

Figure 1

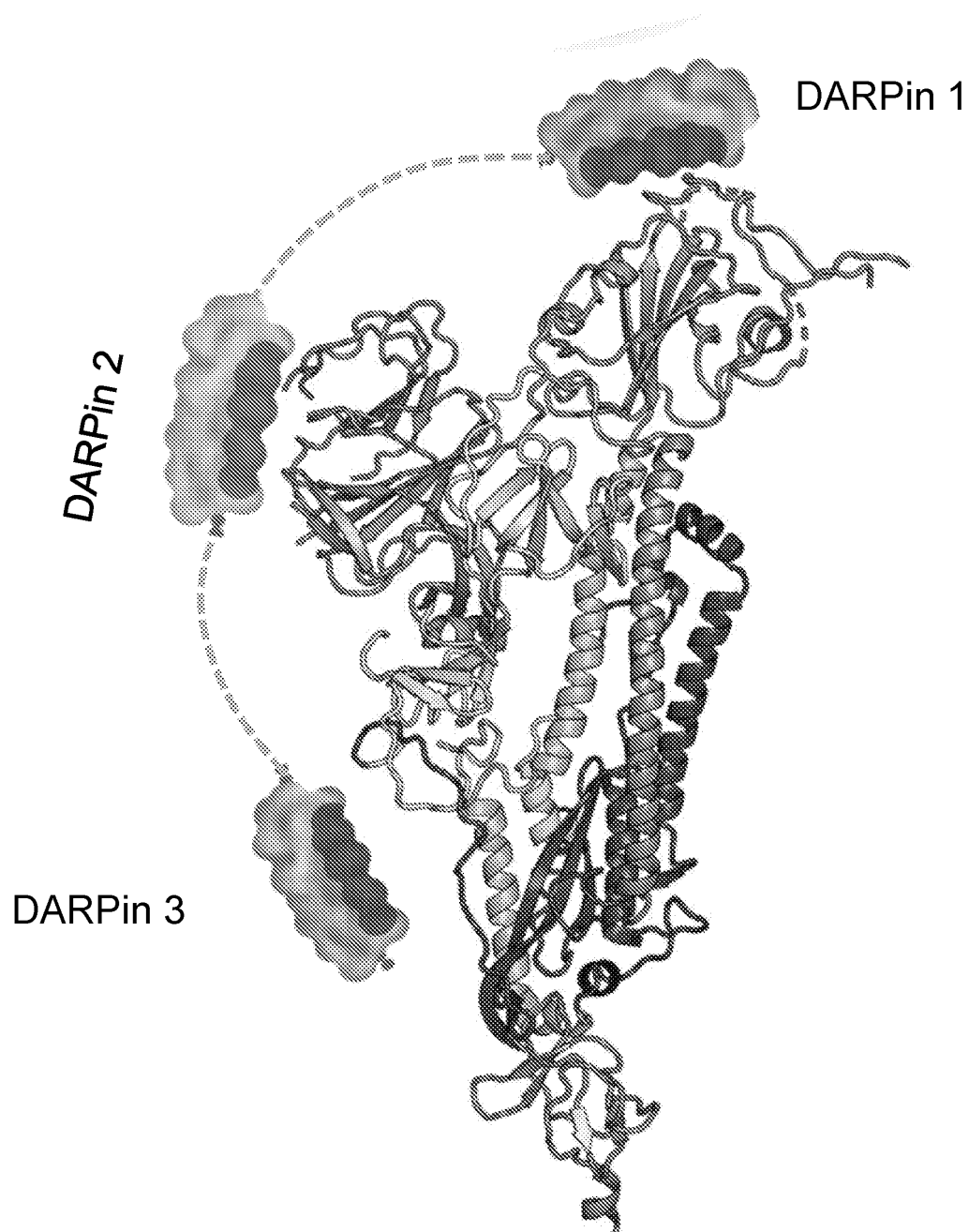


Figure 2



Figure 3



Figure 4

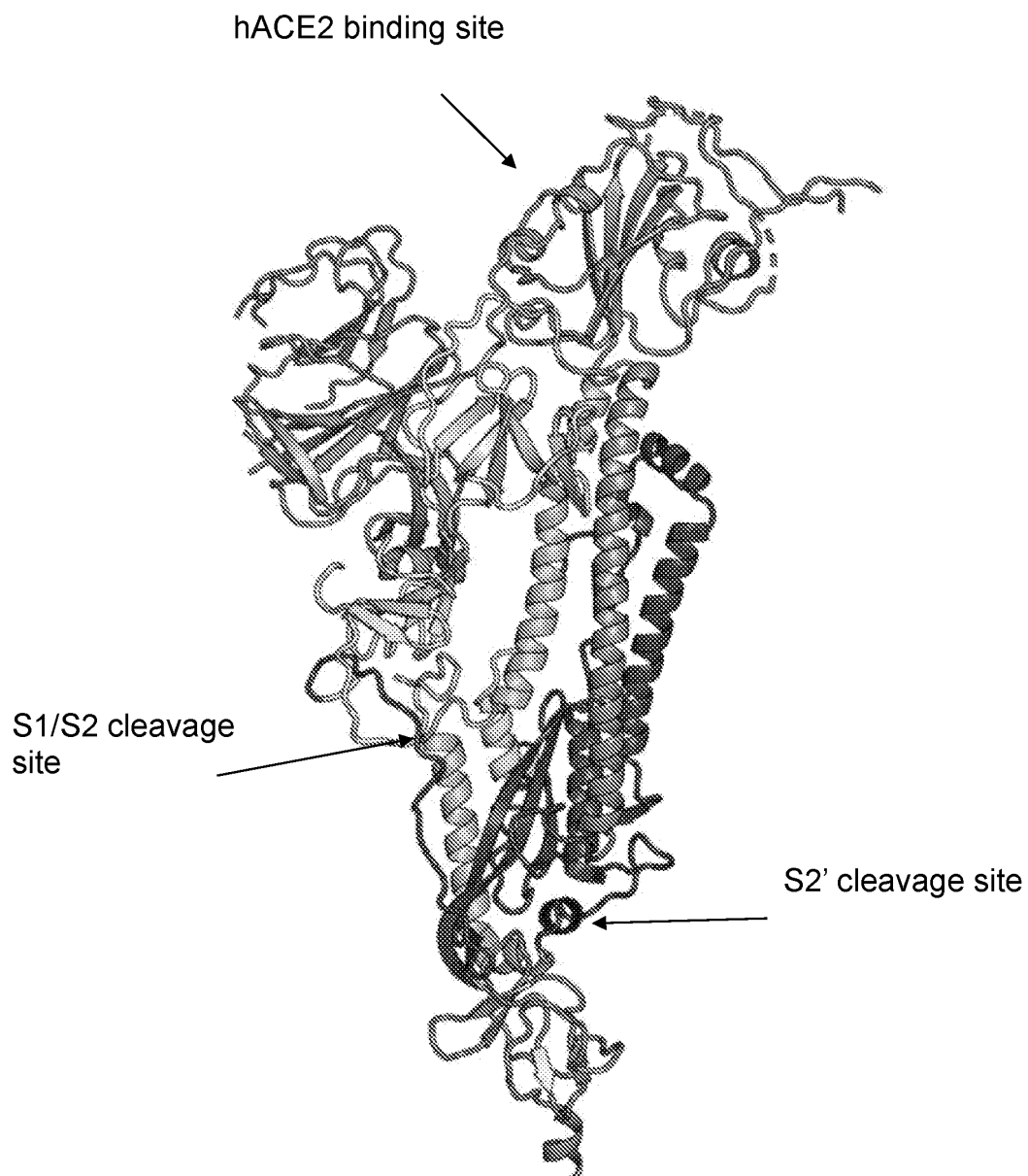


Figure 5

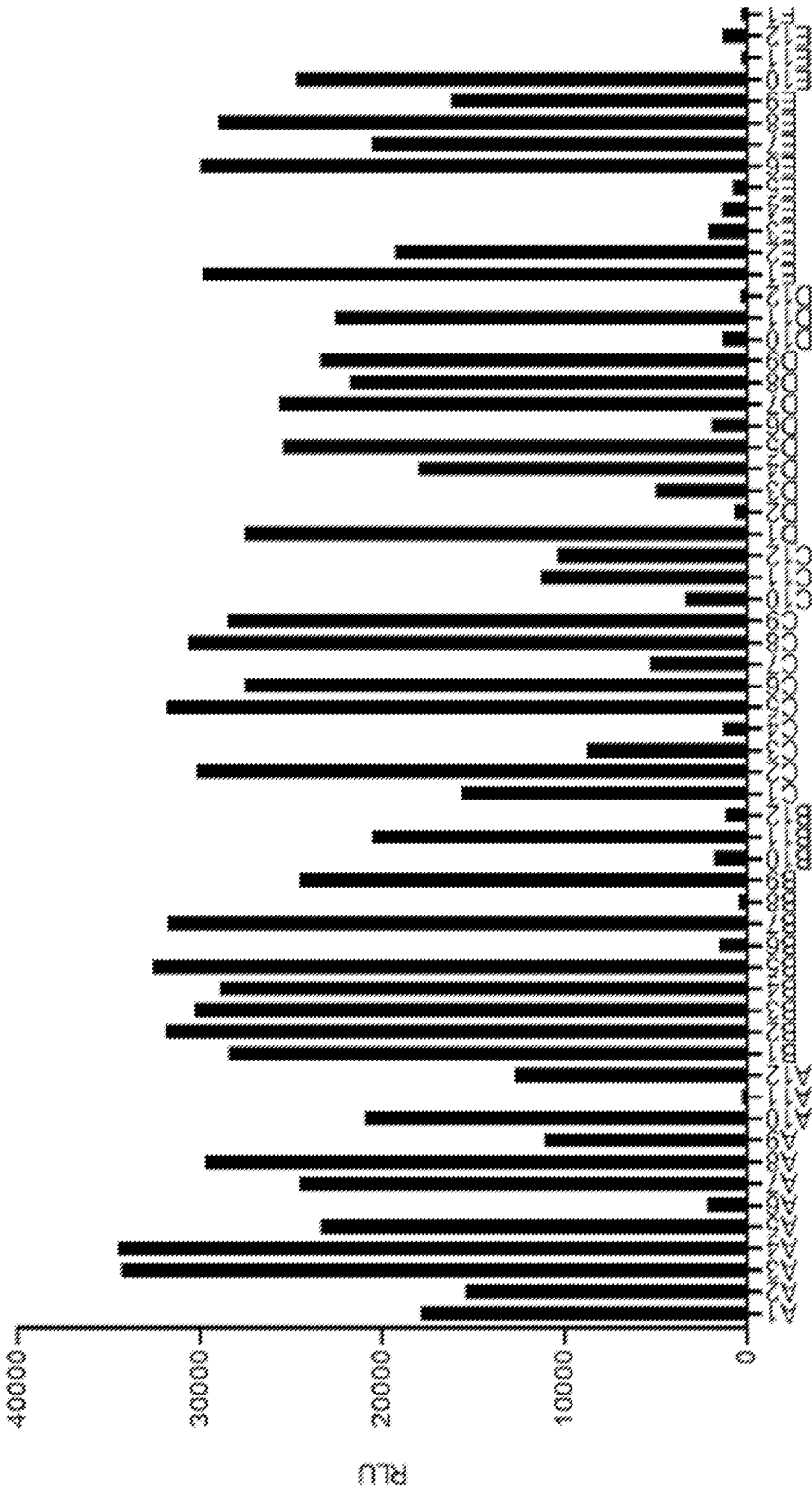


Figure 6

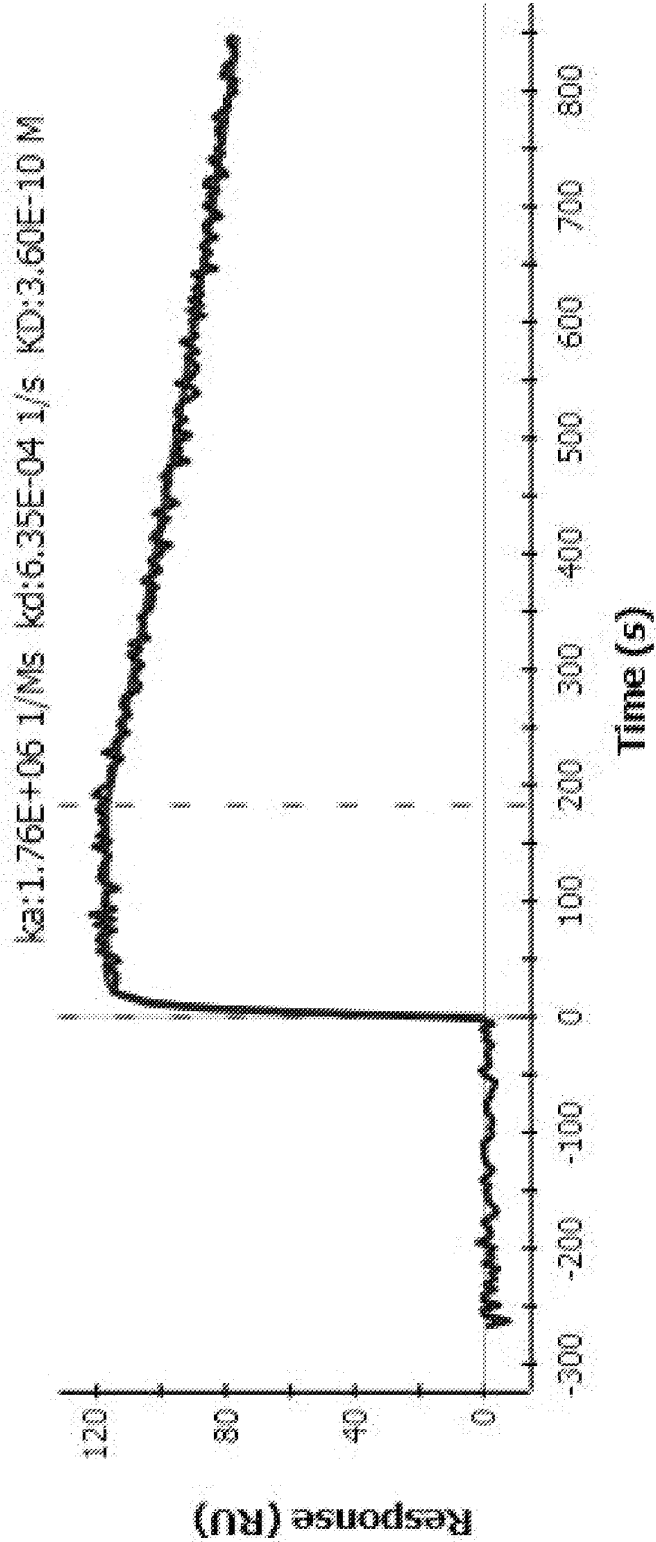


Figure 7

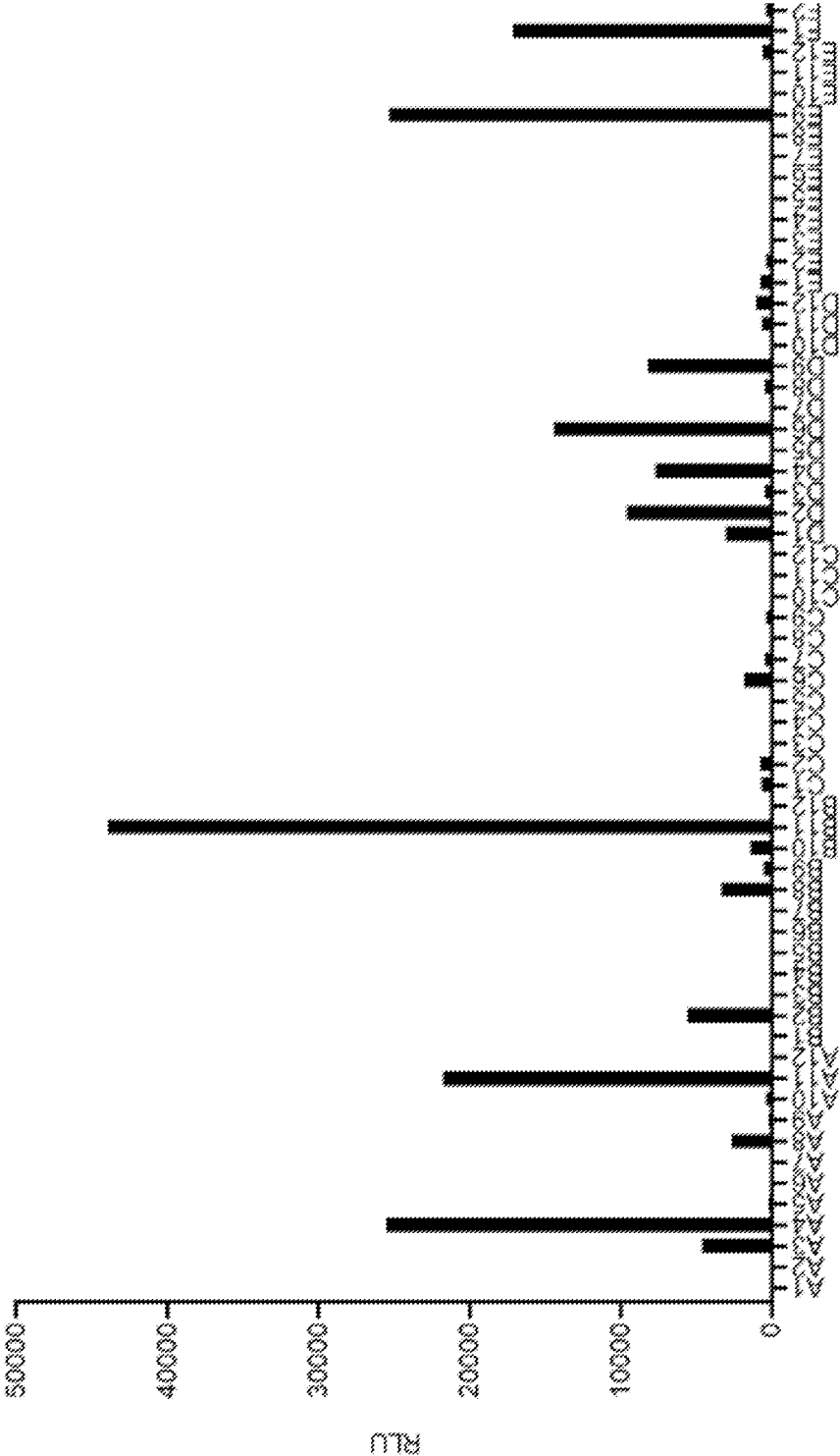


Figure 8

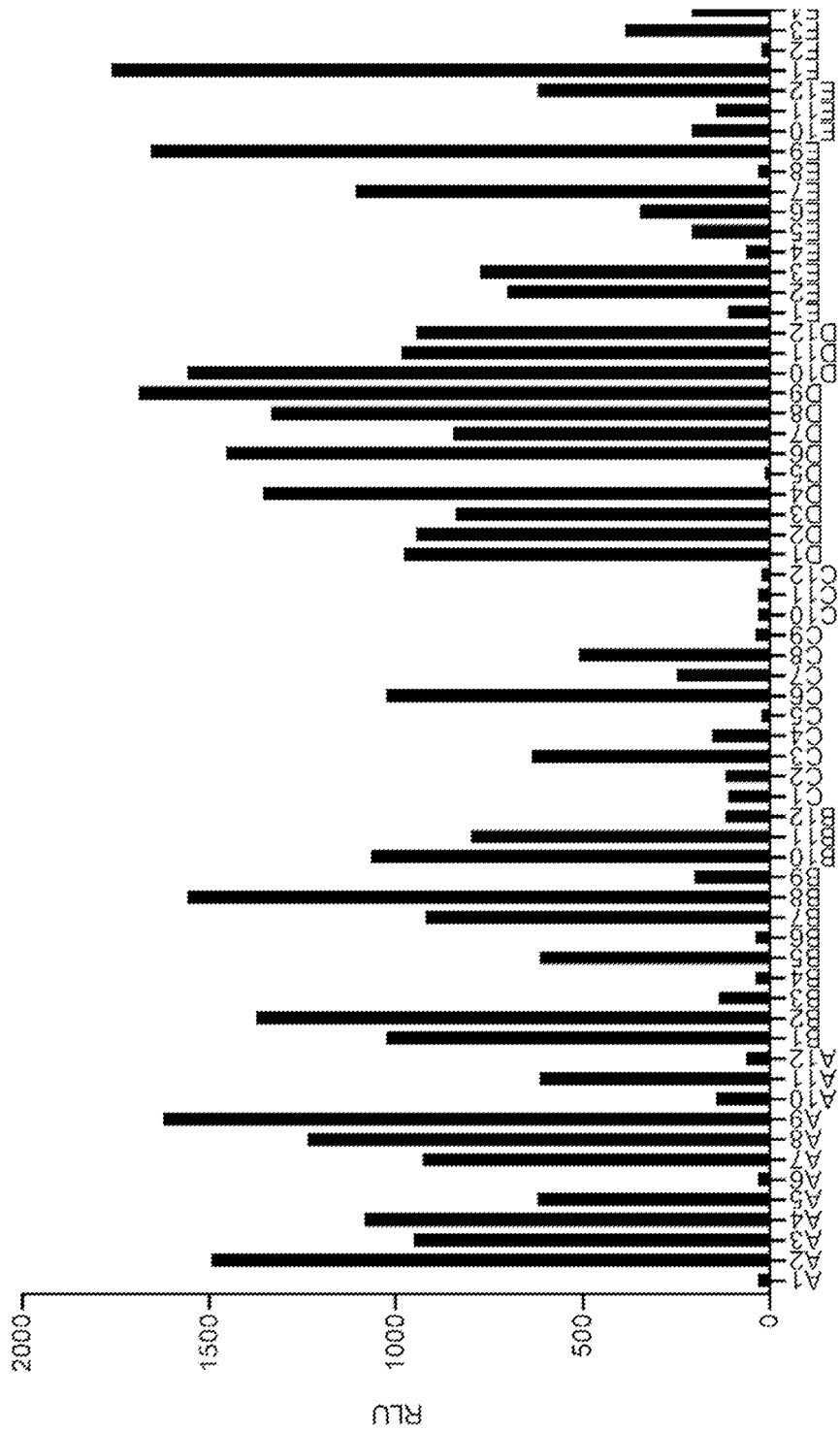
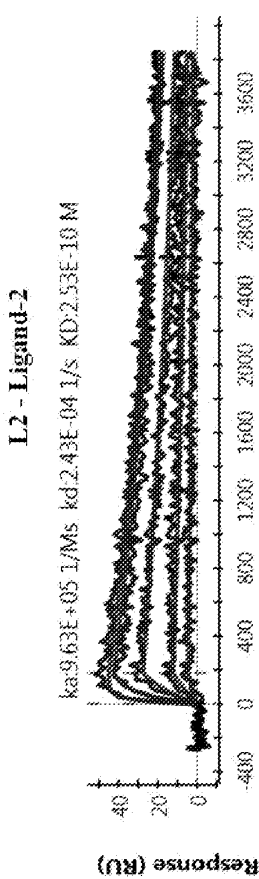
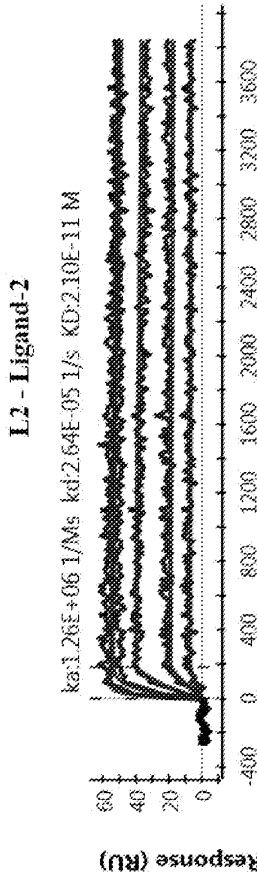


Figure 9a

Step: 14 - R1a_vS07_06F12



Step: 8 - R1b_vS07_12C06



Step: 16 - R2a_vS07_19G10

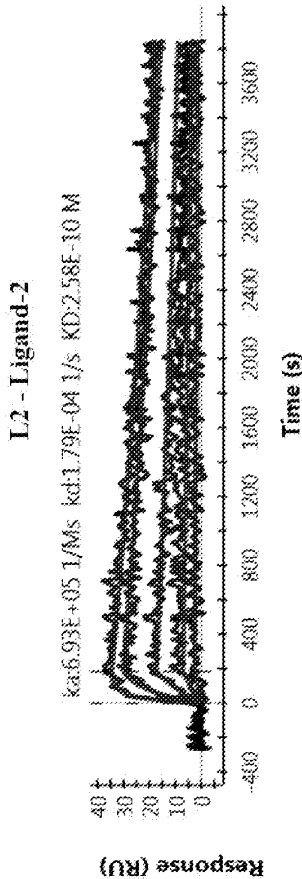


Figure 9b

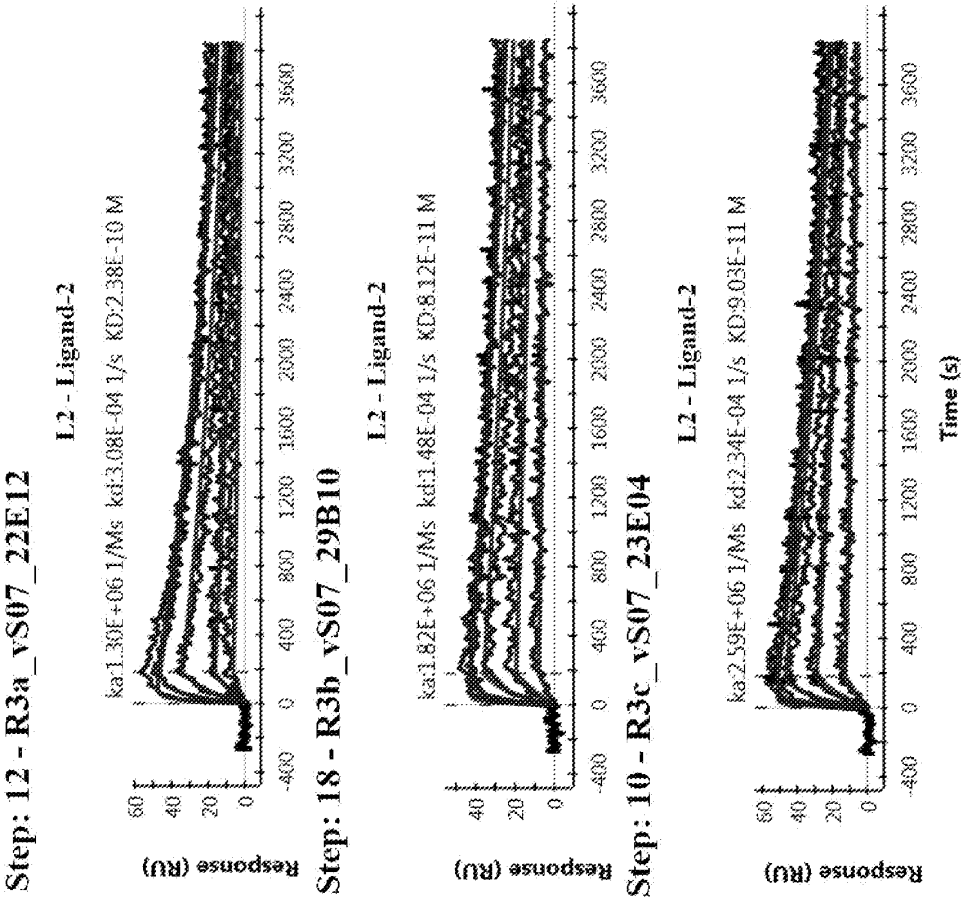


Figure 9c

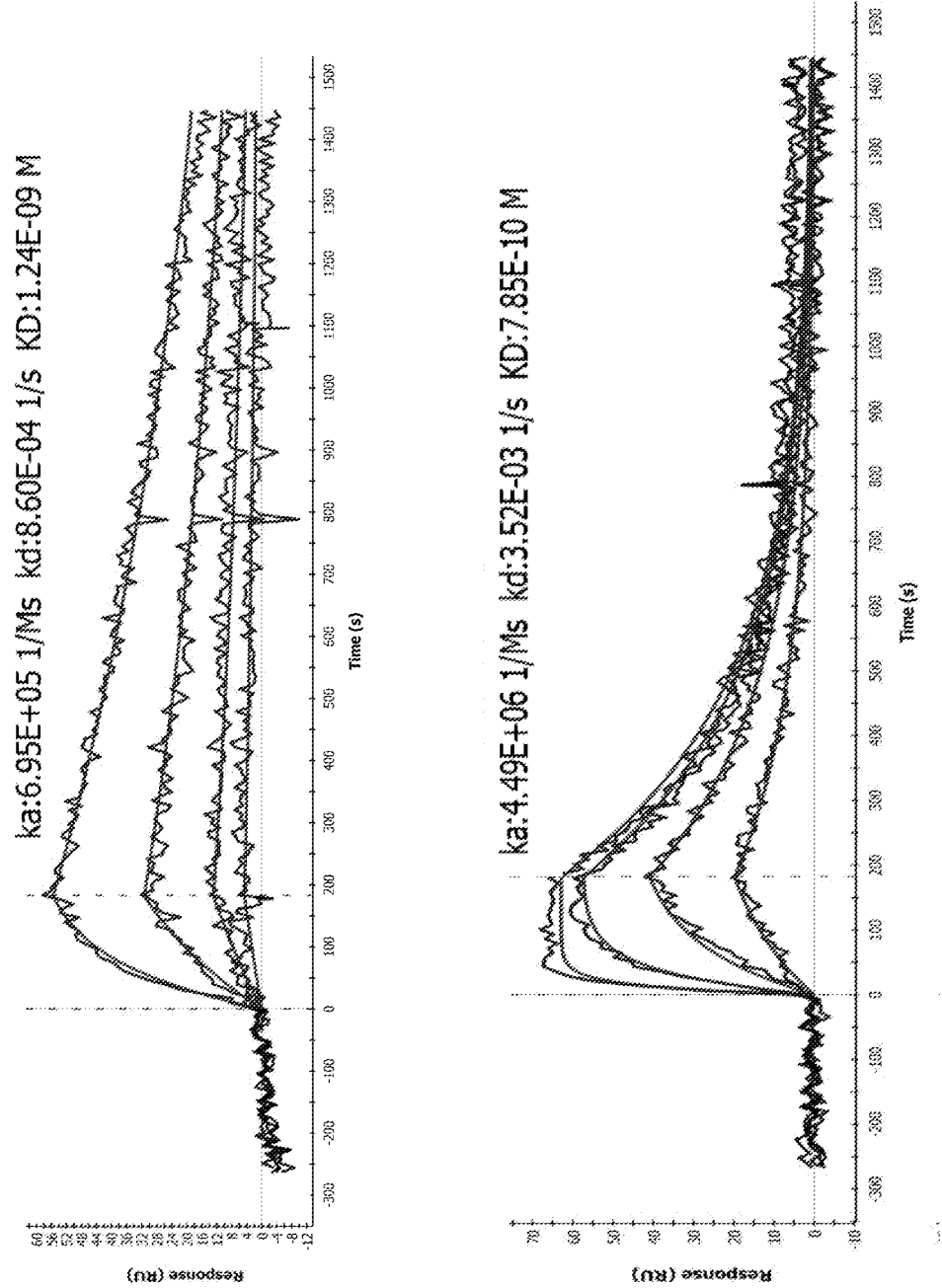


Figure 10

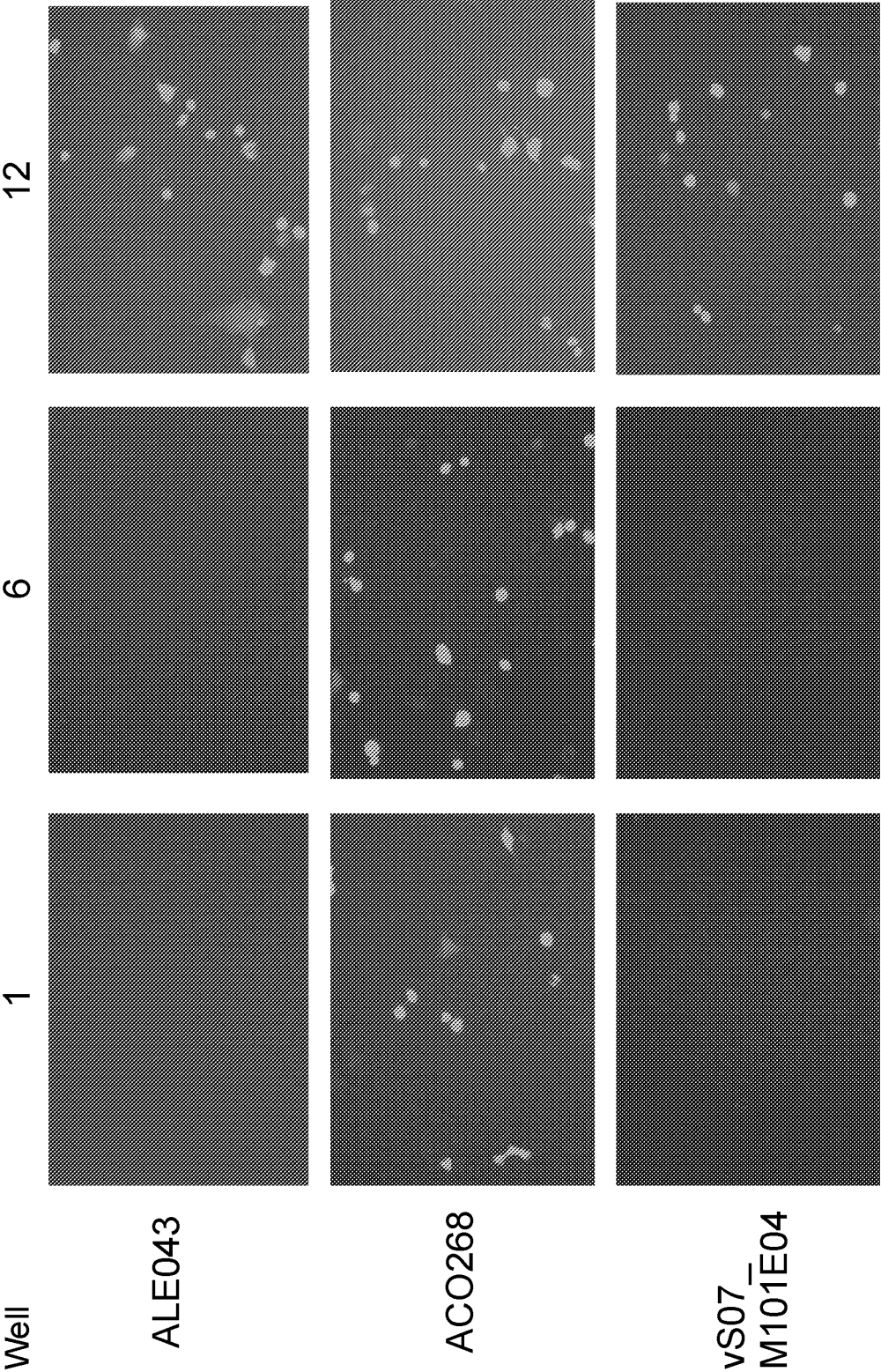


Figure 11

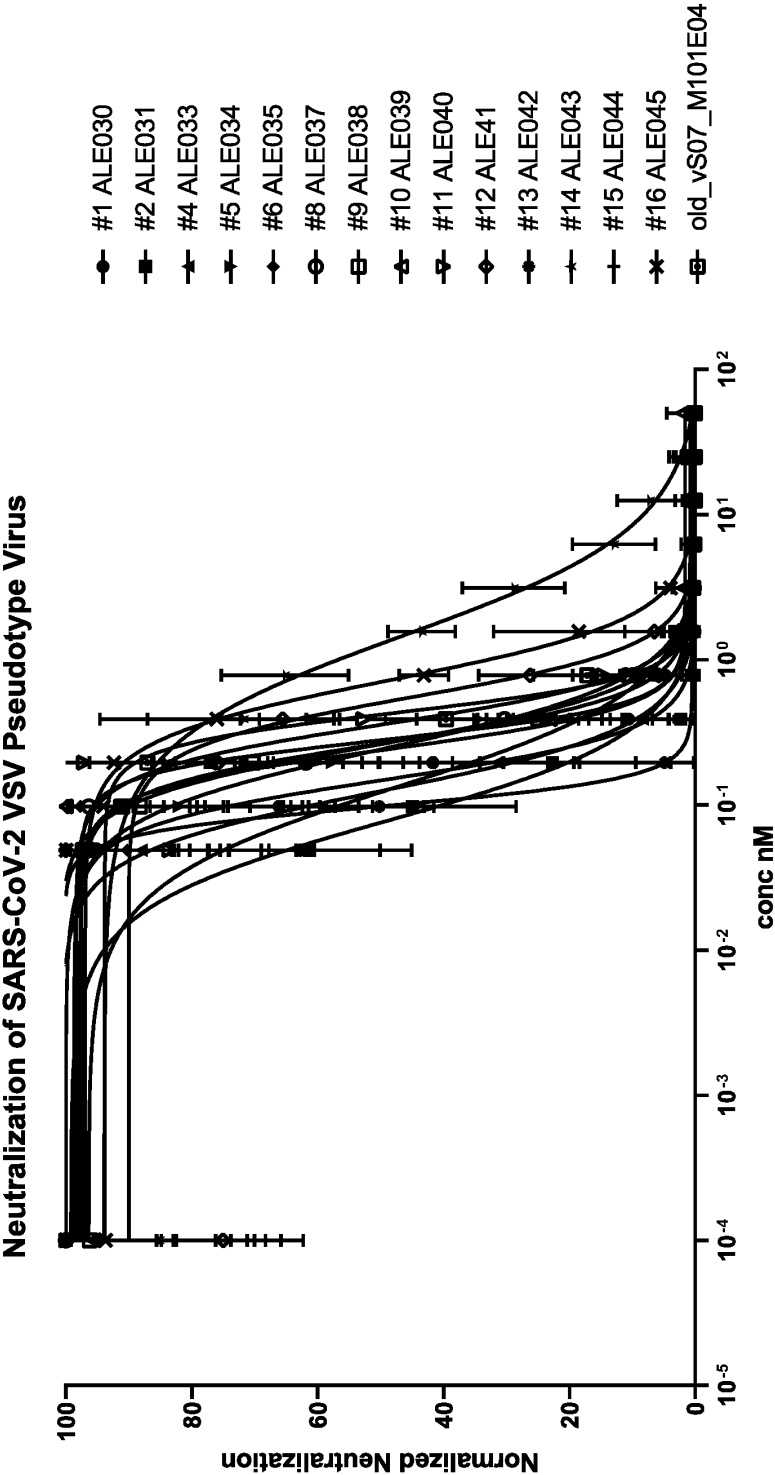


Figure 12

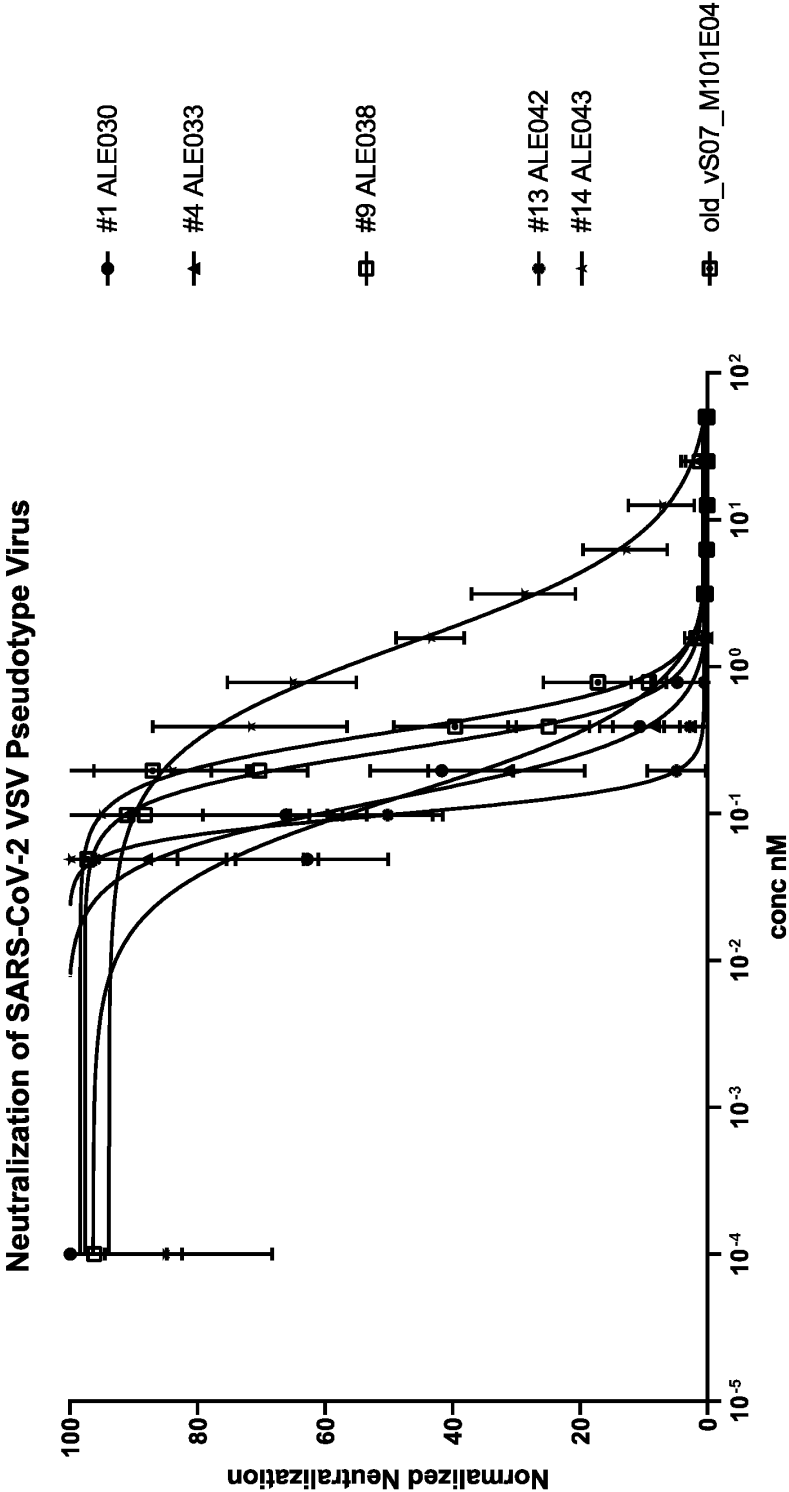


Figure 13

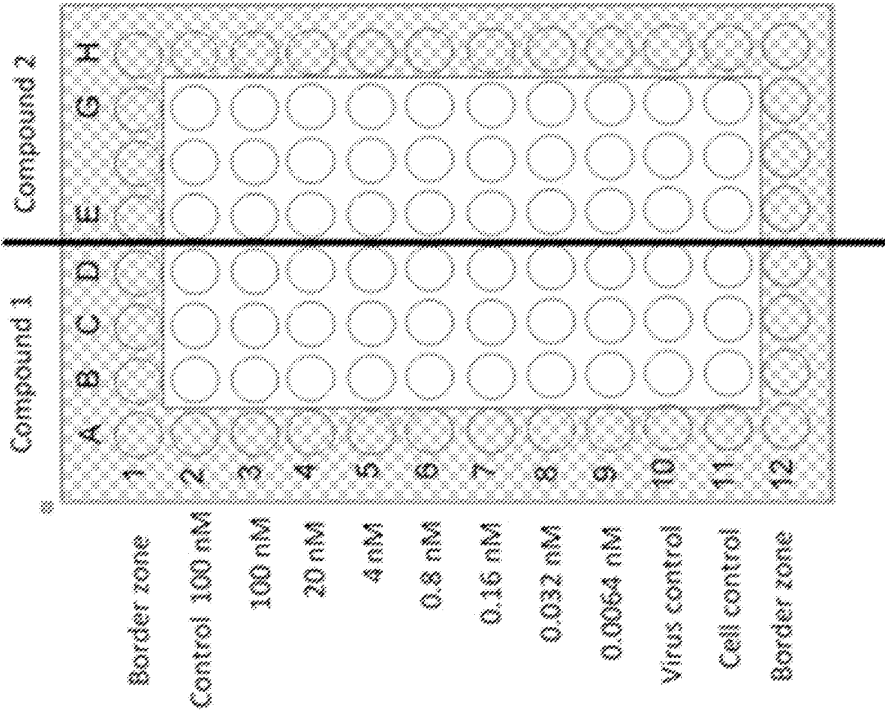


Figure 14a

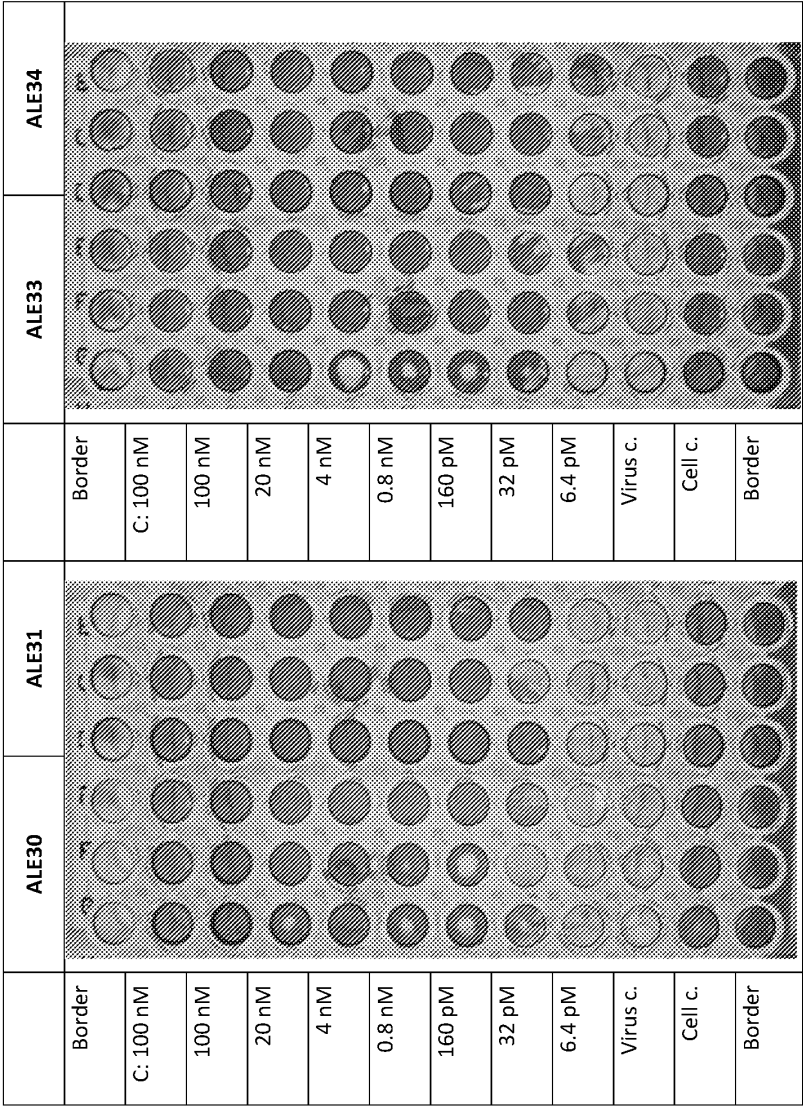


Figure 14b

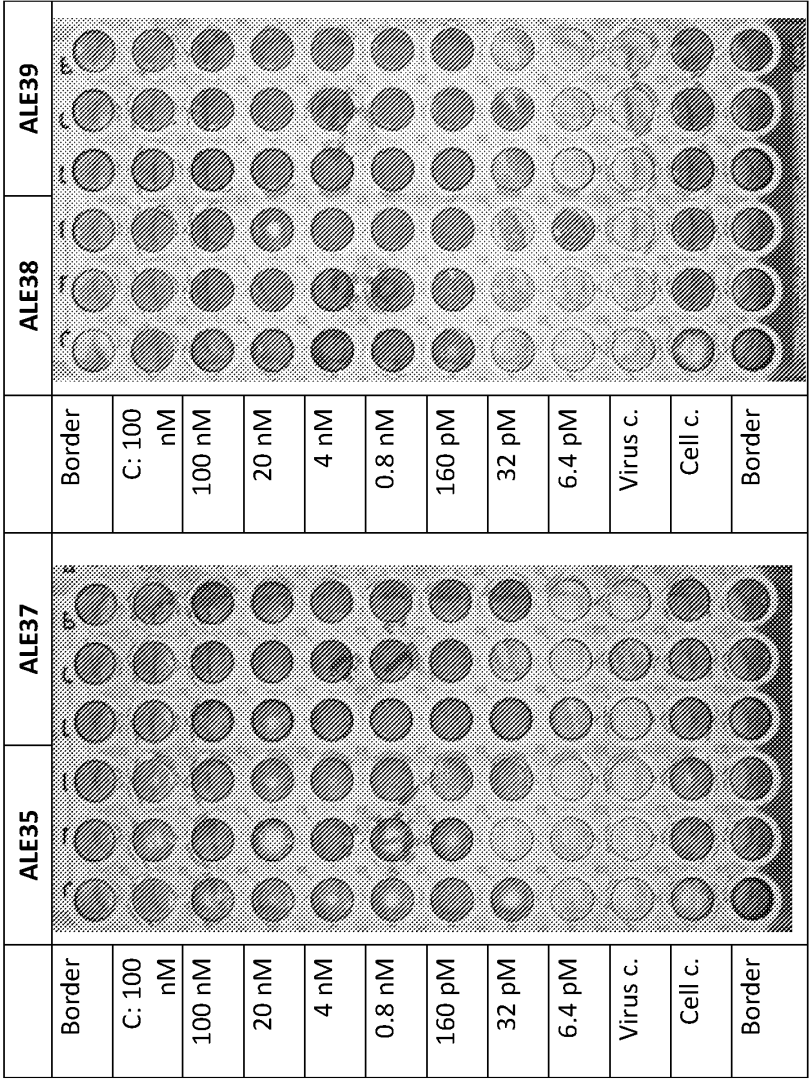


Figure 14c

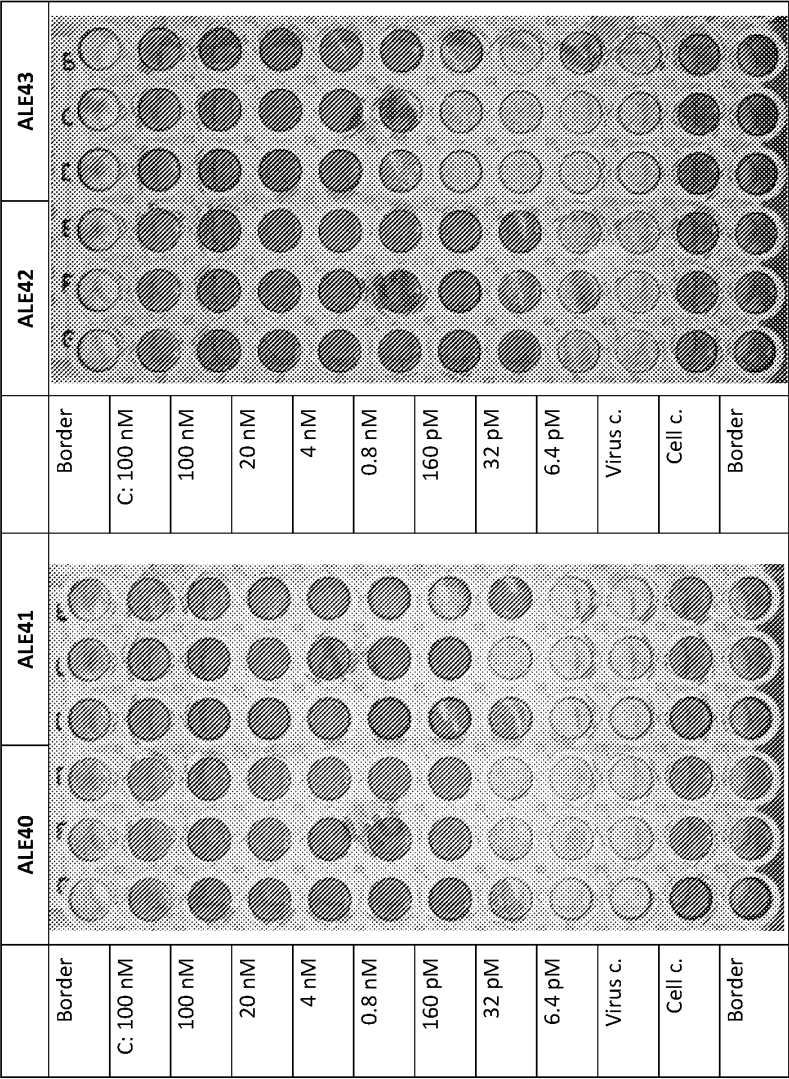


Figure 14d

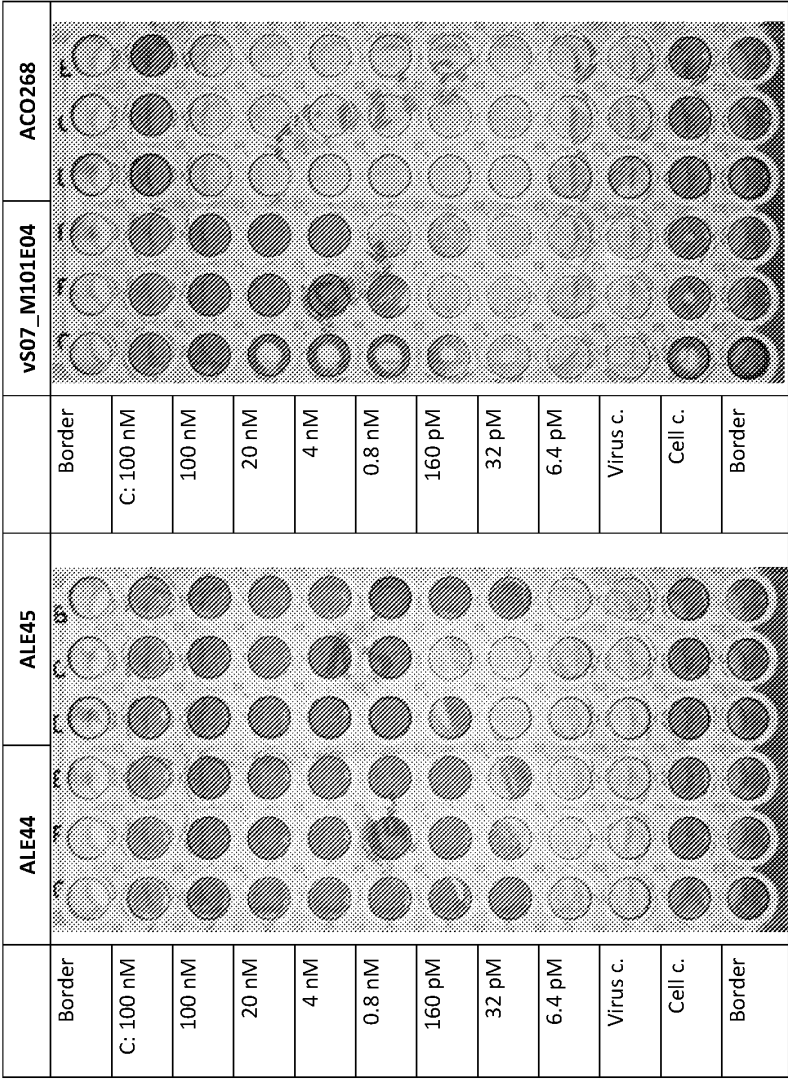


Figure 14e

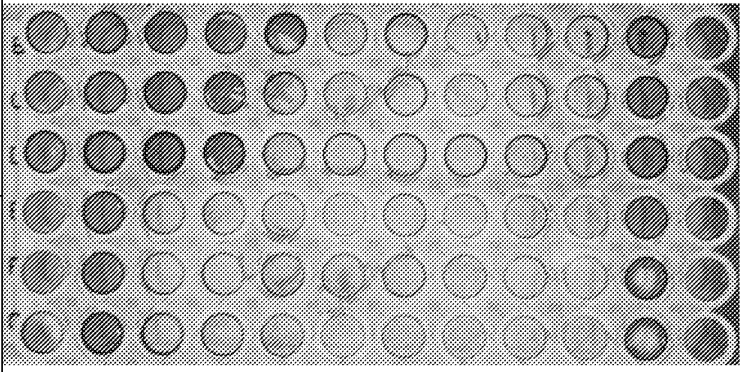
	Neg. serum	Pos. serum (1:100)	
Border			Border
serum control			serum control
1:100			1:100
1:500			1:500
1:2500			1:2500
1:12'500			1:12'500
1:62'500			1:62'500
1:312'500			1:312'500
1:1'562'500			1:1'562'500
Virus c.			Virus c.
Cell c.			Cell c.
Border			Border

Figure 14f

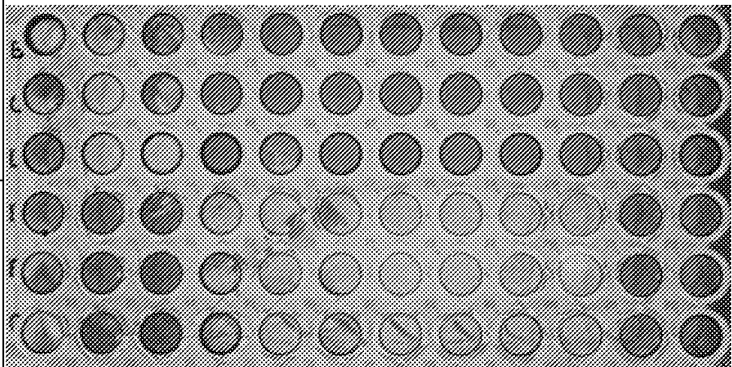
	ACE2	Virus back titration	
Border		Border	
C: 100 nM		100 TCID50	
100 nM		20 TCID50	
20 nM		2 TCID50	
4 nM		0.4 TCID50	
0.8 nM			
160 pM			
32 pM			
6.4 pM			
Virus c.			
Cell c.		Cell c.	
Border		Border	

Figure 15a

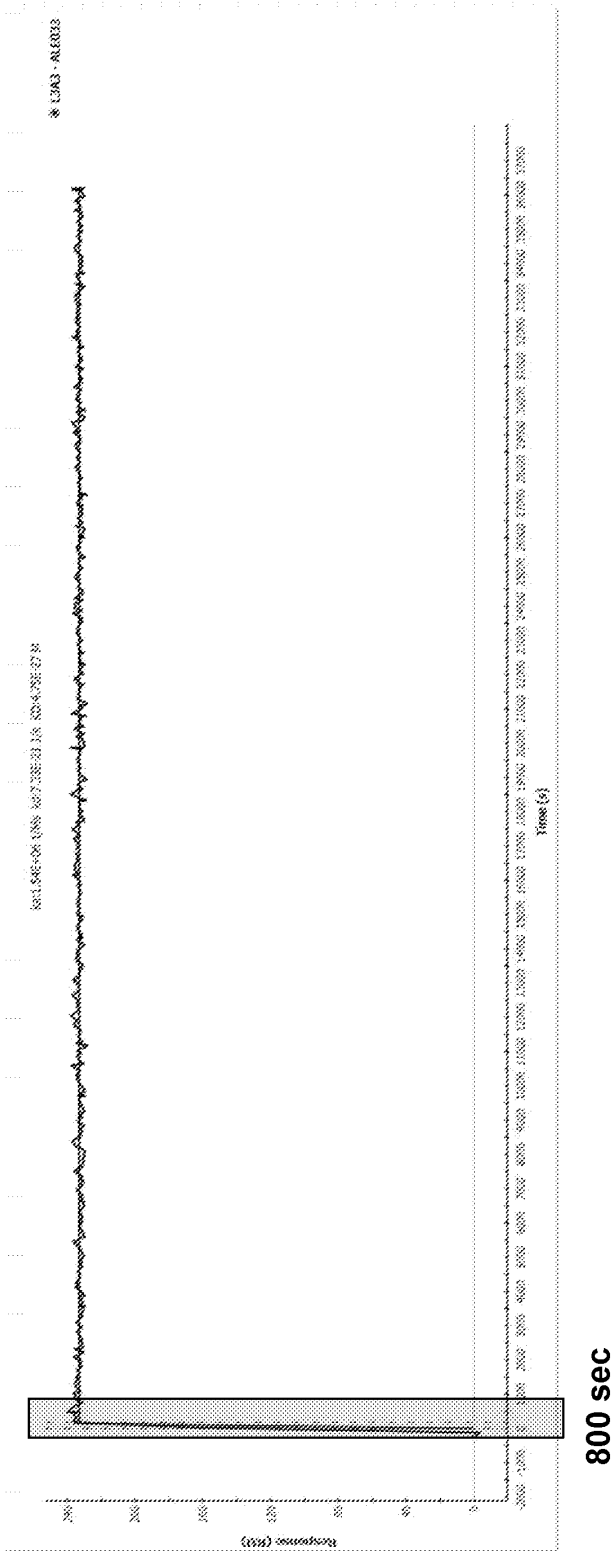


Figure 15b

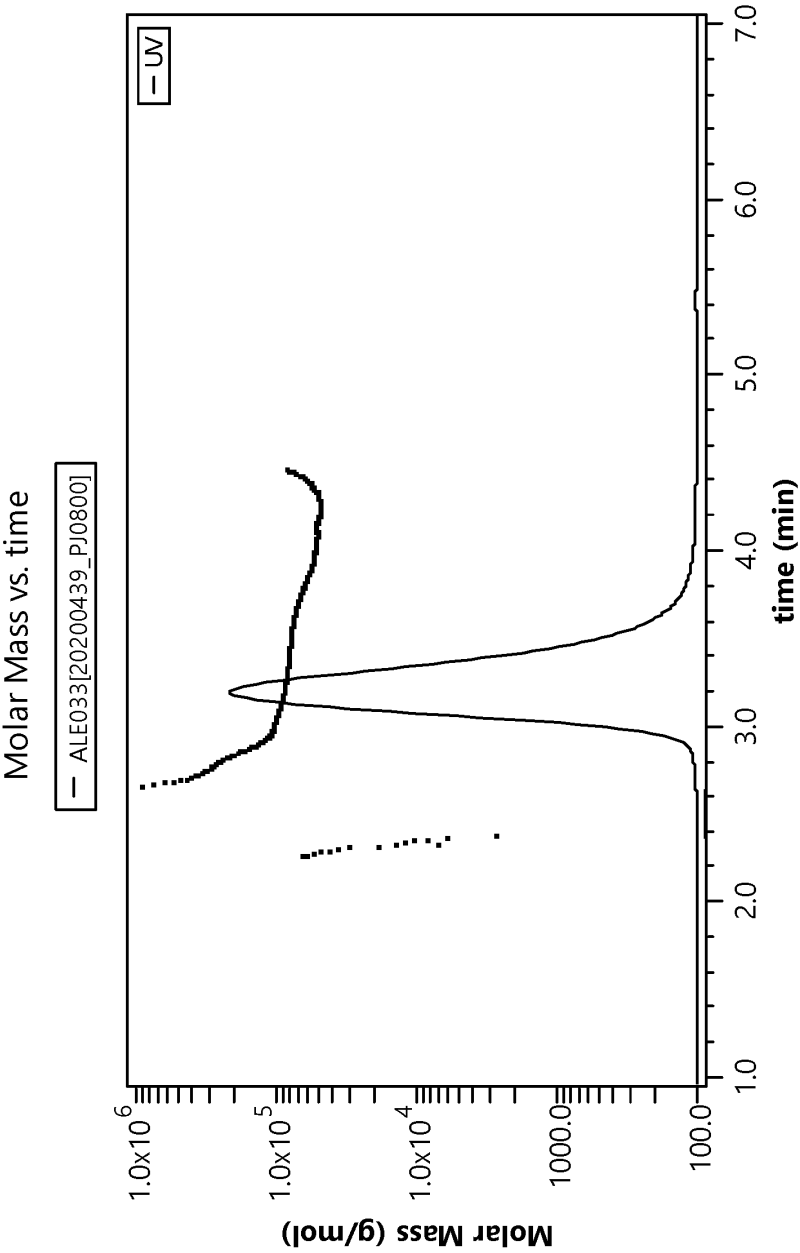


Figure 16

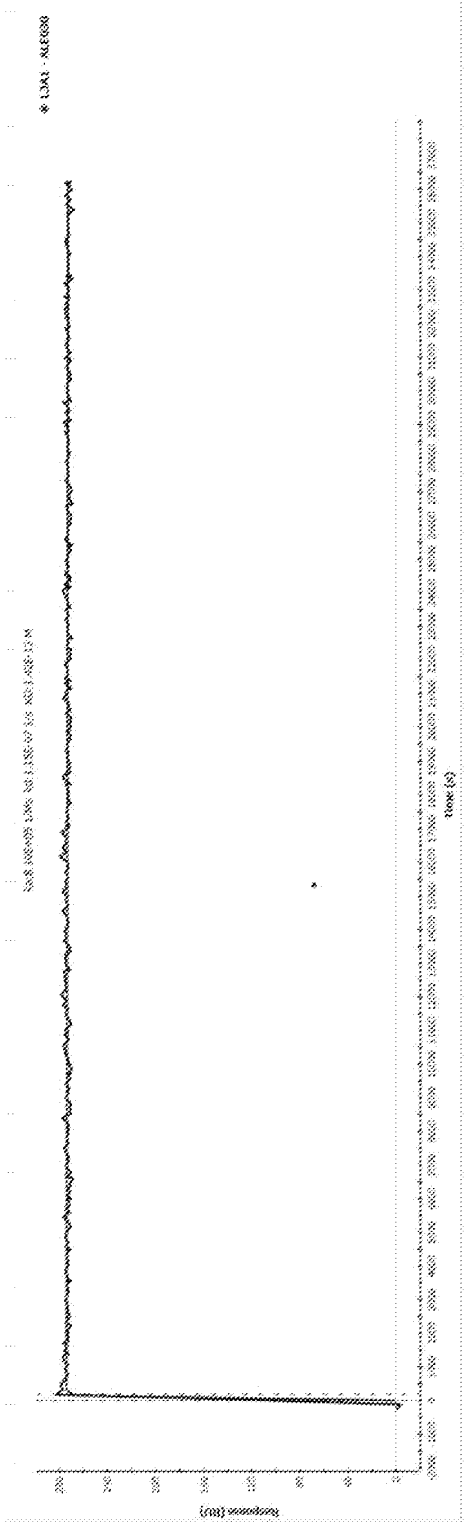


Figure 17

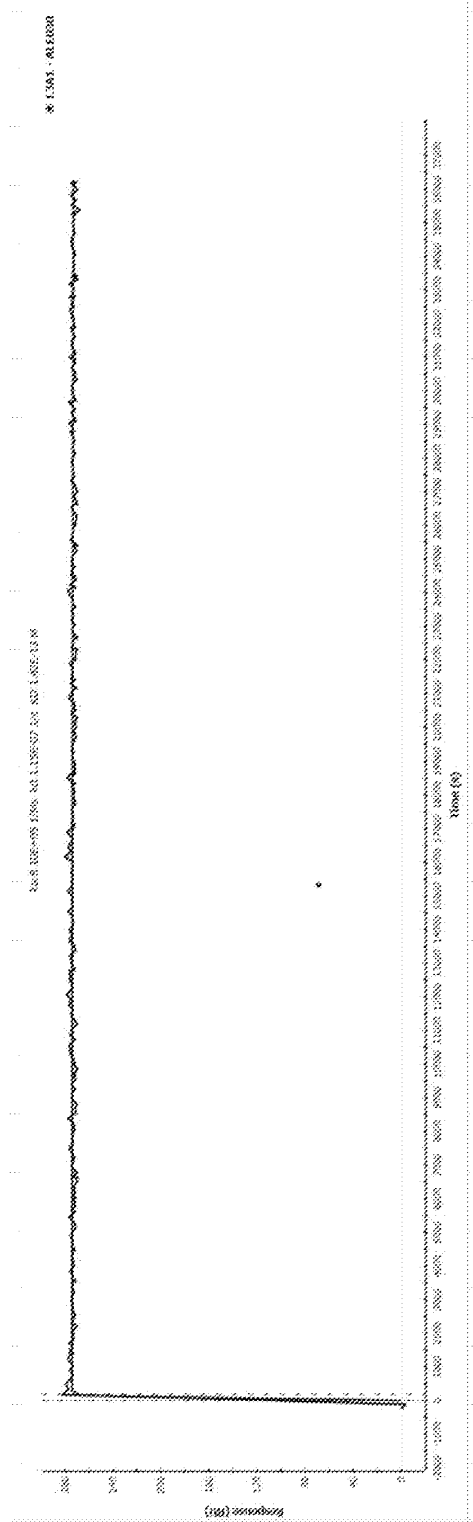


Figure 18a

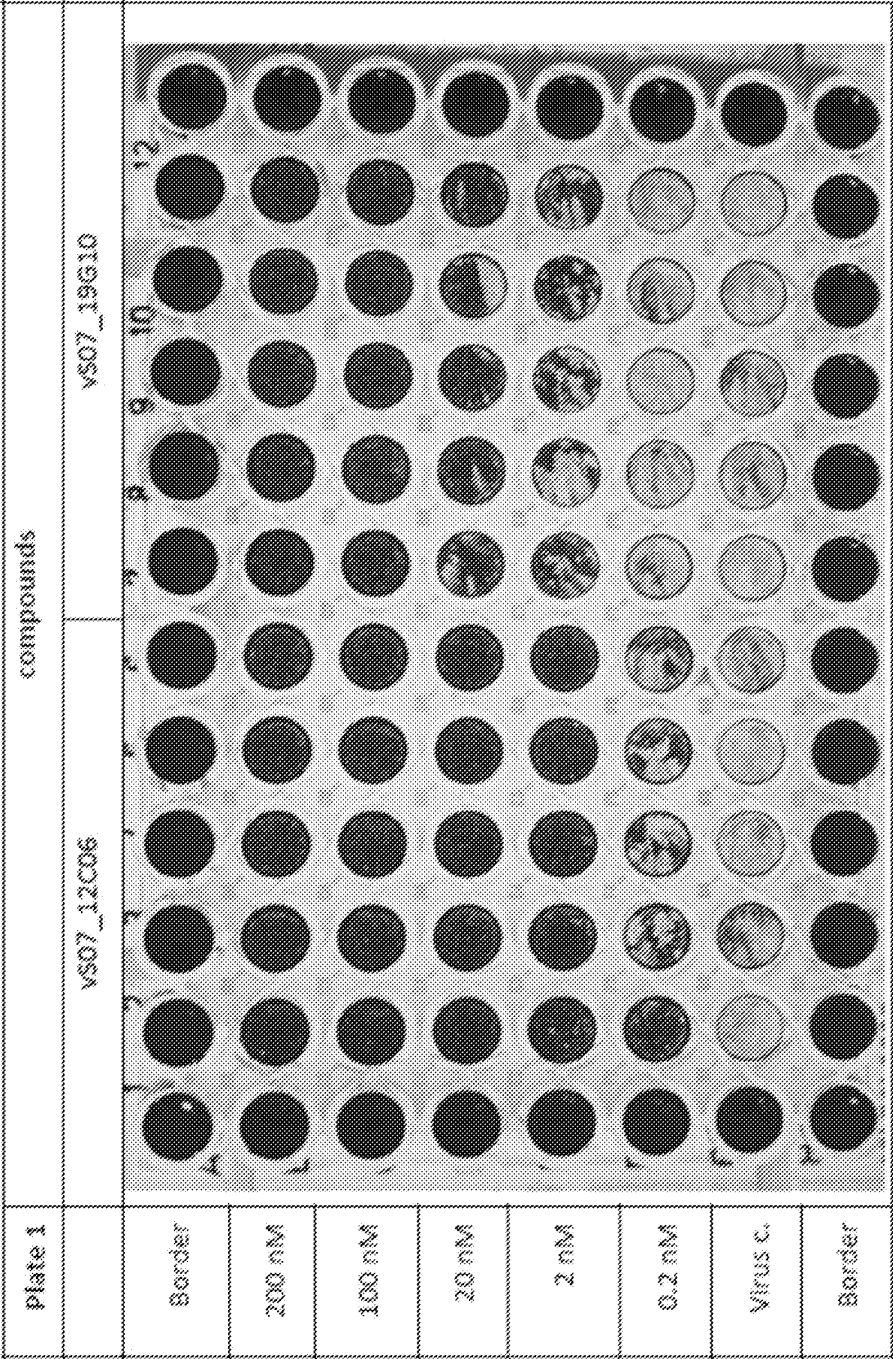


Figure 18b

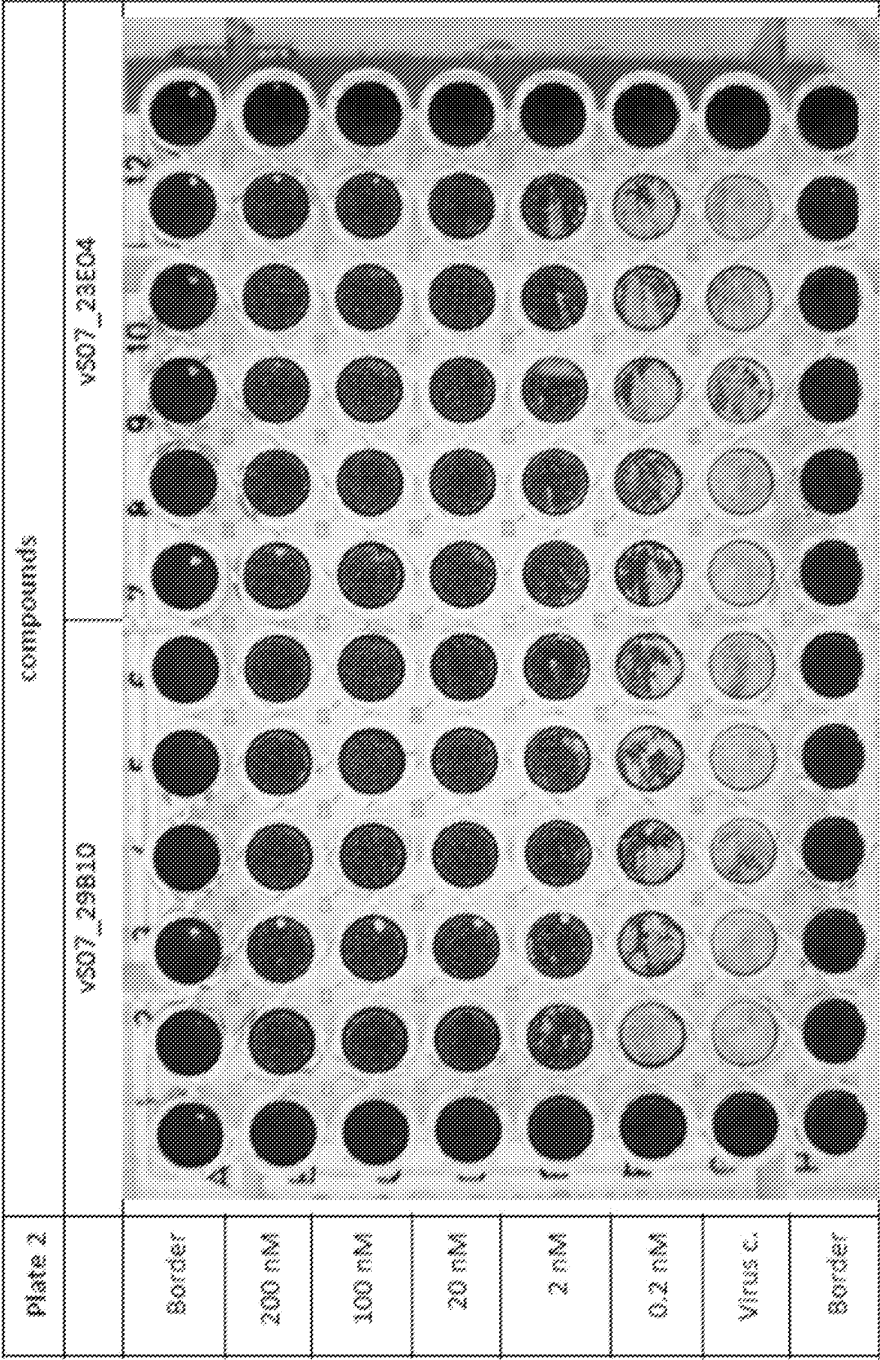


Figure 18c

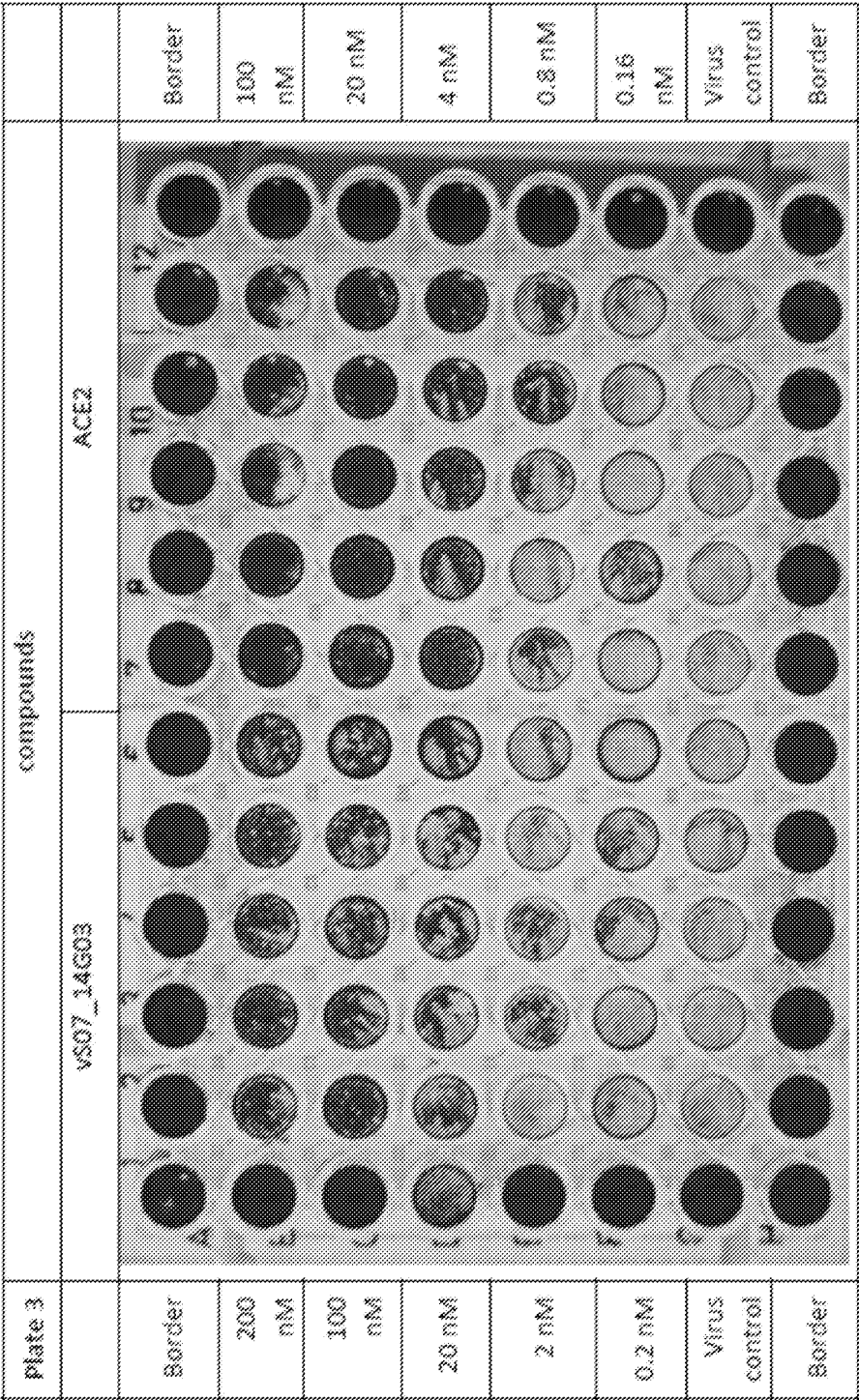


Figure 18d

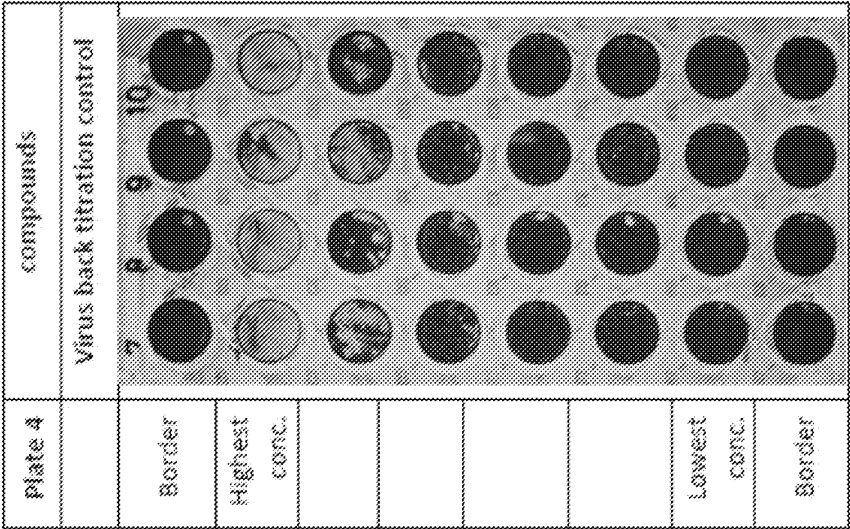


Figure 19

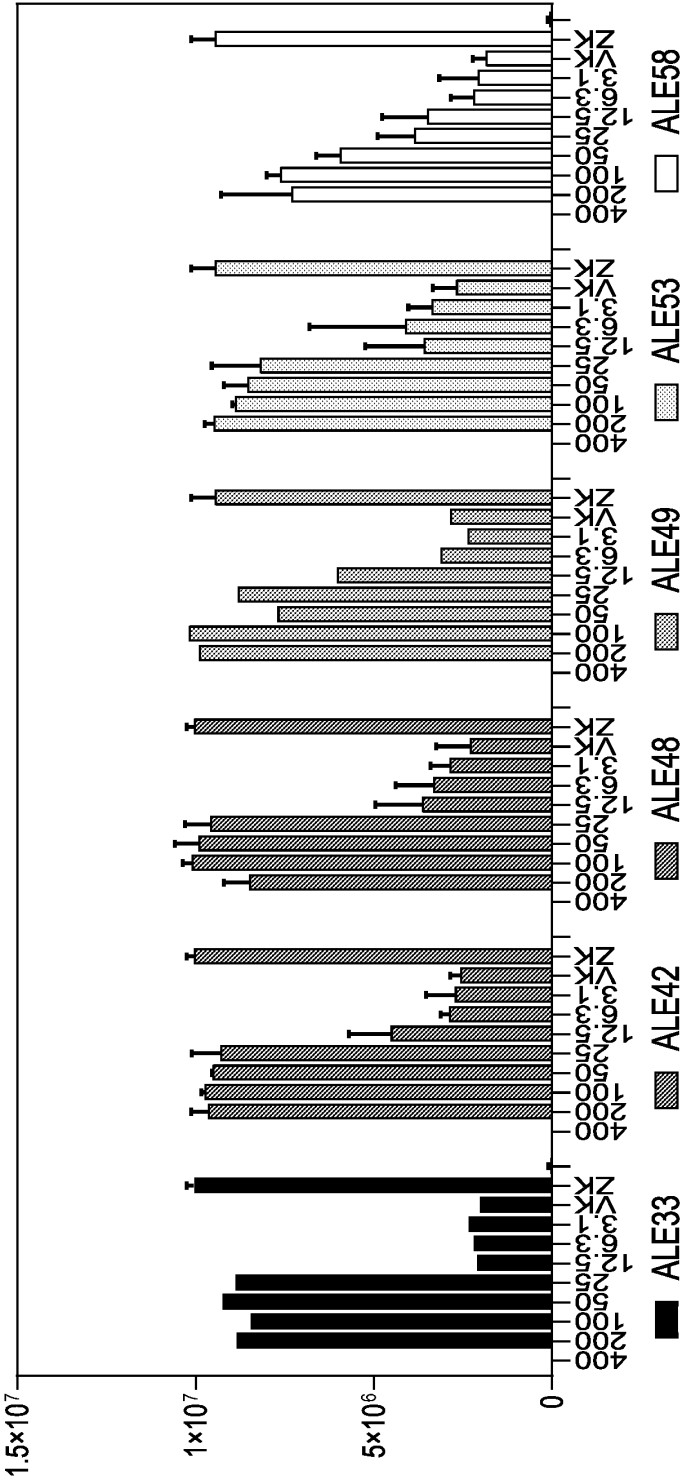


Figure 20

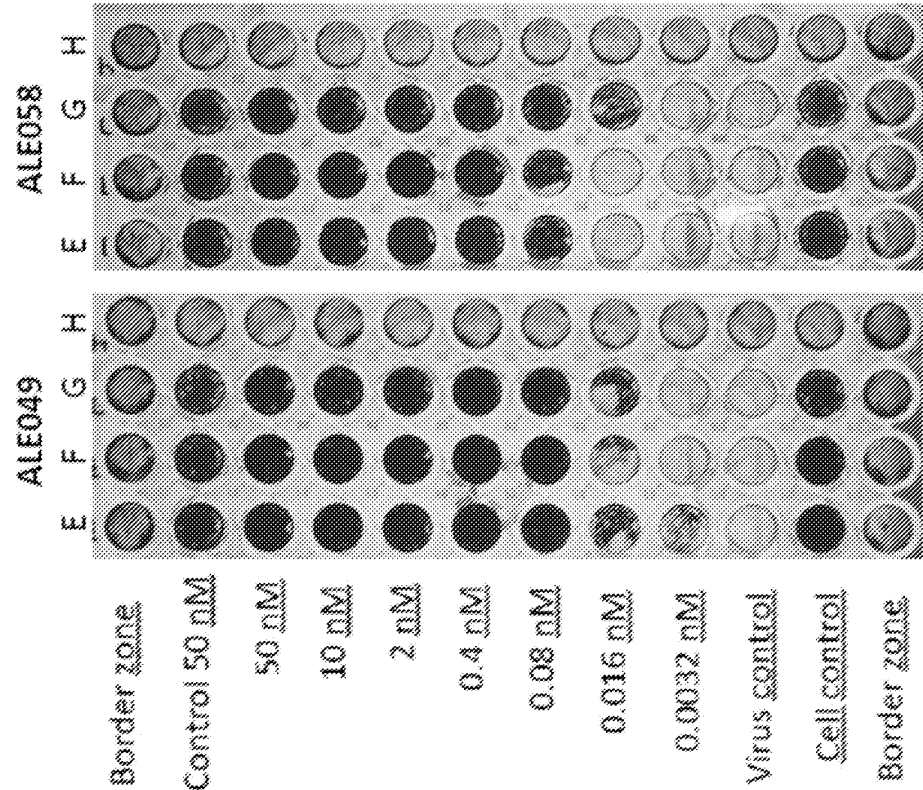


Figure 21a

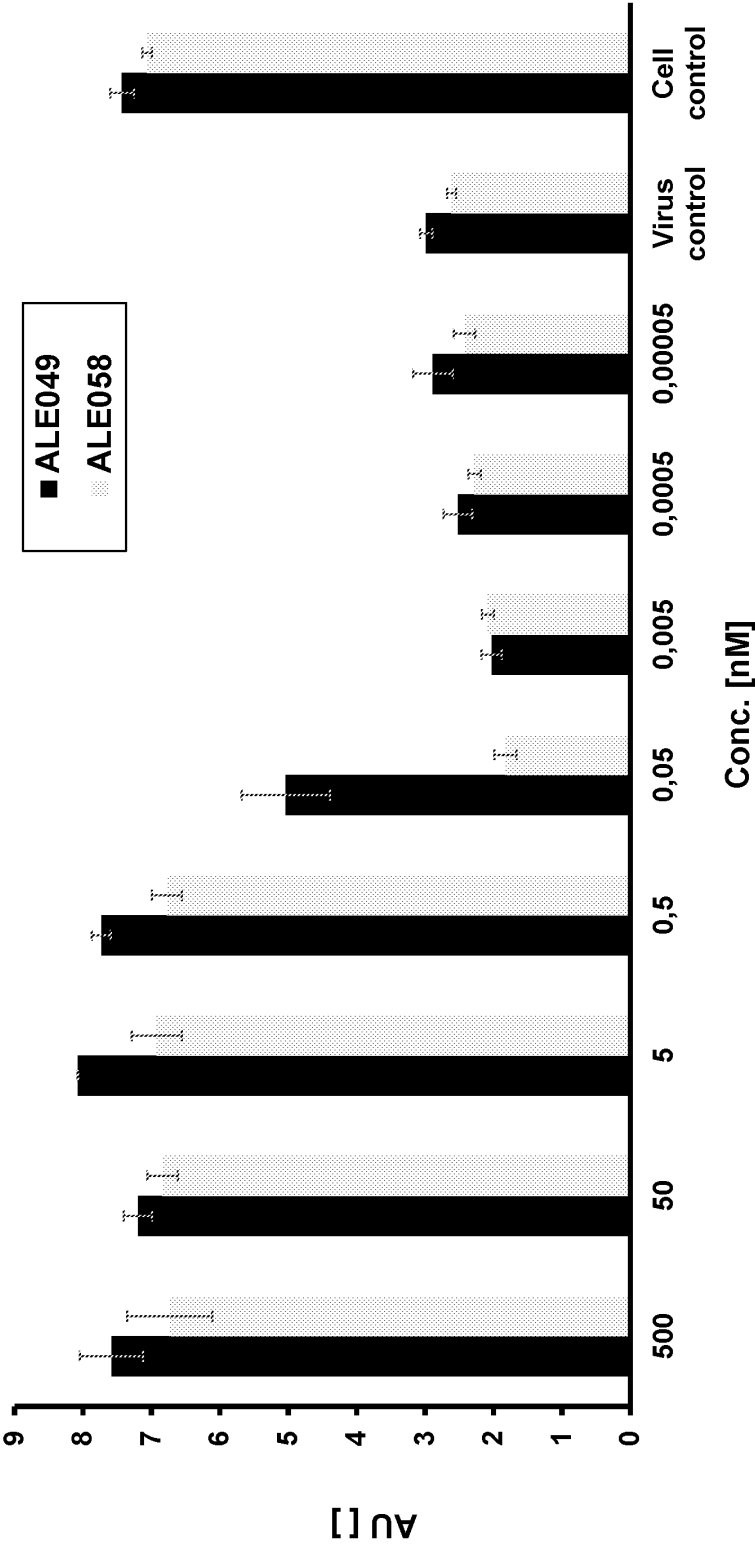


Figure 21b

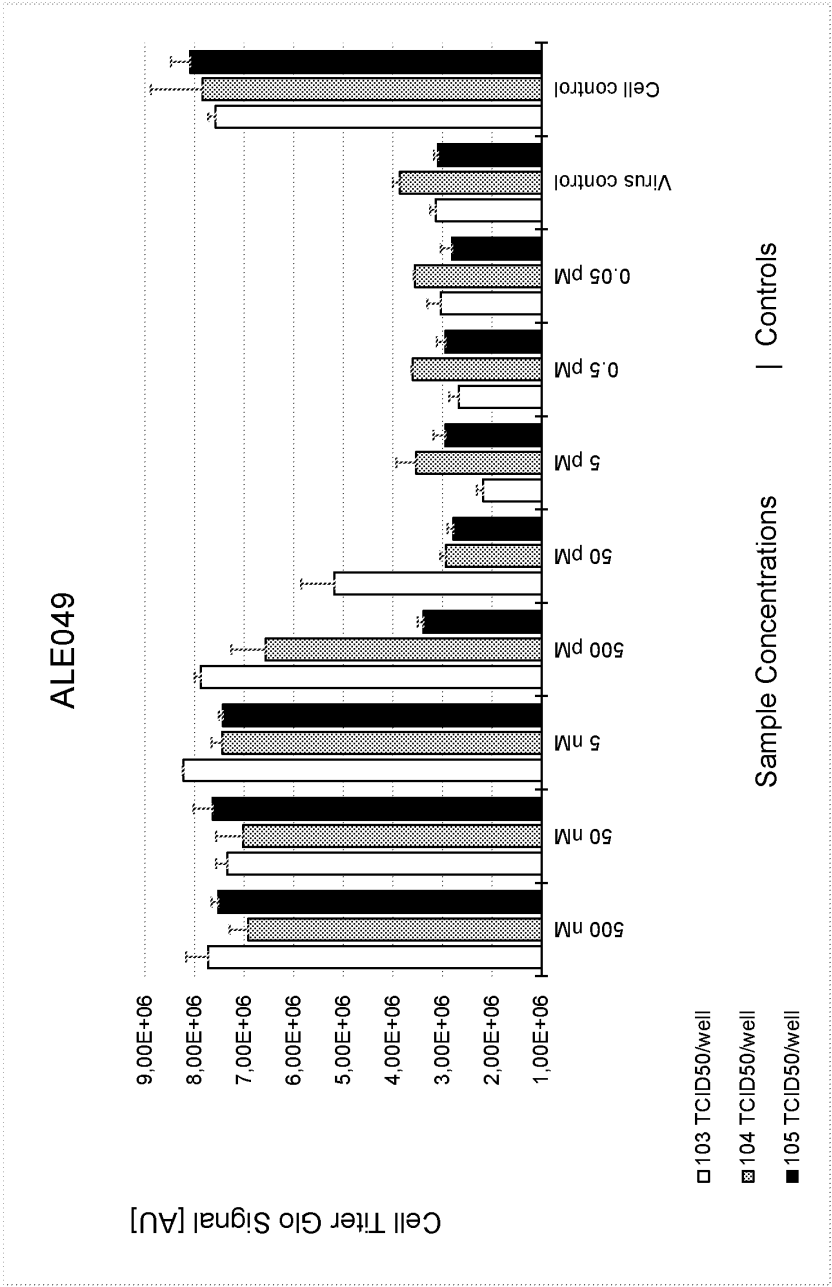
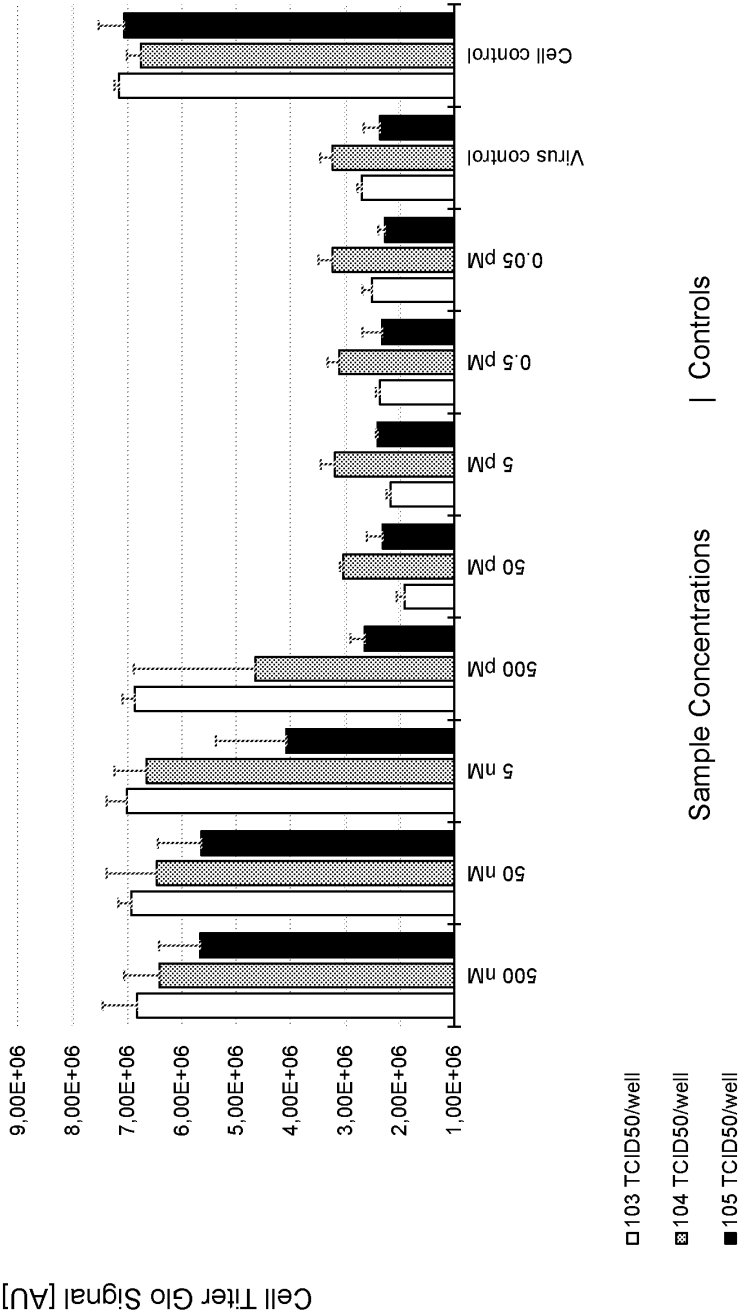


Figure 21c

ALE058



Figures 22a & 22b

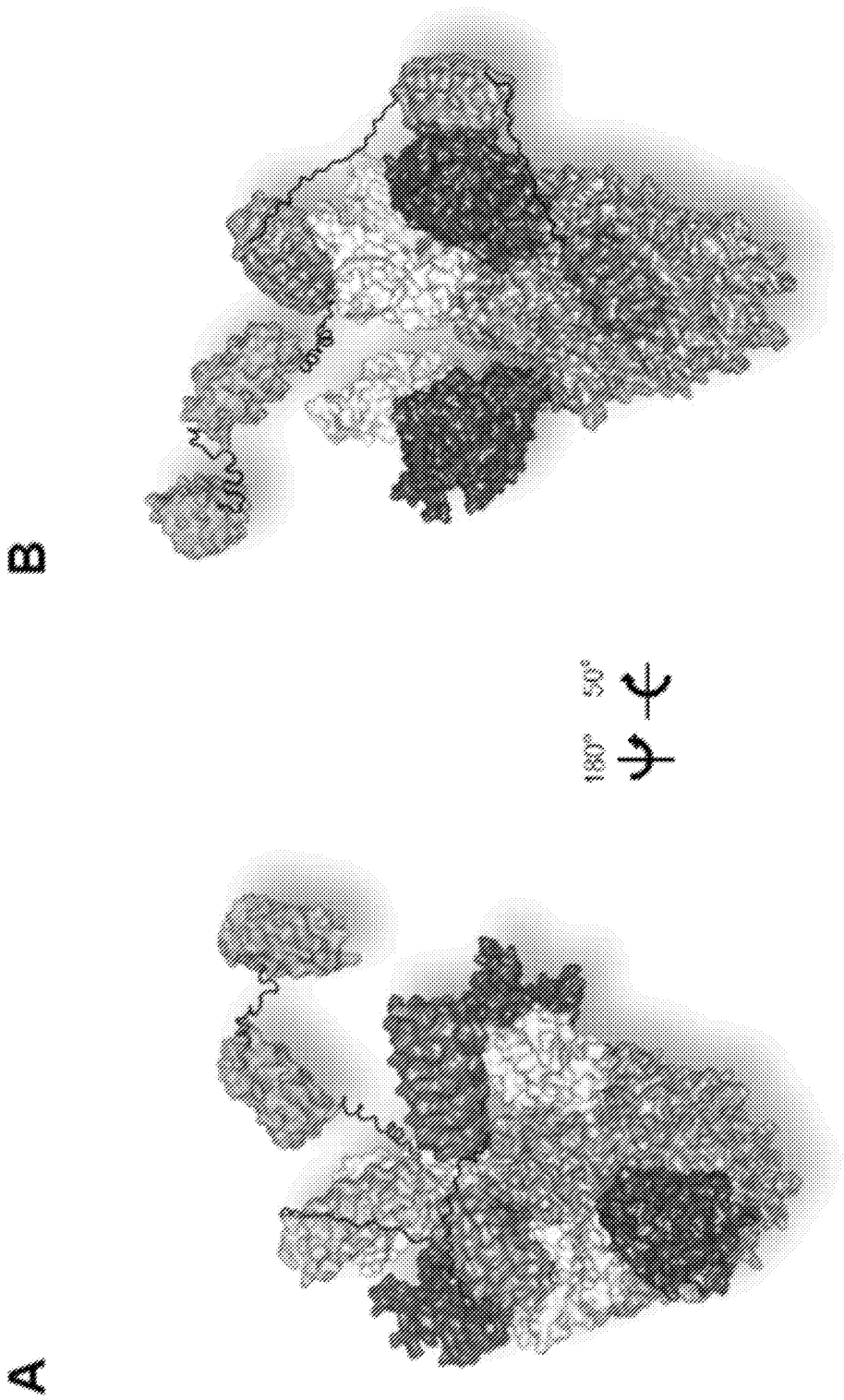


Figure 23

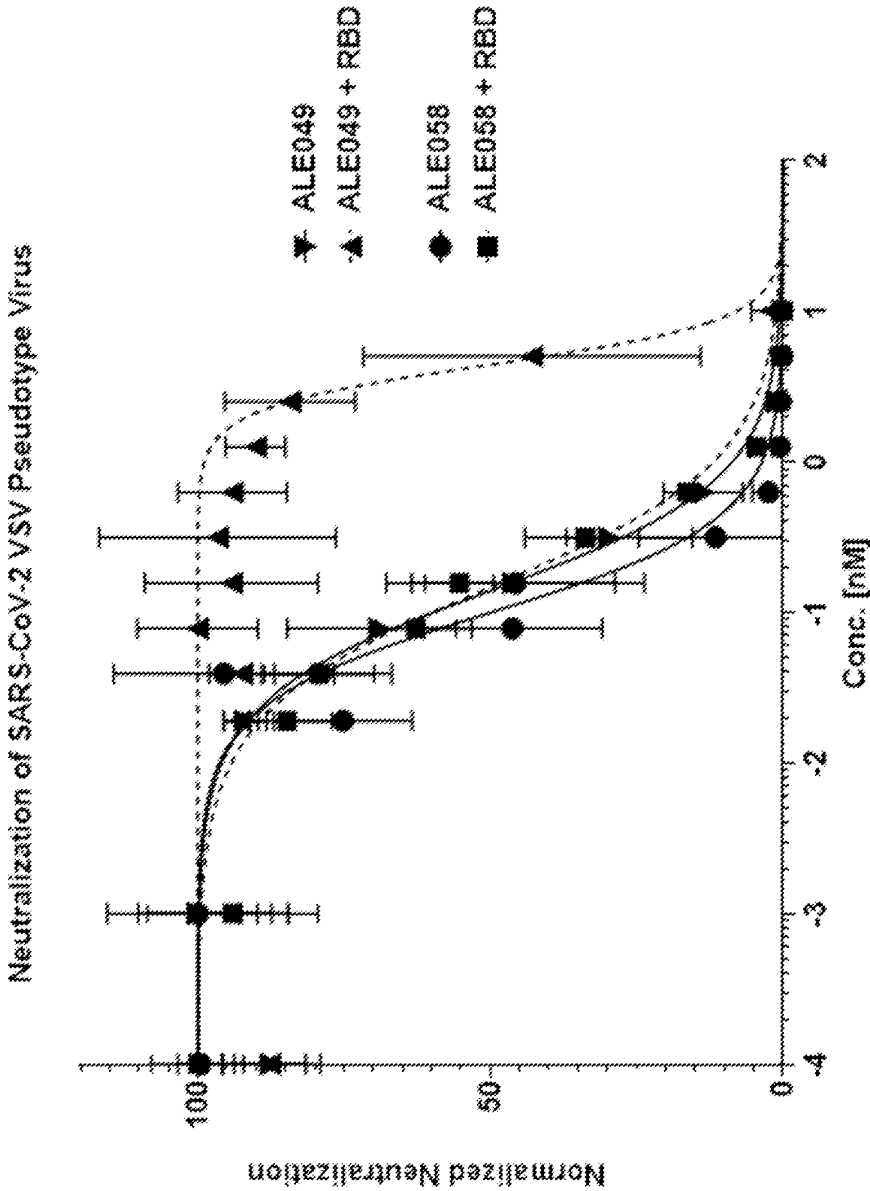


Figure 24

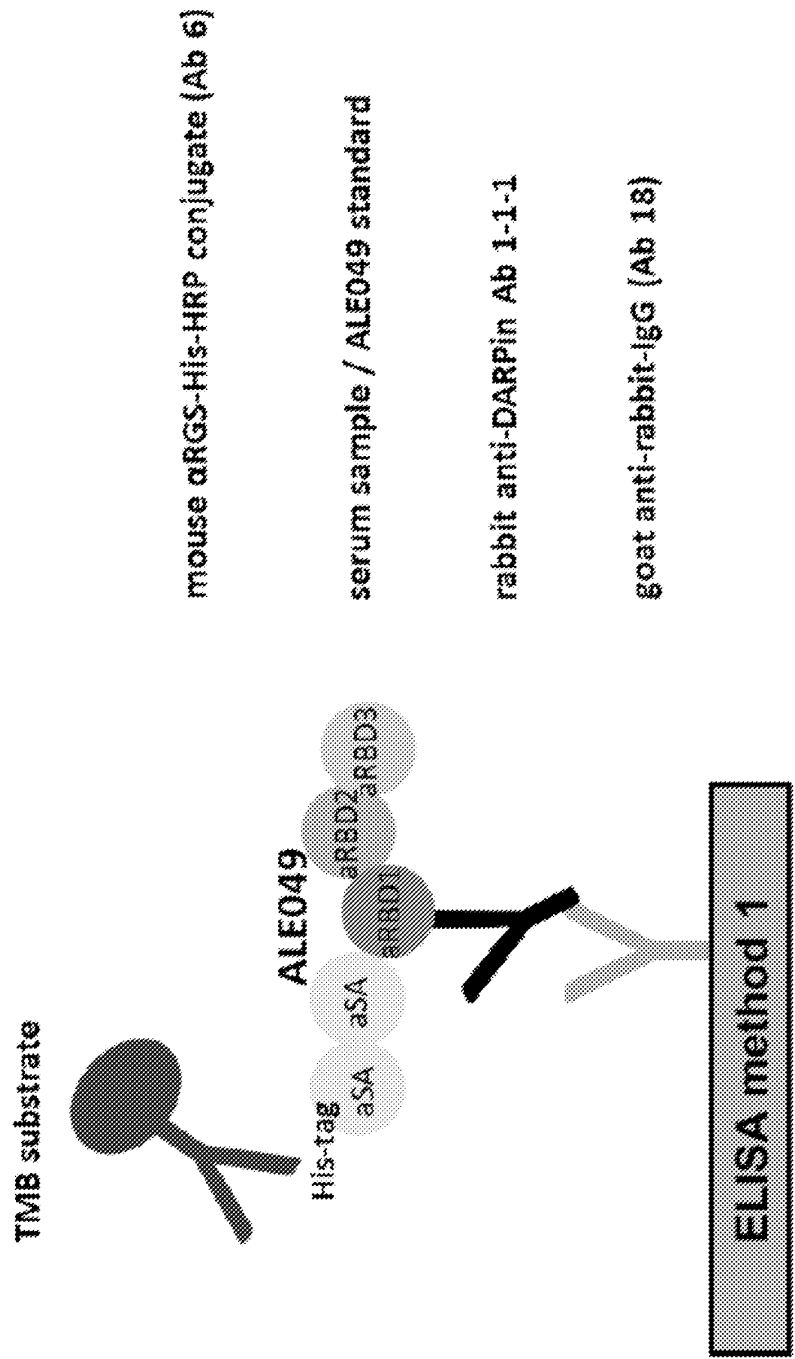


Figure 25

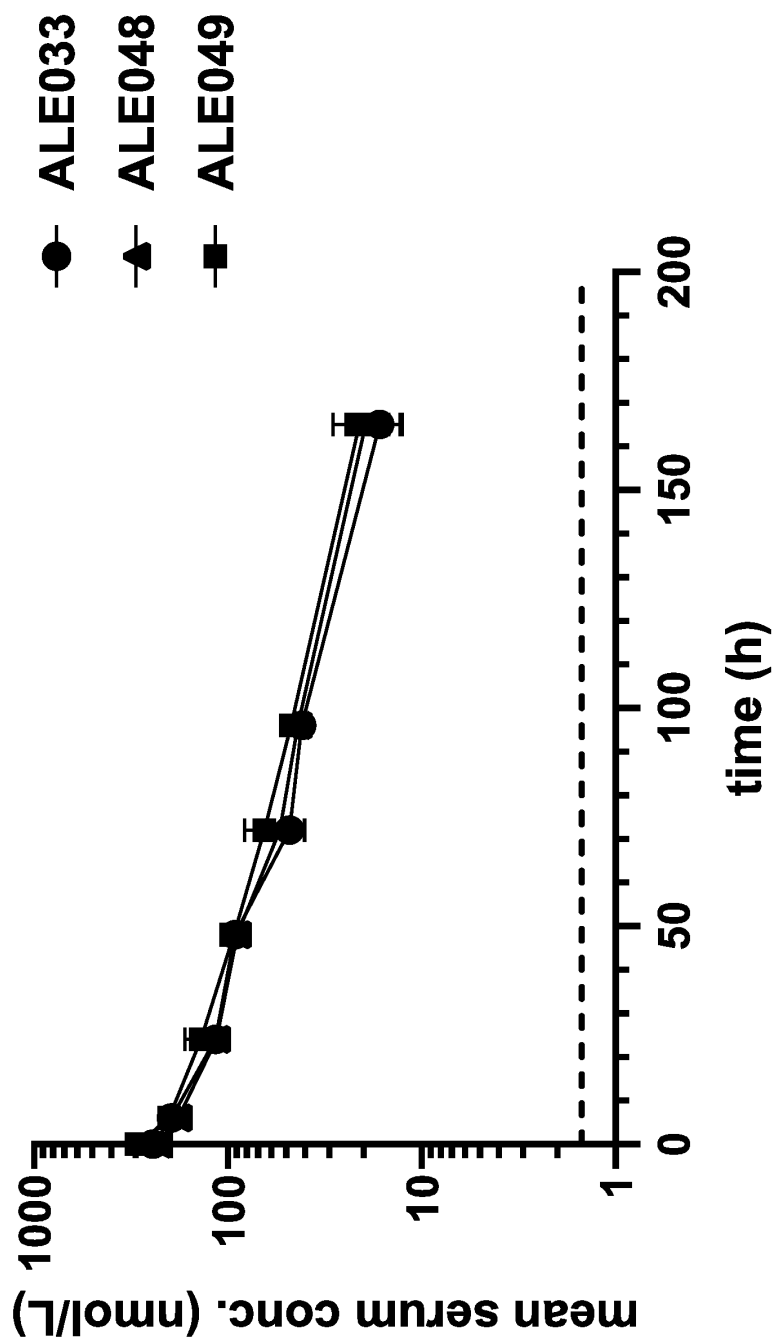
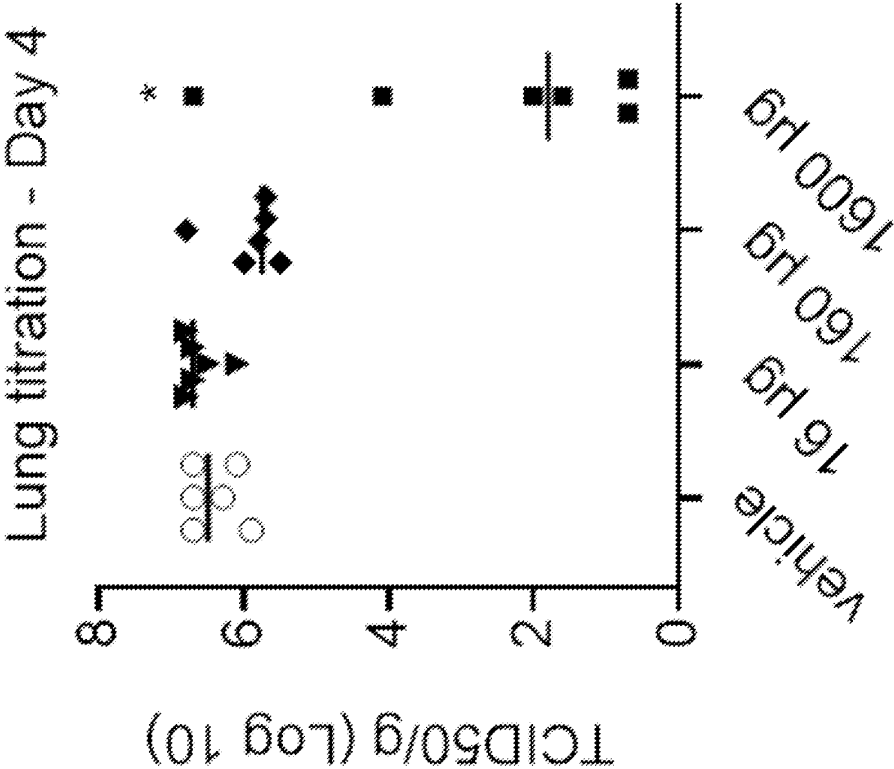


Figure 26a



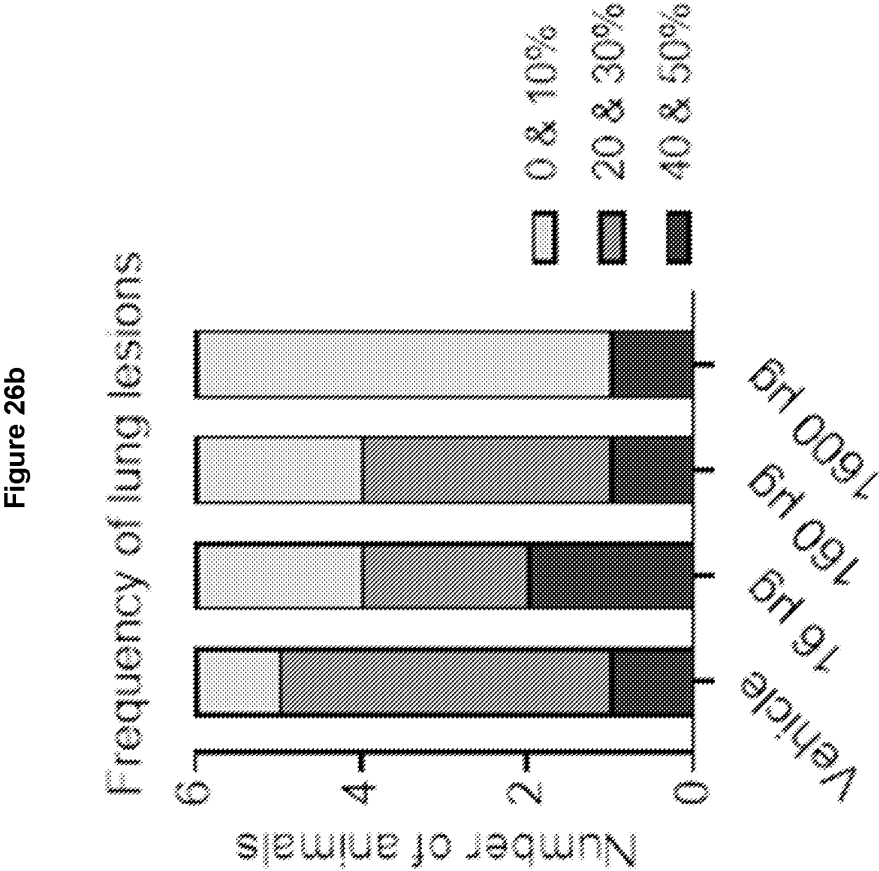


Figure 26c

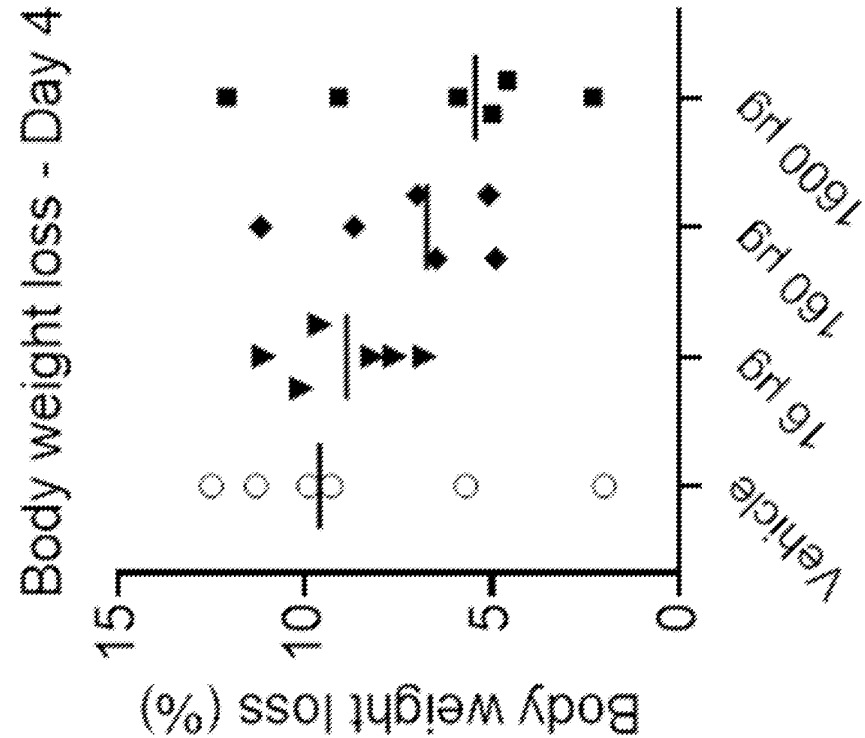


Figure 26d

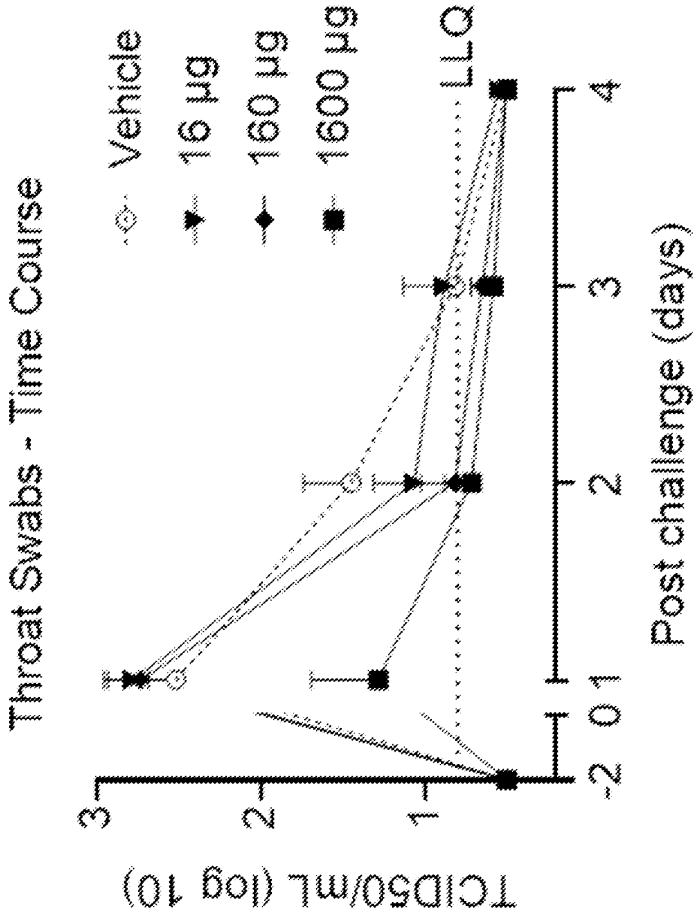
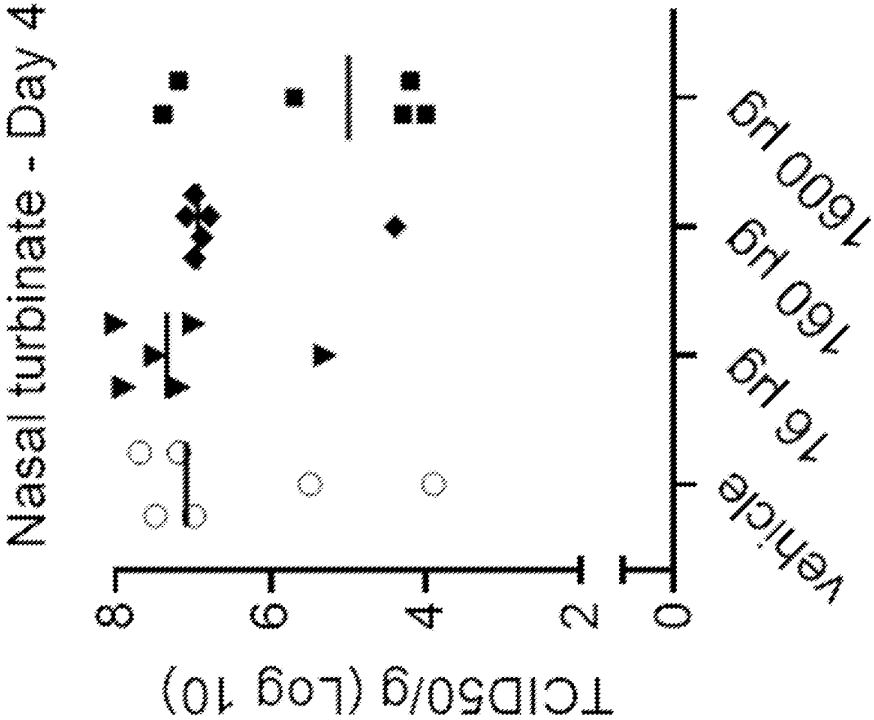


Figure 26e



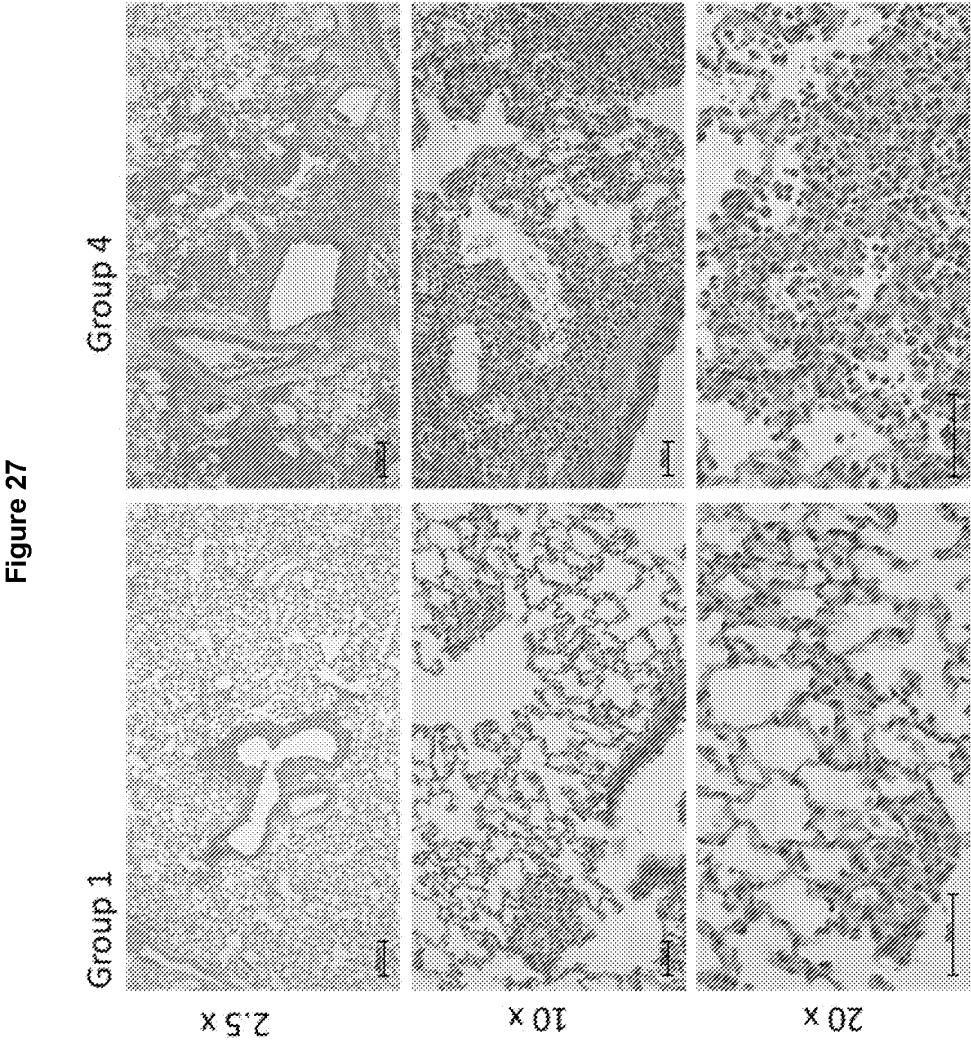


Figure 28

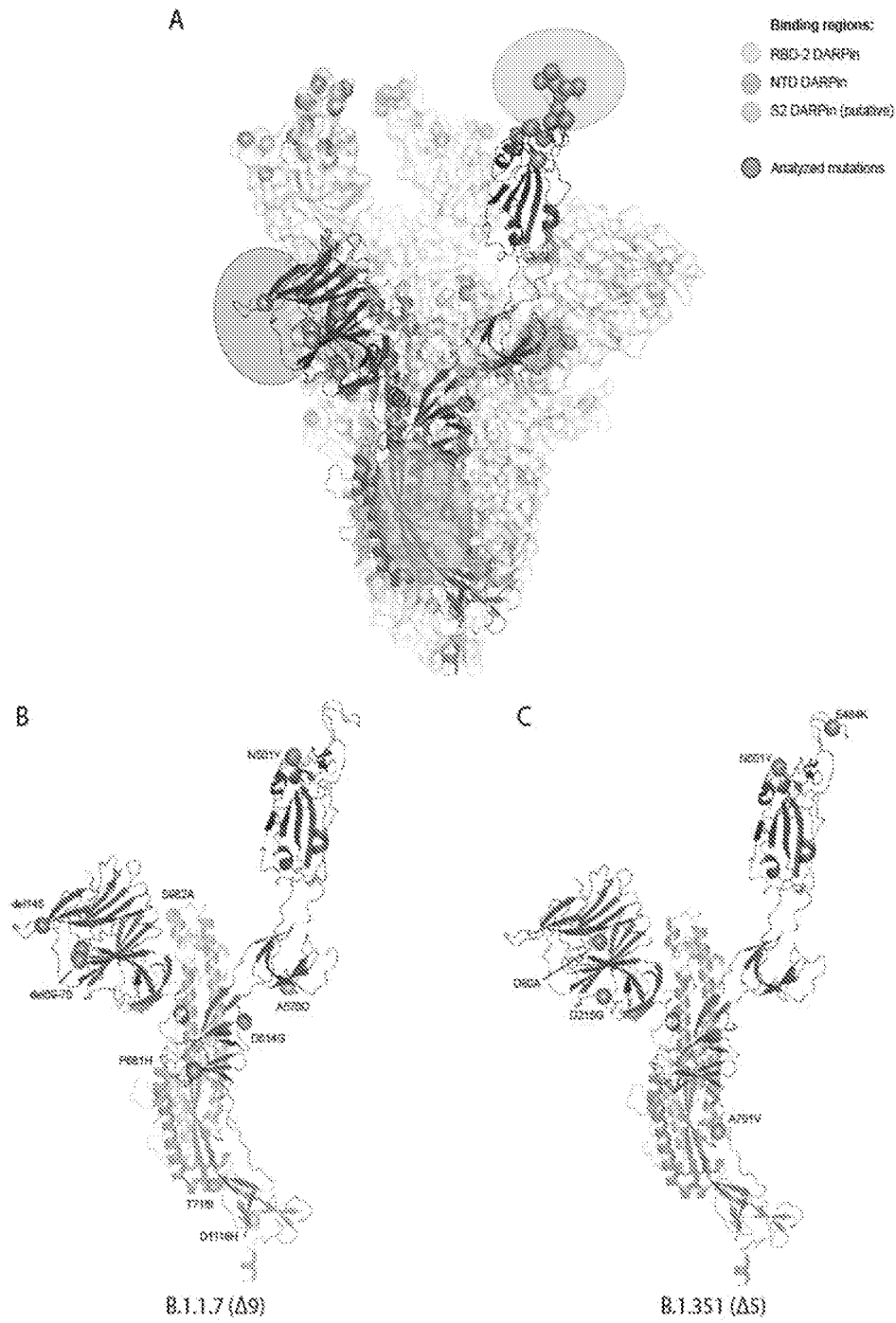


Figure 29

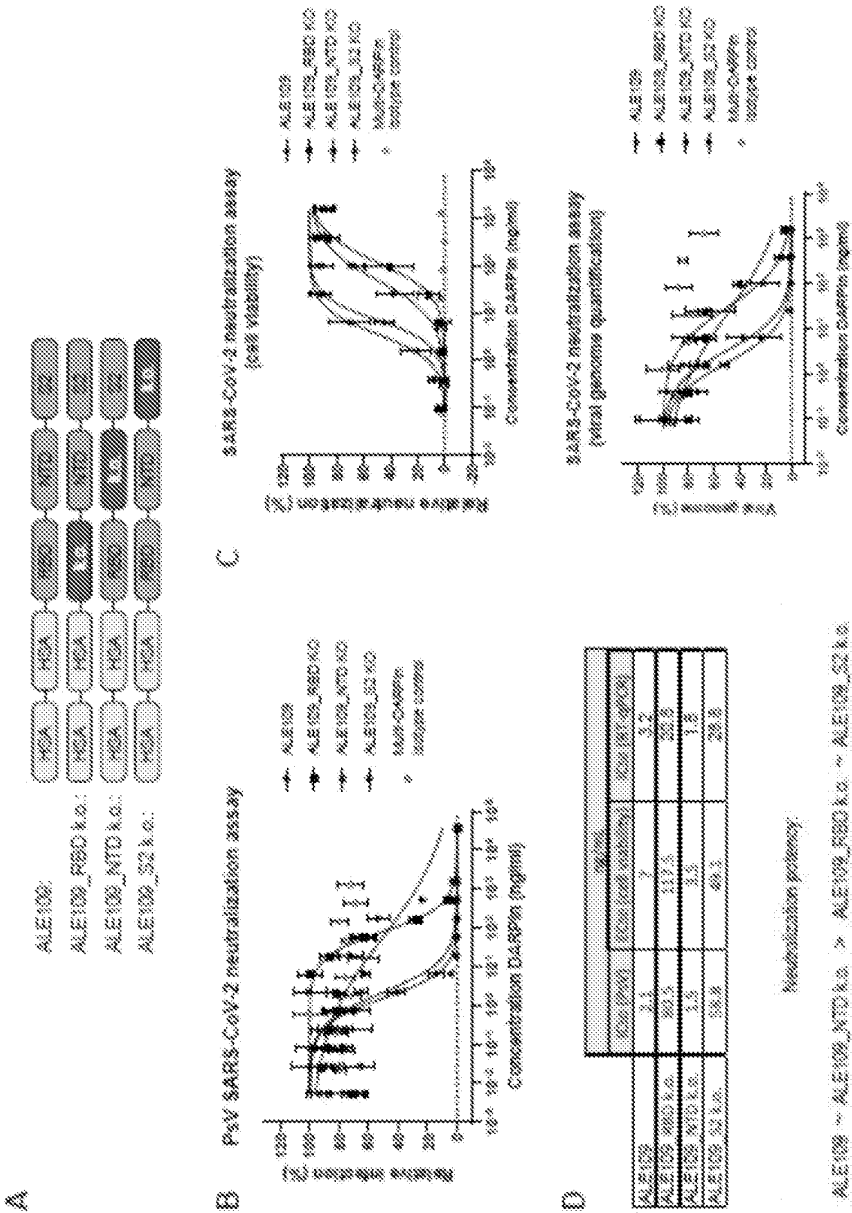


Figure 30

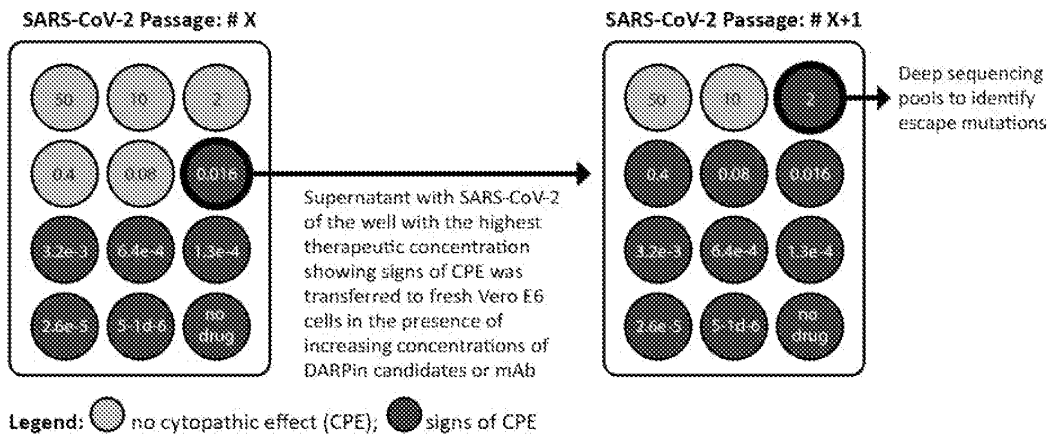


Figure 31

Passage #1	DARPin or Antibody Concentrations [μ g/mL]							Passage #2	DARPin or Antibody Concentrations [μ g/mL]								
	Constructs	50	10	2	0.4	0.08	0.016		no drug	Constructs	50	10	2	0.4	0.08	0.016	no drug
		Cytotoxic Effect [%]							Cytotoxic Effect [%]								
DARPin Candidates	RBD - 2	0%	0%	0%	5%	$\geq 90\%$	$\geq 90\%$		RBD - 2	0%	60%	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$		
	ALE049	0%	0%	0%	0%	$\geq 90\%$	$\geq 90\%$		ALE049	0%	0%	0%	0%	0%	50%	$\geq 90\%$	
	ALE109	0%	0%	0%	0%	$\geq 90\%$	$\geq 90\%$		ALE109	0%	0%	0%	0%	0%	$\geq 90\%$	$\geq 90\%$	
	ALE049 & ALE109								ALE049 & ALE109								
	Antibody Candidates								Antibody Candidates								
IgG Negative Control	S309	0%	0%	60%	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$		S309	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$		
	RA1	0%	0%	0%	5%	$\geq 90\%$	$\geq 90\%$		RA1	0%	0%	80%	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$		
	RA2	80%	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$		RA2	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$		
	RA1 & RA2	0%	0%	0%	0%	$\geq 90\%$	$\geq 90\%$		RA1 & RA2	0%	0%	0%	0%	0%	$\geq 90\%$	$\geq 90\%$	
	IgG Negative Control	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$		IgG Negative Control	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$		
Passage #3	DARPin or Antibody Concentrations [μ g/mL]							Passage #4	DARPin or Antibody Concentrations [μ g/mL]								
	Constructs	50	10	2	0.4	0.08	0.016		no drug	Constructs	50	10	2	0.4	0.08	0.016	no drug
		Cytotoxic Effect [%]							Cytotoxic Effect [%]								
DARPin Candidates	RBD - 2	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$		RBD - 2	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	
	ALE049	0%	0%	0%	0%	$\geq 90\%$	$\geq 90\%$		ALE049	0%	0%	0%	40%	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	
	ALE109	0%	0%	0%	40%	$\geq 90\%$	$\geq 90\%$		ALE109	0%	0%	0%	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	
	ALE049 & ALE109								ALE049 & ALE109								
	Antibody Candidates								Antibody Candidates								
IgG Negative Control	S309	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$		S309	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	
	RA1	0%	0%	5%	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$		RA1	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	
	RA2	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$		RA2	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	
	RA1 & RA2	0%	0%	0%	0%	$\geq 90\%$	$\geq 90\%$		RA1 & RA2	0%	0%	0%	0%	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	
	IgG Negative Control	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$	$\geq 90\%$		IgG Negative Control	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	n.d.	

n.d.: not determined as virus acquired resistance in previous passage

Figure 32

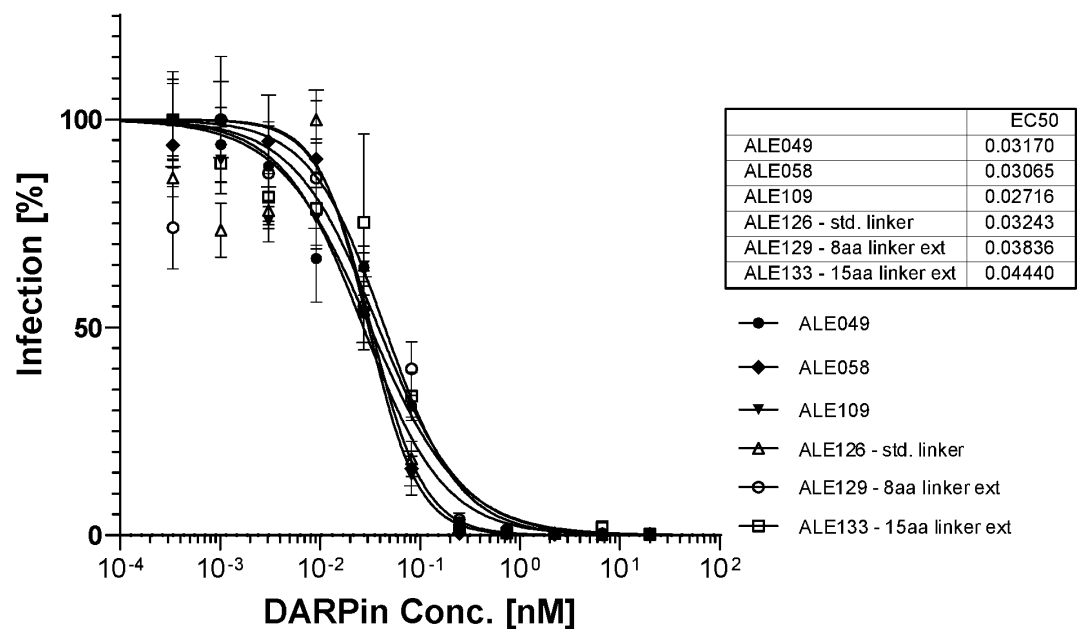


Figure 33

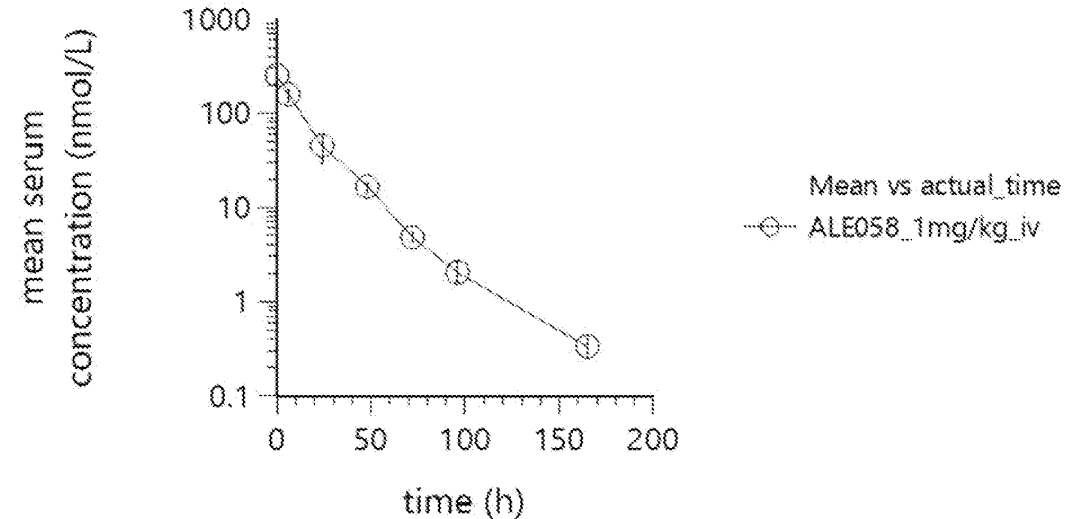


Figure 34

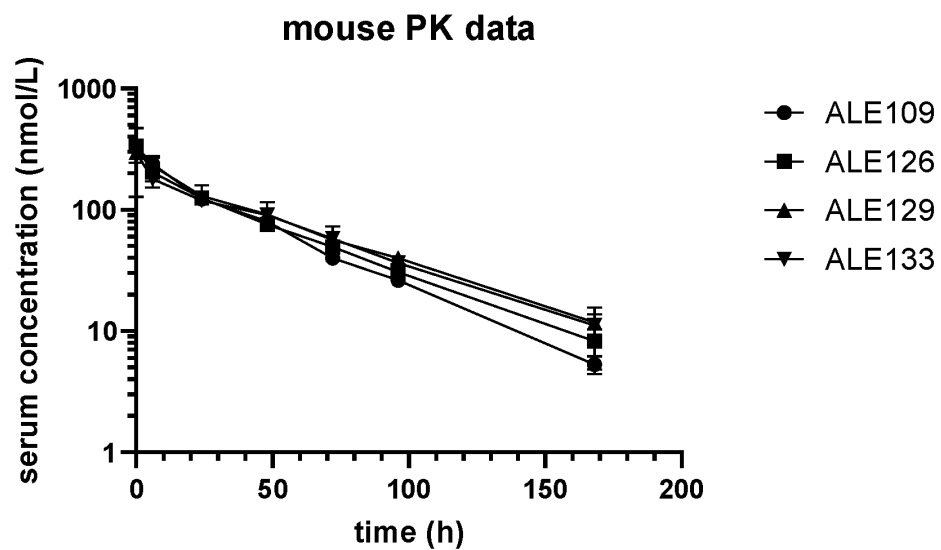


Figure 35

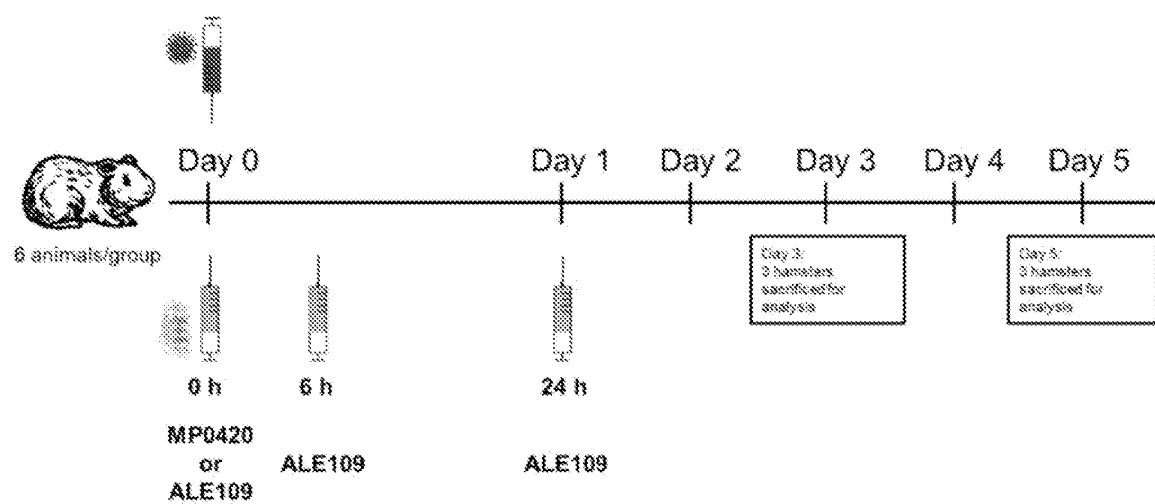
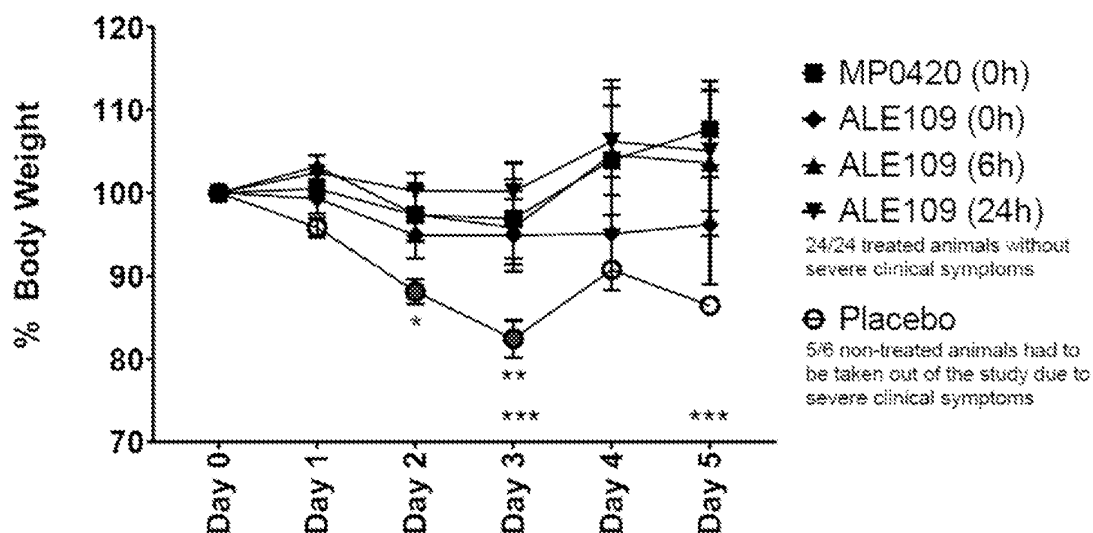


Figure 36



*Two hamsters were taken out of placebo group due to severe clinical symptoms and body weight loss at day 2.

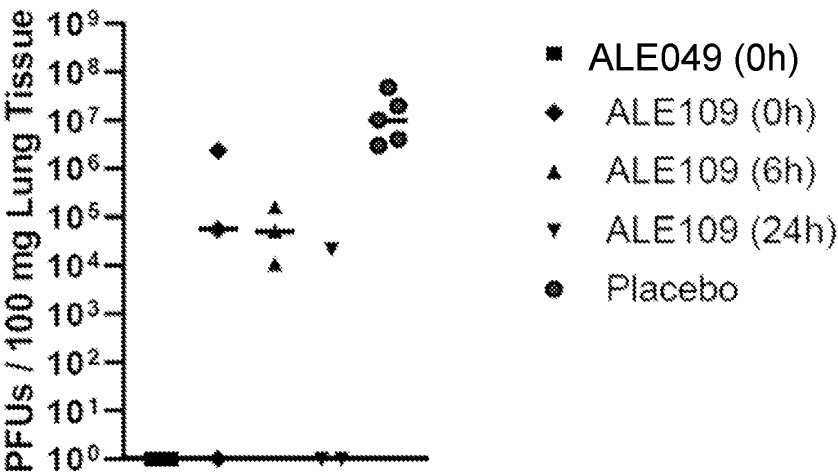
**Three additional hamsters were taken out of placebo group due to severe clinical symptoms and body weight loss at day 3 with only one animal remaining until day 5.

***Three animals of the treated groups were sacrificed at day 3 and the other animals at day 5 for analytical purposes.

Figure 37 (A-B)

A

Virus Titration - Lung Day 3



Placebo: animals taken out of the study (at day 2 and 3) due to severe clinical symptoms and body weight loss.

B

Virus Titration - Lung Day 5

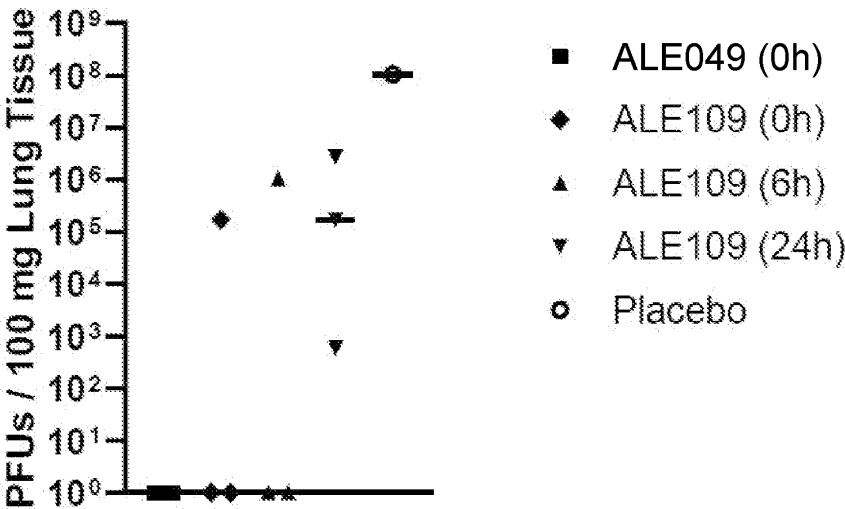
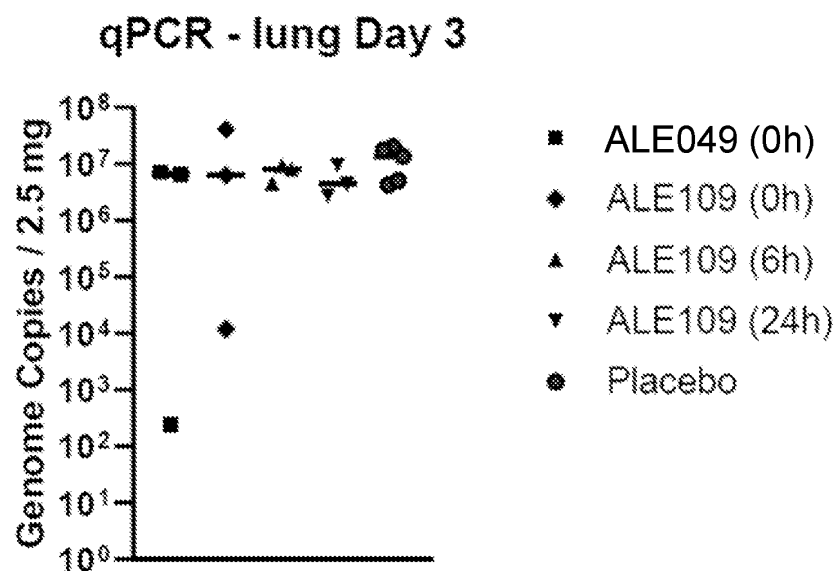


Figure 37 (C-D)

C



Placebo: animals taken out of the study (at day 2 and 3) due to severe clinical symptoms and body weight loss.

D

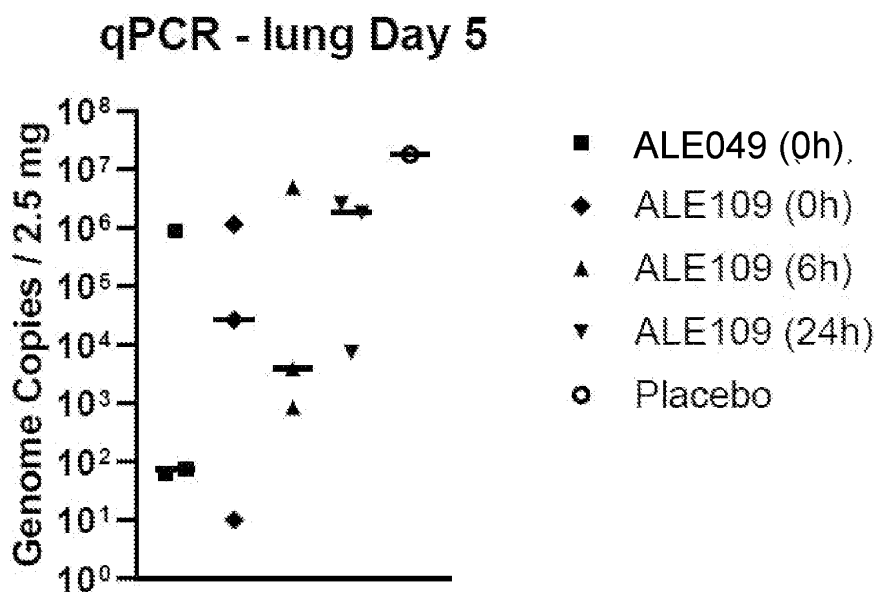
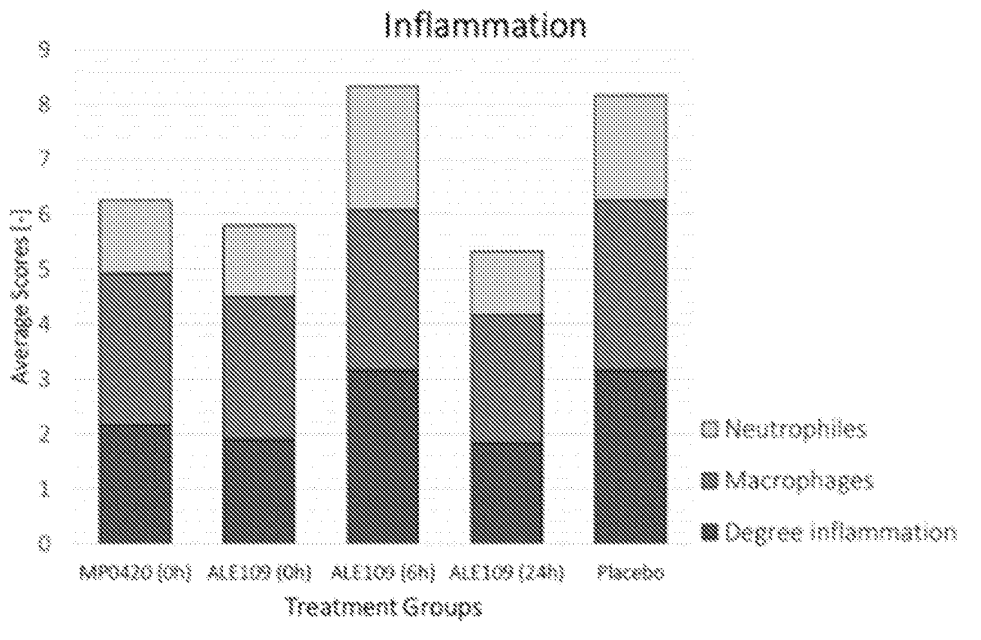


Figure 38 (A-B)

A



B

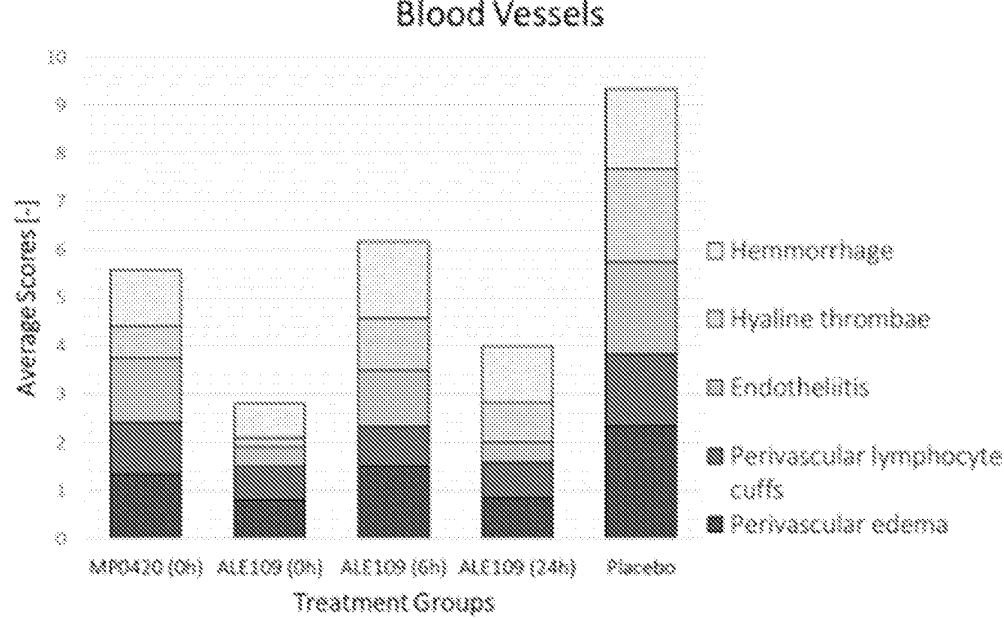
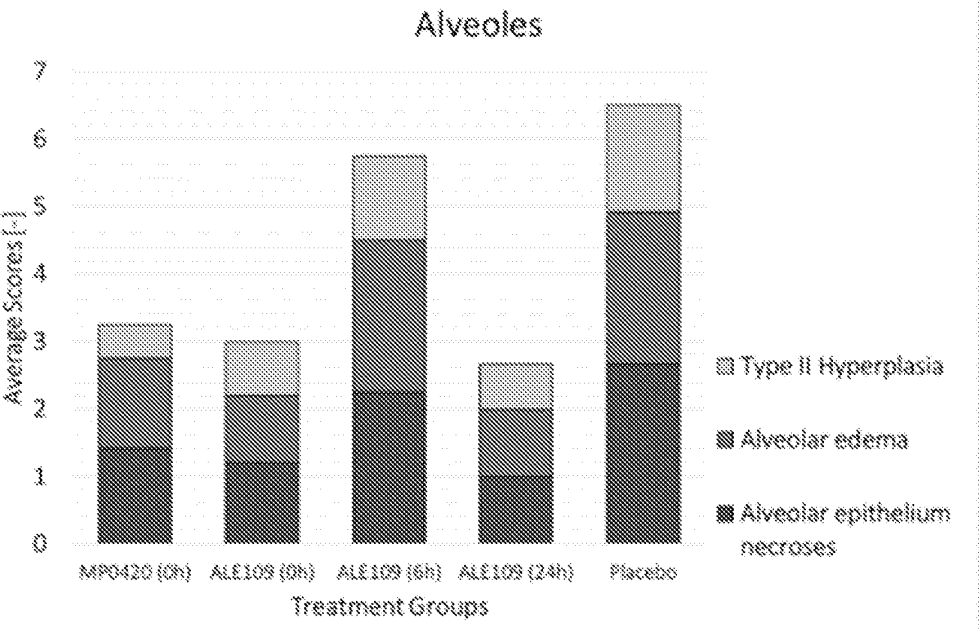


Figure 38 (C-D)

C



D

