Figure 1

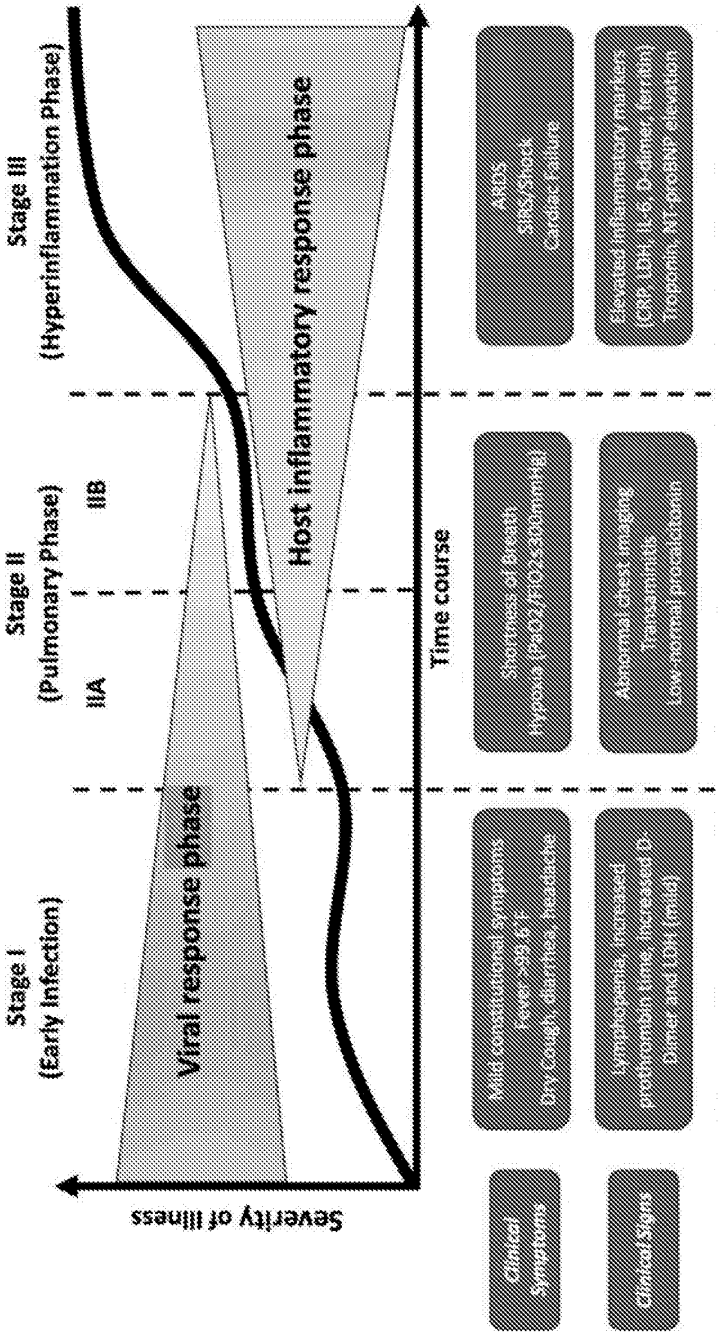

Stage III
(Hyperinflammation Phase)
Stage II
(Pulmonary Phase)
IIB
IIA
Stage I
(Early Infection)
Viral response phase
Host inflammatory response phase
Severity of illness
Time course
Mild constitutional symptoms
Fever ~38-39 C
Dry cough, diarrhea, headache
Shortness of Breath
Hypoxia (PaO2/FiO2<300mmHg)
Symptoms, increased
pneumonitis (fever, increased c
Dyspnea and ARDS (mid)
Abnormal chest imaging
Tachypnoea
Low arterial pressure
ARDS
Sepsis/shock
Cardiac failure
General inflammatory markers
(CRP, LDH, IL6, D-dimer, ferritin)
Thrombi/ Myocardial infection
Clinical Symptoms
Clinical Signs

Figure 2

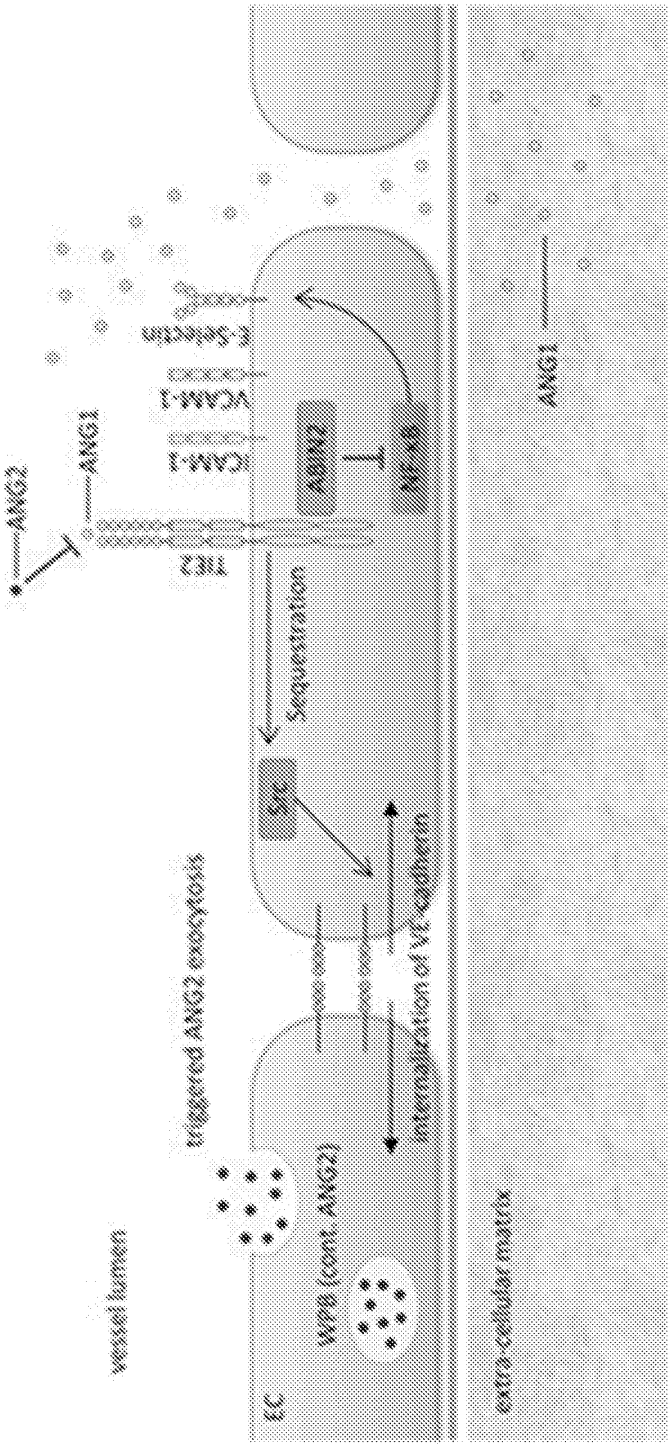

ANG2
ANG1
Tie2
VCAM-1
ICAM-1
E-Selectin
ABIN2
NF-κB
ANG1
Sequestration
Src
internalization of VE-cadherin
triggered ANG2 exocytosis
vessel lumen
WPB (cont. ANG2)
EC
extra-cellular matrix

Figure 3

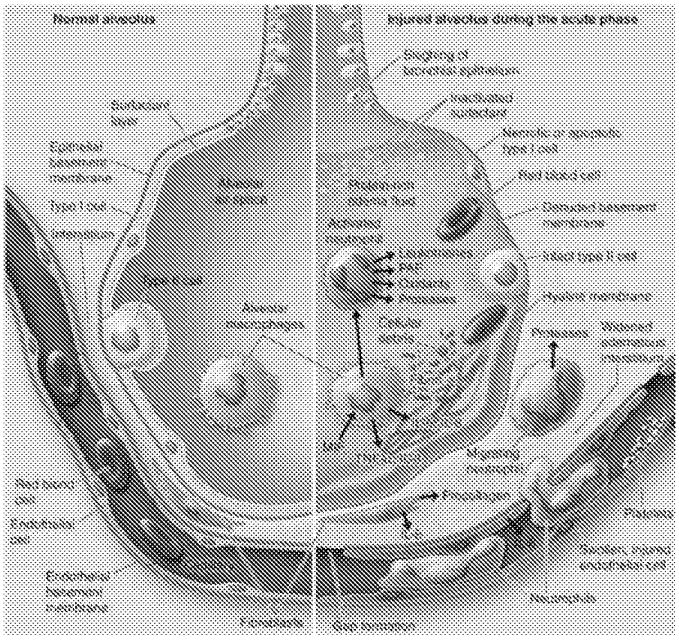

Normal alveolus
Injured alveolus during the acute phase
Surfactant layer
Epithelial basement membrane
Type I cell
Interstitium
Alveolar macrophages
Red blood cell
Endothelial cell
Endothelial basement membrane
Capillary
Sloughing of bronchial epithelium
Inactivated surfactant
Necrotic or apoptotic type I cell
Red blood cell
Disrupted basement membrane
Activated type II cell
Hyaline membrane
Thickened interstitium
Migrating neutrophil
Fibrin/fibrin
Platelets
Swollen, injured endothelial cell
Neutrophils

Figure 4

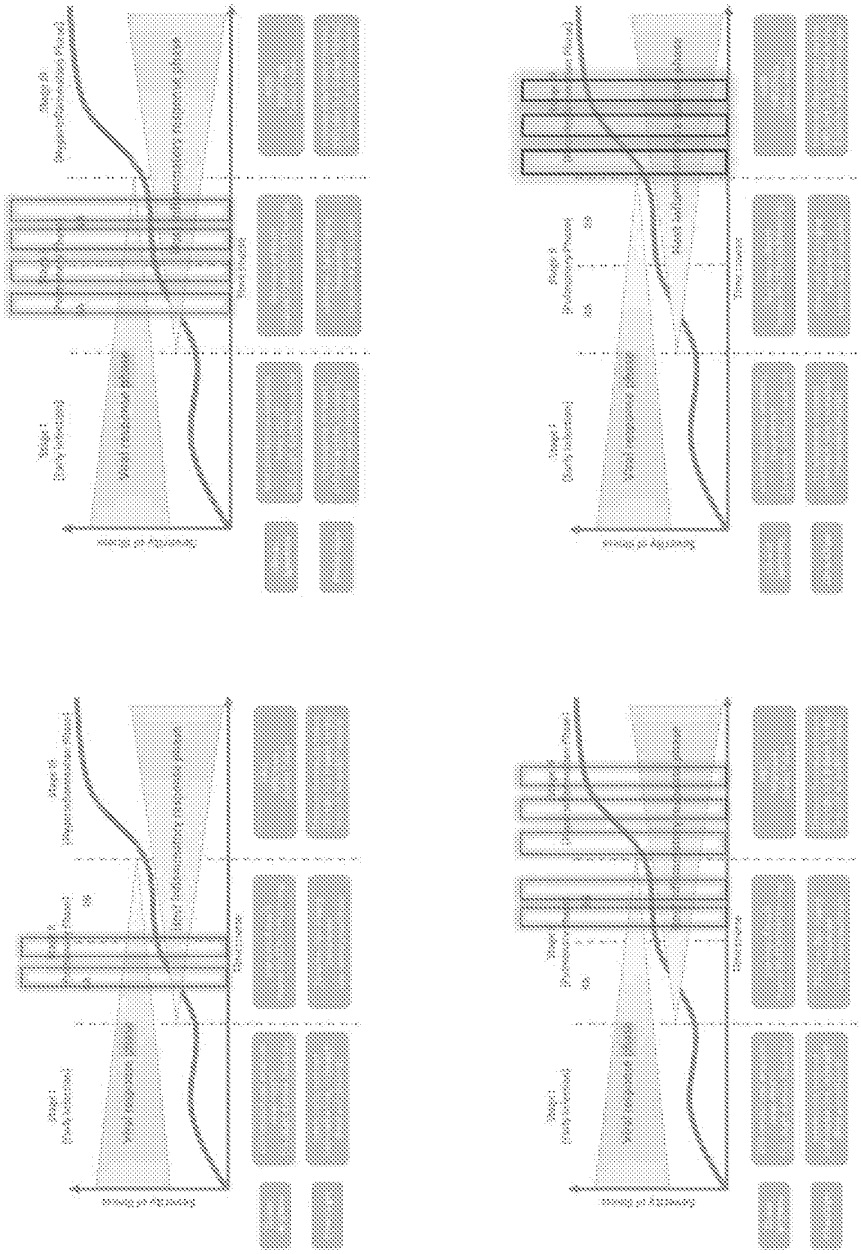


Figure 5

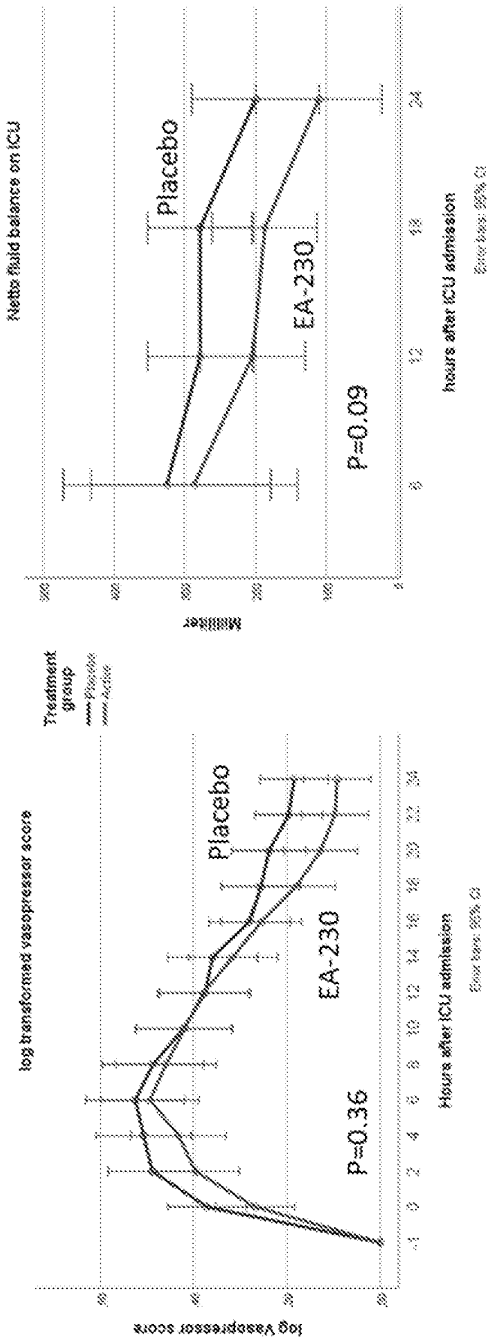

Netto fluid balance on ICU
Placebo
EA-230
P=0,09
hours after ICU admission
log transformed vasopressor score
Placebo
EA-230
P=0.36
Hours after ICU admission
log Vasopressor score
Treatment group

Figure 6

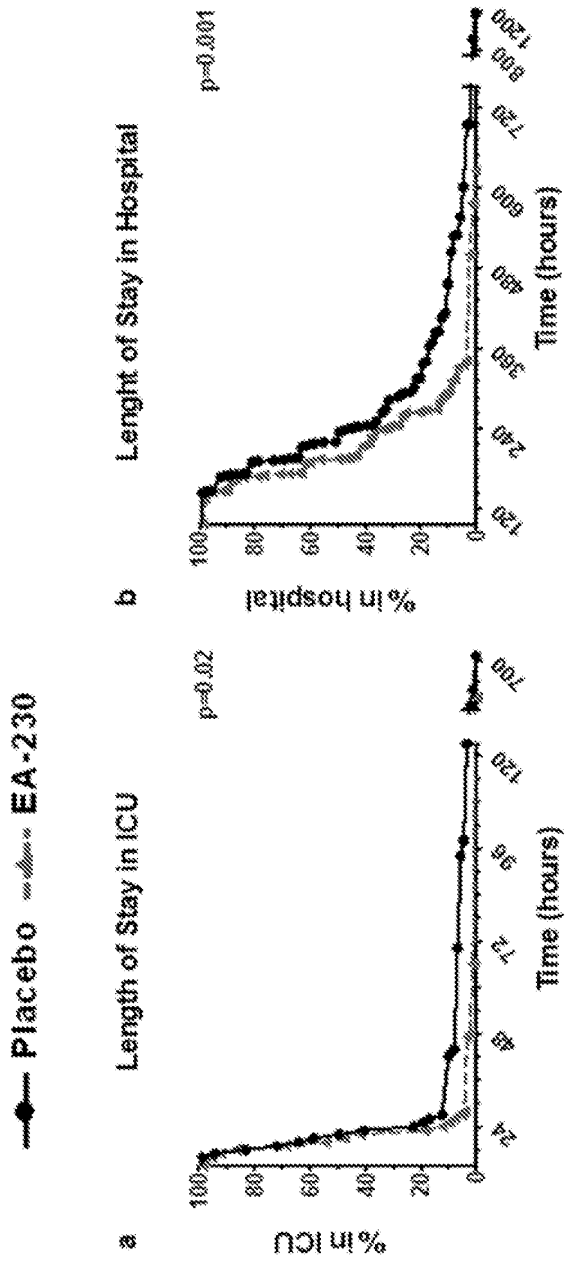

Placebo
EA-230
a
% in ICU
Length of Stay in ICU
p=0.02
Time (hours)
b
% in hospital
Lenght of Stay in Hospital
p=0.001
Time (hours)

Figure 7

Table 1: summary of experiments

Entry		mmol	Added amount 19-1	22-1	23-1	24-1	25-1	26-1	31-1	01-02	Solubility mmol/mL
1	citric acid	1.75	500	0.25 mmol	0.5 mmol			0.25 mmol	X	X	>2,75mmol/ 500 uL
			Added uL (9g NaCl/L H_2O)								
2	maleic acid	1	200 (clear) but crystallized over the weekend	50	50	150	200 (clear)	X	X	X	1 mmol/ 650 uL
3	$KHSO_4$	1	200	50	50	100	50	150	150	150 (clear)	1 mmol/ 900 uL
4	(+)-tartaric acid	1	200	50	50	50 (clear)	X	X	Some Solids again	50 (clear)	1 mmol/ 400 uL
5	acetic acid	1	200	50	50	150	50 (clear)	X	X	X	1 mmol/ 500 uL
6	adenosine mono-phosphate	0.5	200	100	50	300	200	300	2200	Vial full	<<0,5 mmol/ 3350 uL
7	adenosine	0.5	200	100	50	300	200	300	2200	Vial full	<<0,5 mmol/ 3350 uL

Figure 8

Table 2: Solubility of different salt of AQGV in 0.9% NaCl.

Acid	Solubility (in 0.9% NaCl)
citric acid	> 5.5 mmol/ mL
maleic acid	1.54 mmol/mL
$KHSO_4$	1.11 mmol/mL
(+)-tartaric acid	2.5 mmol/mL
acetic acid	2 mmol/mL
adenosine mono-phosphate	< 0.15 mmol/mL
Adenosine	< 0.15 mmol/mL

Figure 9

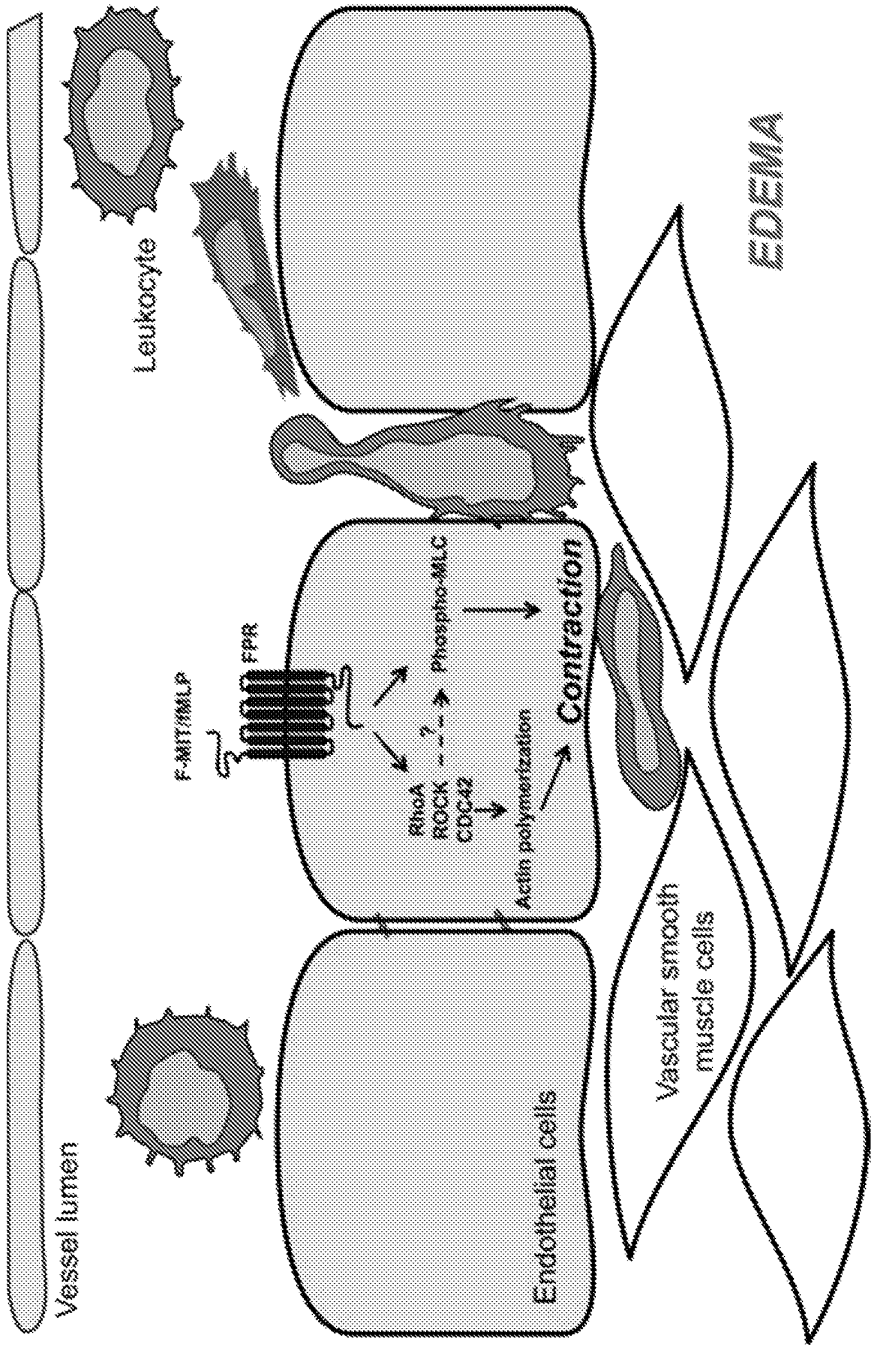

Vessel lumen
Leukocyte
EDEMA
Endothelial cells
Vascular smooth muscle cells
Contraction
Phospho-MLC
FPR
F-MIT/fMLP
RhoA
ROCK
CDC42
Actin polymerization
?

Figure 10a

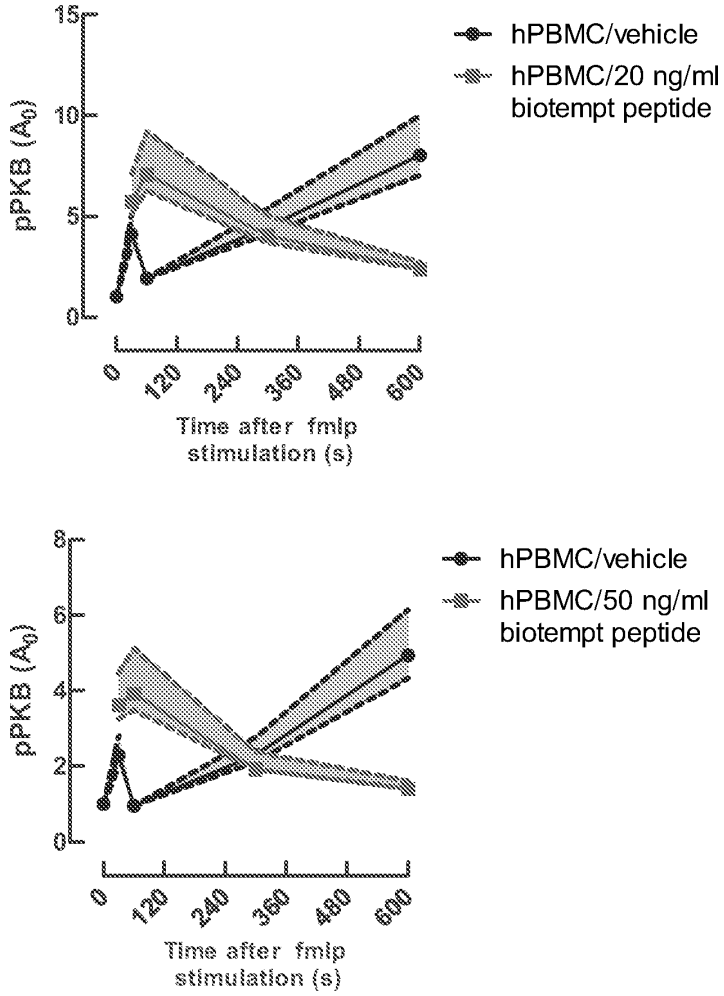

15
10
5
0
pPKB (A0)
0
120
240
360
480
600
Time after fmlp stimulation (s)
hPBMC/vehicle
hPBMC/20 ng/ml biotempt peptide
8
6
4
2
0
pPKB (A0)
0
120
240
360
480
600
Time after fmlp stimulation (s)
hPBMC/vehicle
hPBMC/50 ng/ml biotempt peptide

Figure 10b

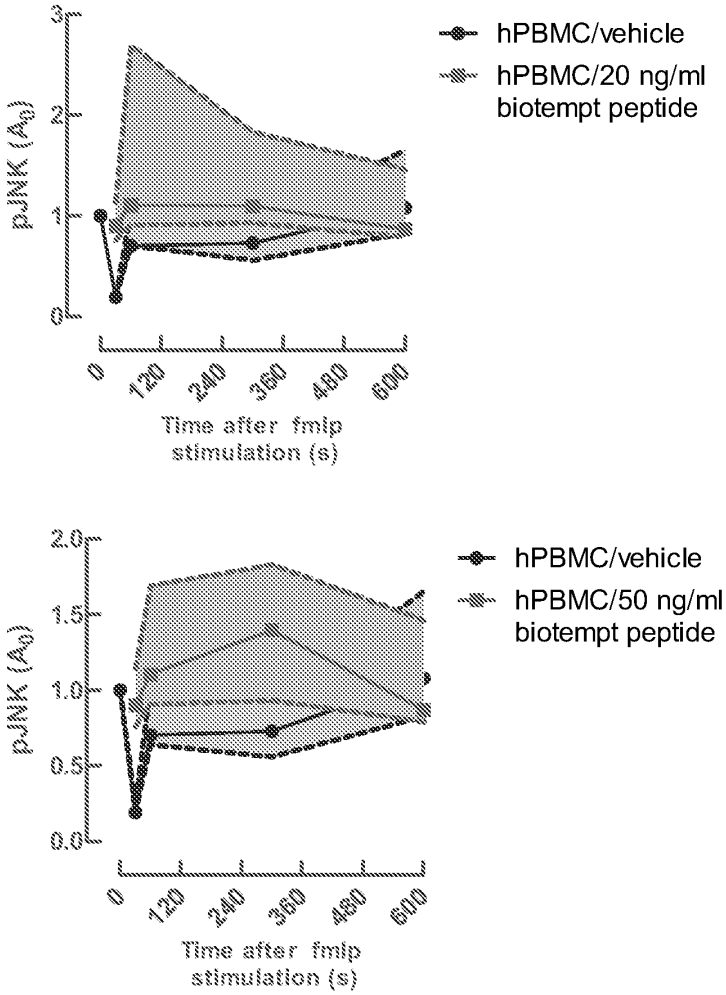

pJNK (A0)
3
2
1
0
0
120
240
360
480
600
Time after fmlp stimulation (s)
hPBMC/vehicle
hPBMC/20 ng/ml biotempt peptide
pJNK (A0)
2.0
1.5
1.0
0.5
0.0
0
120
240
360
480
600
Time after fmlp stimulation (s)
hPBMC/vehicle
hPBMC/50 ng/ml biotempt peptide

Figure 10c

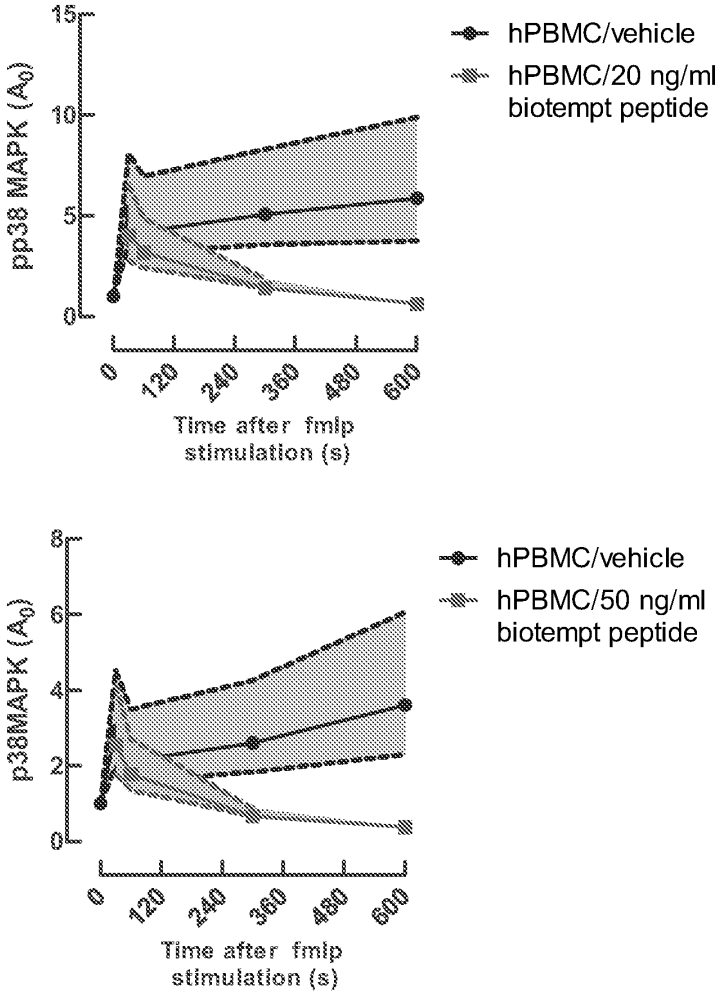

15
10
5
0
pp38 MAPK (A0)
0
120
240
360
480
600
Time after fmlp stimulation (s)
hPBMC/vehicle
hPBMC/20 ng/ml biotempt peptide
8
6
4
2
0
p38MAPK (A0)
0
120
240
360
480
600
Time after fmlp stimulation (s)
hPBMC/vehicle
hPBMC/50 ng/ml biotempt peptide

Figure 10d

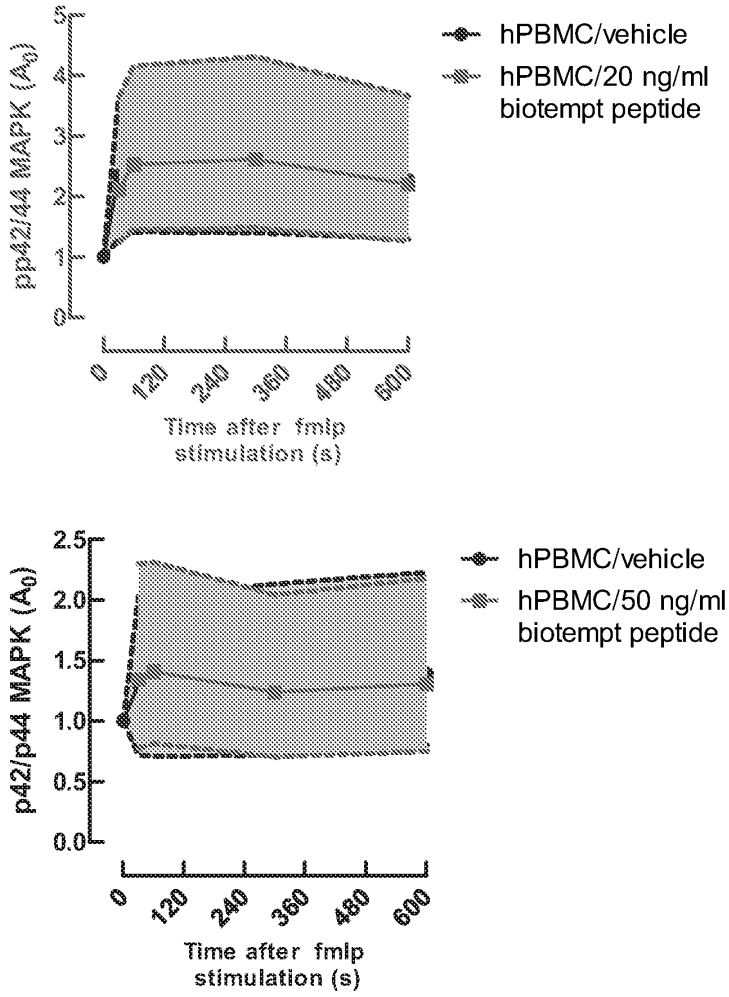

pp42/44 MAPK (A_0)
0
1
2
3
4
5
0
120
240
360
480
600
Time after fmlp stimulation (s)
hPBMC/vehicle
hPBMC/20 ng/ml biotempt peptide
p42/p44 MAPK (A_0)
0.0
0.5
1.0
1.5
2.0
2.5
0
120
240
360
480
600
Time after fmlp stimulation (s)
hPBMC/vehicle
hPBMC/50 ng/ml biotempt peptide

Figure 11

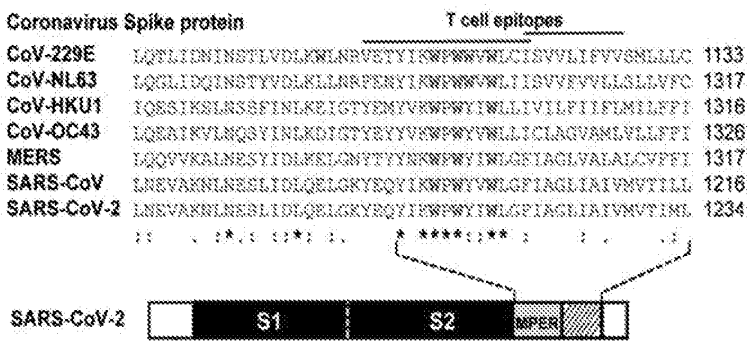

Coronavirus Spike protein
T cell epitopes
CoV-229E 1133
CoV-NL63 1317
CoV-HKU1 1316
CoV-OC43 1326
MERS 1317
SARS-CoV 1216
SARS-CoV-2 1234
SARS-CoV-2
S1
S2

Figure 12

```
SARS-CoV-1      LGKYEQYIKWPWYVWLGF
SARS-CoV-1                KWPWYVWLGFIAGLIAIV
```

Fusogenic sequence

```
SARS-CoV-1                KWPWYVWLGF
SARS-CoV-2                KWPWYIWLGF
MERS-CoV                  KWPWYIWLGF
```

Figure 13

Alignment of 36-mer AA sequences of near-C-terminal (position 1183-1218 in SARS-COV-2) with coronavirus spike proteins that have shown binding to FPR-receptor (with increased binding at polymorphism W190/N192). Synthesised 11/12-meric peptides having FPR-binding activity shown in red.

Mills, Biochim Biophys Acta Mol Basis Dis. 2006 Jul; 1762(7): 693–703.	CORONAVIRUS	OC43	MNRLQEAIKVLNQSYINLKDIGTYEYYVKWPWYVWL
	CORONAVIRUS	HKU-1	MNLIQESIKSLNNSYINLKDIGTYEMYVKWPWYVWL
	CORONAVIRUS	229E	VQKLQTLIDNINSTLVDLKWLNRVETYIKWPWWVWL
	CORONAVIRUS	NL63	TVELQGLIDQINSTYVDLKLLNREFNYIKWPWWVWL
	CORONAVIRUS	SARS	IDRLNEVAKNLNESLIDLQELGKYEQYIKWPWYVWL
			********************************.**
EBI-finding	*CORONAVIRUS*	*SARS-COV-2*	*IDRLNEVAKNLNESLIDLQELGKYEQYIKWPWYIWL*
	SARS sequence has 97.2% homology with all 249 SARS-COV-2 spike sequences (Uniprot 11/02/21)		