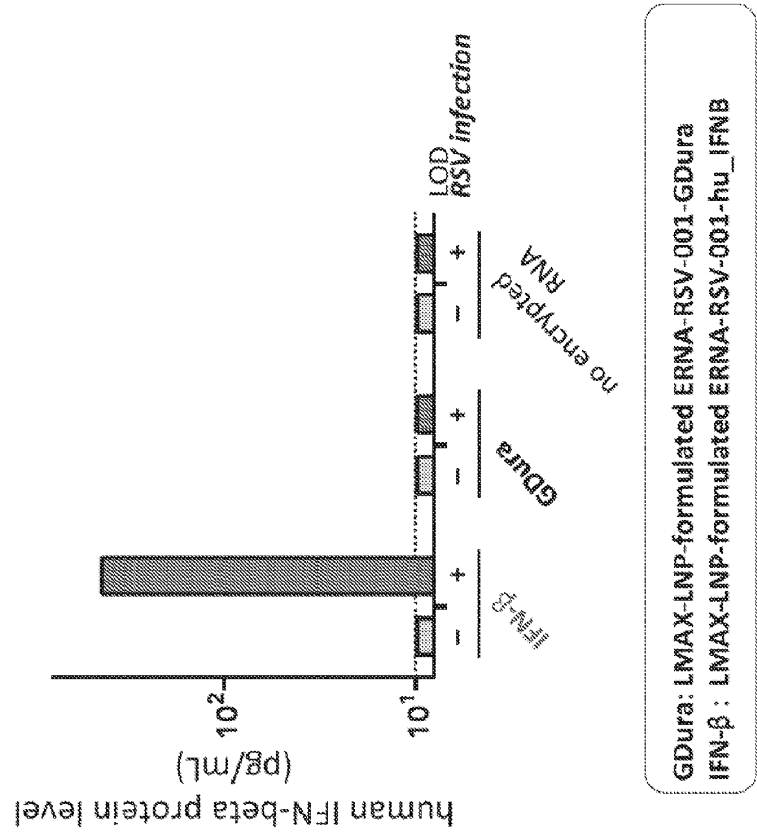
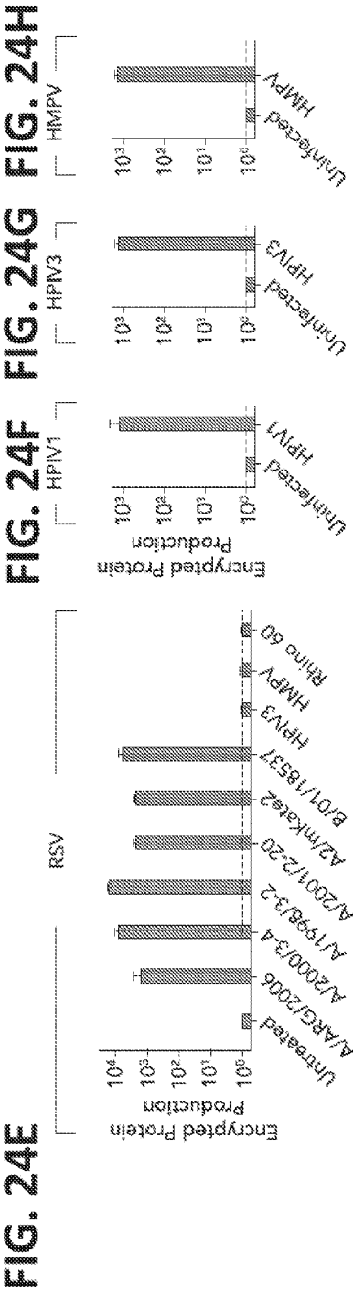
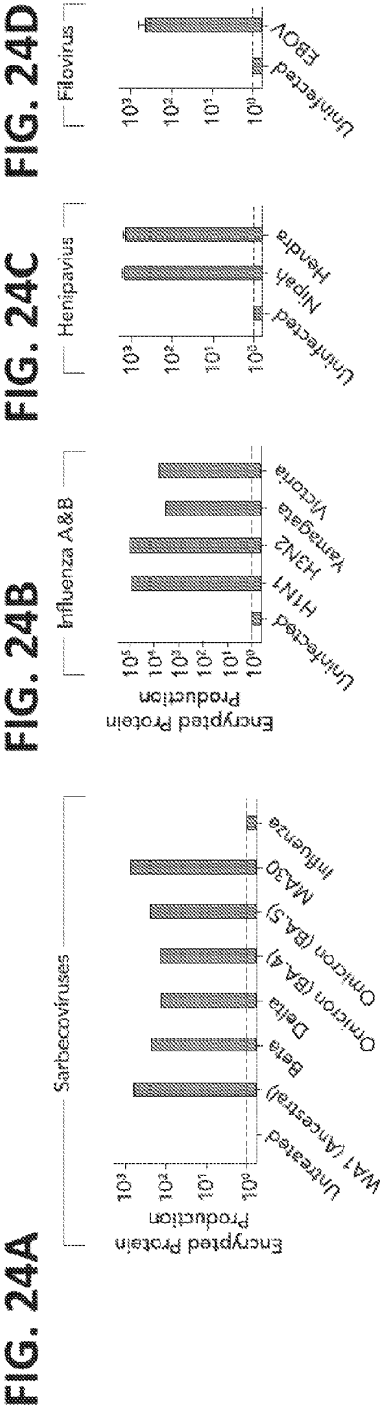
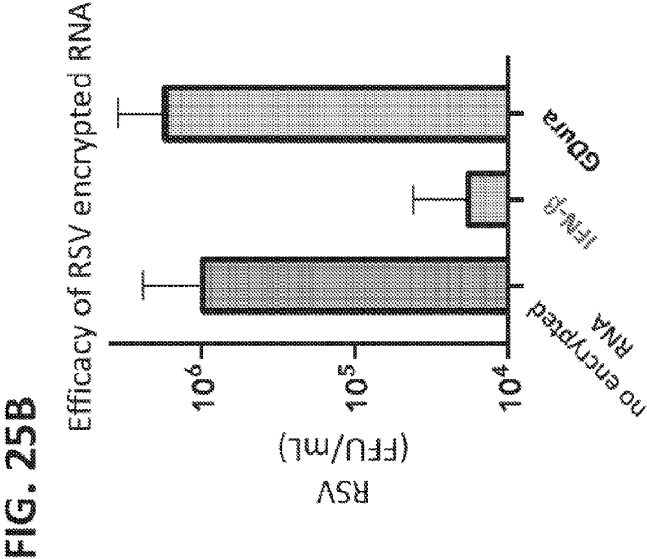
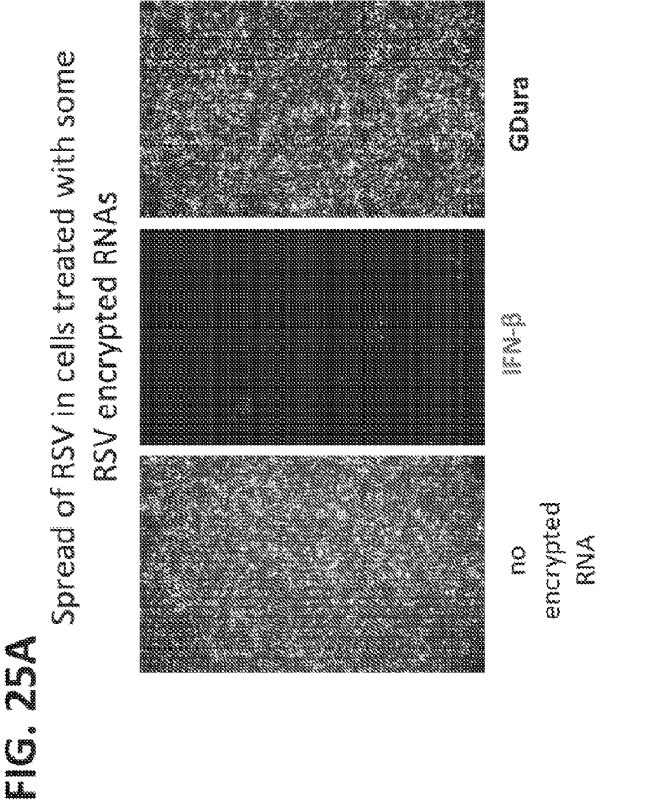


FIG. 23

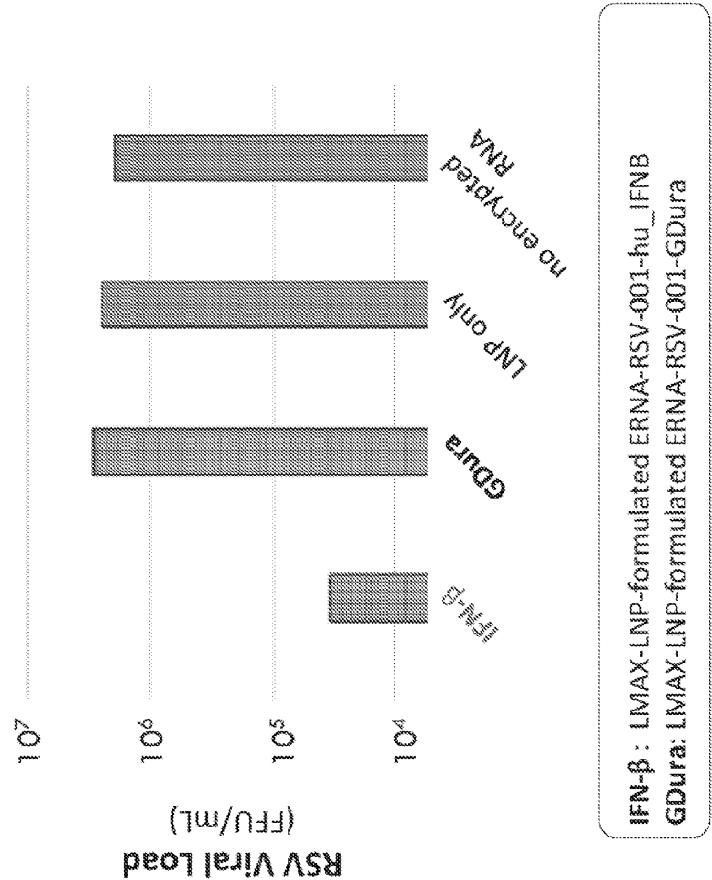


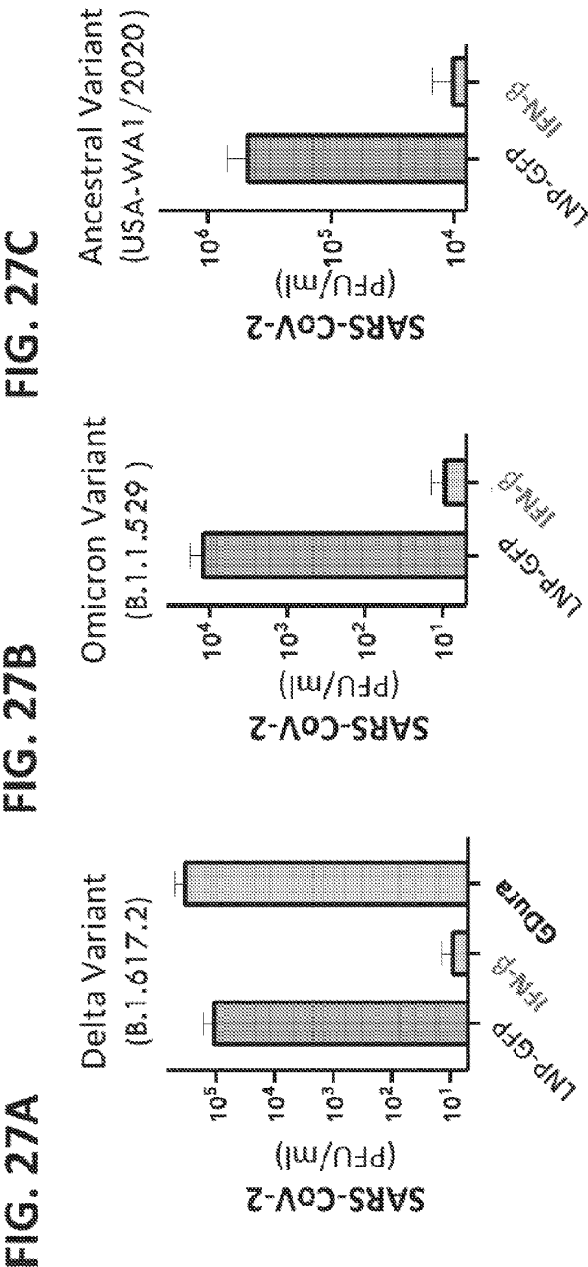




IFN-β : LMAX-LNP formulated ERNA-RSV-001-hu_IFNB (RSV encrypted RNA encoding human IFN-β)
GDura: LMAX-LNP formulated ERNA-RSV-001-GDura (RSV encrypted RNA encoding GDura)

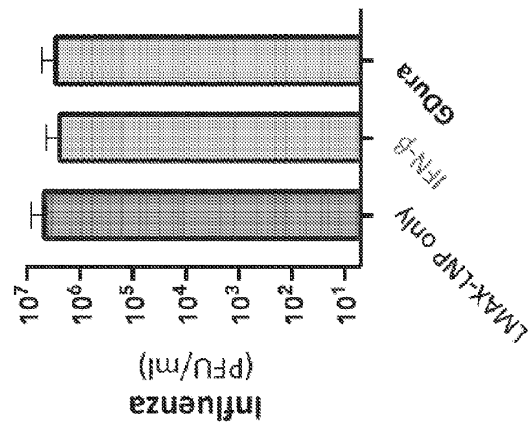
FIG. 26





GDura: LNP-formulated ERNA-SARS2-101-GDura (sarbecovirus encrypted RNA encoding GDura)
IFN-β : LNP-formulated ERNA-SARS2-101-hu_IFNB (sarbecovirus encrypted RNA encoding human IFN-β)
LNP-GFP: LNP-formulated mRNA encoding a GFP

FIG. 28



GDura: LMAX-LNP-formulated ERNA-SARS2-101-GDura (sarbecovirus encrypted RNA encoding GDura)
IFN-β : LMAX-LNP-formulated ERNA-SARS2-101-hu_IFNB (therapeutic sarbecovirus encrypted RNA encoding human IFN-β)
LMAX-LNP only: LMAX-LNP only

FIG. 29A

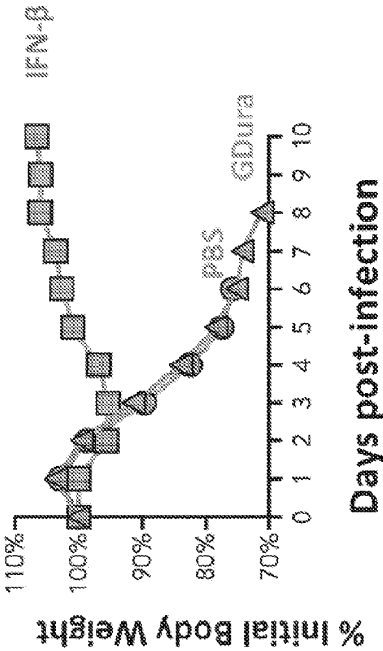
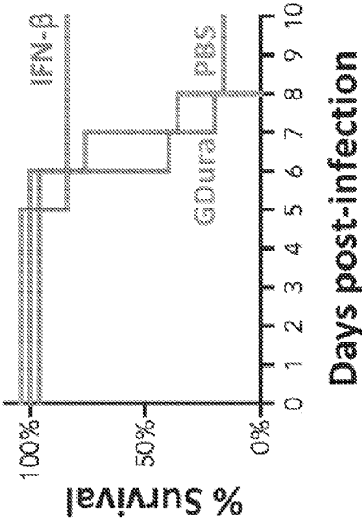


FIG. 29B



IFN-β : LNP-formulated capped ERNA-SARS2-001-m_IFNB
GDura: LNP-formulated capped ERNA-SARS2-001-GDura
PBS: PBS + 5% sucrose (vehicle only)

FIG. 30

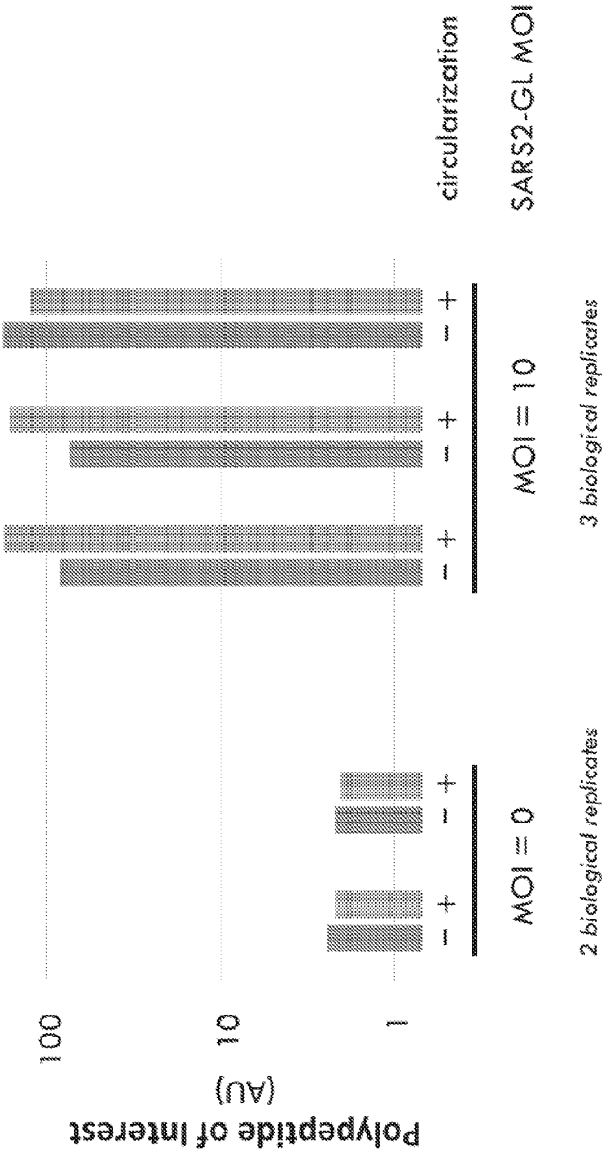
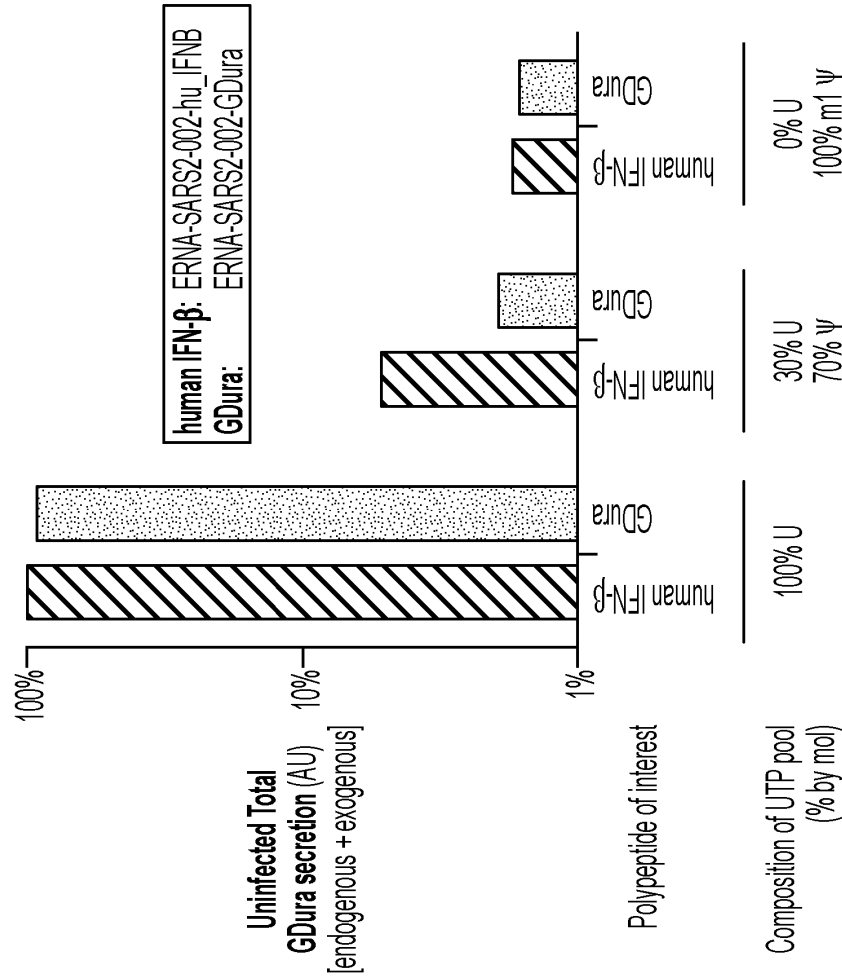


FIG. 31



Representative Viral Vectors to Deliver DNA-encoded Encrypted RNA Cassettes
(Lentiviral vectors)

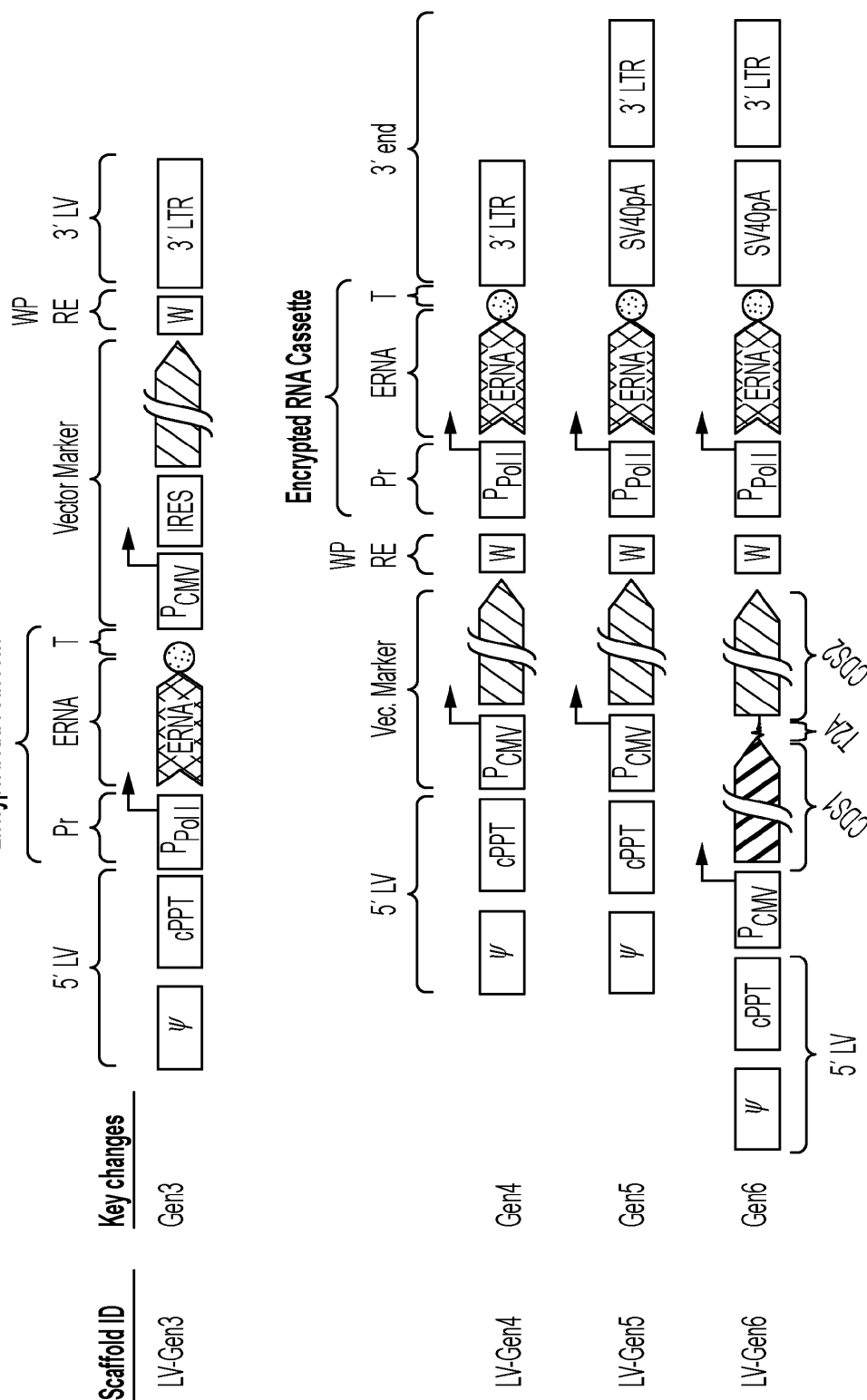


FIG. 33

Sequence of 3' end of RNA transcript (3'-RACE)		Poll terminator sequence	
3' end of desired sequence ...gcu:cccc Extra nt in transcript cccc (Residues 1 through 17 of SEQ ID NO: 355) (Residues 1 through 13 of SEQ ID NO: 357) (Residues 1 through 12 of SEQ ID NO: 356) mouse terminator mouse enhanced terminator		cccccacacttcggag... ccaacttcggag... mouse terminator (d4)	
...gcu:cccc	5 extra C	73% (8 of 11)	0% (0 of 10)
...gcu:cccc	4 extra C	18% (2 of 11)	0% (0 of 10)
...gcu:ccc	3 extra C	0% (0 of 11)	0% (0 of 10)
...gcu:cc	2 extra C	9% (1 of 11)	0% (0 of 10)
...gcu:c	1 extra C	0% (0 of 11)	0% (0 of 10)
...gcu:	0 extra C	0% (0 of 11)	100% (10 of 10)

Statistics of
interpreted
genotypes of
3'-RACE
sequences

FIG. 34

An RSV encrypted RNA with a 5'-monophosphate is competent for activation

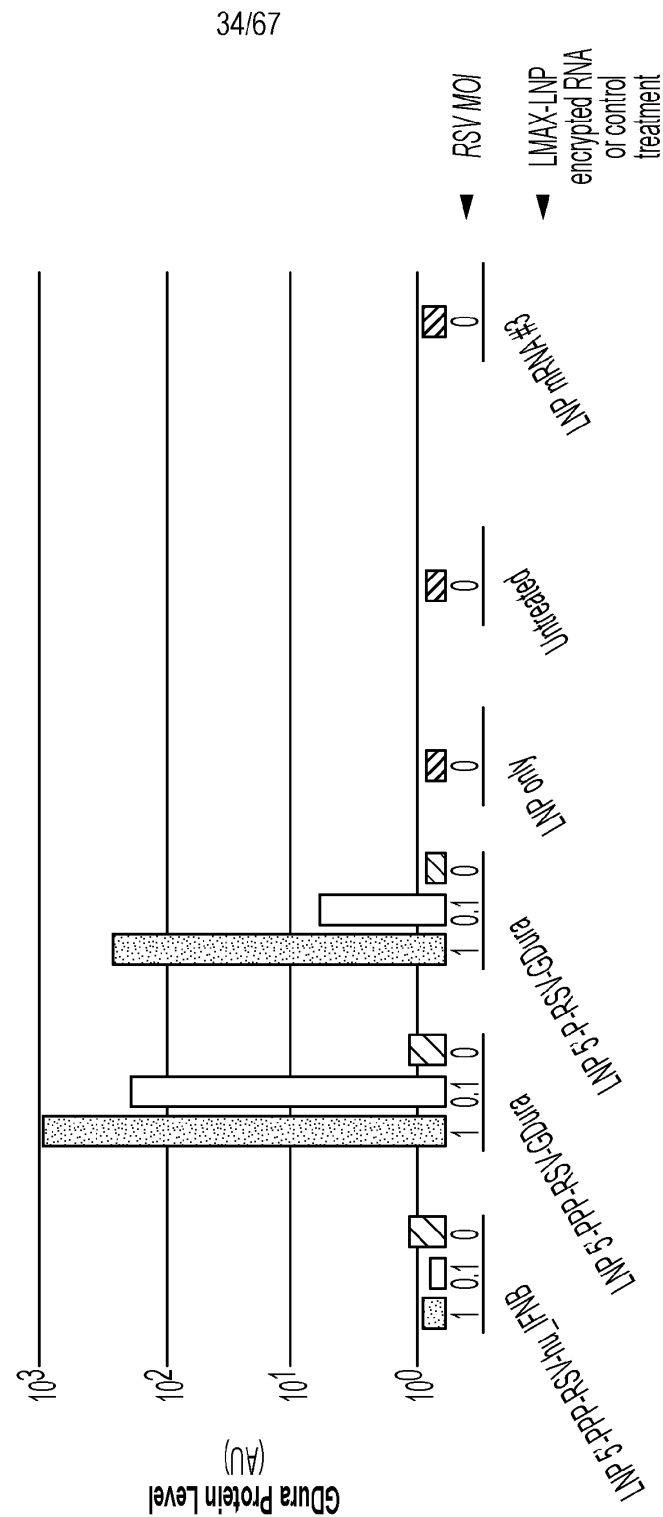


FIG. 35
An RSV encrypted RNA lacking a RIG-I agonist (5'-triphosphate) is competent for activation

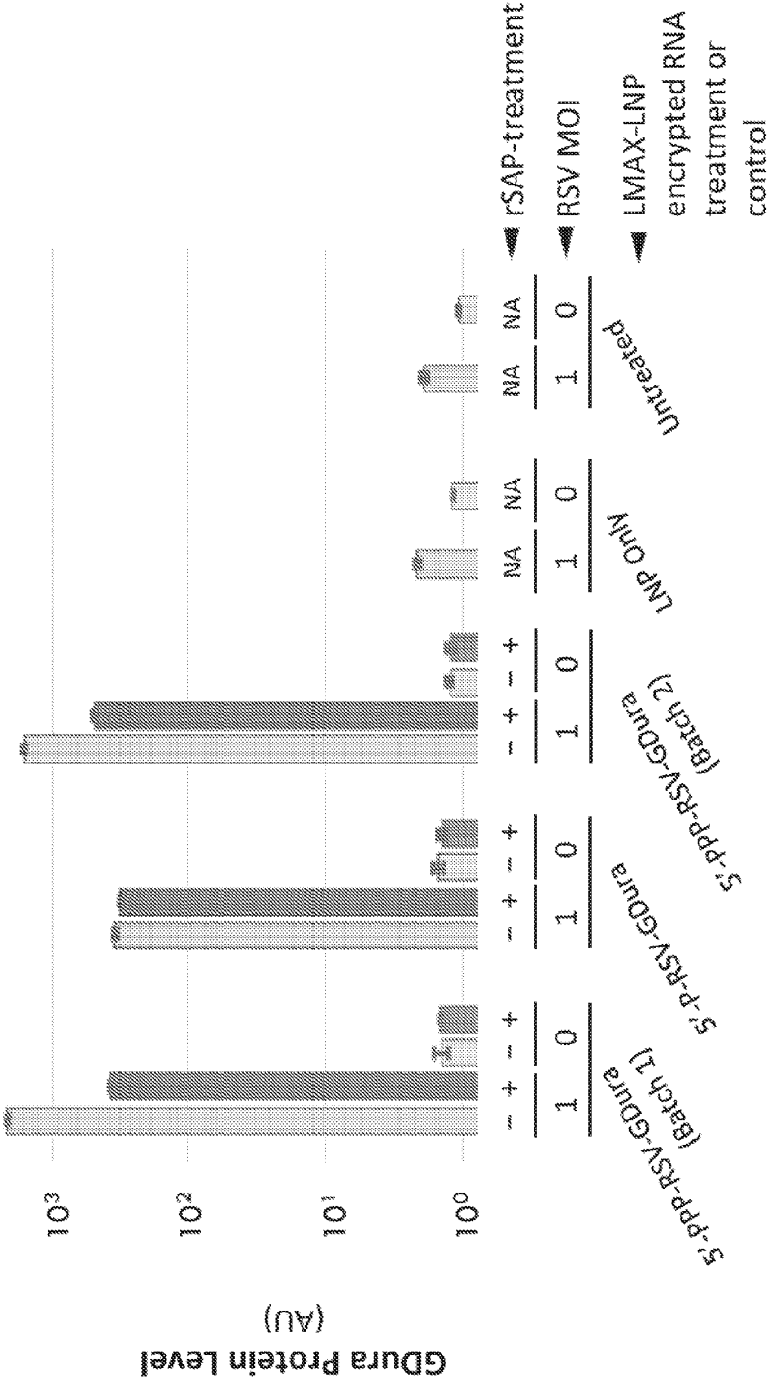
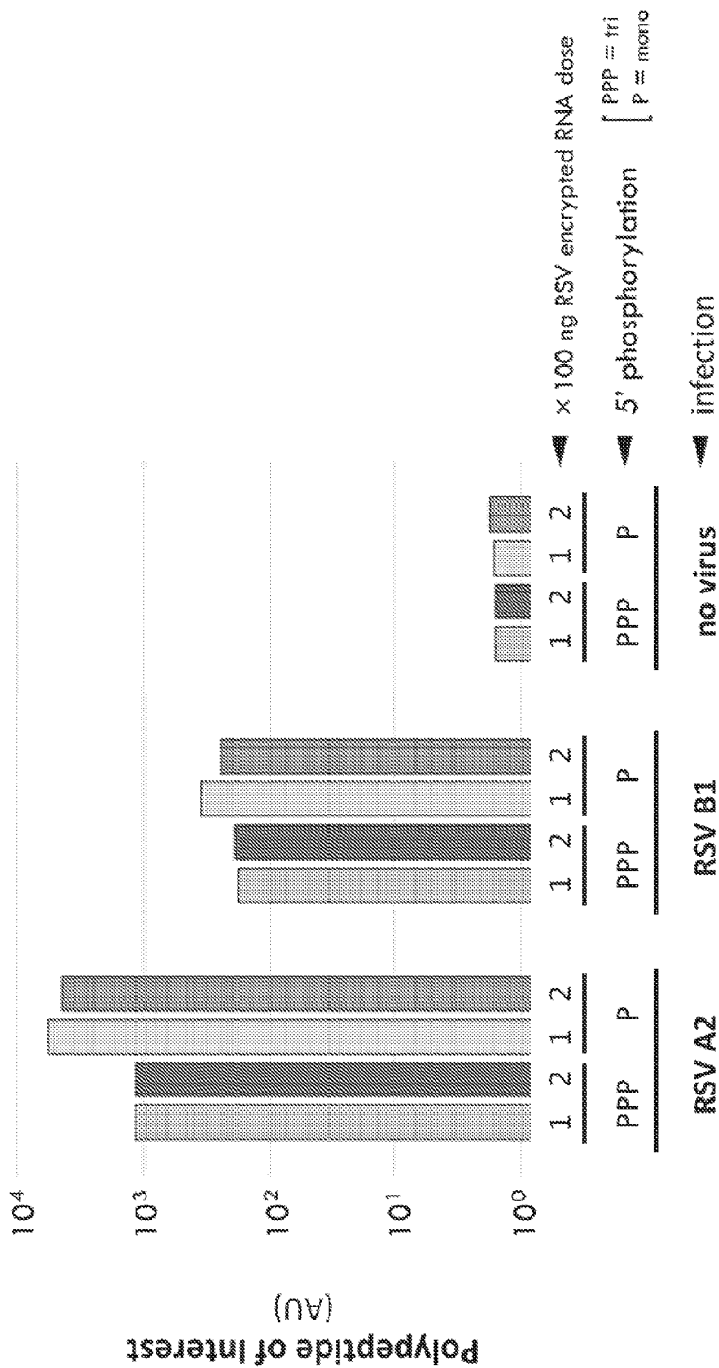


FIG. 37

An RSV encrypted RNA can be activated by distinct RSV strains



33

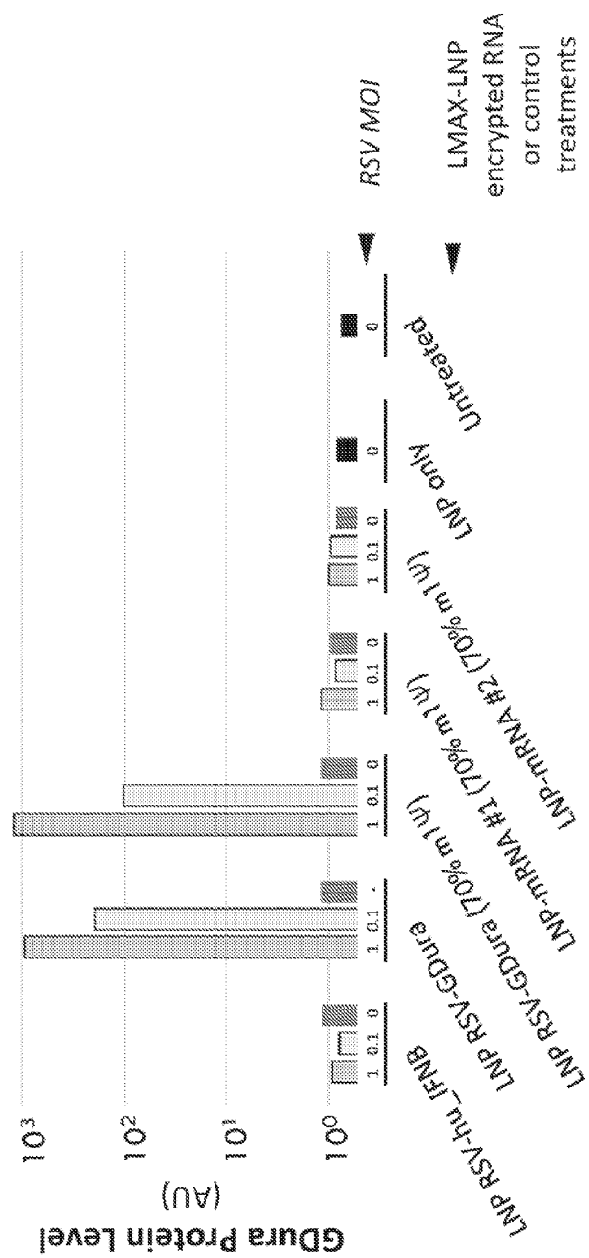


FIG. 39

Lipid-formulated RSV encrypted RNA can be activated days after dosing

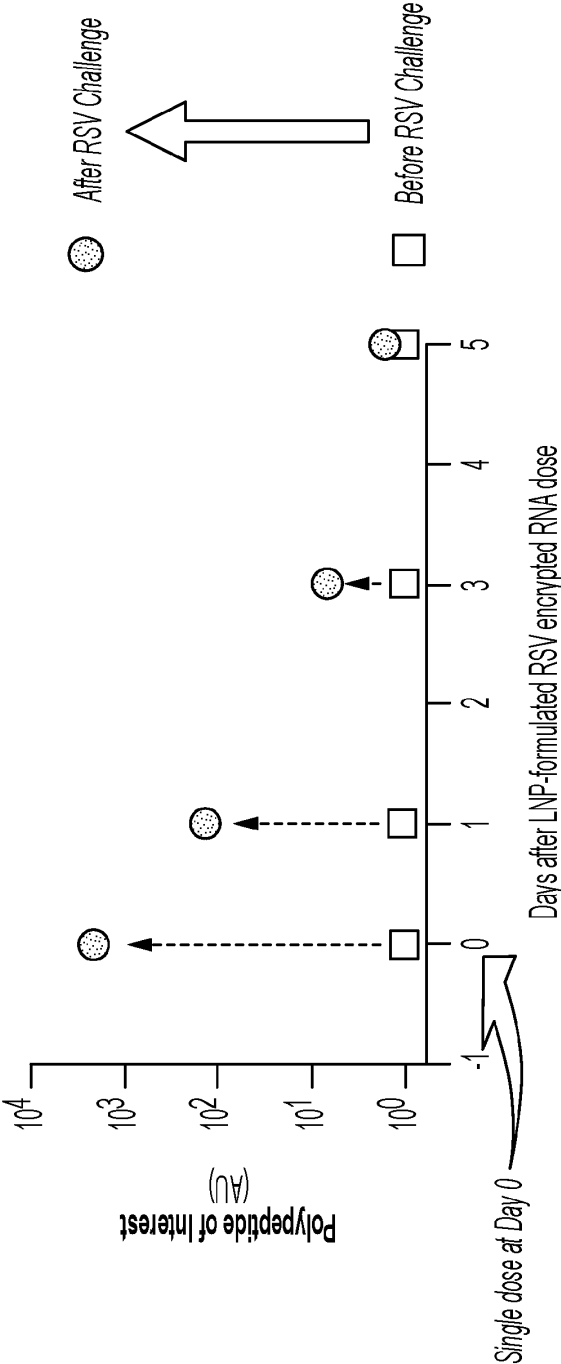


FIG. 40A

Activation with non-cognate TRS
Encrypted RNA: WT TRS (ERNA-SARS2-002-GDura)
Virus challenge: SARS2-GL

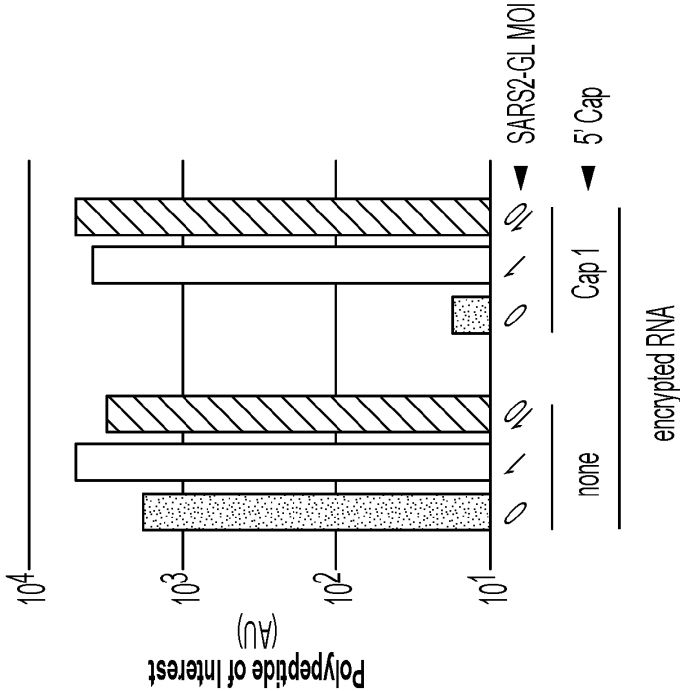
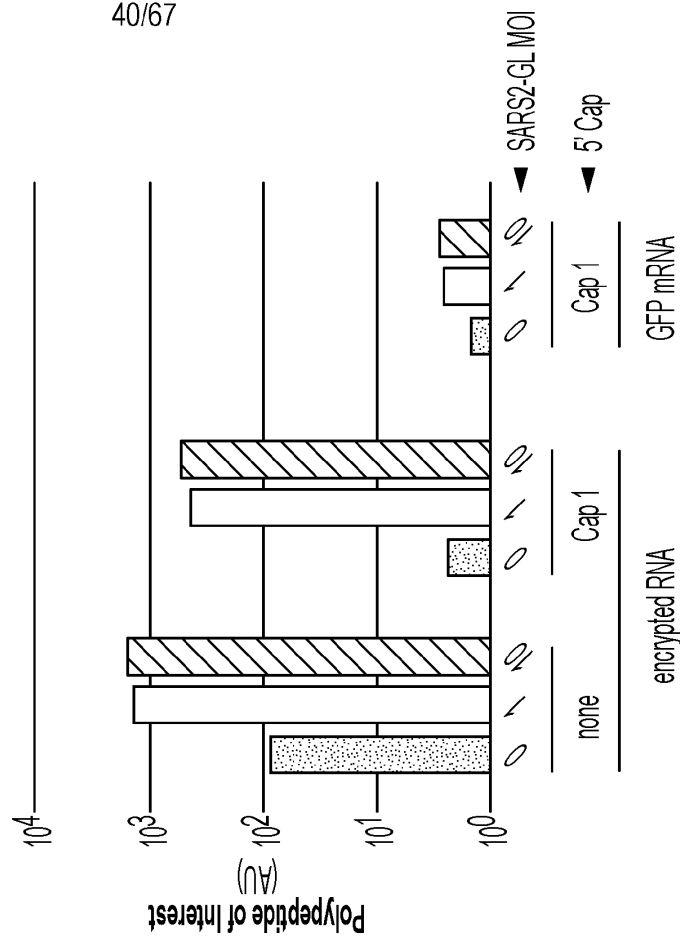


FIG. 40B

Activation with cognate SARS2-GL TRS
Encrypted RNA: SARS2-GL TRS (ERNA-SARS2-102-GDura)
Virus challenge: SARS2-GL



45

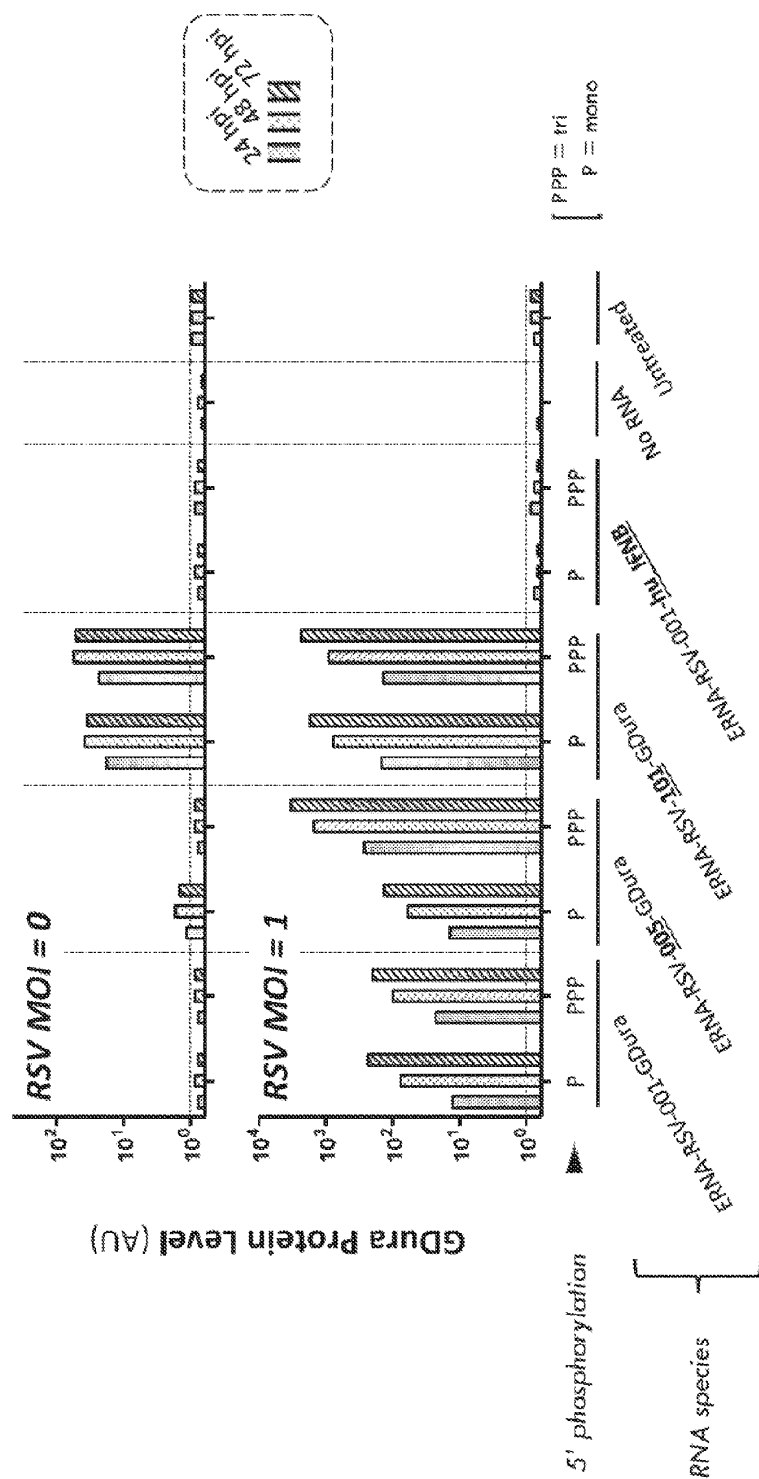


FIG. 42

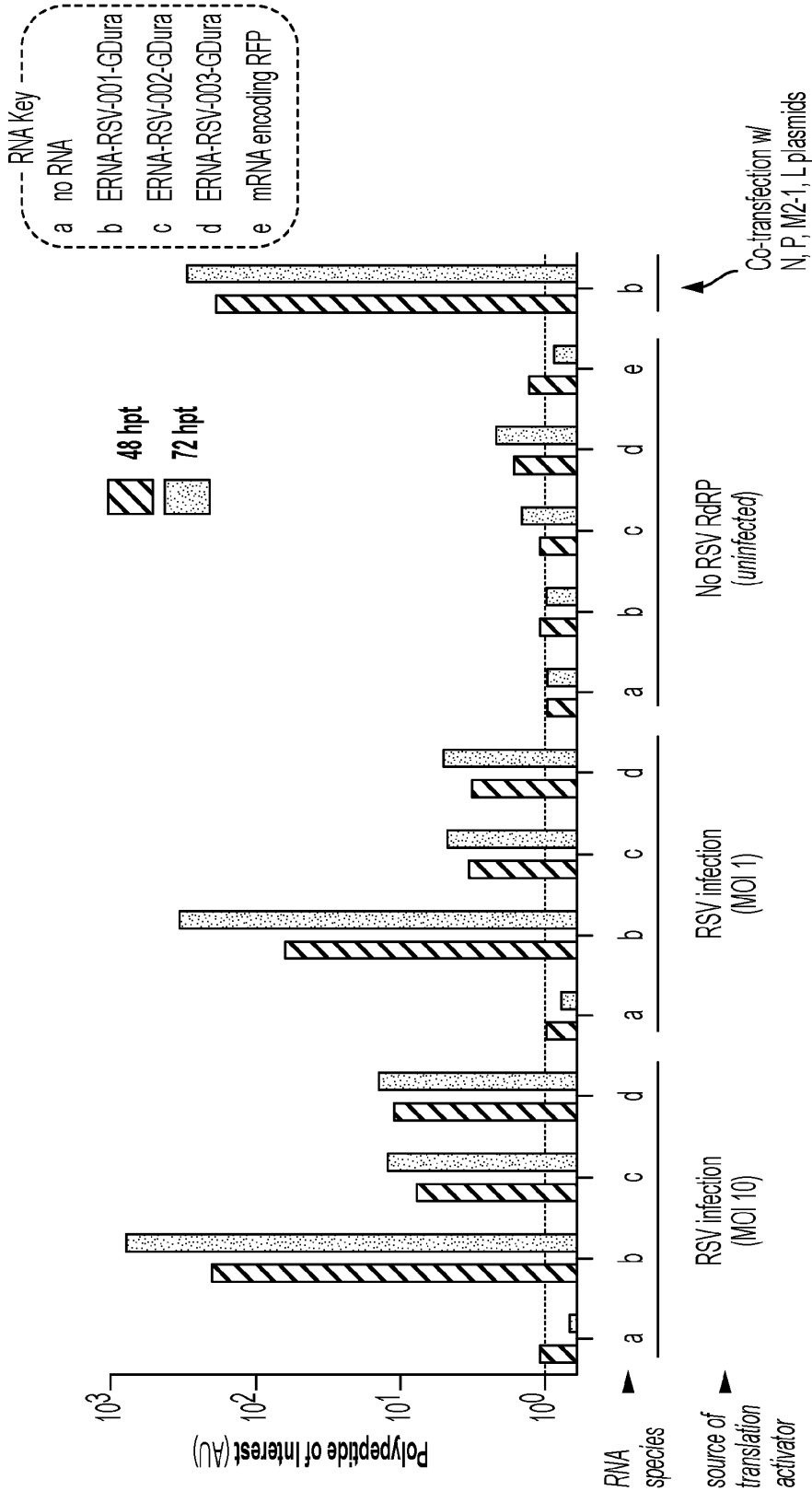
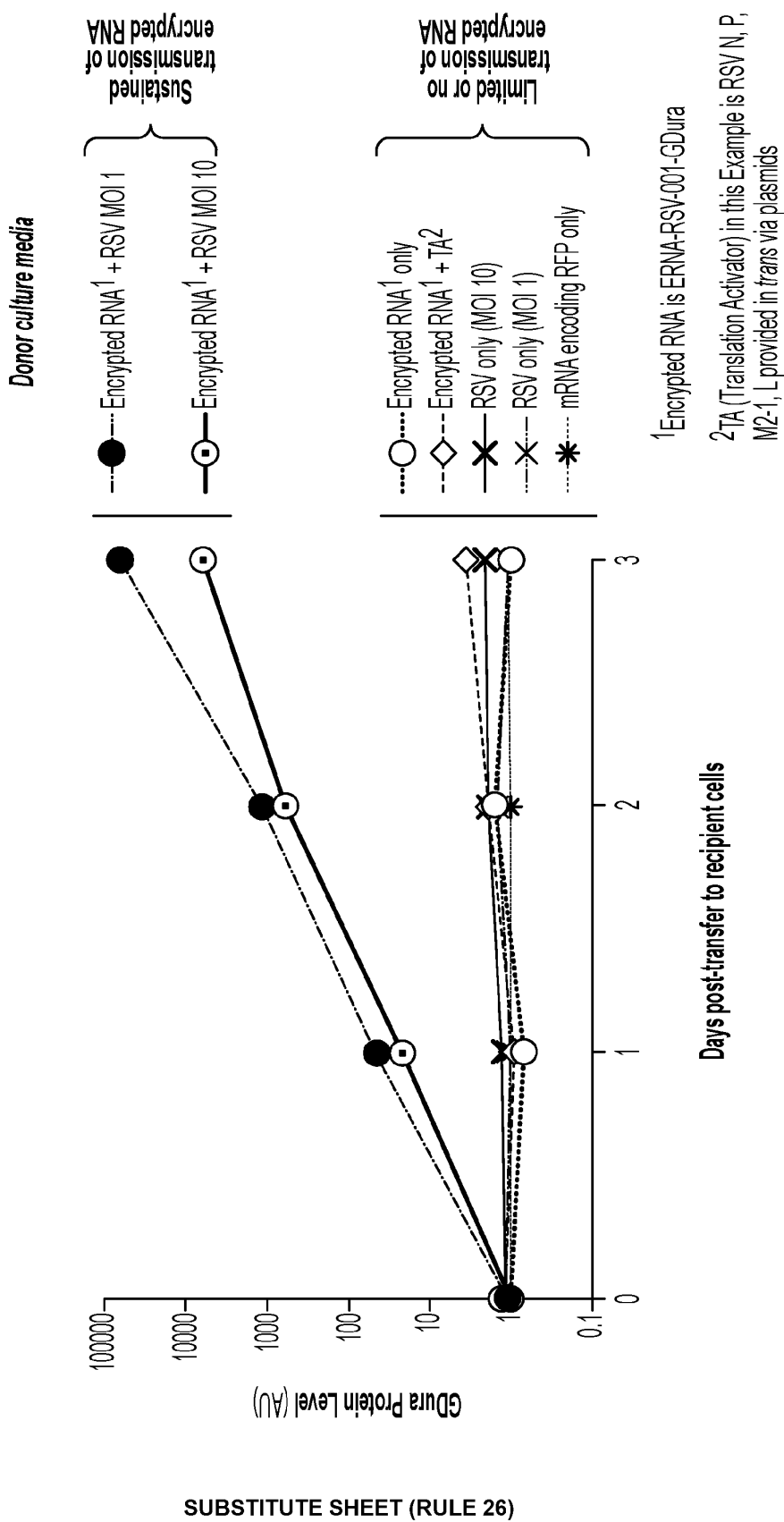


FIG. 43



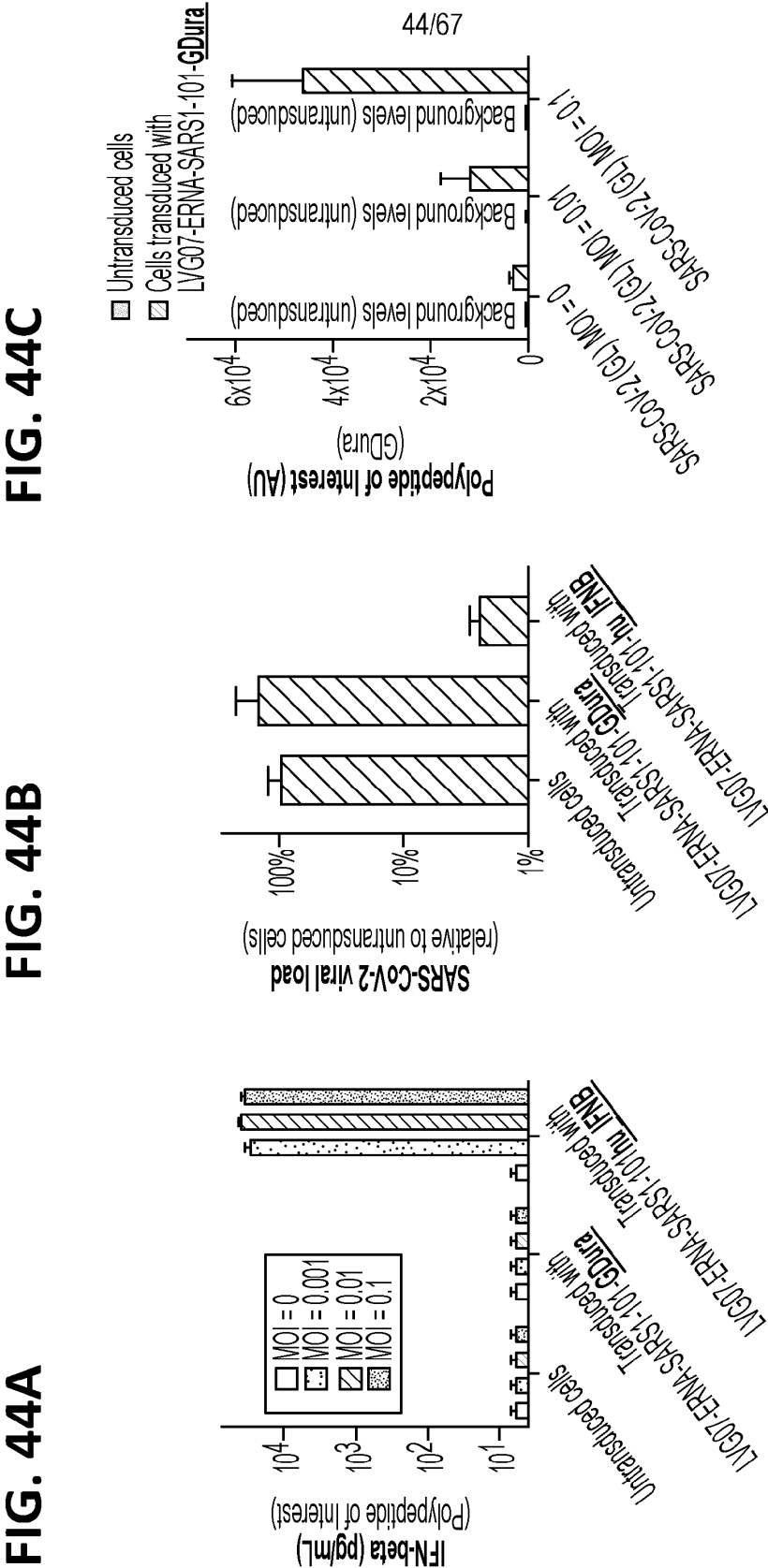


FIG. 45

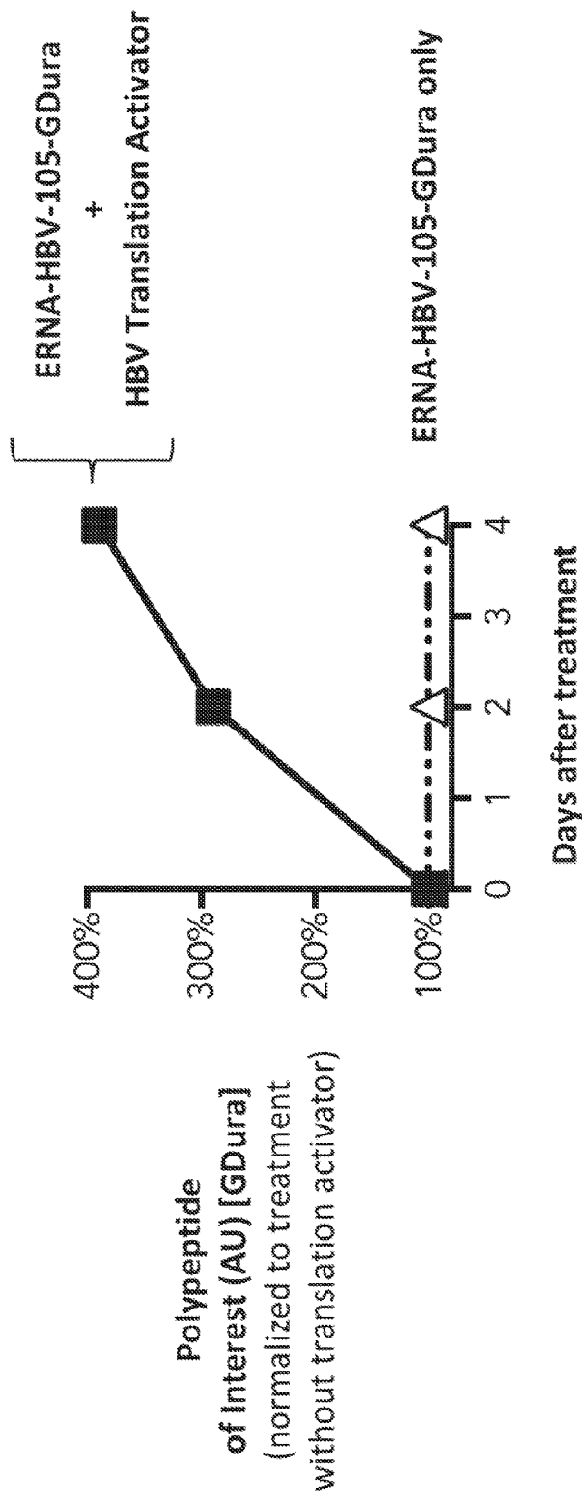
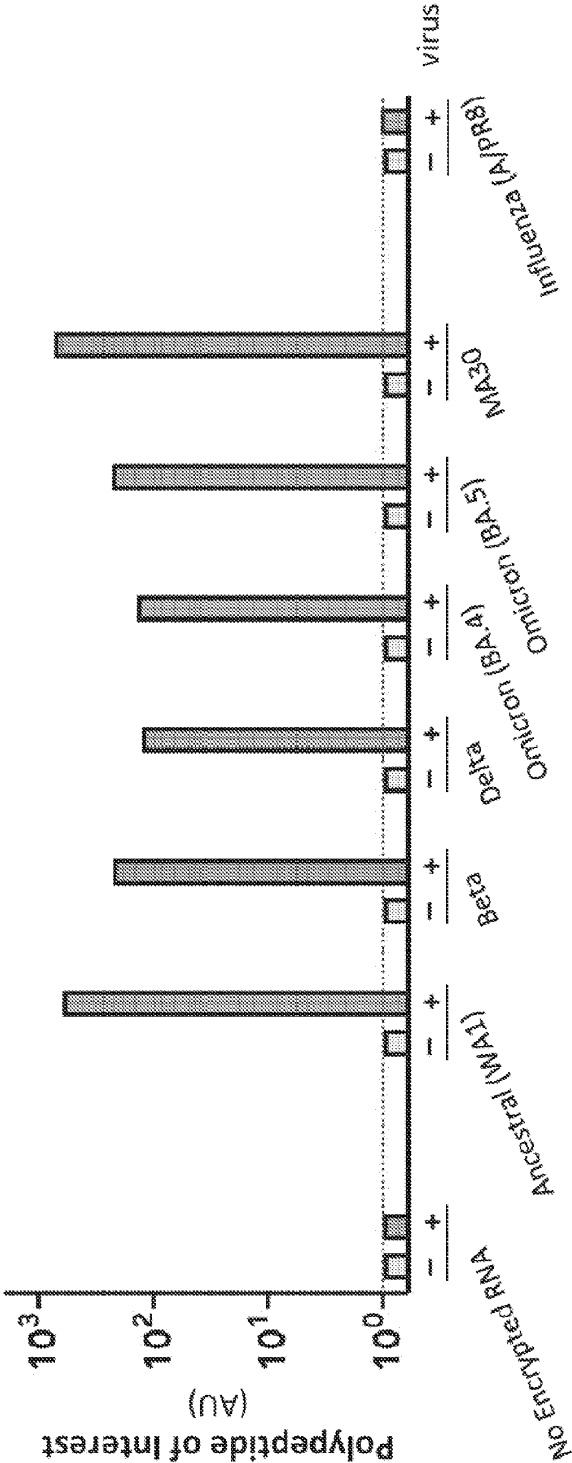


FIG. 46



LNP-formulated ERNA-SARS2-001-GDura ($\pm$ a SARS-CoV-2 or influenza variant)

WA1, Beta, Delta, BA.4, BA.5, and MA30 are variants of SARS-CoV-2

FIG. 47A

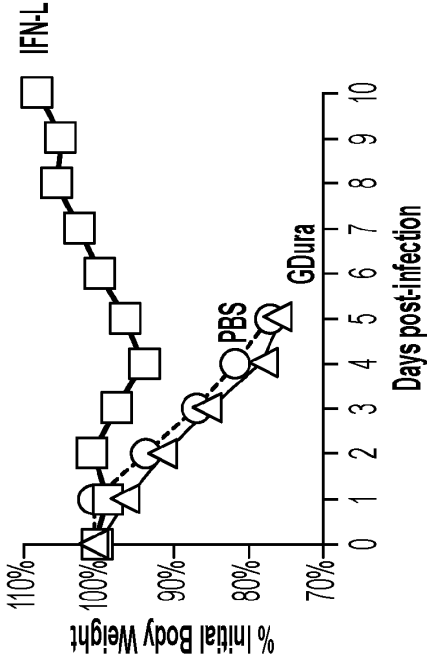
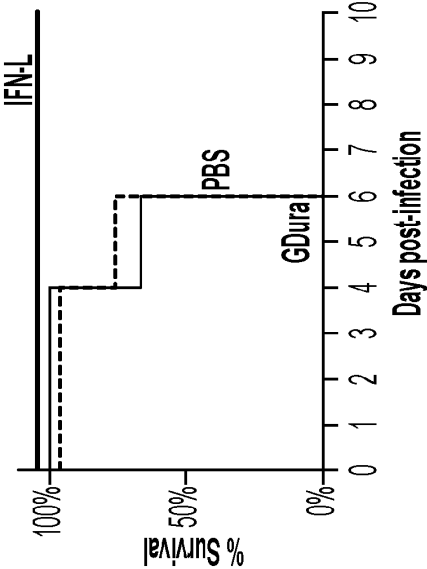


FIG. 47B



IFN-L: LNP-formulated capped ERNA-SARS2-001-m_IFN_Lambda_2
GDura: LNP-formulated capped ERNA-SARS2-001-GDura
PBS: PBS + 5% sucrose (vehicle only)

FIG. 48A

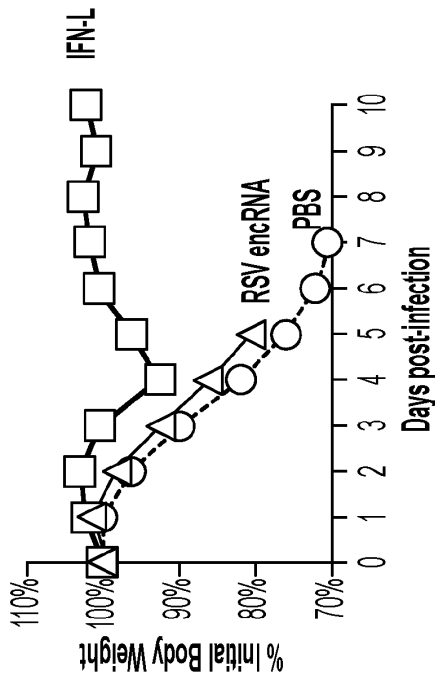
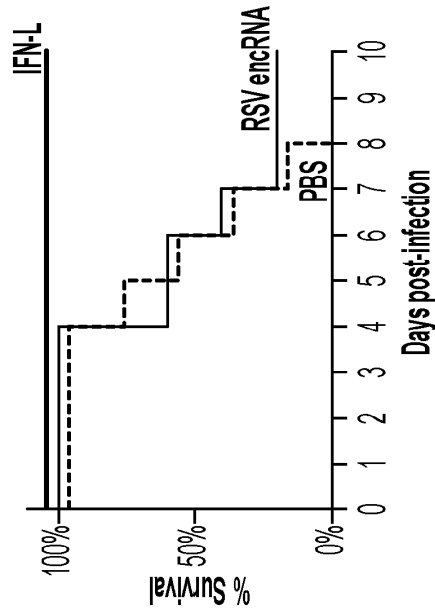


FIG. 48B



IFN-L: LNP-formulated capped ERNA-SARS2-001-m_IFN_lambda_2
RSV encRNA: LNP-formulated capped ERNA-RSV-005-m_IFN_lambda_2
PBS: PBS + 5% sucrose (vehicle only)

FIG. 49A

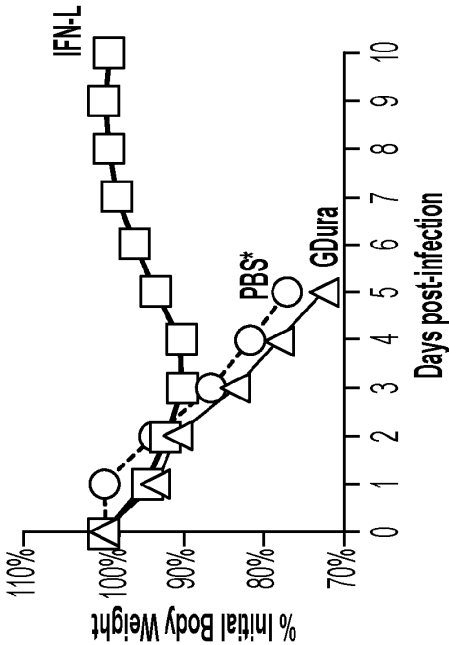
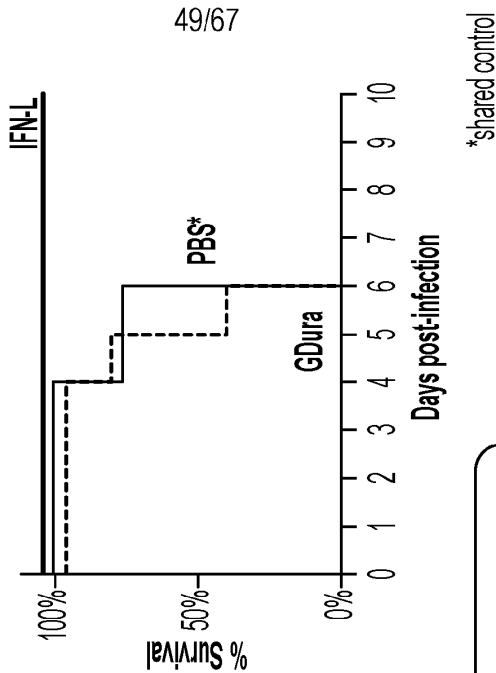


FIG. 49B



IFN-L: LNP-formulated capped ERNA-SARS2-001-m_IFN_lambda_2
GDura: LNP-formulated capped ERNA-SARS2-001-GDura
PBS: PBS + 5% sucrose (vehicle only)

*shared control

FIG. 50A

Encrypted RNA safety in hamsters

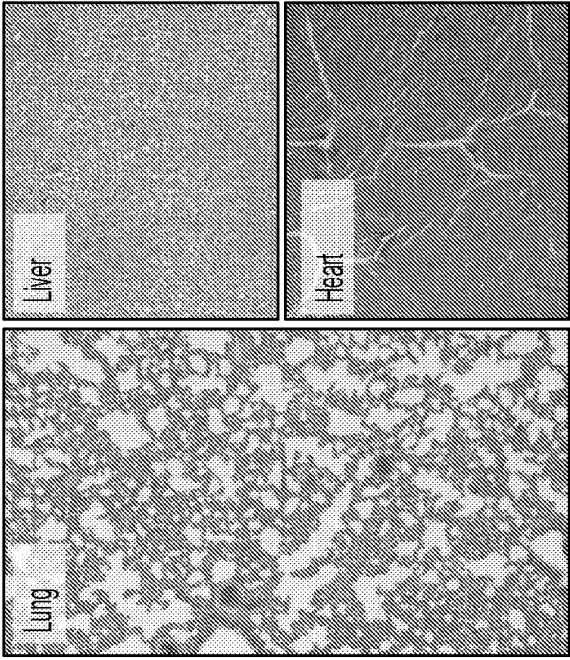
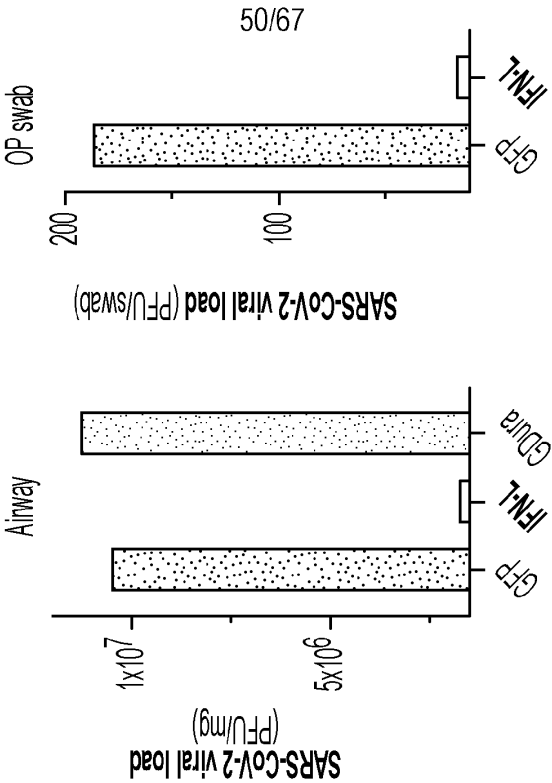


FIG. 50B

Encrypted RNA efficacy in hamsters



IFN-L: LNP-formulated capped ERNA-SARS2-001-hamster_IFN_lambda_3
GDura: LNP-formulated capped ERNA-SARS2-001-GDura
GFP: LNP-formulated capped mRNA encoding a GFP

FIG. 51A

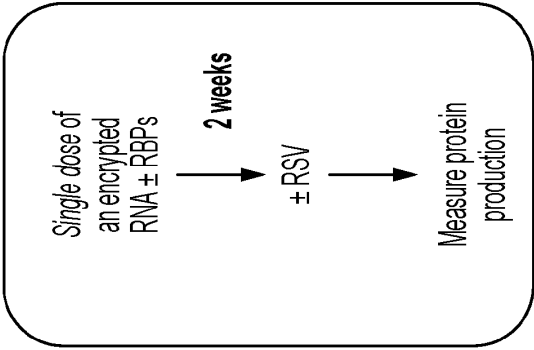


FIG. 51B

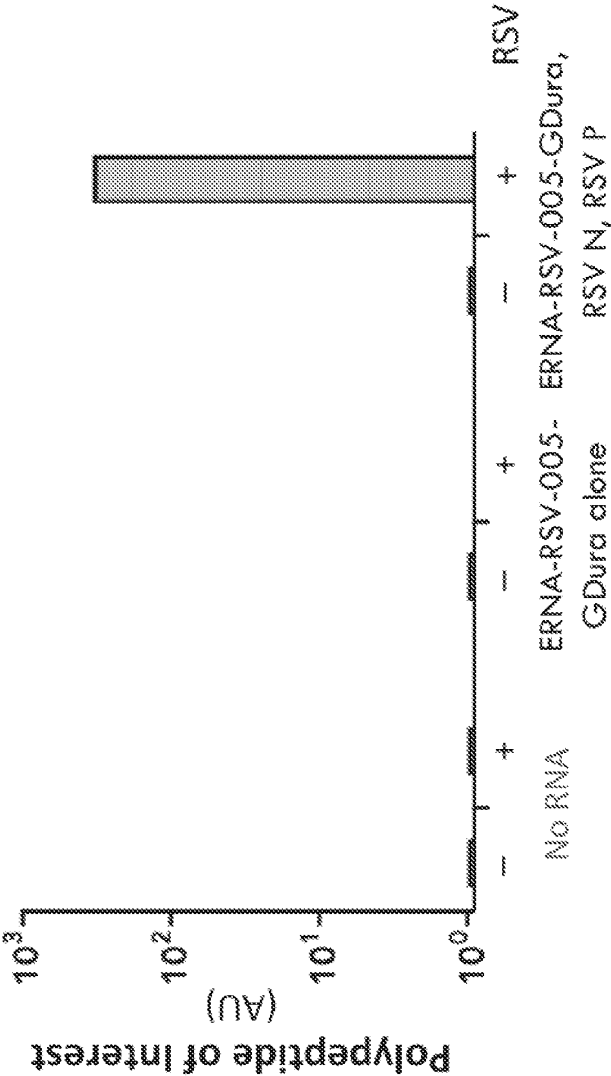


FIG. 52

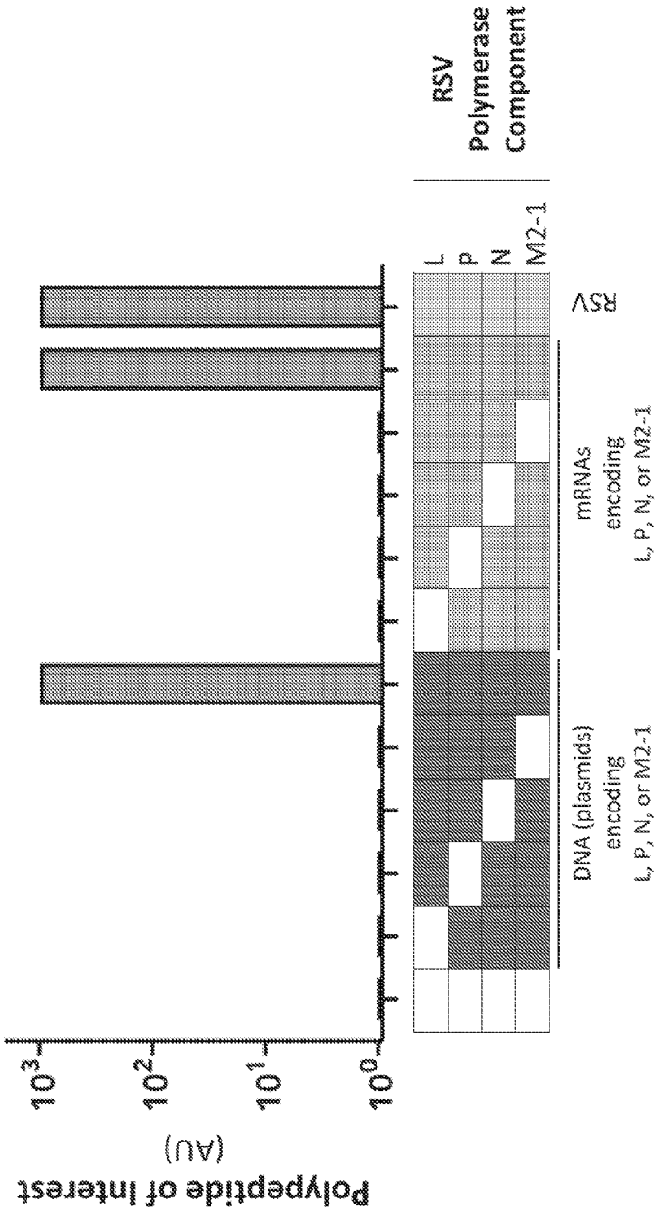
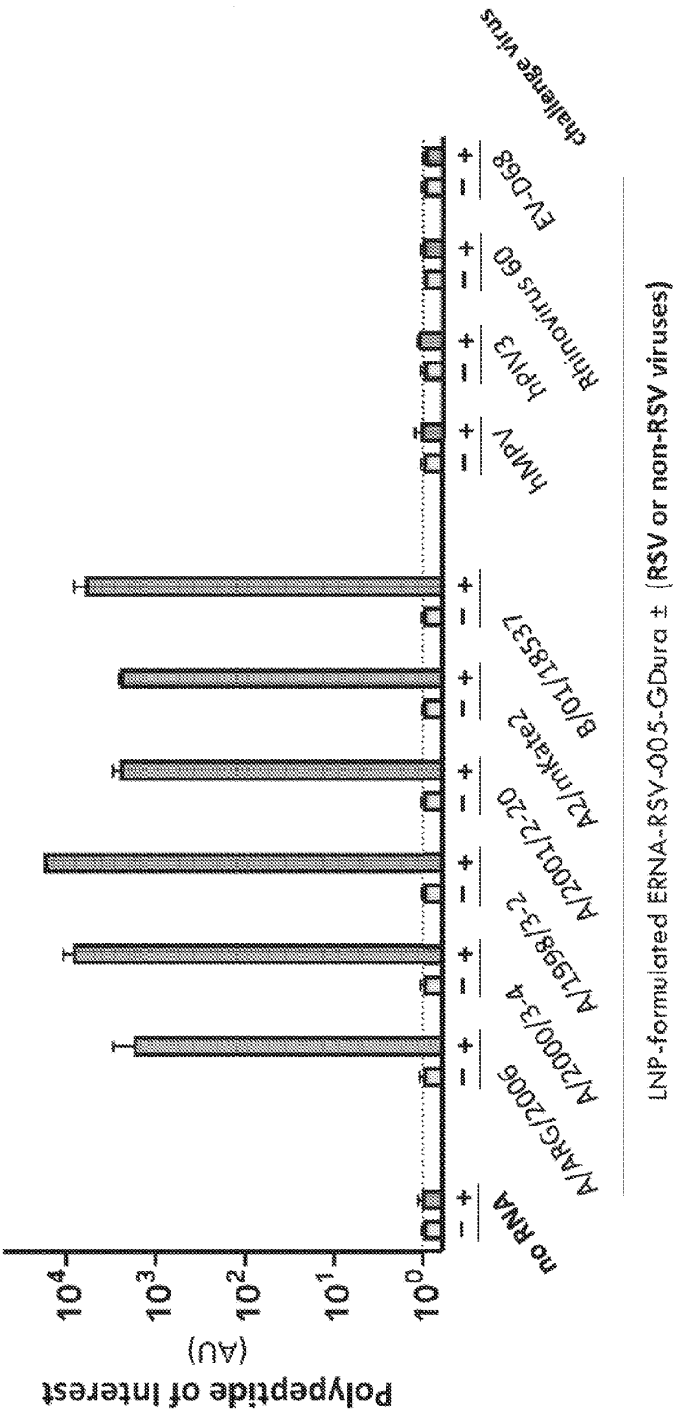


FIG. 53



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FIG. 54B

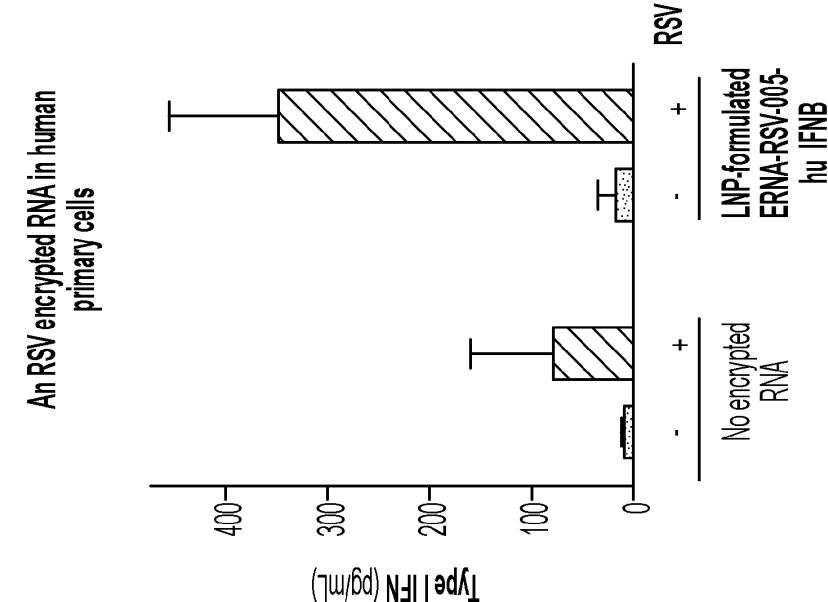


FIG. 54A

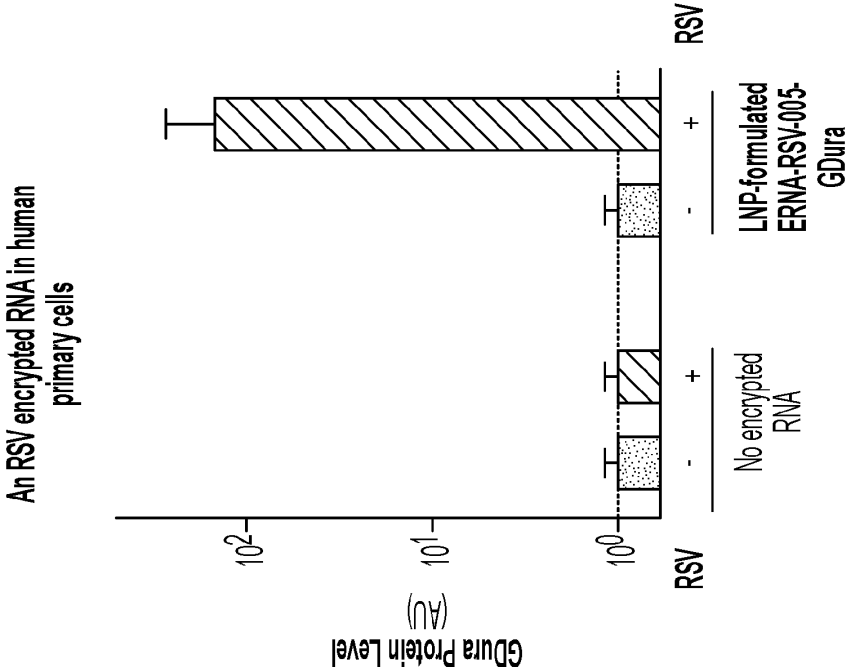


FIG. 55A

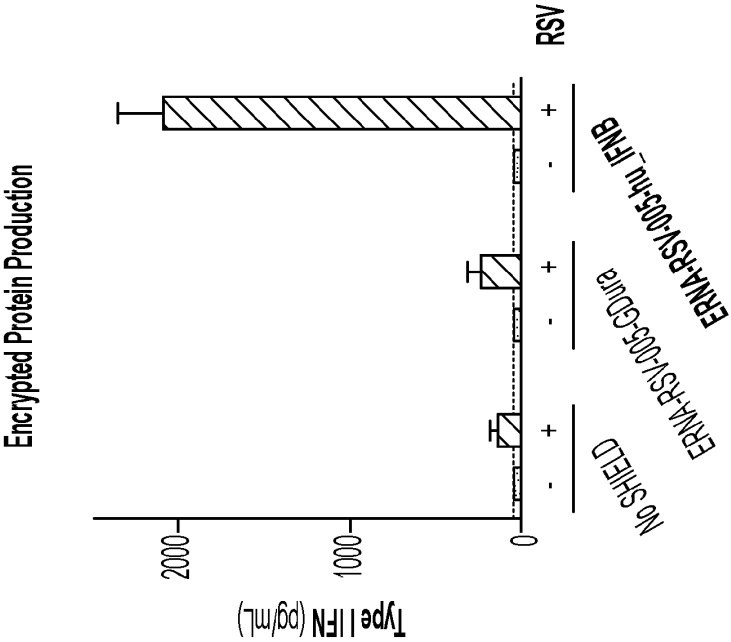


FIG. 55B

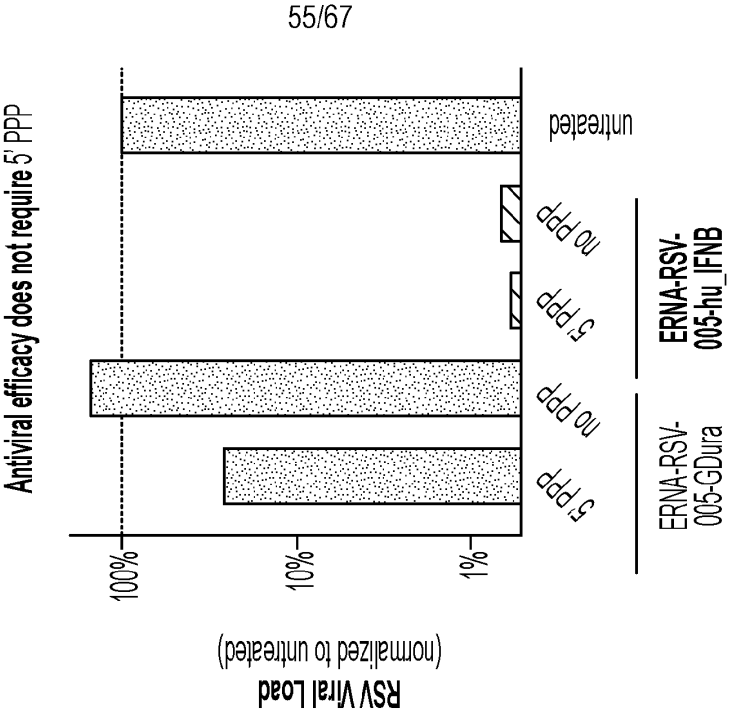
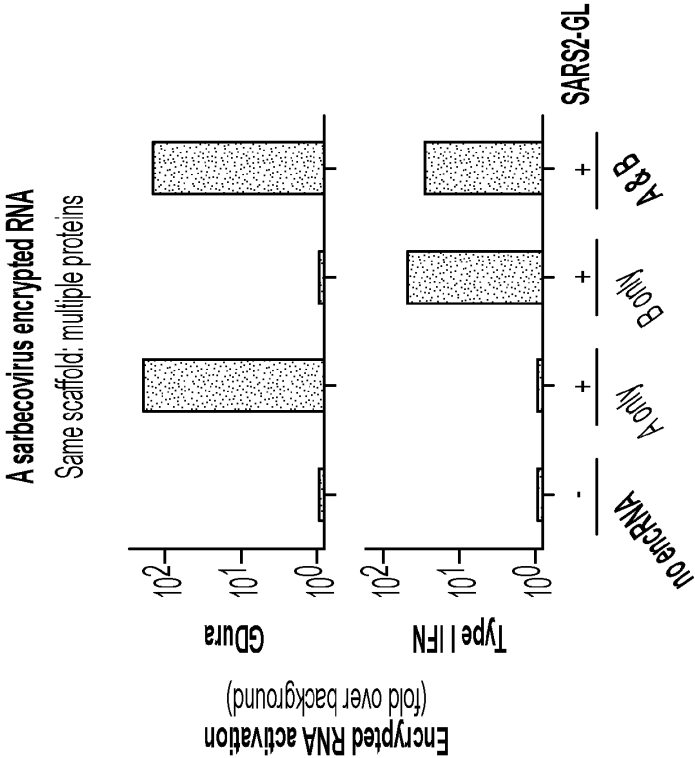
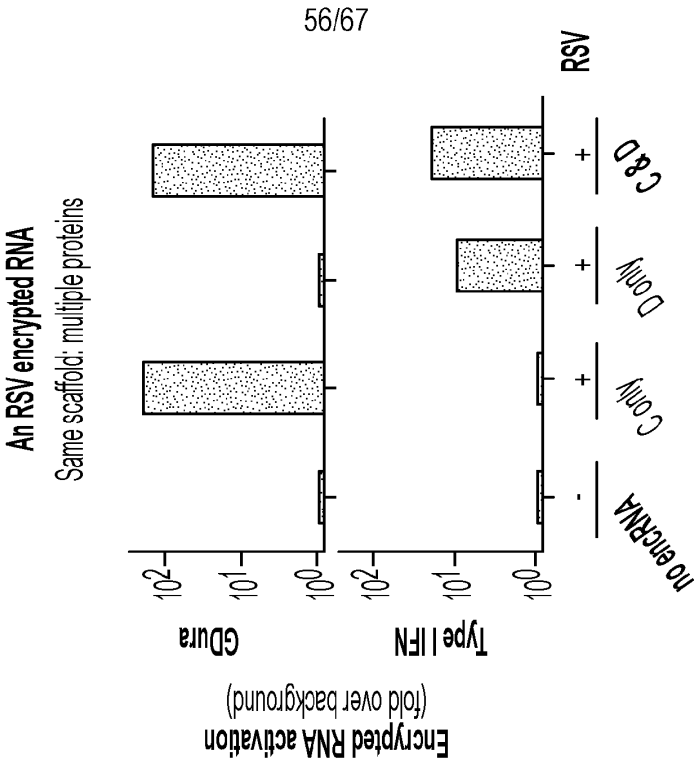


FIG. 56A



A = ERNA-SARS2-101-GDura
B = ERNA-SARS2-101-hu-IFNB

FIG. 56B



C = ERNA-RSV-005-GDura
D = ERNA-RSV-005-hu-IFNB

FIG. 57B

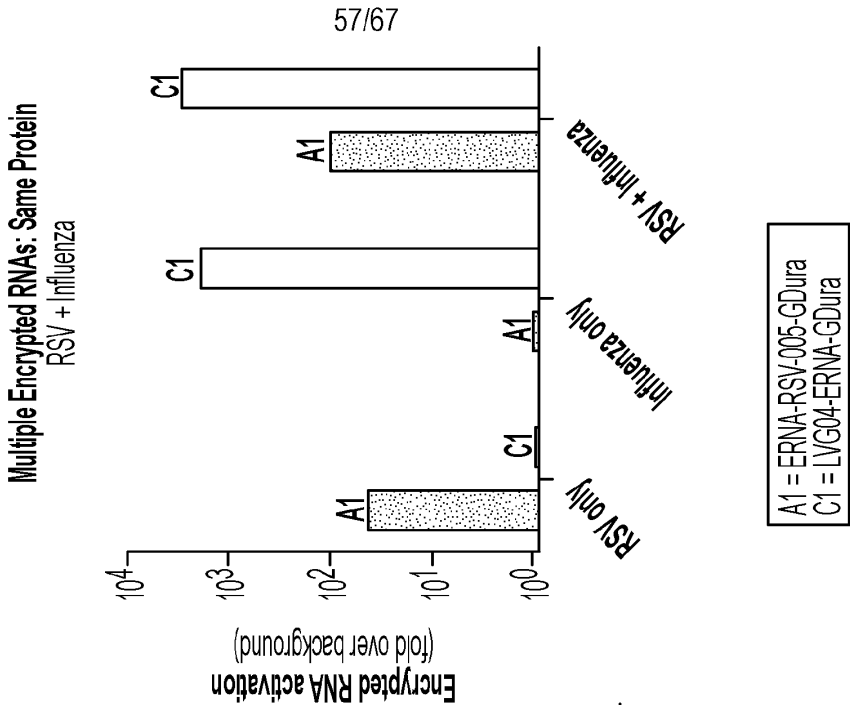


FIG. 57A

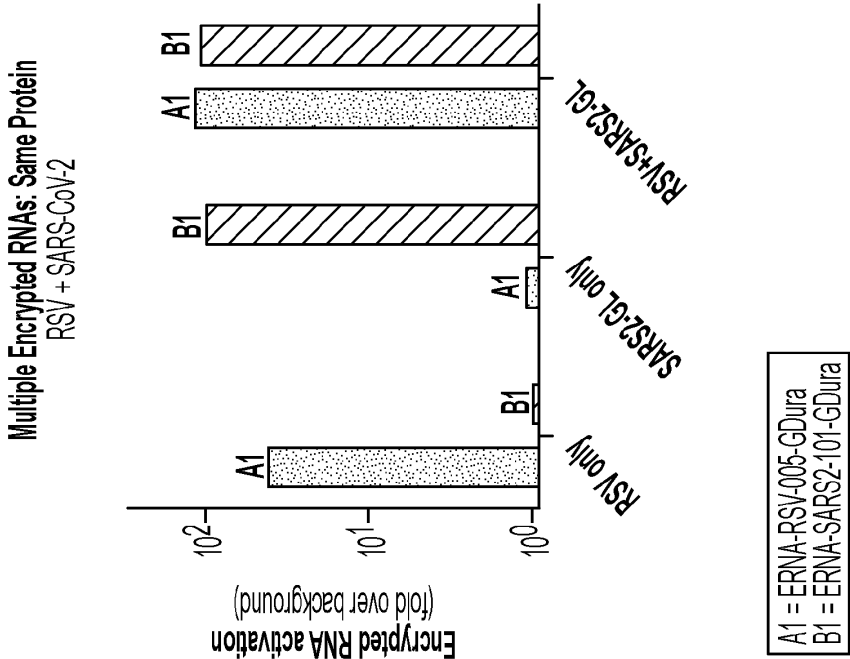


FIG. 58A

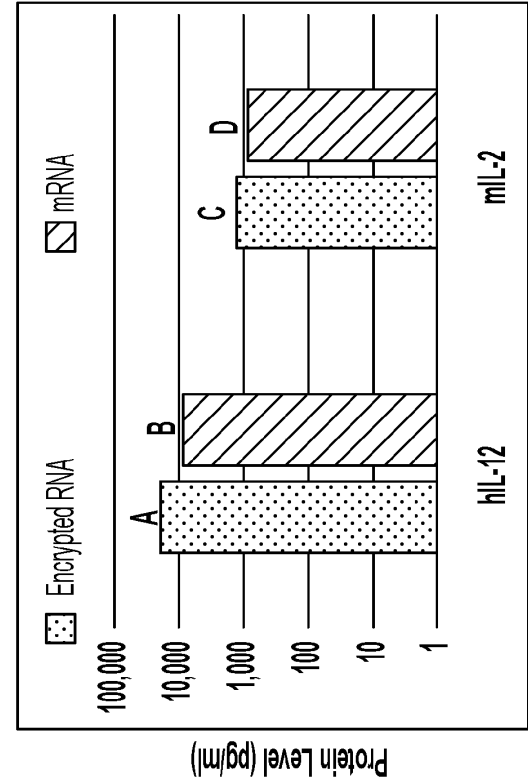


FIG. 58B

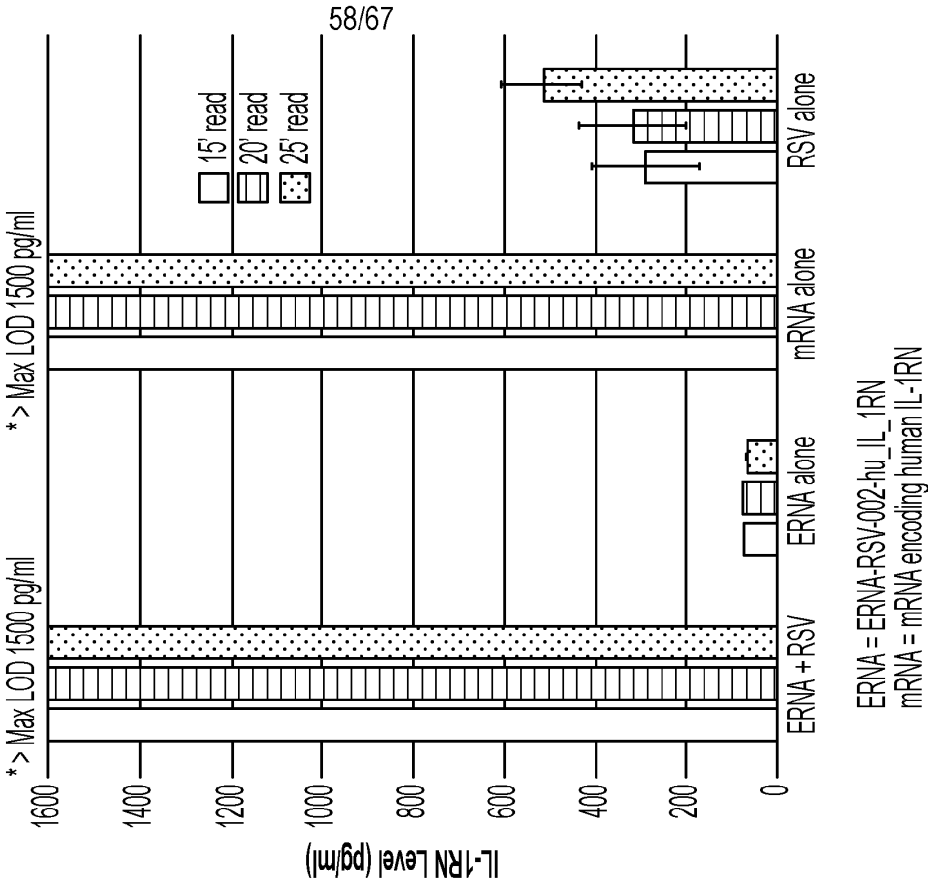


FIG. 59

A sarbecovirus encrypted RNA with modified nucleotides
can be substantially activated by SARS-CoV-2

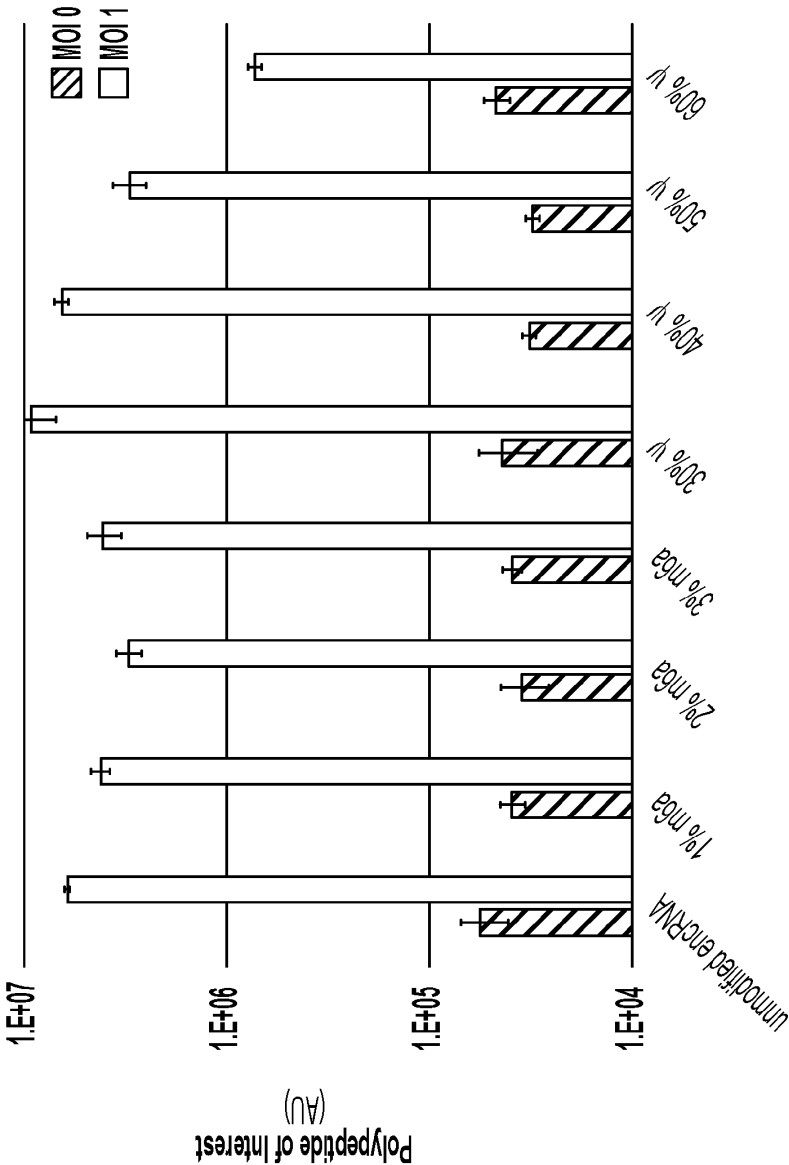


FIG. 60

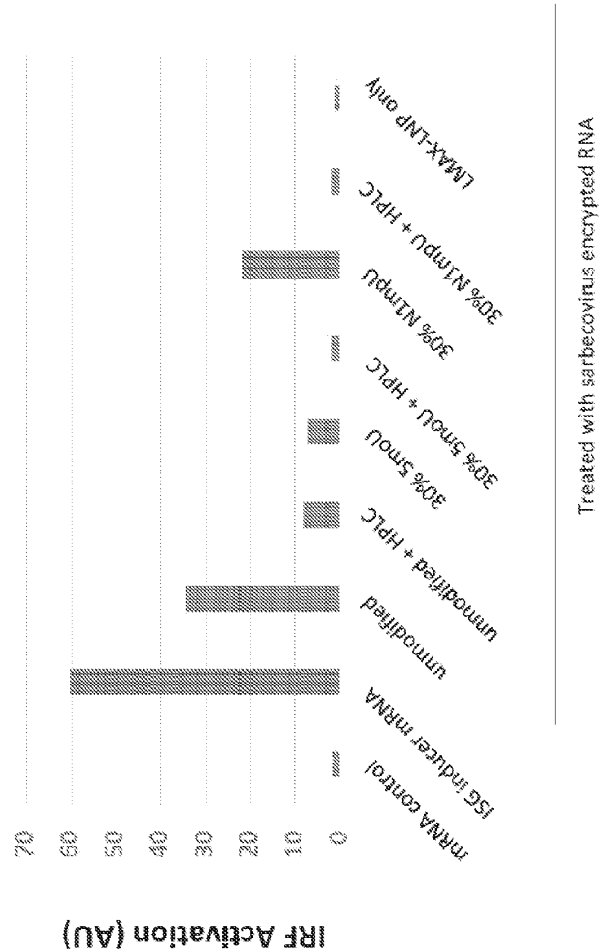


FIG. 61

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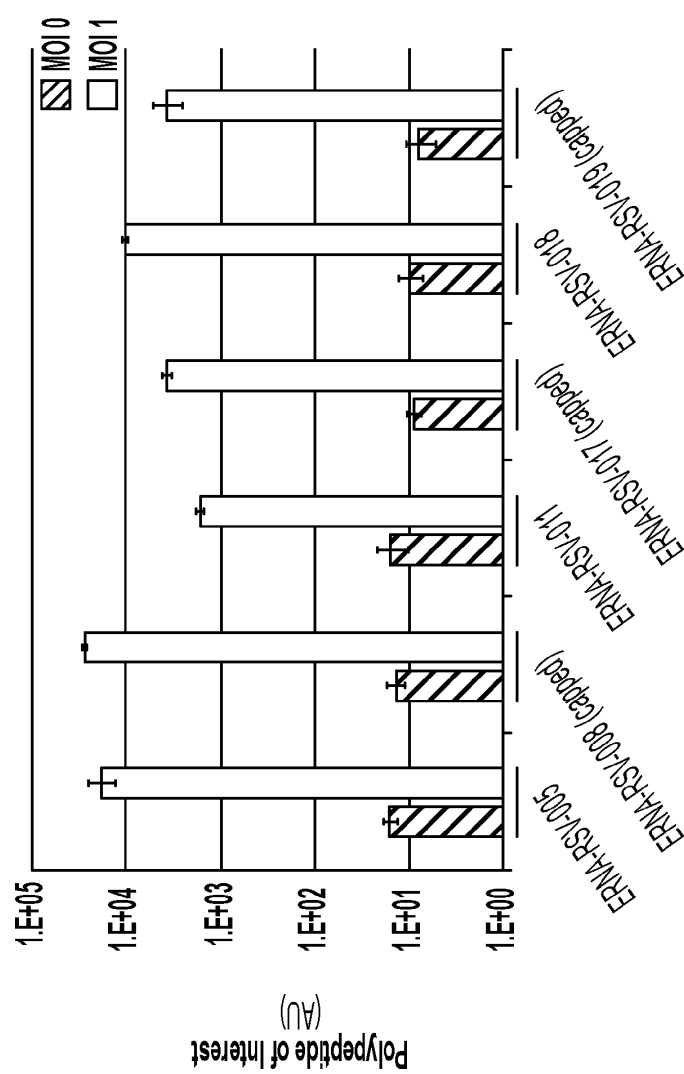


FIG. 62

An RSV encrypted RNA with modified nucleotides
can be substantially activated by RSV



FIG. 63

An RSV encrypted RNA with modified nucleotides
can be substantially activated by RSV

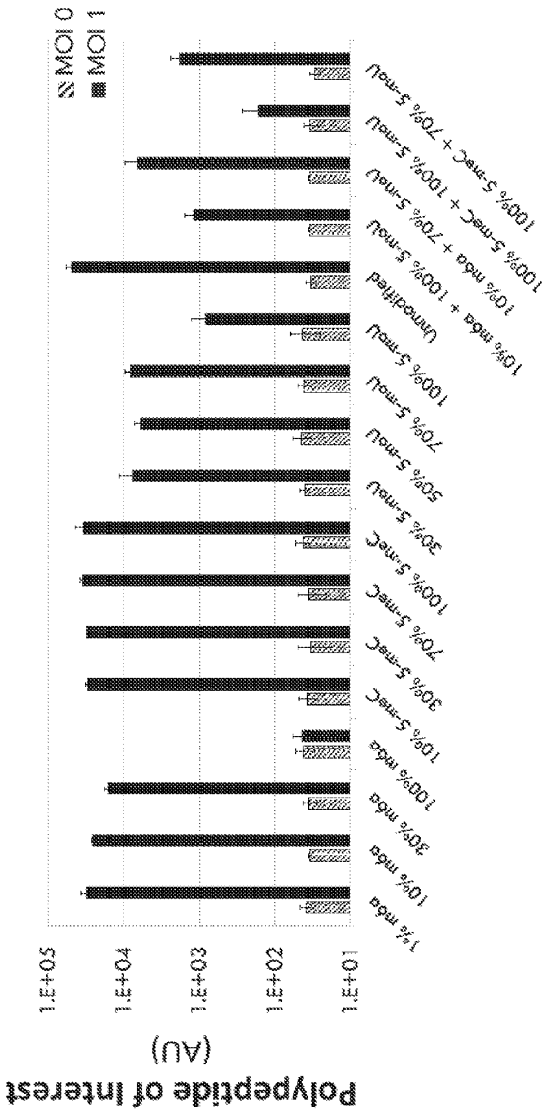


FIG. 64

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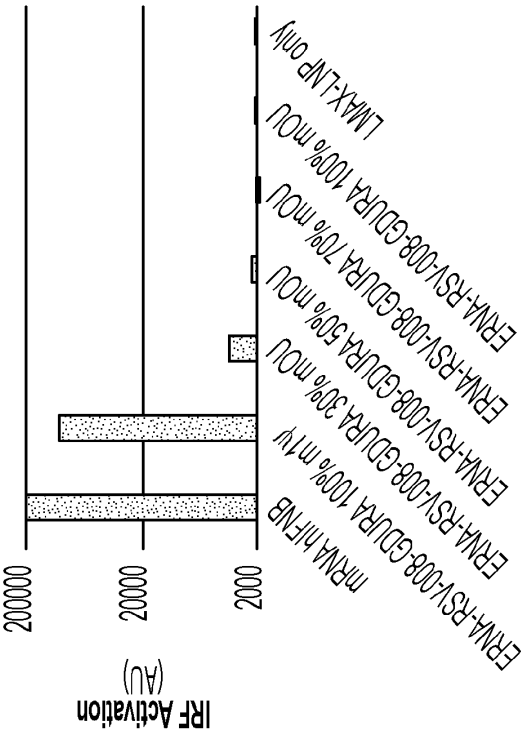
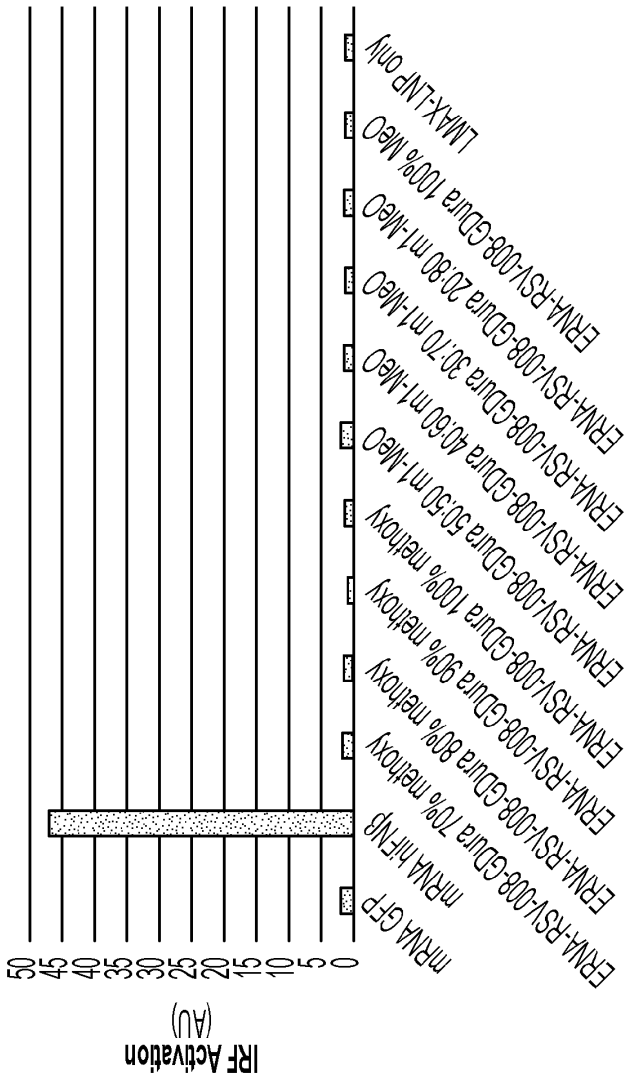


FIG. 65

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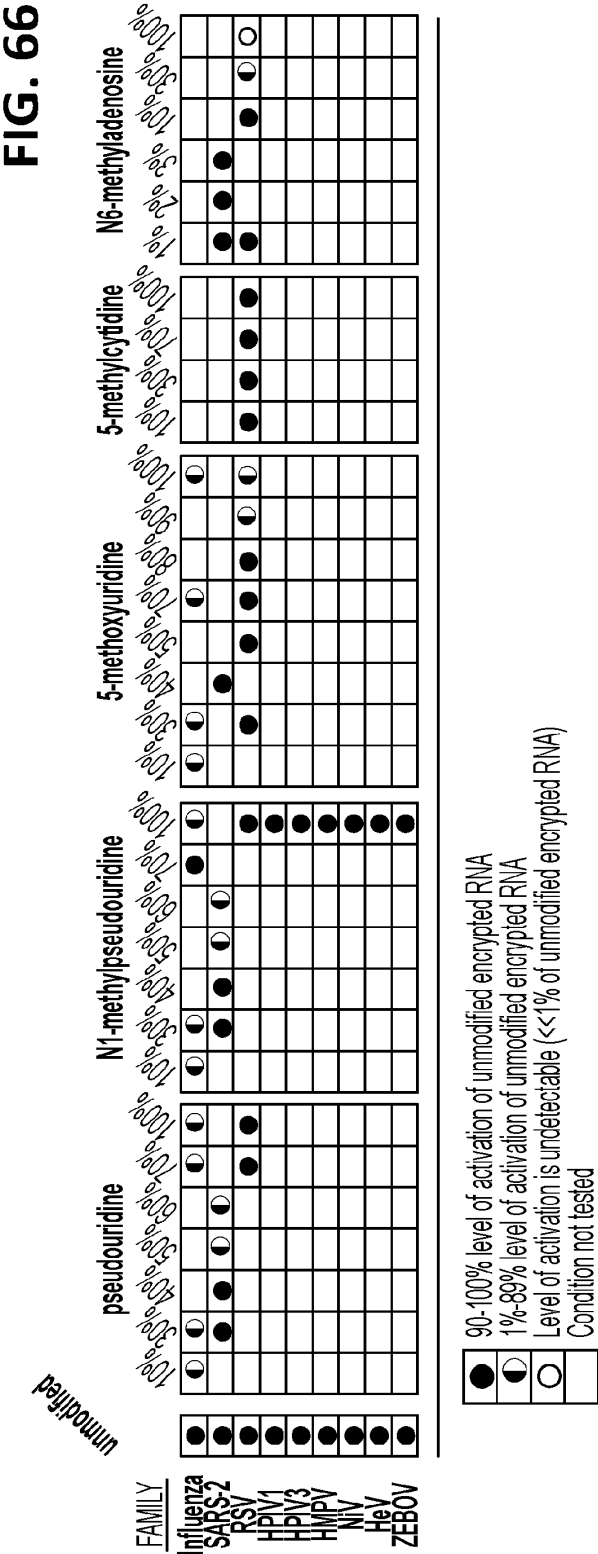


FIG. 67

Preparation	A-modification	C-modification	G-modification	U-modification	Relative Activation Level (Normalized to Prep 1 (nonmodified))
1					100% ↑
2	N6mA (10%)			mo5U (100%)	65% ↑
3	N6mA (10%)			mo5U (70%)	90% ↑
4		m5c (100%)		mo5U (100%)	20% ↑
5		m5c (100%)		mo5U (70%)	70% ↑
6				N1mpU (50%) & mo5U (50%)	100% ↑
7				N1mpU (60%) & mo5U (40%)	60% ↑
8				N1mpU (70%) & mo5U (30%)	50% ↑
9				N1mpU (80%) & mo5U (20%)	50% ↑

Test Scaffold: ERNA-RSV-008
N6mA: N6-methyladenosine; N1mpU: N1-methylpseudouridine; m5c: 5-methylcytidine; mo5U: 5-methoxyuridine