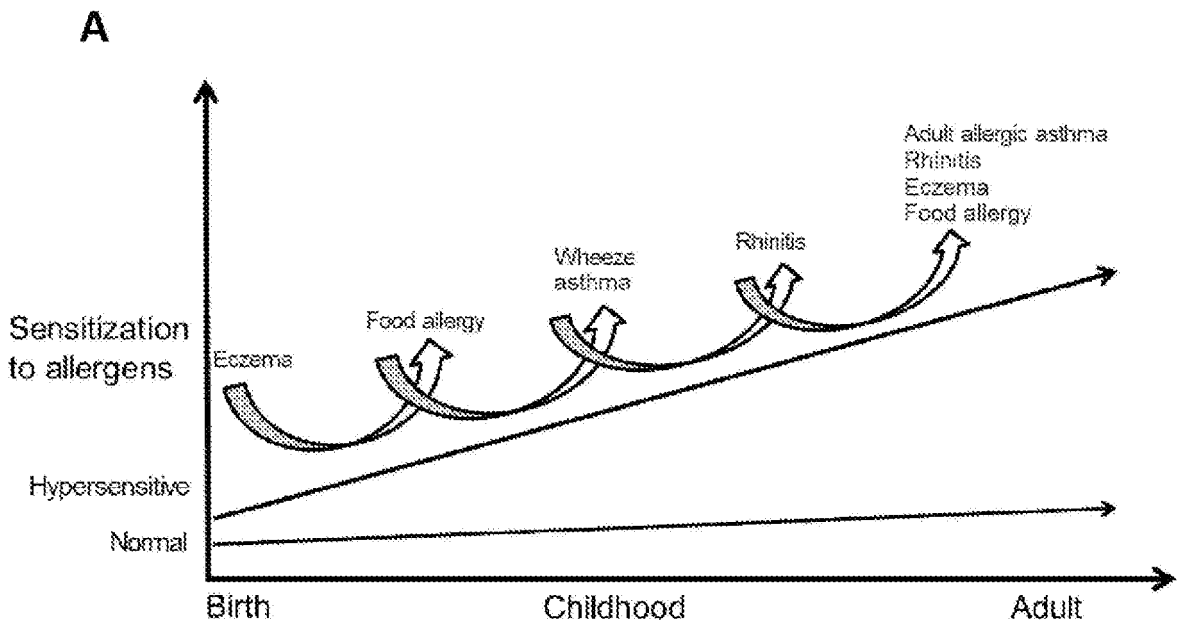

A
Adult allergic asthma
Rhinitis
Eczema
Food allergy
Wheeze asthma
Rhinitis
Food allergy
Eczema
Sensitization to allergens
Hypersensitive
Normal
Birth
Childhood
Adult

FIGURE 1

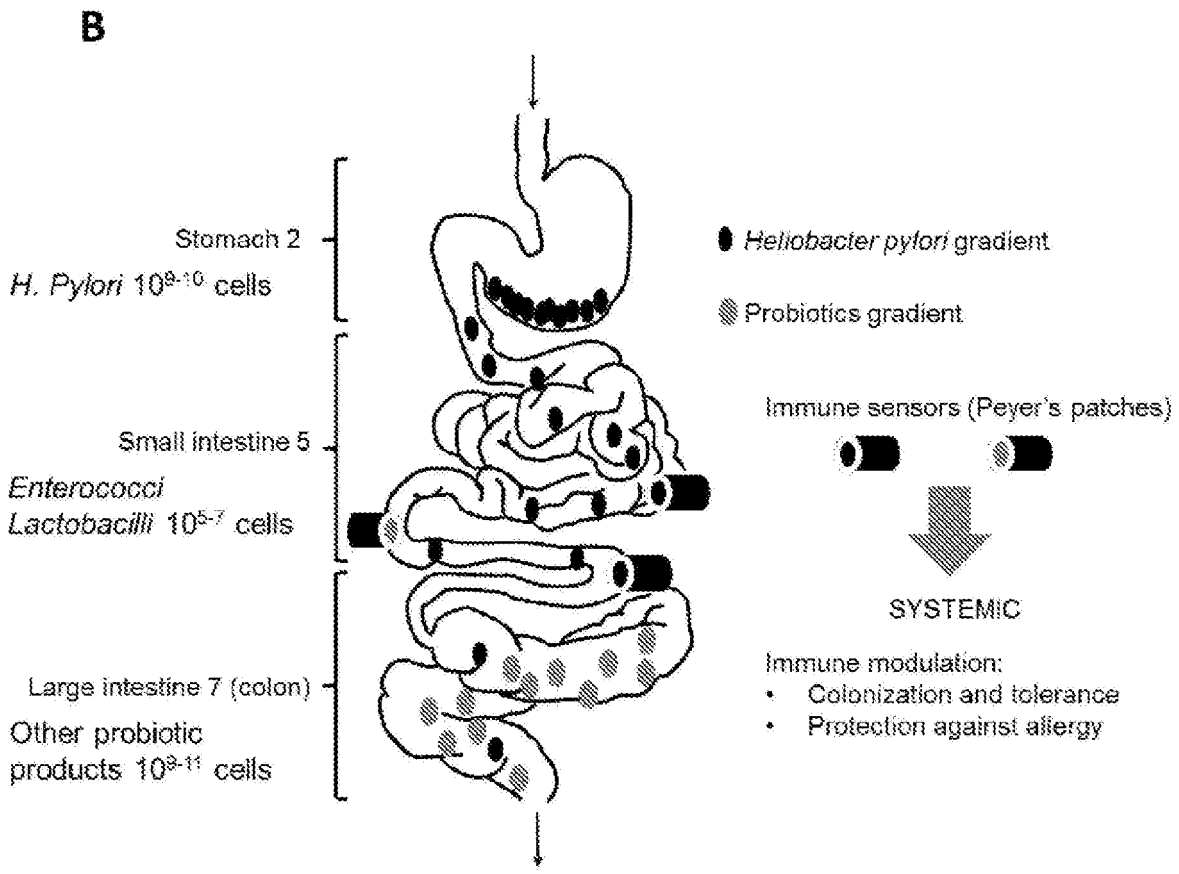

B
Stomach 2
H. Pylori 10^8-10 cells
Small intestine 5
Enterococci
Lactobacilli 10^5-7 cells
Large intestine 7 (colon)
Other probiotic products 10^8-11 cells
Heliobacter pylori gradient
Probiotics gradient
Immune sensors (Peyer's patches)
SYSTEMIC
Immune modulation:
• Colonization and tolerance
• Protection against allergy

FIGURE 1

C

Acute Allergic Asthma Model – OVA Sensitization / Challenge Model

6-8 week old C57BL/6 mice acclimatized for at least 1 week

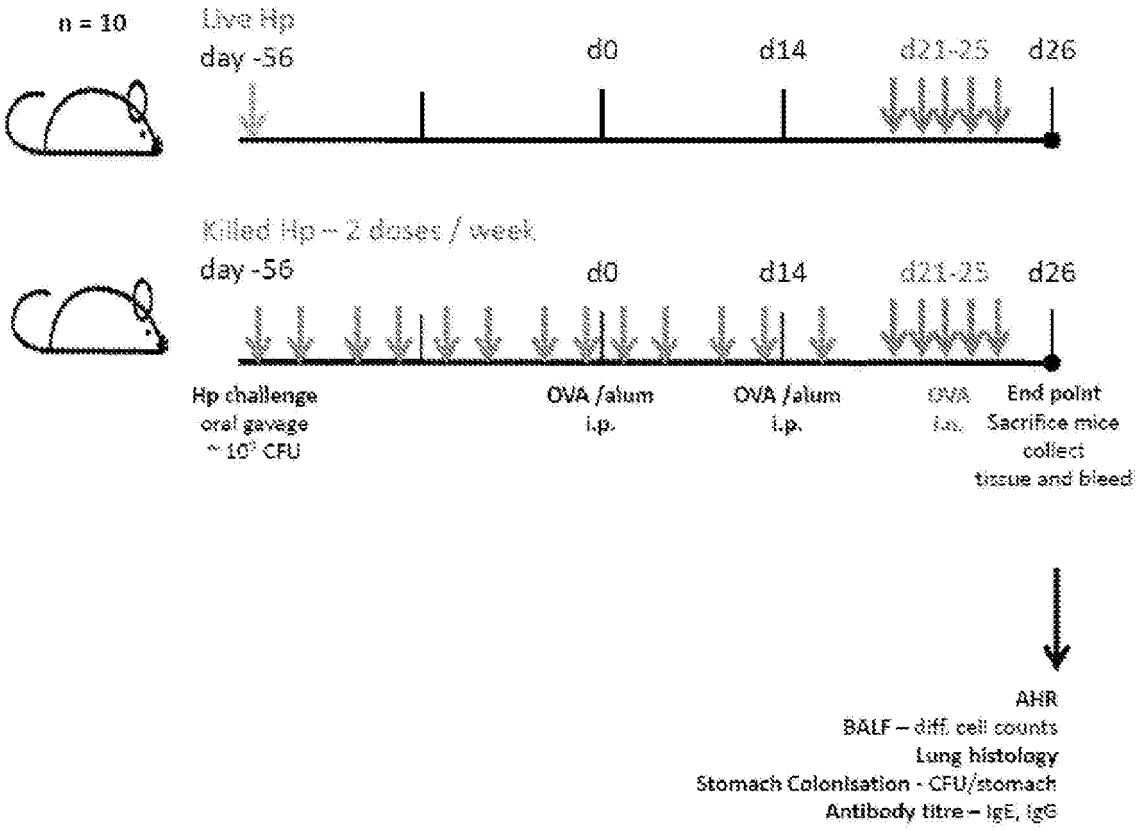


FIGURE 1

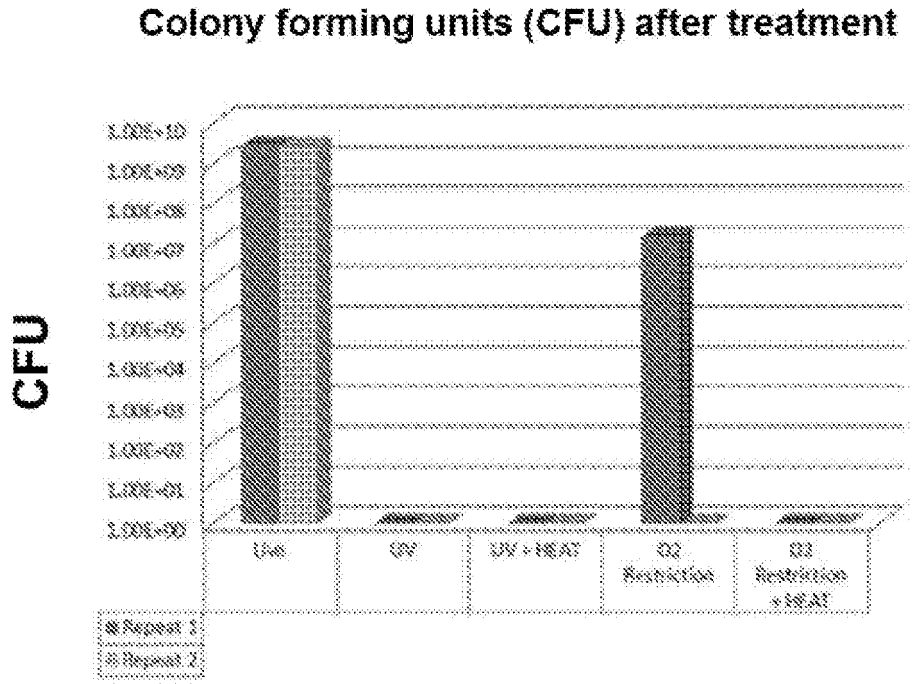

Colony forming units (CFU) after treatment
CFU
Repeat 1
Repeat 2

FIGURE 2

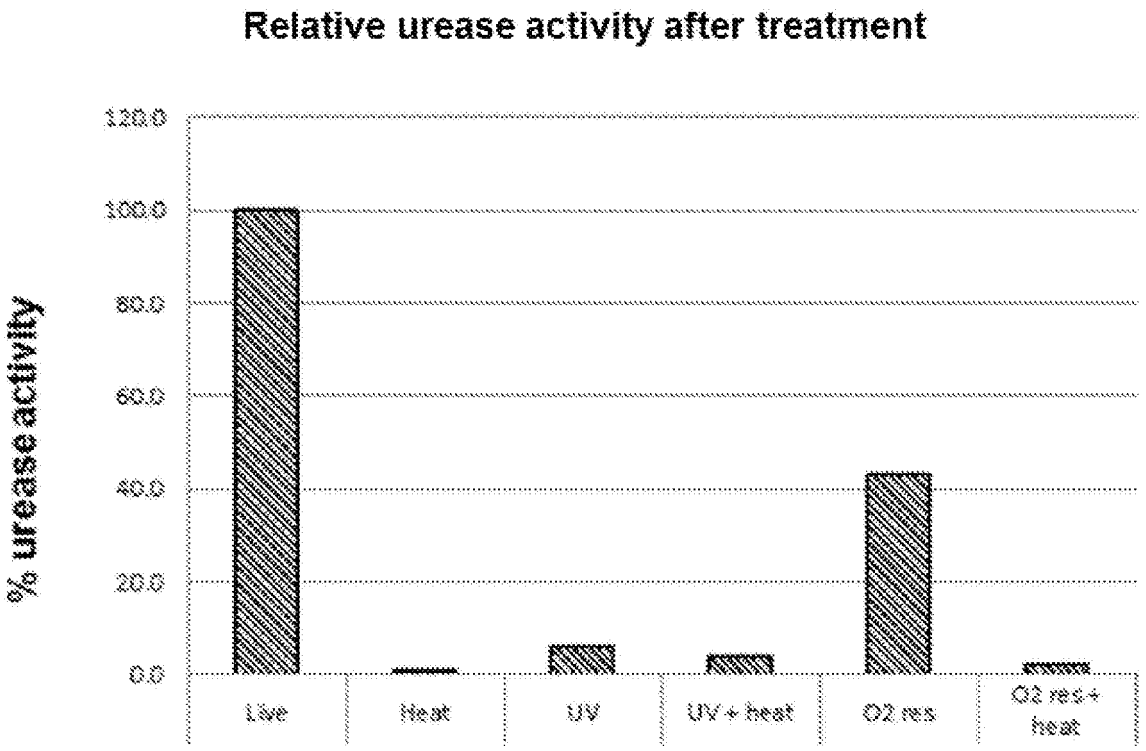

Relative urease activity after treatment
% urease activity
120.0
100.0
80.0
60.0
40.0
20.0
0.0
Live
Heat
UV
UV + heat
O2 res
O2 res + heat

FIGURE 3

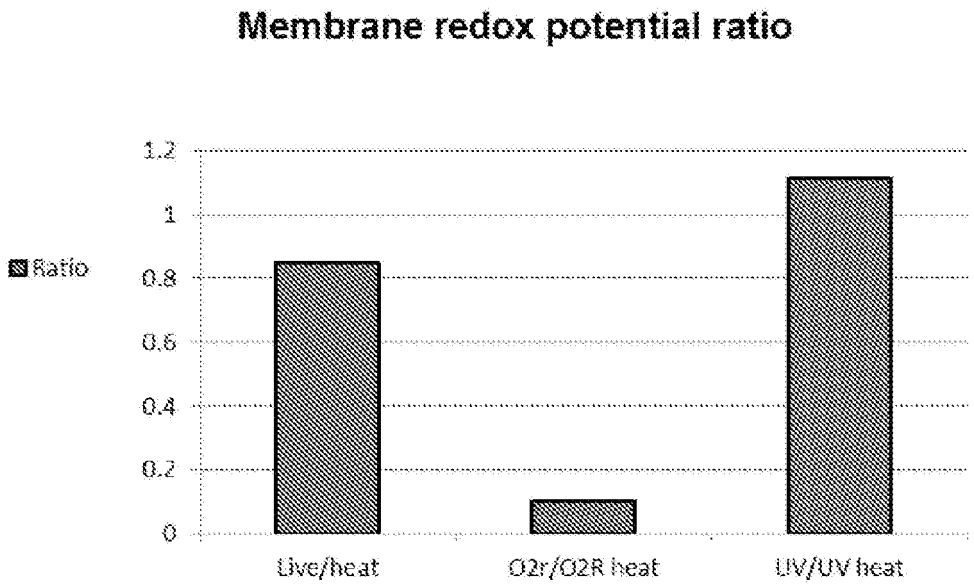

Membrane redox potential ratio
Ratio
1.2
1
0.8
0.6
0.4
0.2
0
Live/heat
O2r/O2R heat
UV/UV heat

FIGURE 4

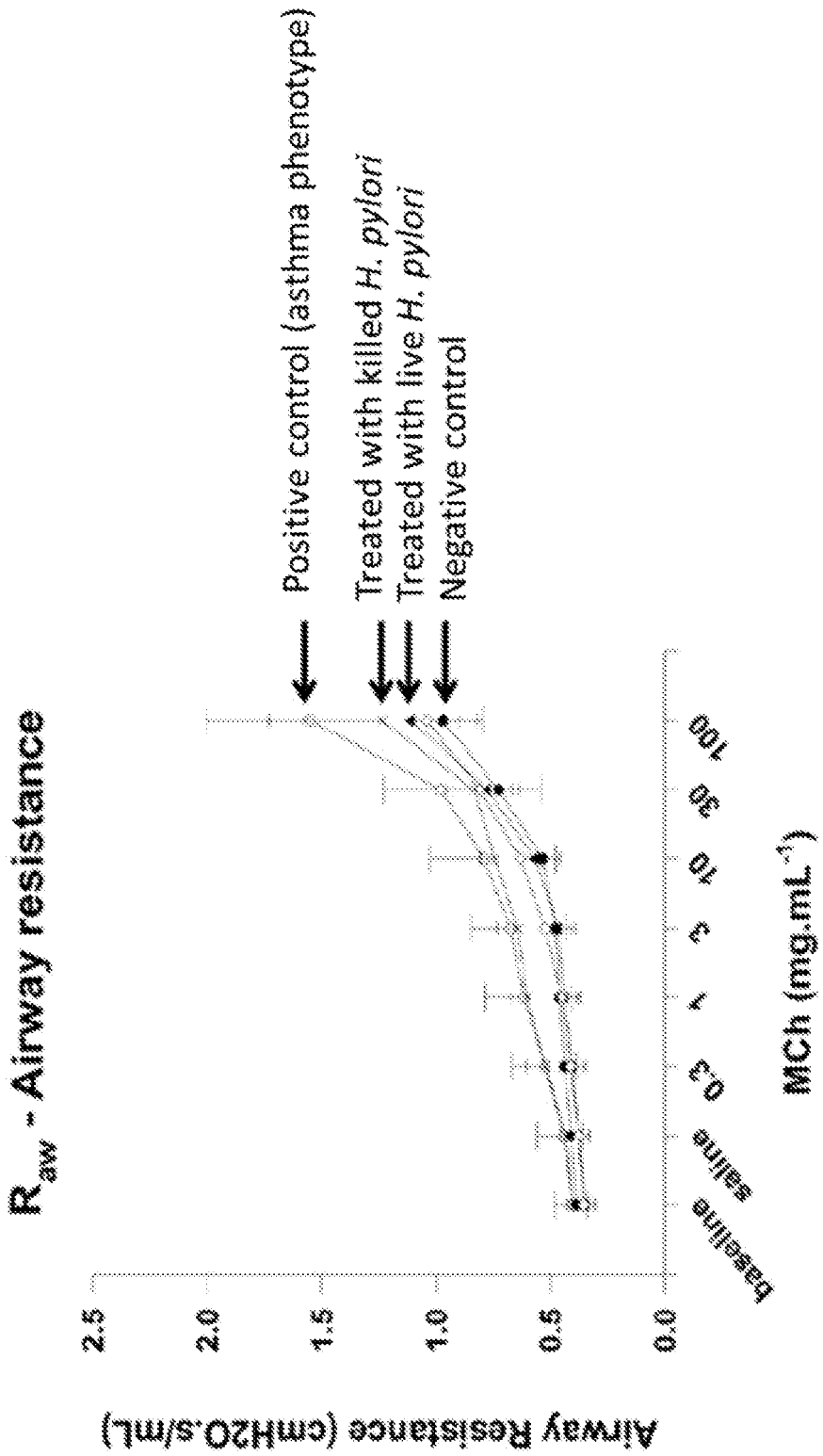

Positive control (asthma phenotype)
Treated with killed H. pylori
Treated with live H. pylori
Negative control
R_{aw} - Airway resistance
Airway Resistance (cmH2O.s/mL)
2.5
2.0
1.5
1.0
0.5
0.0
baseline
saline
0.3
1
3
10
30
100
MCh (mg.mL-1)

FIGURE 5

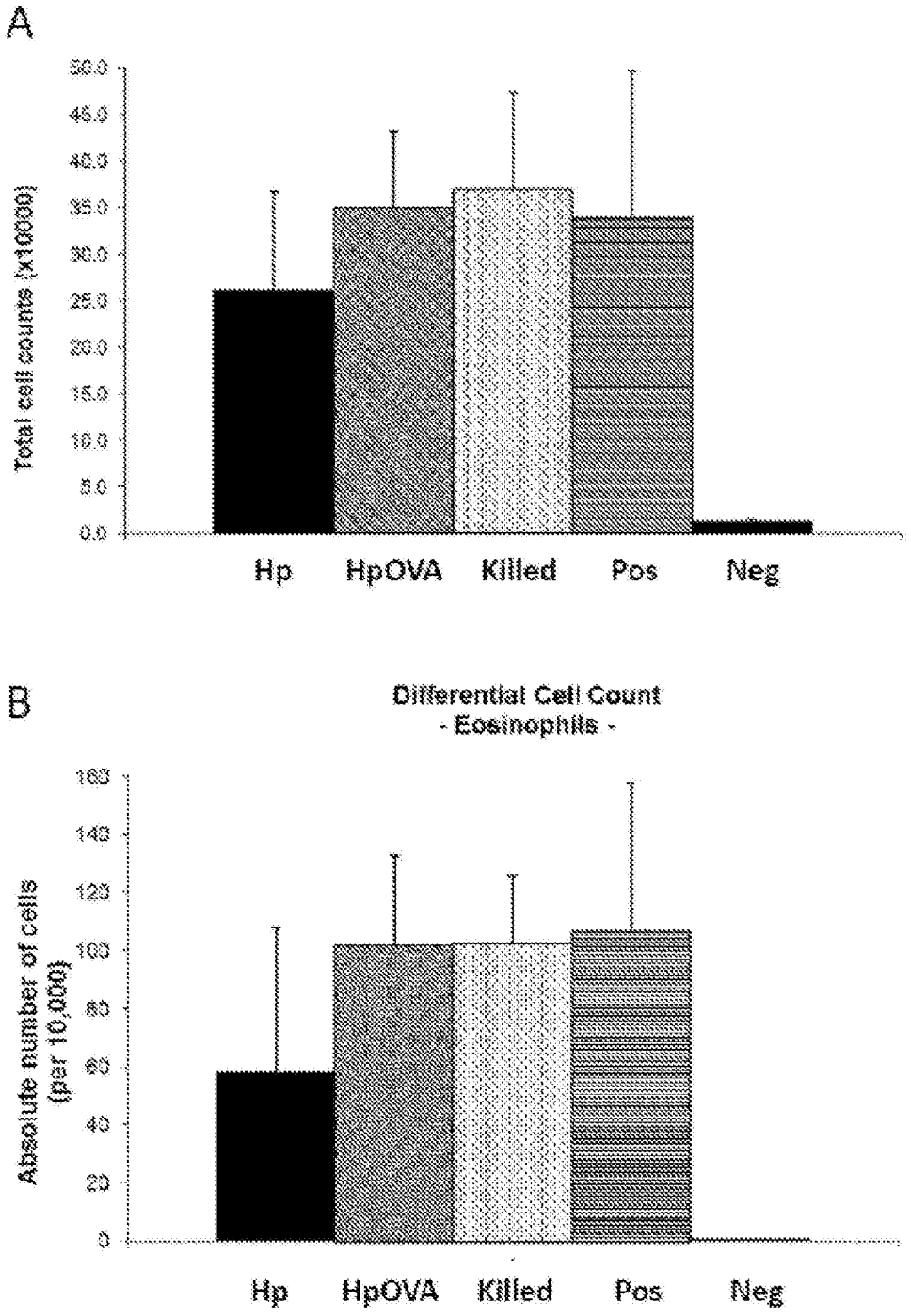

A
Total cell counts (x10000)
50.0
45.0
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
Hp
HpOVA
Killed
Pos
Neg
B
Differential Cell Count
- Eosinophils -
Absolute number of cells
(per 10,000)
160
140
120
100
80
60
40
20
0
Hp
HpOVA
Killed
Pos
Neg

FIGURE 6

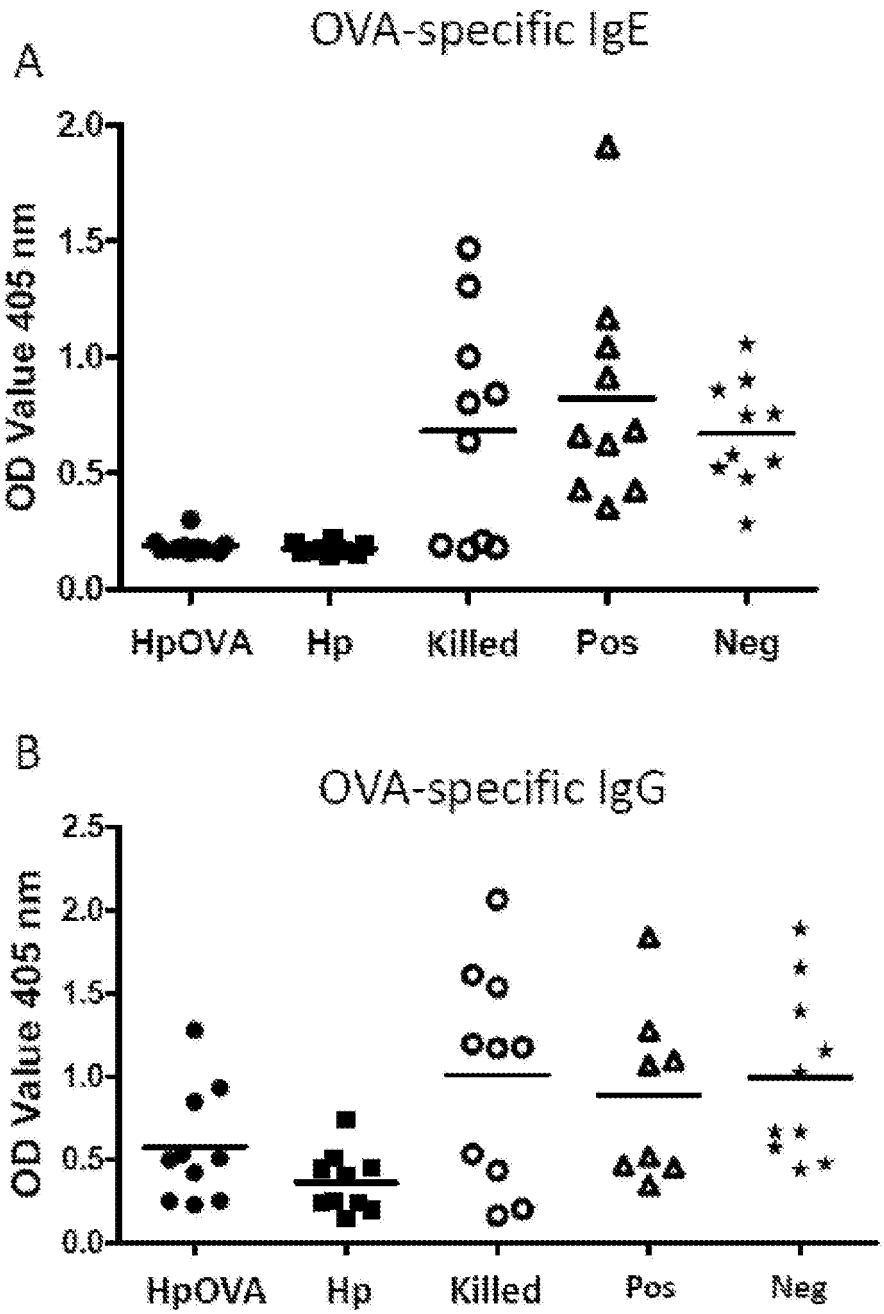

A
OVA-specific IgE
OD Value 405 nm
2.0
1.5
1.0
0.5
0.0
HpOVA
Hp
Killed
Pos
Neg
B
OVA-specific IgG
OD Value 405 nm
2.5
2.0
1.5
1.0
0.5
0.0
HpOVA
Hp
Killed
Pos
Neg

FIGURE 7

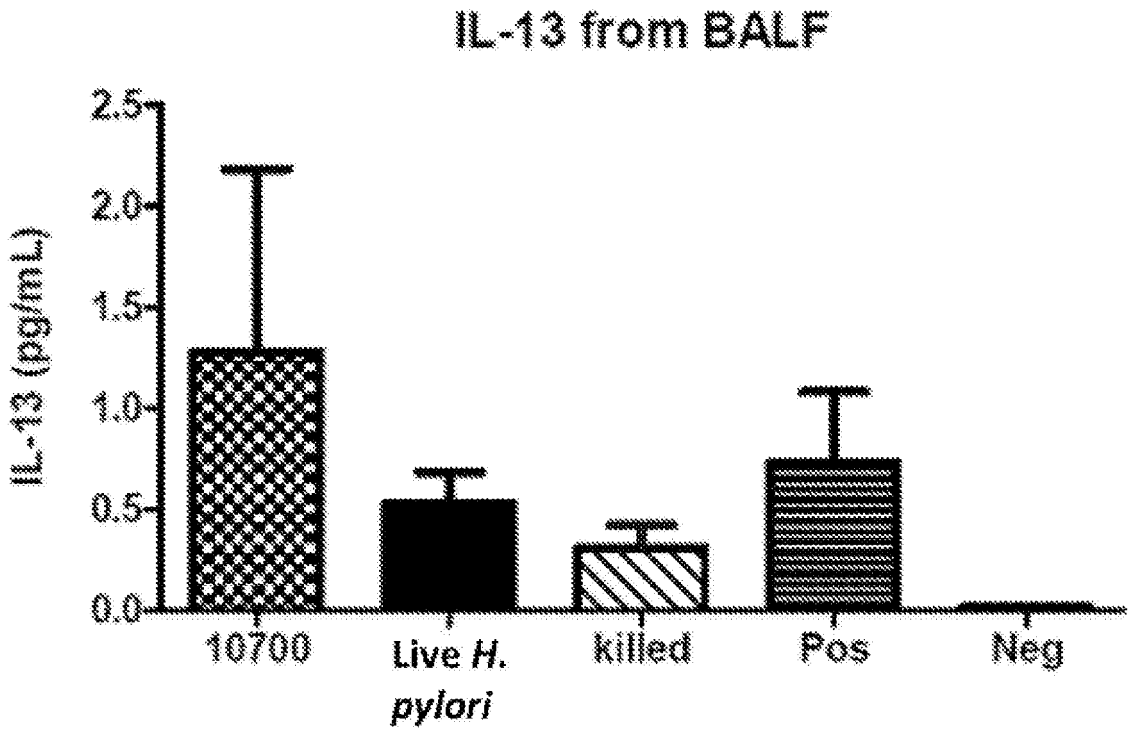

IL-13 from BALF
IL-13 (pg/mL)
2.5
2.0
1.5
1.0
0.5
0.0
10700
Live H. pylori
killed
Pos
Neg

FIGURE 8

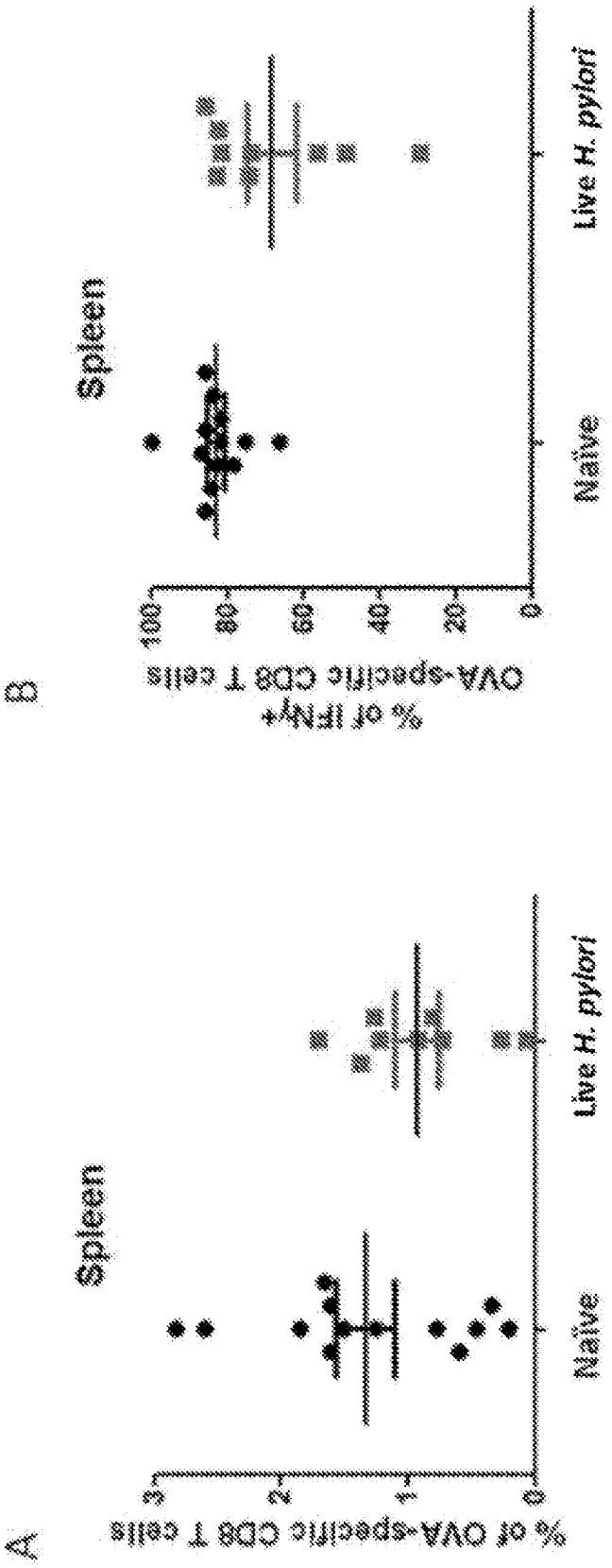

A
% of OVA-specific CD8 T cells
3
2
1
0
Spleen
Naïve
Live H. pylori
B
% of IFNγ+
OVA-specific CD8 T cells
100
80
60
40
20
0
Spleen
Naïve
Live H. pylori

FIGURE 9

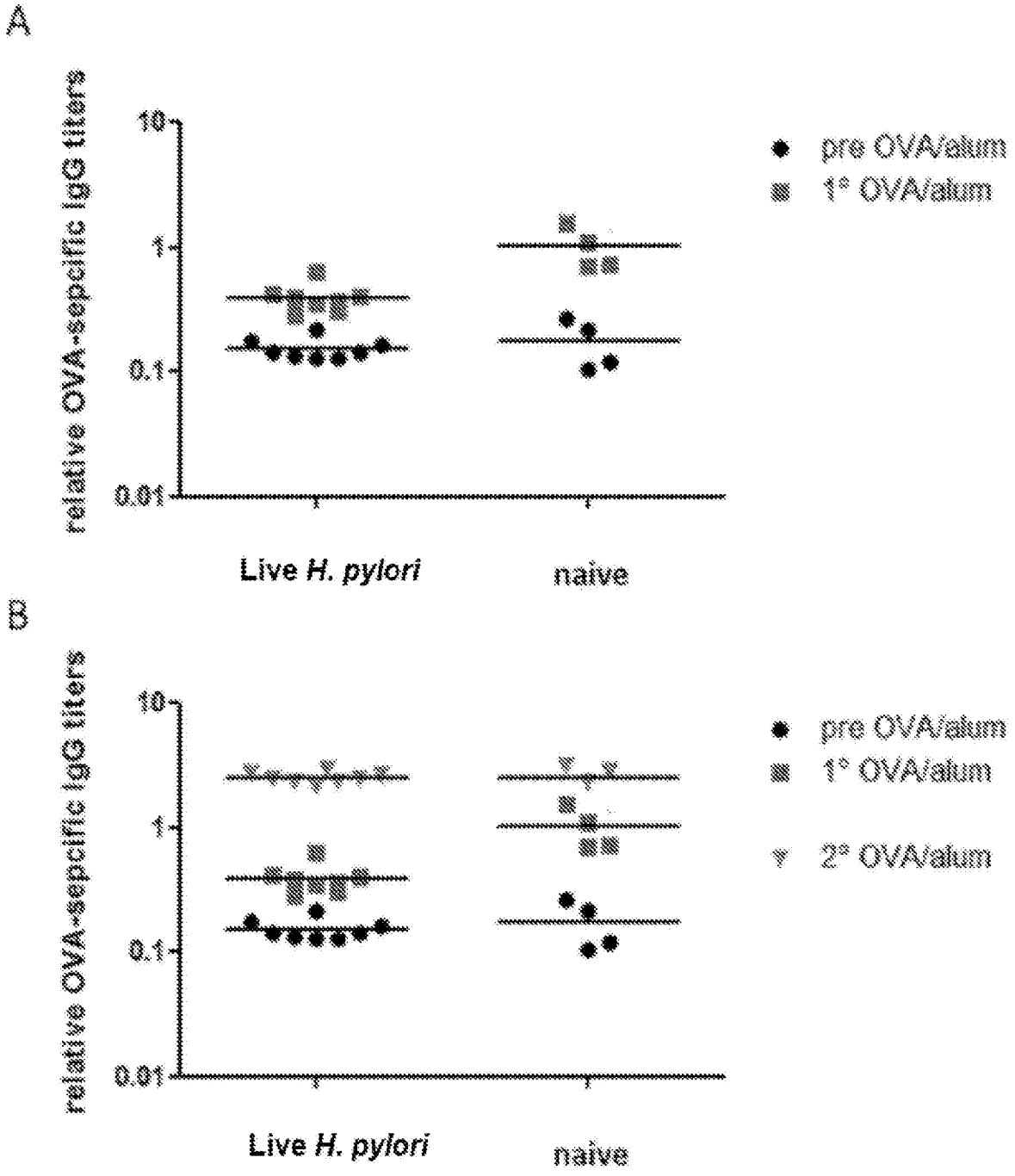

A
relative OVA-sepcific IgG titers
10
1
0.1
0.01
pre OVA/alum
1° OVA/alum
Live H. pylori
naive
B
relative OVA-sepcific IgG titers
10
1
0.1
0.01
pre OVA/alum
1° OVA/alum
2° OVA/alum
Live H. pylori
naive

FIGURE 10

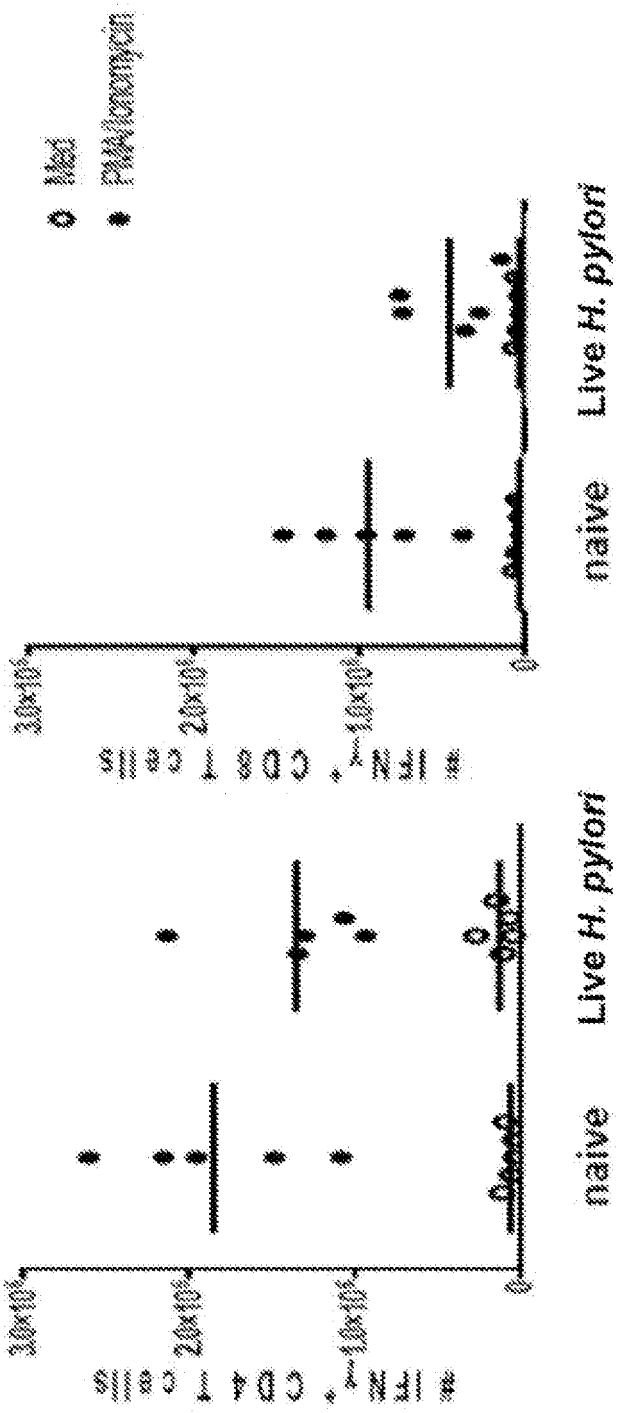

Med
PMA/ionomycin
IFNγ+ CD8 T cells
3.0x10⁴
2.0x10⁴
1.0x10⁴
0
naive
Live H. pylori
IFNγ+ CD4 T cells
3.0x10⁴
2.0x10⁴
1.0x10⁴
0
naive
Live H. pylori

FIGURE 11

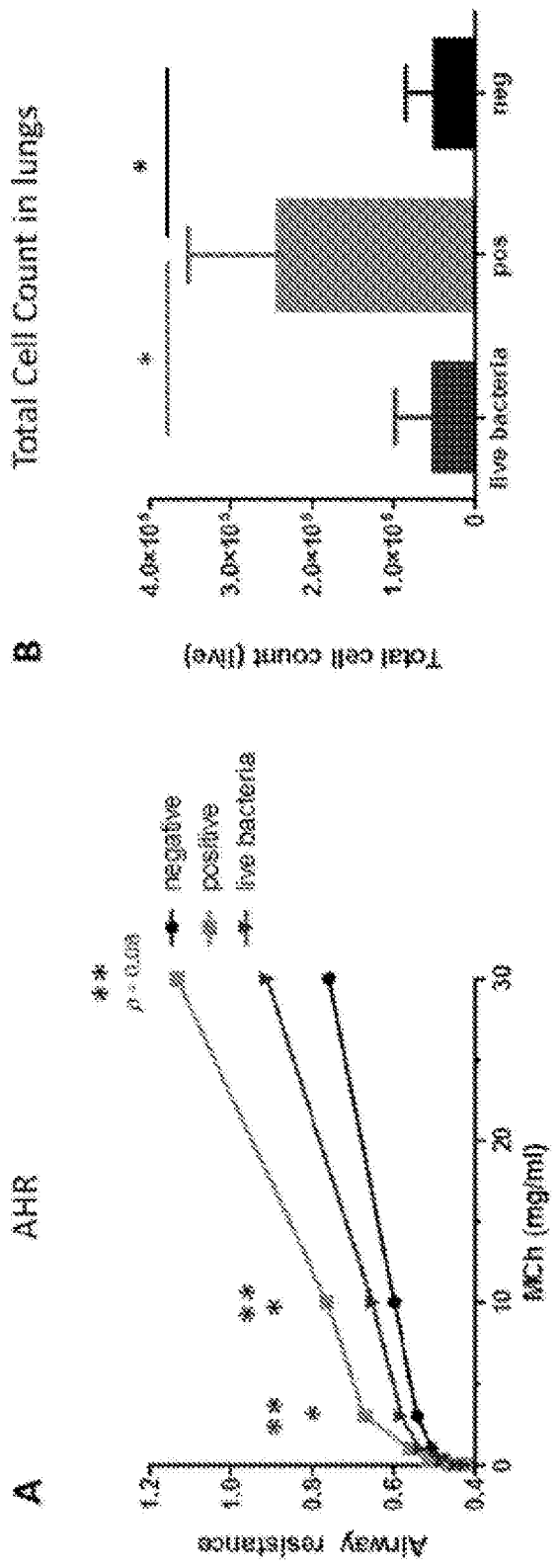

A
AHR
Airway resistance
MCh (mg/ml)
negative
positive
live bacteria
B
Total Cell Count in lungs
Total cell count (live)
live bacteria
pos
neg

FIGURE 12

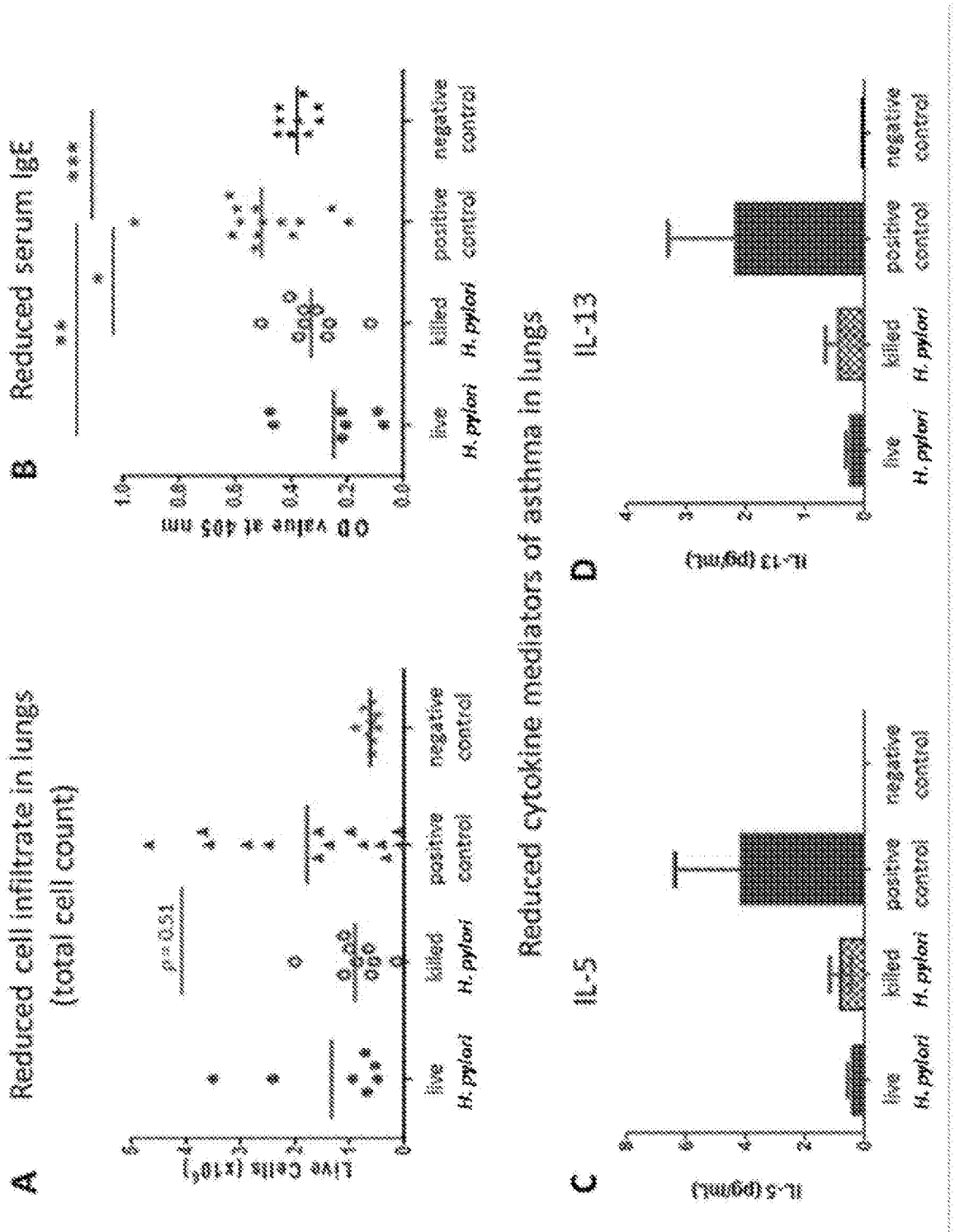

A
Reduced cell infiltrate in lungs
(total cell count)
B
Reduced serum IgE
Reduced cytokine mediators of asthma in lungs
C
IL-5
D
IL-13
live H. pylori
killed H. pylori
positive control
negative control

FIGURE 13

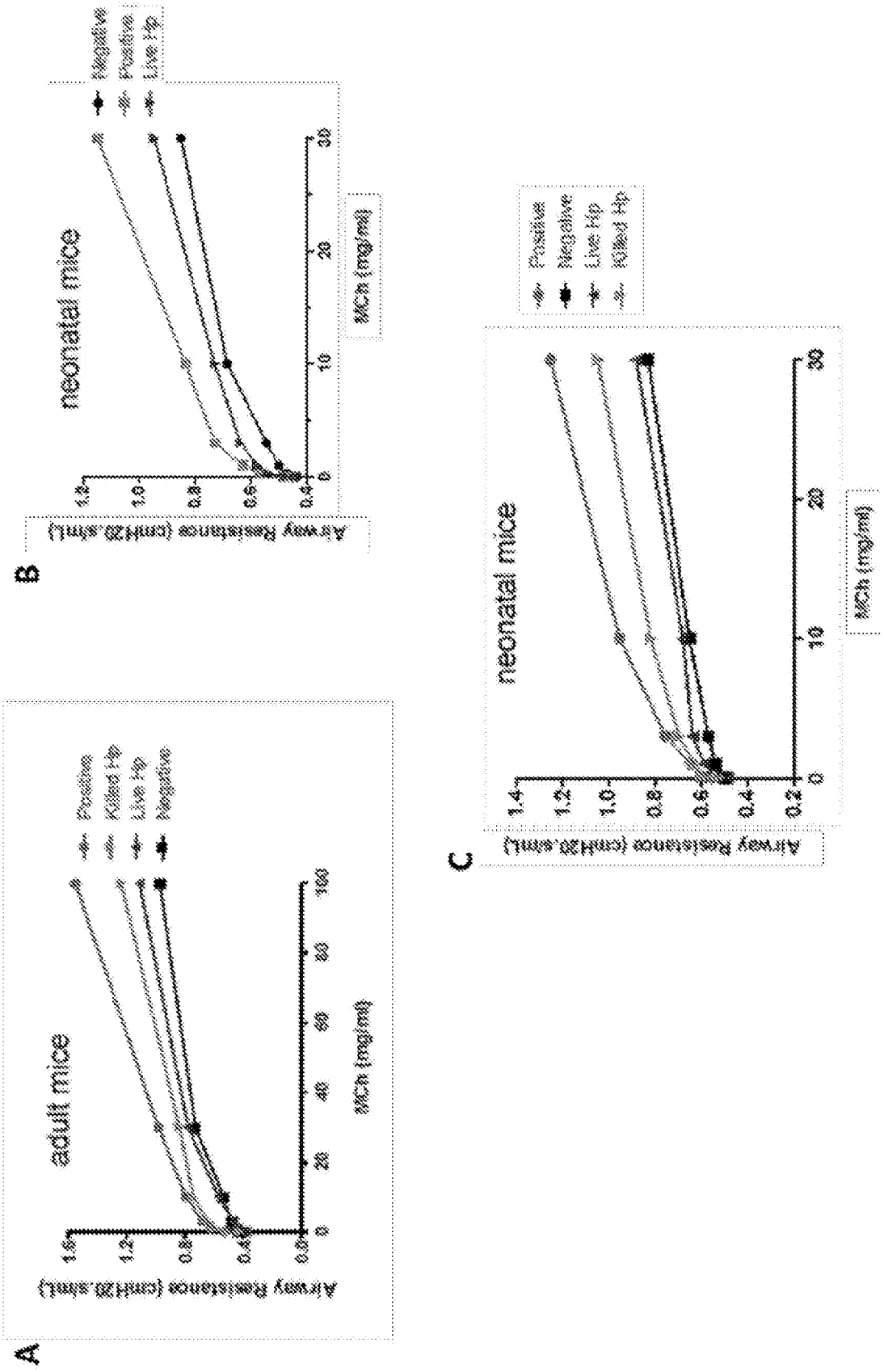

A
adult mice
Positive
Killed Hp
Live Hp
Negative
Airway Resistance (cmH2O.s/mL)
MCh (mg/ml)
B
neonatal mice
Negative
Positive
Live Hp
Airway Resistance (cmH2O.s/mL)
MCh (mg/ml)
C
neonatal mice
Positive
Negative
Live Hp
Killed Hp
Airway Resistance (cmH2O.s/mL)
MCh (mg/ml)

FIGURE 14

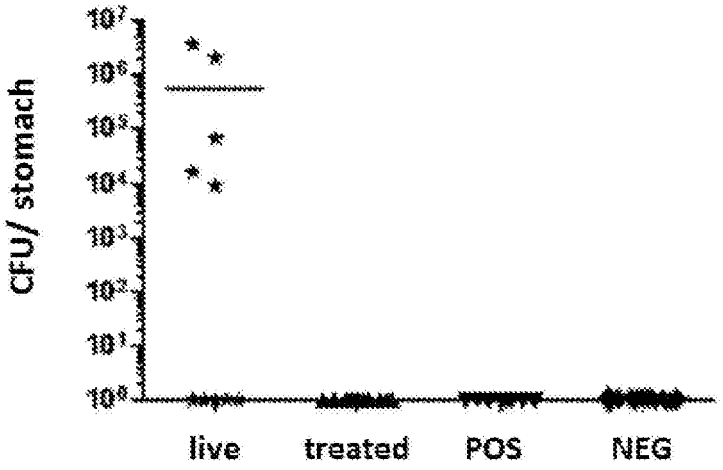

CFU/ stomach
10^7
10^6
10^5
10^4
10^3
10^2
10^1
10^0
live
treated
POS
NEG

FIGURE 15

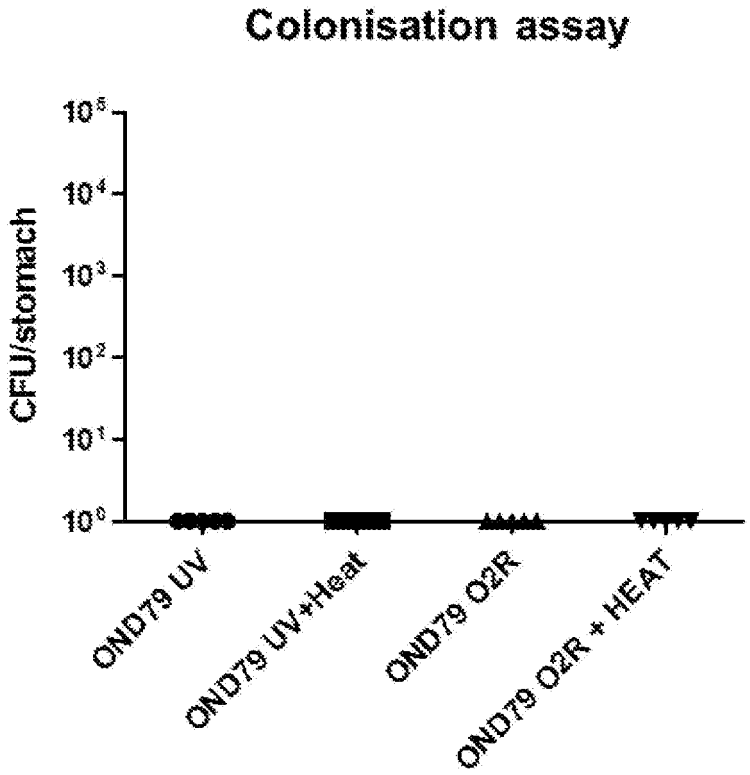

Colonisation assay
CFU/stomach
10^5
10^4
10^3
10^2
10^1
10^0
OND79 UV
OND79 UV+Heat
OND79 O2R
OND79 O2R + HEAT

FIGURE 16

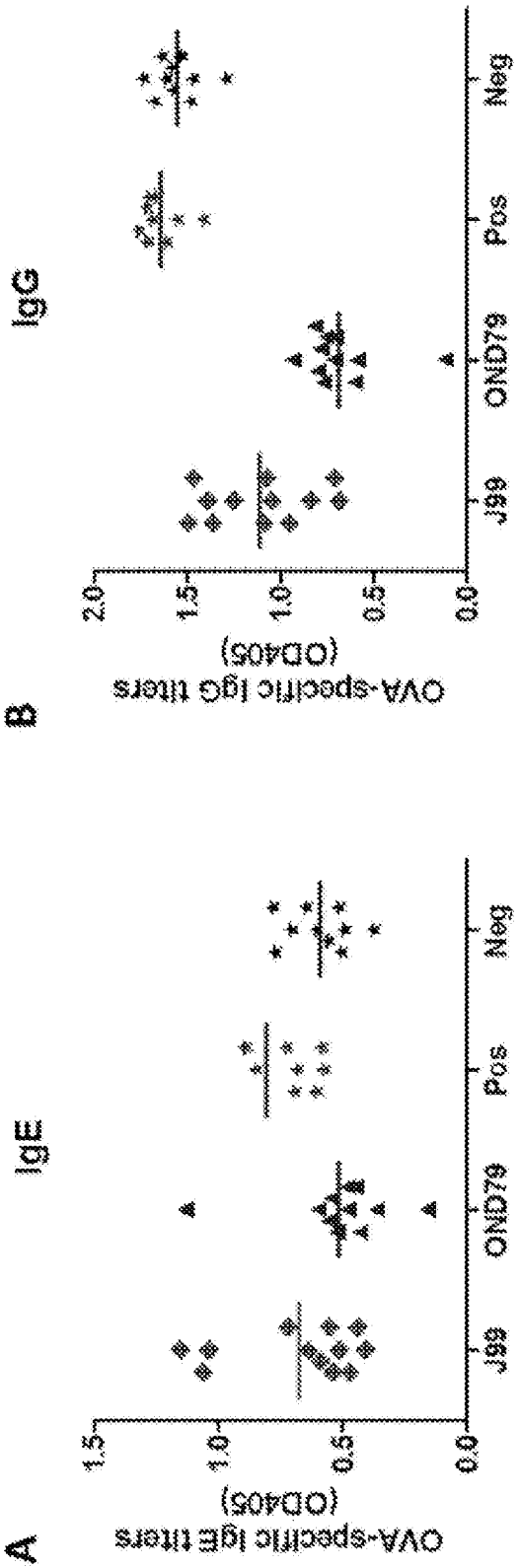

A
IgE
OVA-specific IgE titers
(OD405)
1.5
1.0
0.5
0.0
J99
OND79
Pos
Neg
B
IgG
OVA-specific IgG titers
(OD405)
2.0
1.5
1.0
0.5
0.0
J99
OND79
Pos
Neg

FIGURE 17

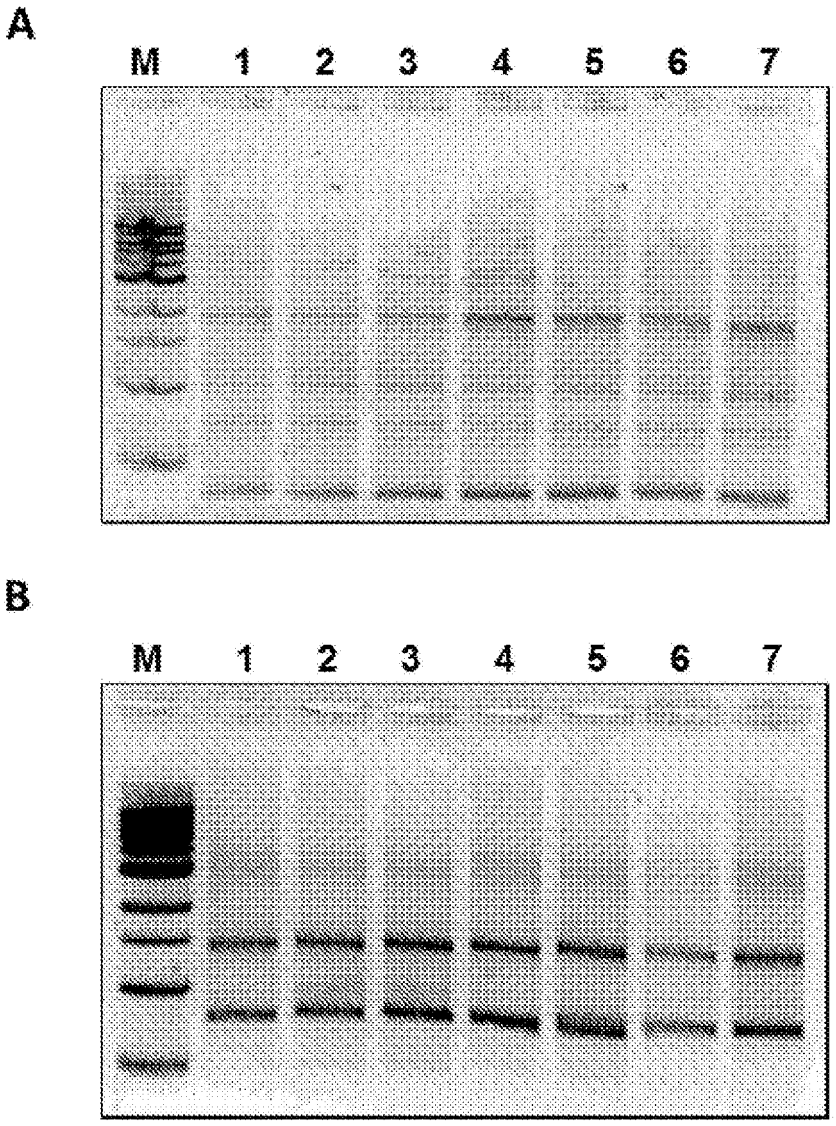


FIGURE 18

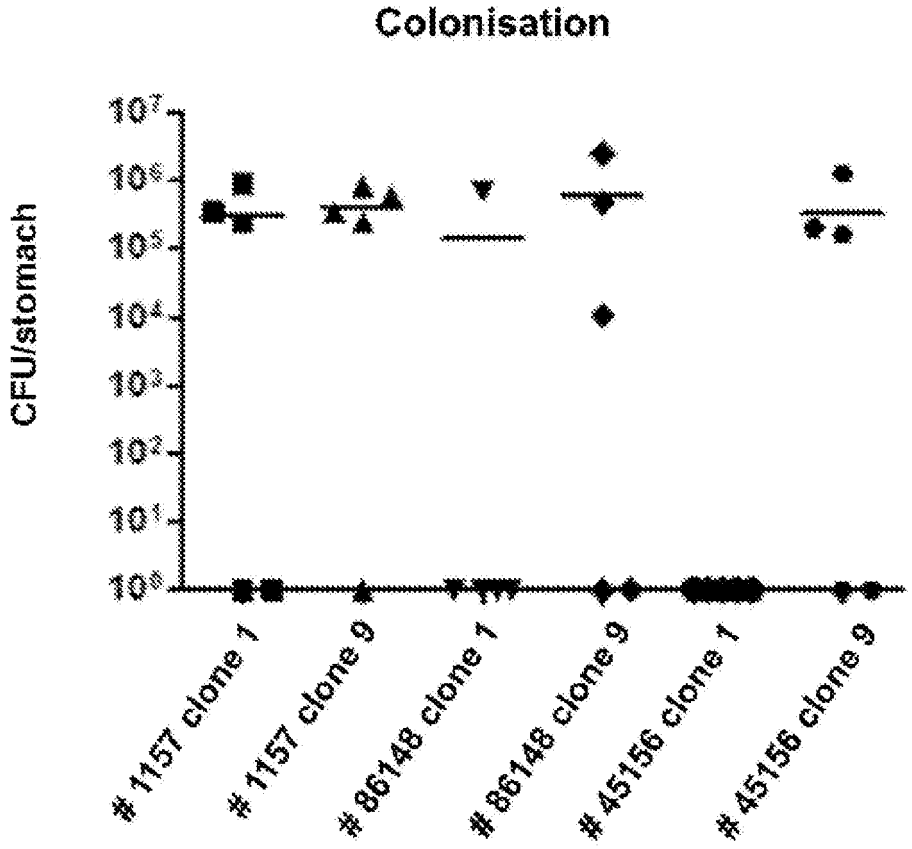

Colonisation
CFU/stomach
10^7
10^6
10^5
10^4
10^3
10^2
10^1
10^0
1157 clone 1
1157 clone 9
86148 clone 1
86148 clone 9
45156 clone 1
45156 clone 9

FIGURE 19

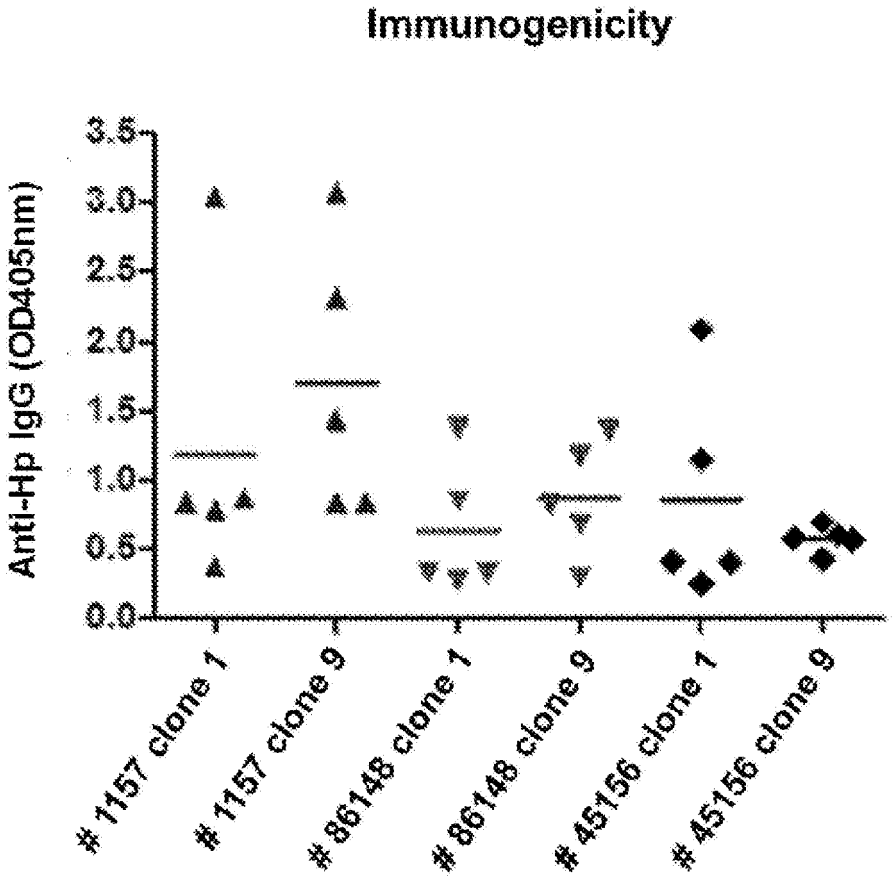

Immunogenicity
Anti-Hp IgG (OD405nm)
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1157 clone 1
1157 clone 9
86148 clone 1
86148 clone 9
45156 clone 1
45156 clone 9

FIGURE 20

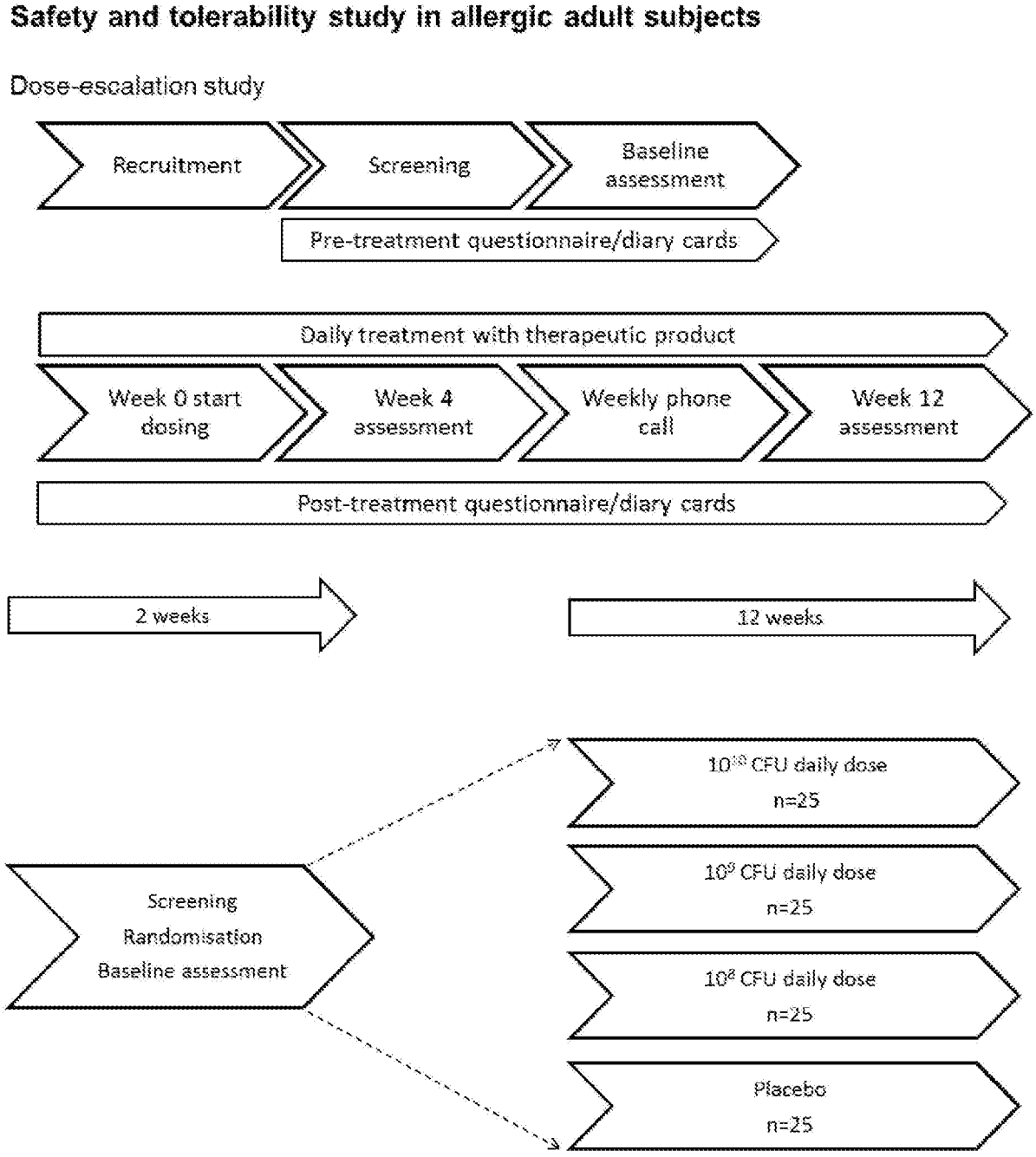

Safety and tolerability study in allergic adult subjects
Dose-escalation study
Recruitment
Screening
Baseline assessment
Pre-treatment questionnaire/diary cards
Daily treatment with therapeutic product
Week 0 start dosing
Week 4 assessment
Weekly phone call
Week 12 assessment
Post-treatment questionnaire/diary cards
2 weeks
12 weeks
Screening
Randomisation
Baseline assessment
10^10 CFU daily dose
n=25
10^9 CFU daily dose
n=25
10^8 CFU daily dose
n=25
Placebo
n=25

FIGURE 21