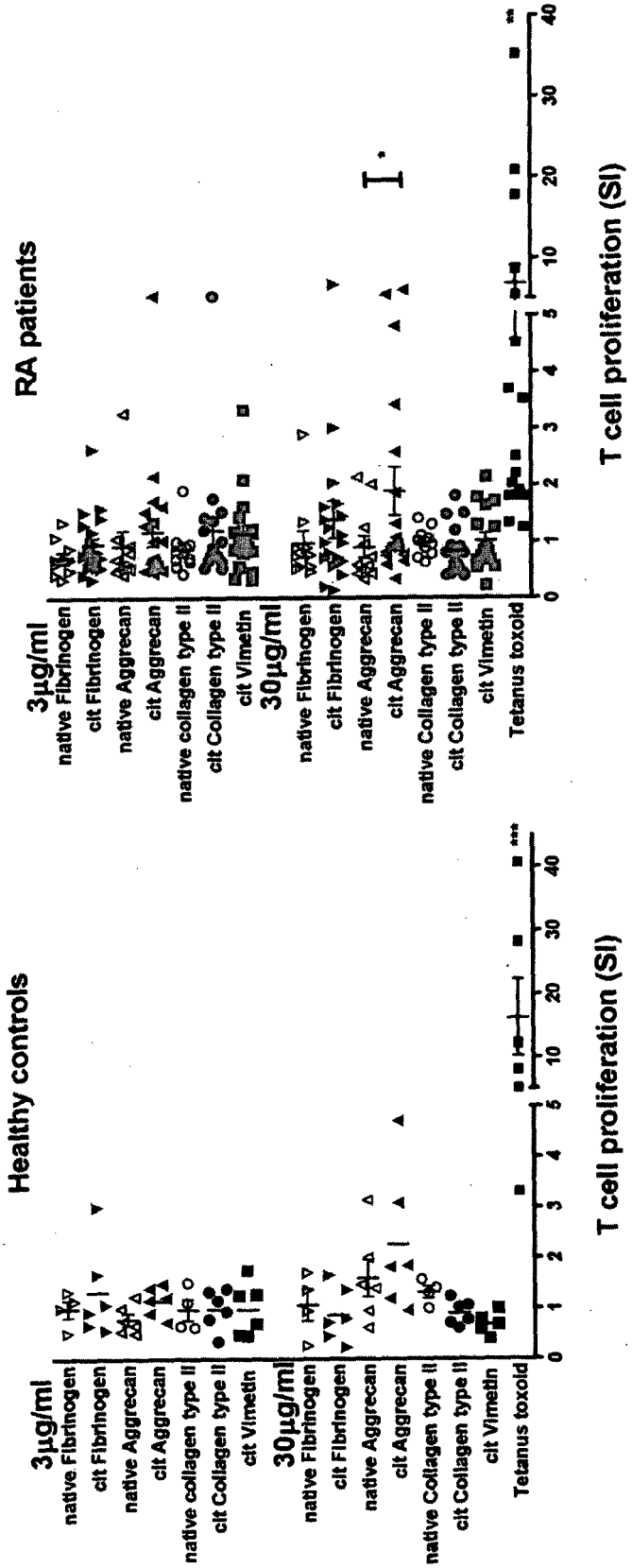
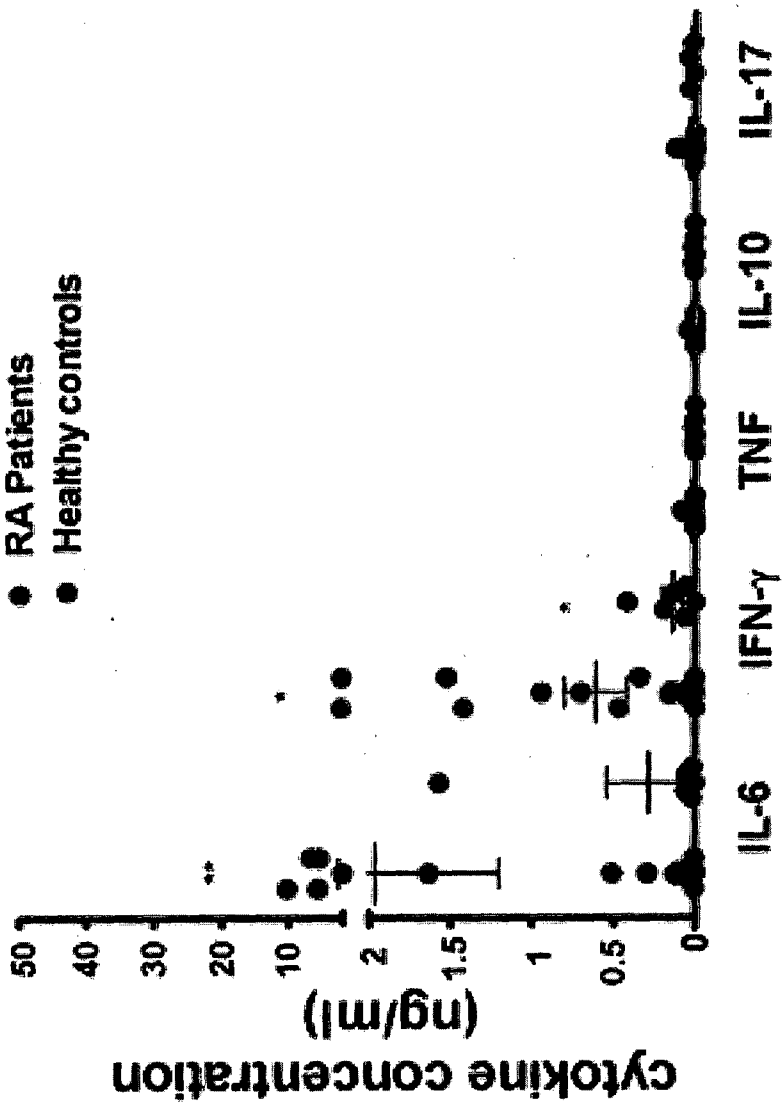

Healthy controls
RA patients
3µg/ml
30µg/ml
native Fibrinogen
cit Fibrinogen
native Aggrecan
cit Aggrecan
native collagen type II
cit Collagen type II
cit Vimetin
Tetanus toxoid
T cell proliferation (SI)
0
1
2
3
4
5
10
20
30
40
***
**

FIGURE 1


RA Patients
Healthy controls
cytokine concentration
(ng/ml)
50
40
30
20
10
2
1.5
1
0.5
0
IL-6
IFN-γ
TNF
IL-10
IL-17

A

FIGURE 2

B

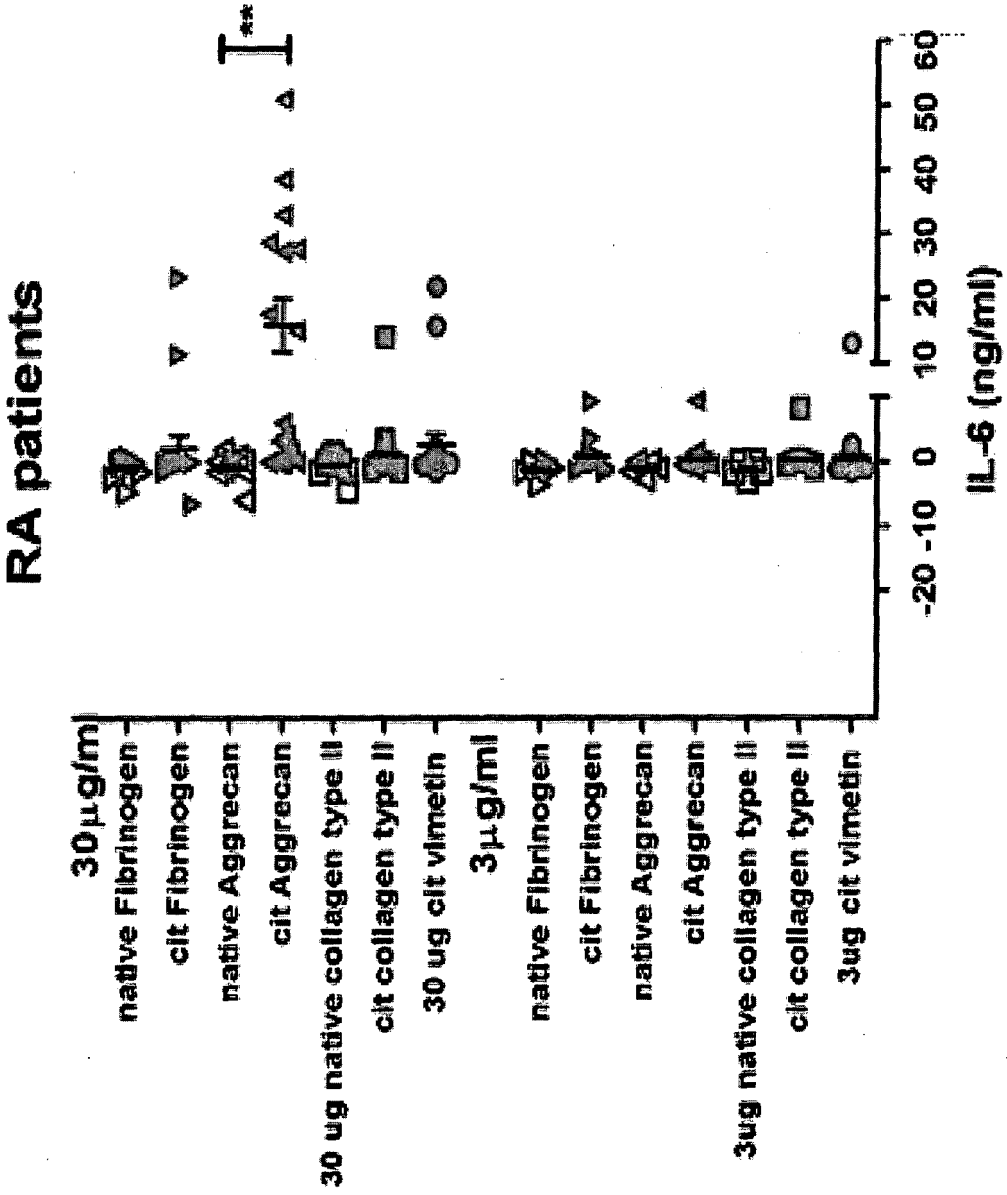



FIGURE 2 continued

B continued

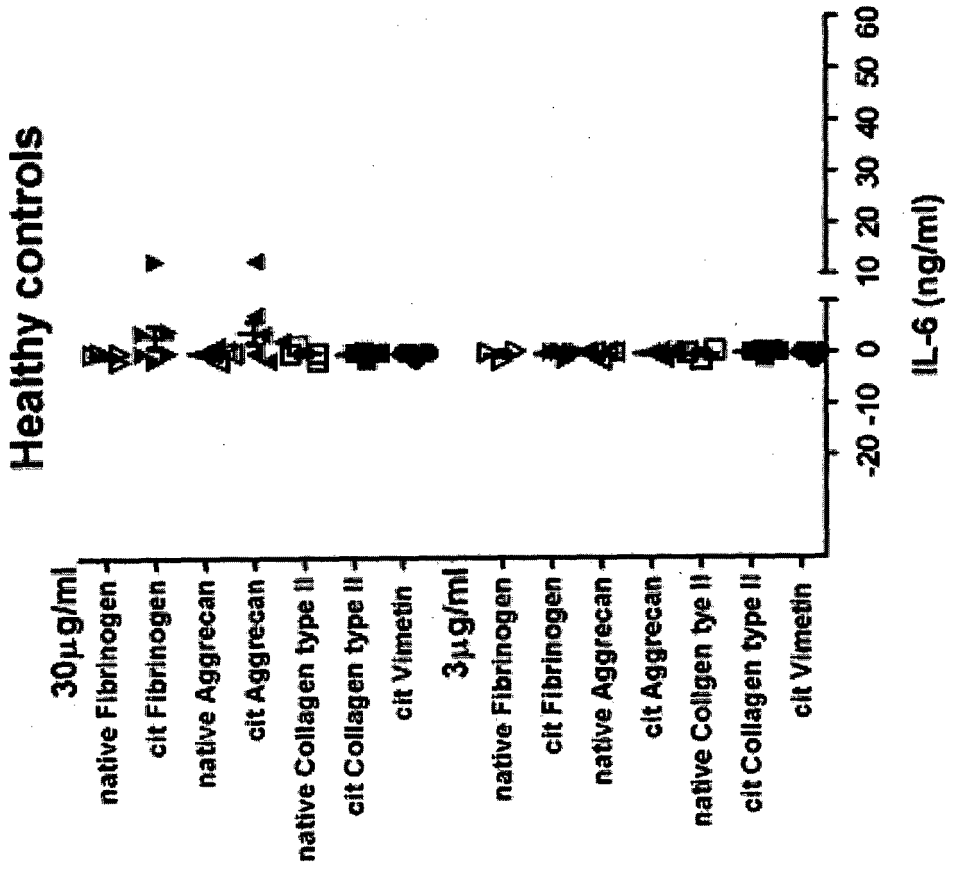



FIGURE 2 continued

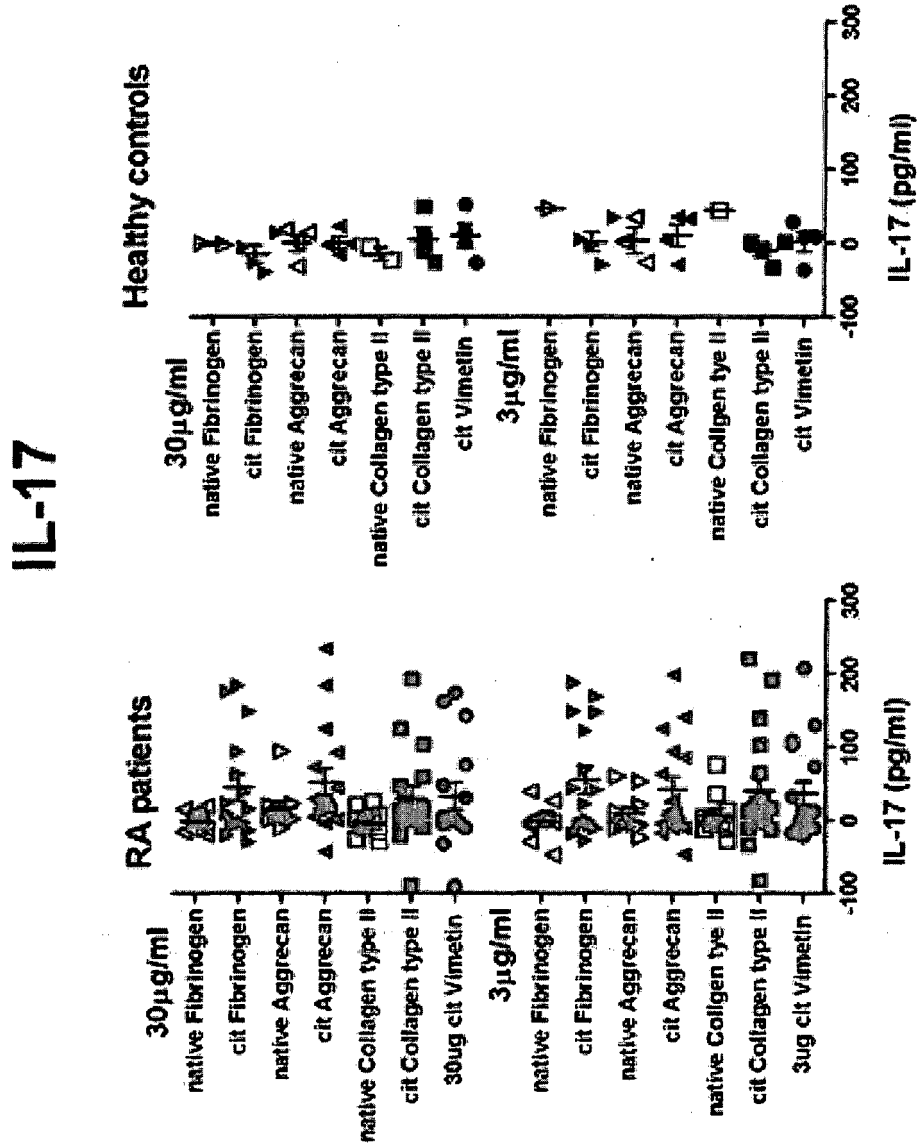

IL-17
RA patients
Healthy controls
30µg/ml
native Fibrinogen
cit Fibrinogen
native Aggrecan
cit Aggrecan
native Collagen type II
cit Collagen type II
30ug cit Vimetin
3µg/ml
native Fibrinogen
cit Fibrinogen
native Aggrecan
cit Aggrecan
native Collgen tye II
cit Collagen type II
3ug cit Vimetin
-100
0
100
200
300
IL-17 (pg/ml)

FIGURE 3

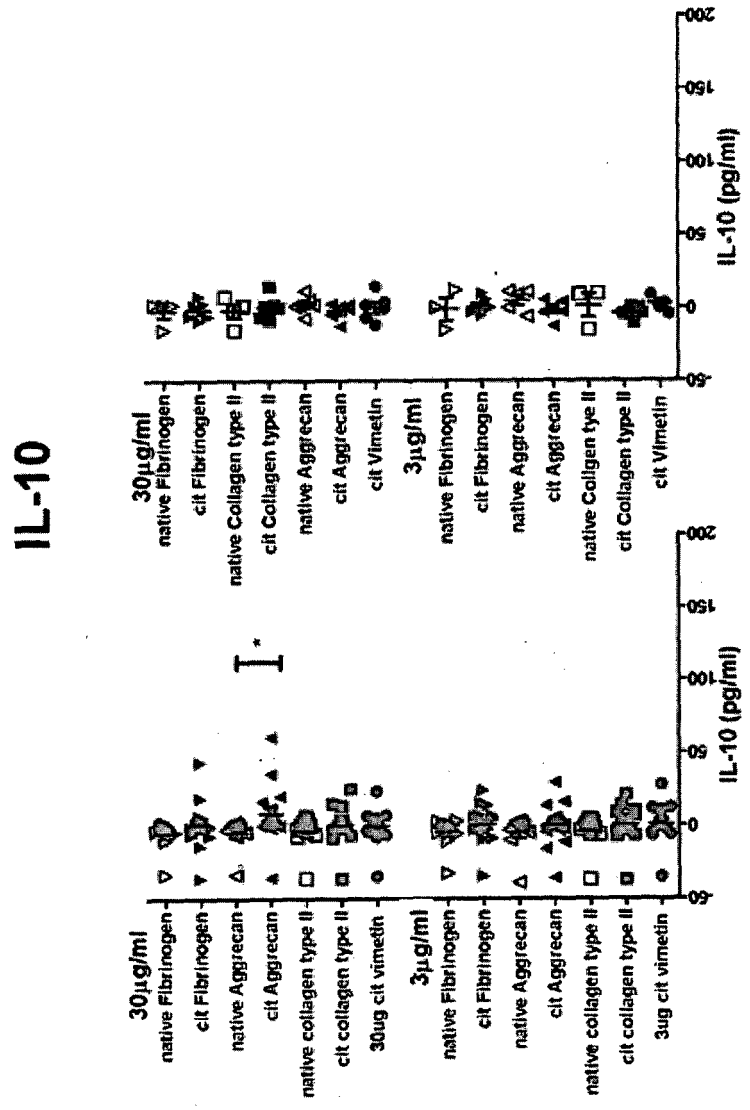



FIGURE 3 continued

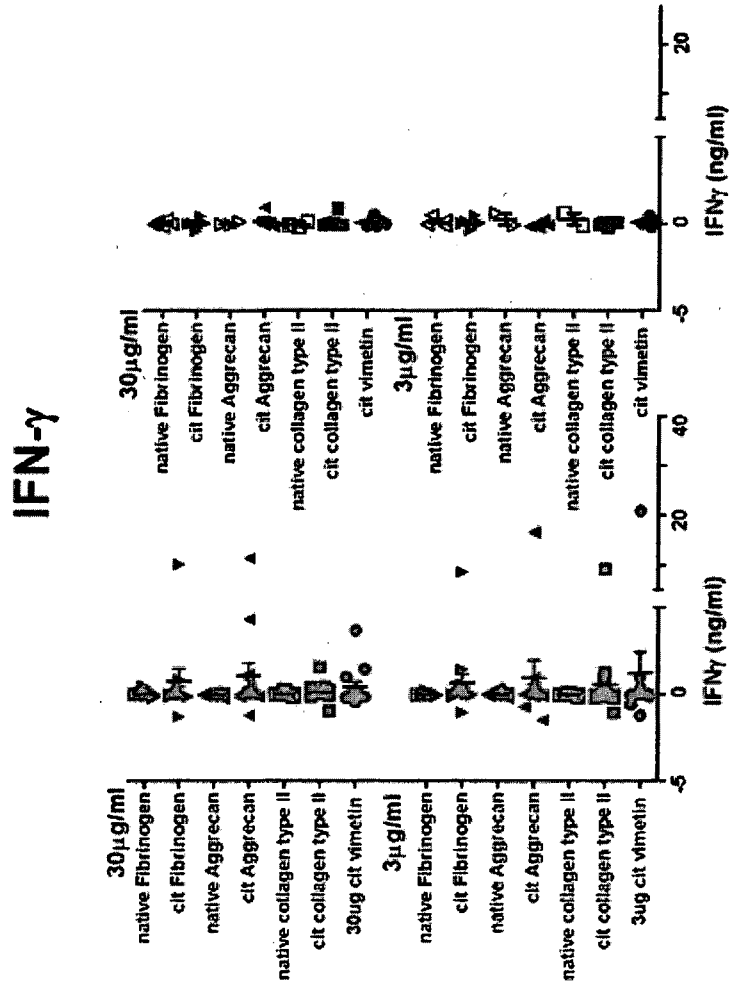



FIGURE 3 continued

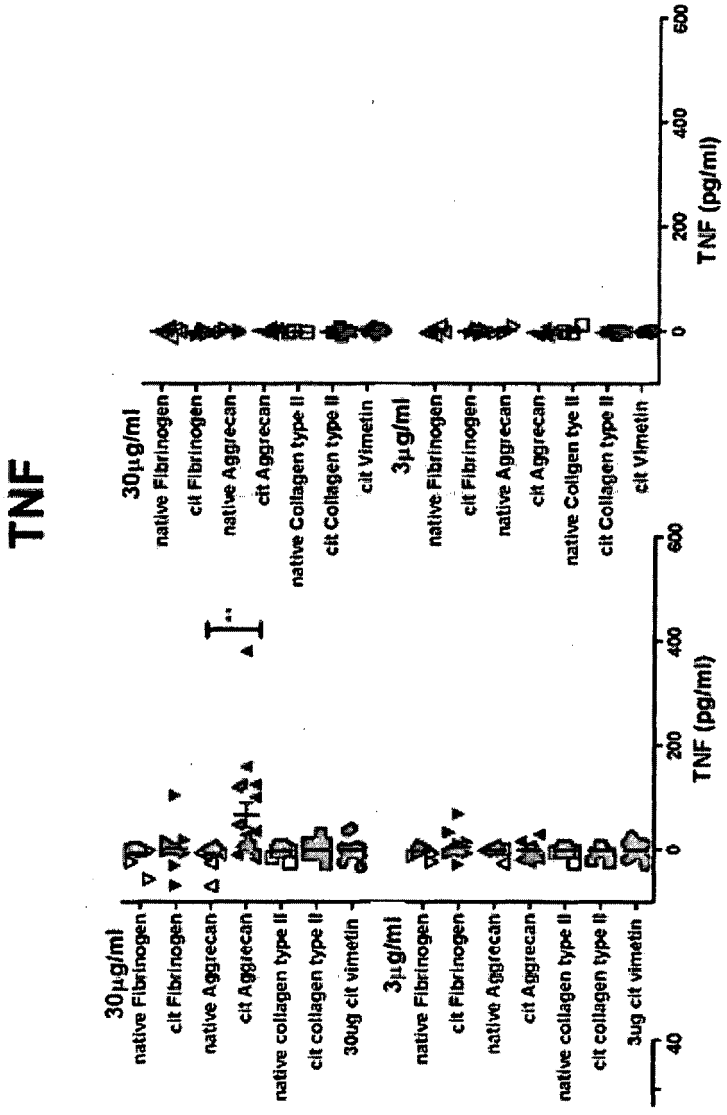



FIGURE 3 continued

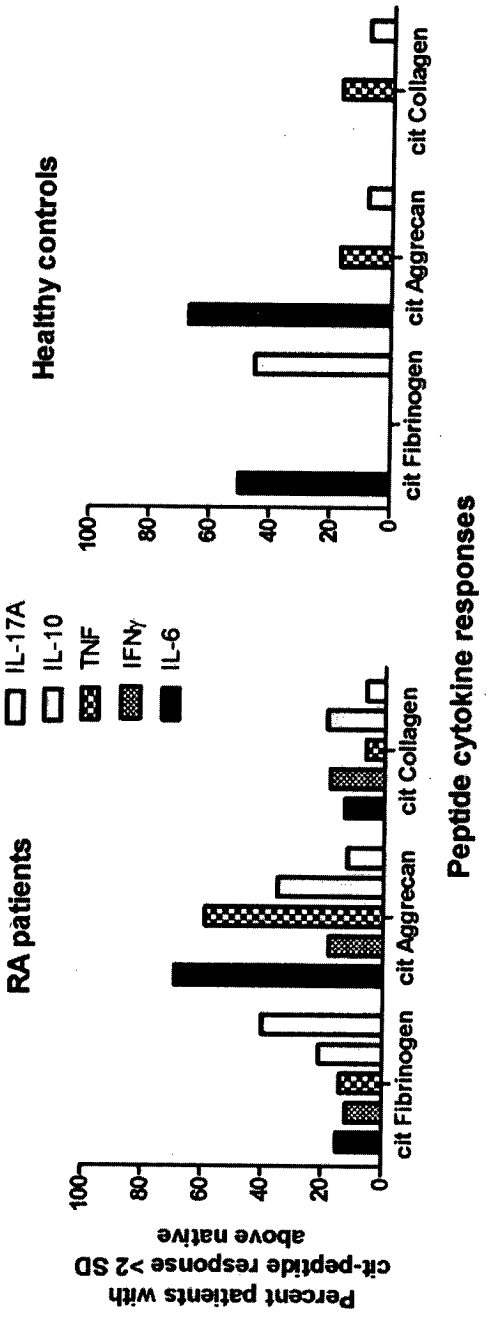

Healthy controls
RA patients
IL-17A
IL-10
TNF
IFNγ
IL-6
Percent patients with cit-peptide response >2 SD above native
0
20
40
60
80
100
cit Fibrinogen
cit Aggrecan
cit Collagen
Peptide cytokine responses

FIGURE 4

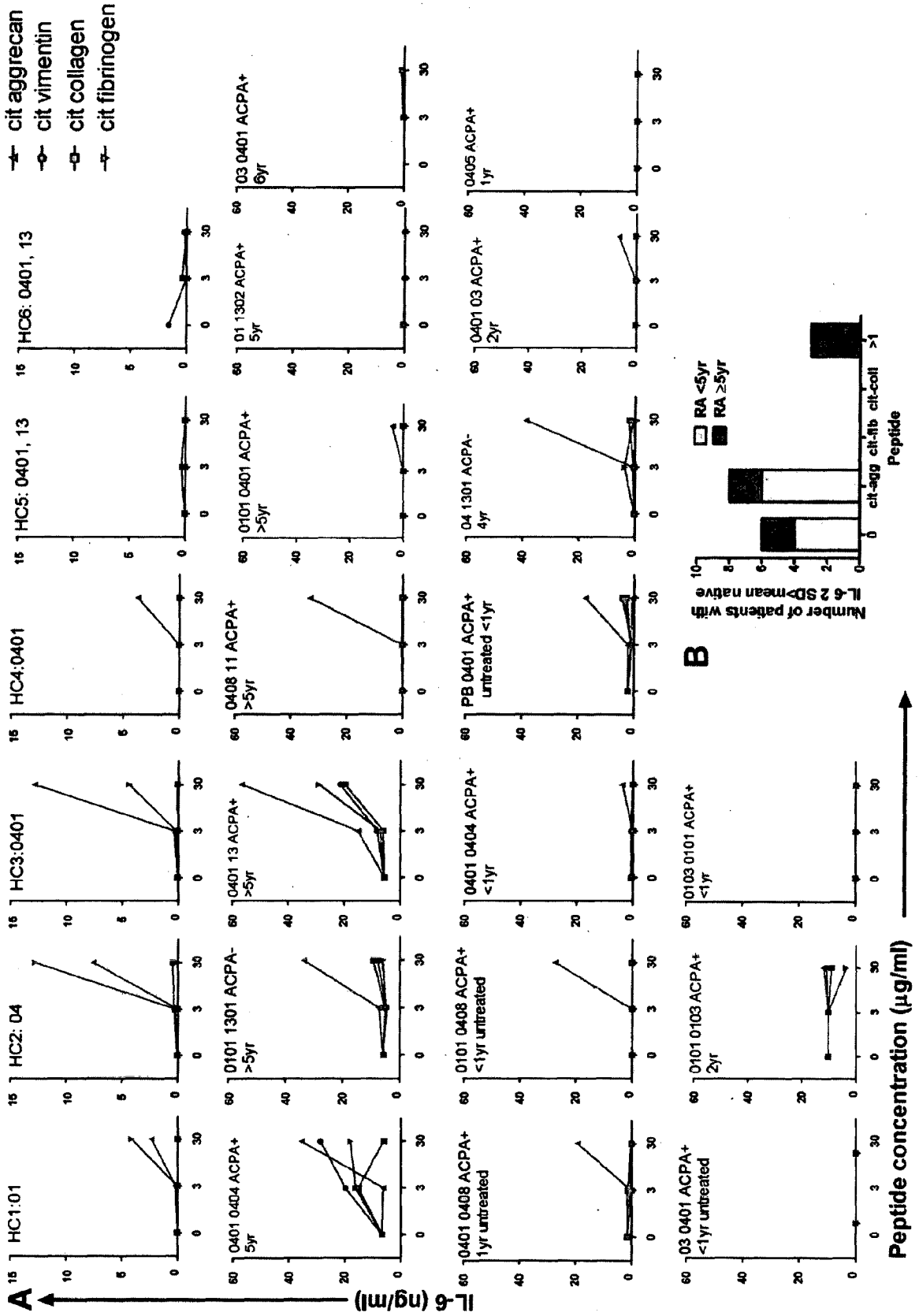

A
IL-6 (ng/ml)
cit aggrecan
cit vimentin
cit collagen
cit fibrinogen
HC1:01
HC2: 04
HC3:0401
HC4:0401
HC5: 0401, 13
HC6: 0401, 13
0401 0404 ACPA+ 5yr
0101 1301 ACPA- >5yr
0401 13 ACPA+ >5yr
0408 11 ACPA+ >5yr
0101 0401 ACPA+ >5yr
01 1302 ACPA+ 5yr
03 0401 ACPA+ 6yr
0401 0408 ACPA+ 1yr untreated
0101 0408 ACPA+ <1yr untreated
0401 0404 ACPA+ <1yr
PB 0401 ACPA+ untreated <1yr
04 1301 ACPA- 4yr
0401 03 ACPA+ 2yr
0405 ACPA+ 1yr
03 0401 ACPA+ <1yr untreated
0101 0103 ACPA+ 2yr
0103 0101 ACPA+ <1yr
Peptide concentration (µg/ml)
B
RA <5yr
RA ≥5yr
Number of patients with IL-6 2 SD>mean naive
cit-agg
cit-fib
cit-coll
>1
Peptide

FIGURE 5

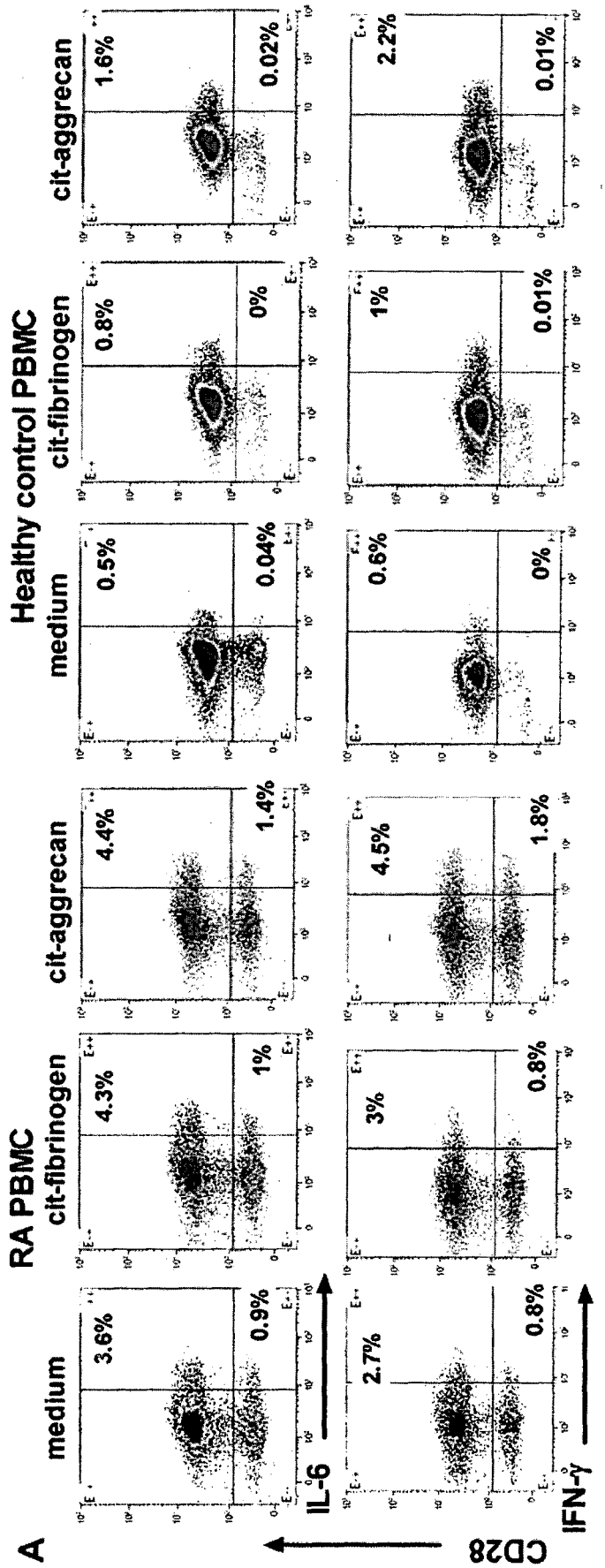

A
RA PBMC
Healthy control PBMC
medium
cit-fibrinogen
cit-aggrecan
3.6%
0.9%
4.3%
1%
4.4%
1.4%
0.5%
0.04%
0.8%
0%
1.6%
0.02%
2.7%
0.8%
3%
0.8%
4.5%
1.8%
0.6%
0%
1%
0.01%
2.2%
0.01%
IL-6
IFN-γ
CD28

FIGURE 6

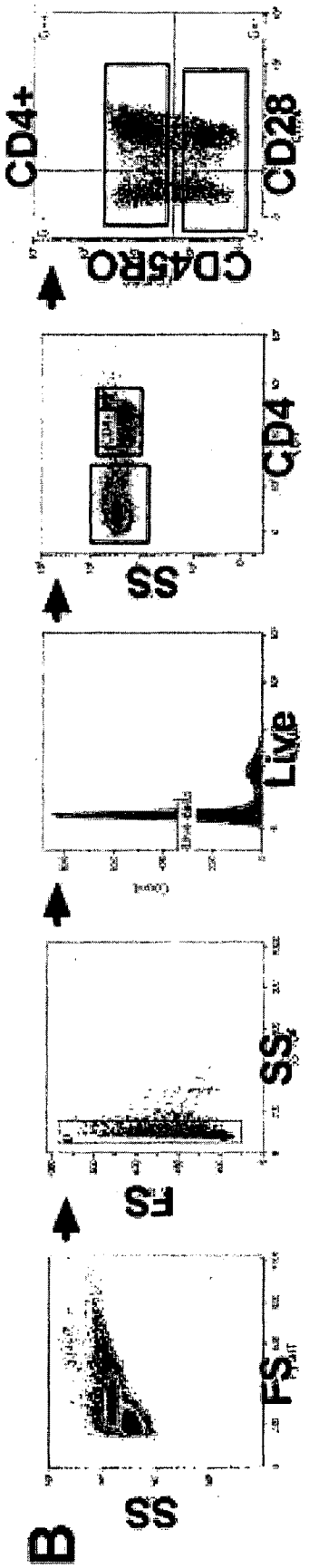



FIGURE 6 continued

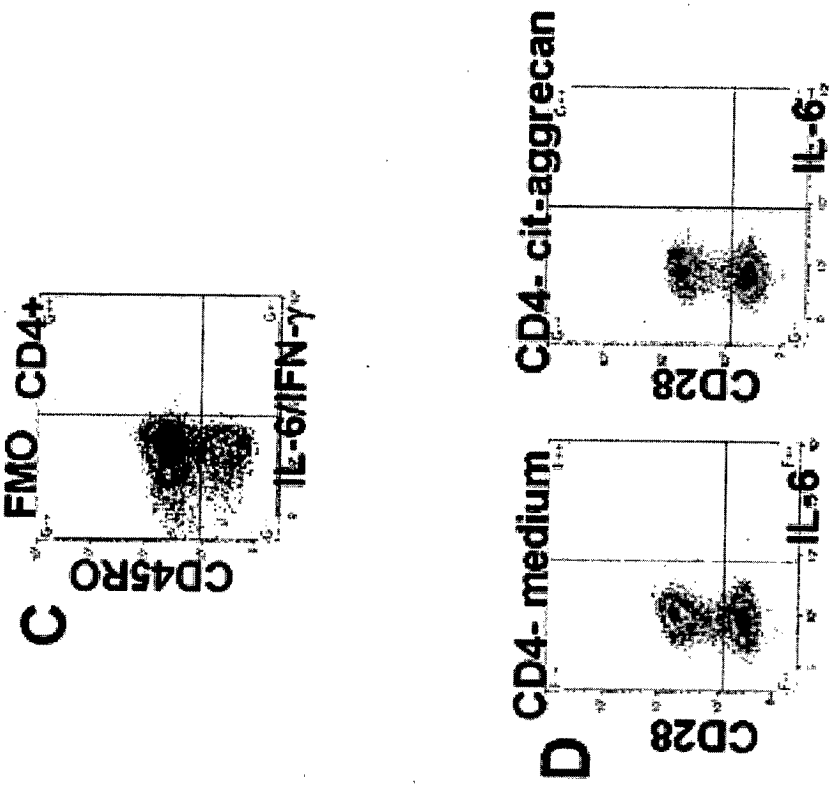



FIGURE 6 continued

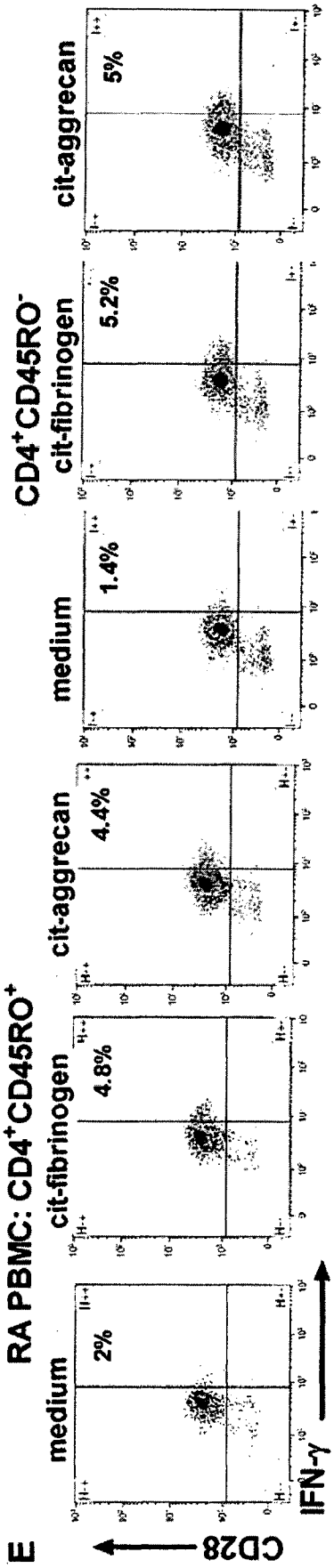



FIGURE 6 continued

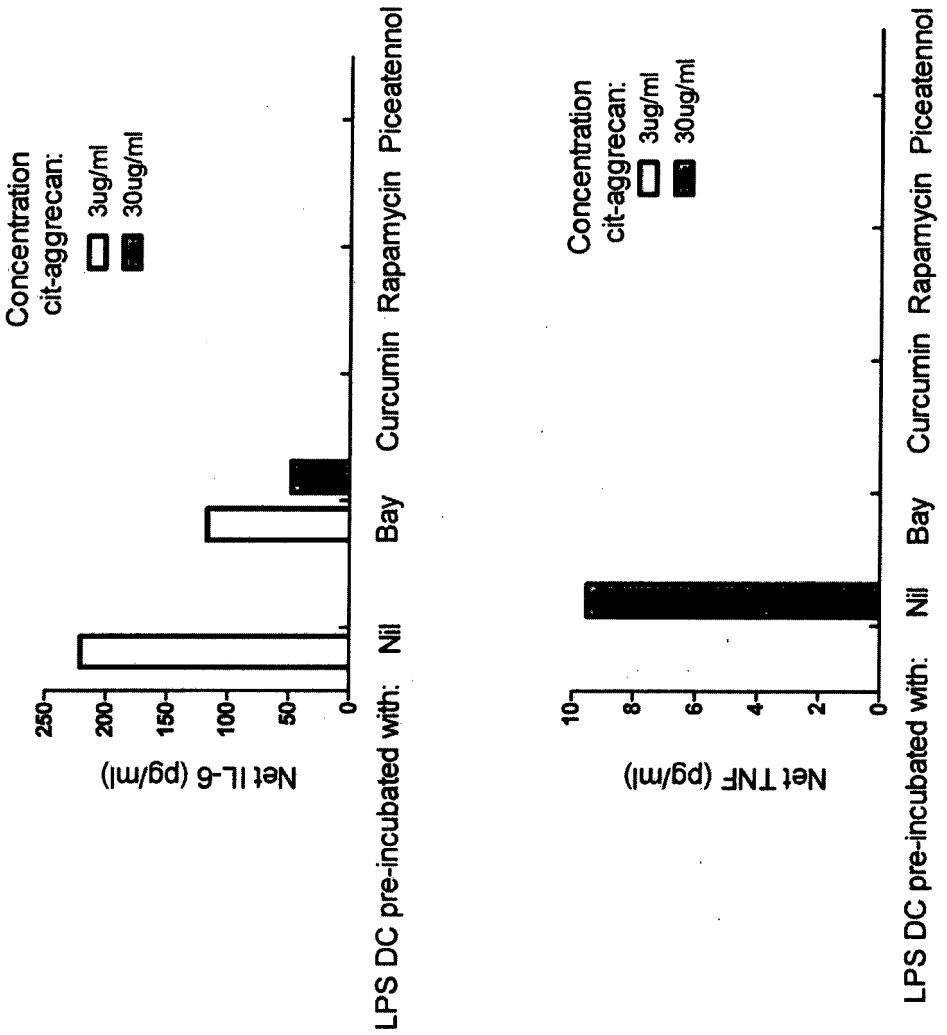

Concentration
cit-aggrecan:
3ug/ml
30ug/ml
Net IL-6 (pg/ml)
250
200
150
100
50
0
LPS DC pre-incubated with:
Nil
Bay
Curcumin
Rapamycin
Piceatennol
Concentration
cit-aggrecan:
3ug/ml
30ug/ml
Net TNF (pg/ml)
10
8
6
4
2
0
LPS DC pre-incubated with:
Nil
Bay
Curcumin
Rapamycin
Piceatennol

FIGURE 7

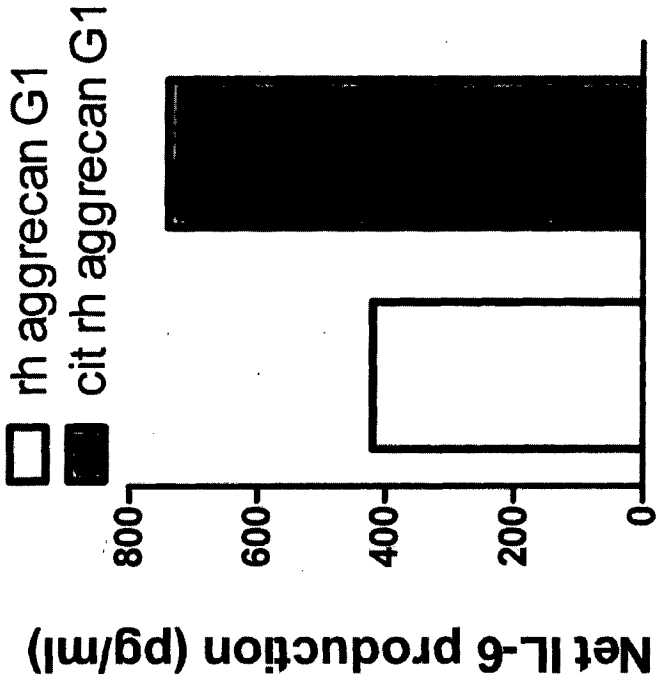

rh aggrecan G1
cit rh aggrecan G1
800
600
400
200
0
Net IL-6 production (pg/ml)

FIGURE 8

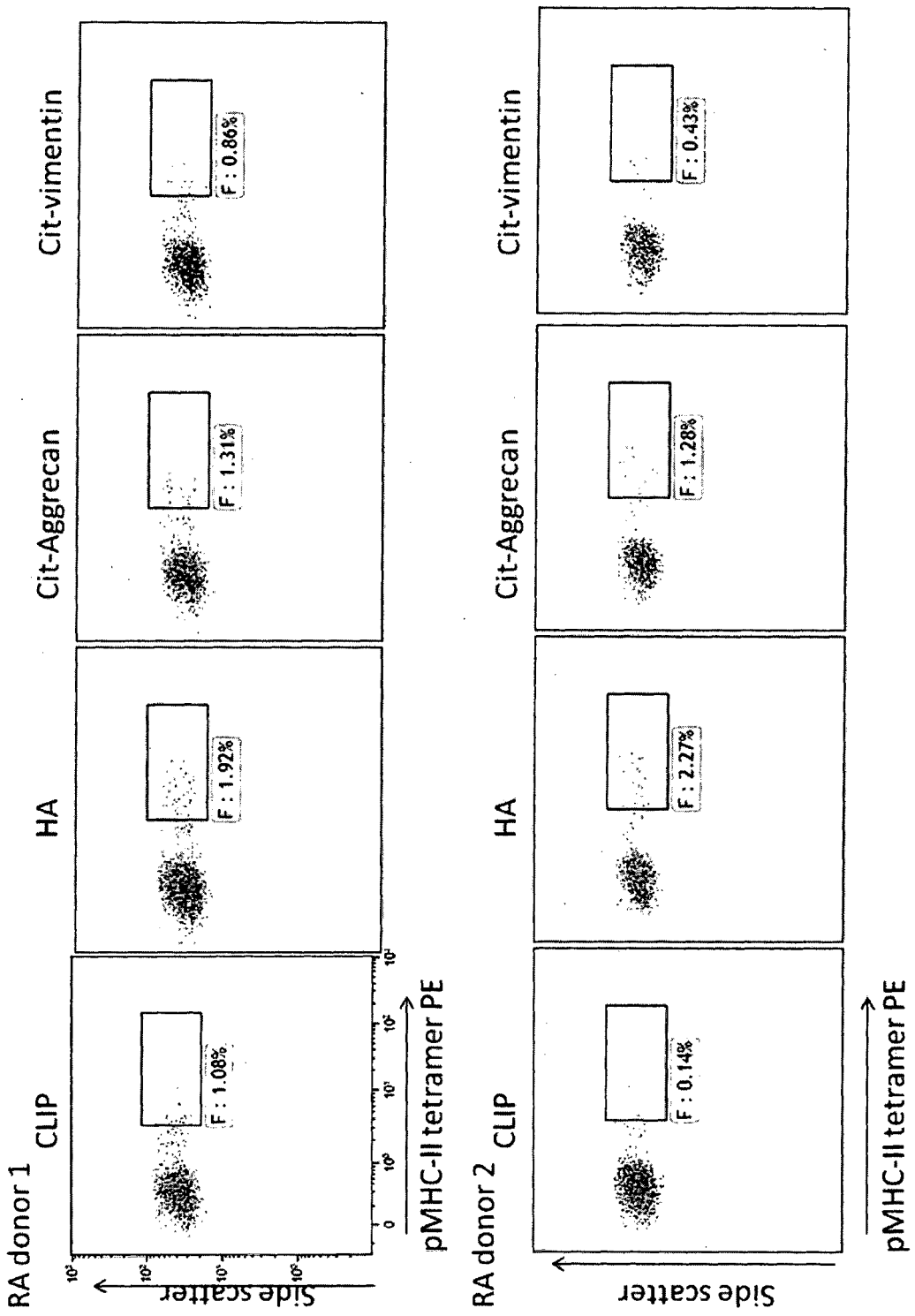

RA donor 1
CLIP
HA
Cit-Aggrecan
Cit-vimentin
F : 1.08%
F : 1.92%
F : 1.31%
F : 0.86%
Side scatter
pMHC-II tetramer PE
RA donor 2
CLIP
HA
Cit-Aggrecan
Cit-vimentin
F : 0.14%
F : 2.27%
F : 1.28%
F : 0.43%
Side scatter
pMHC-II tetramer PE

FIGURE 9

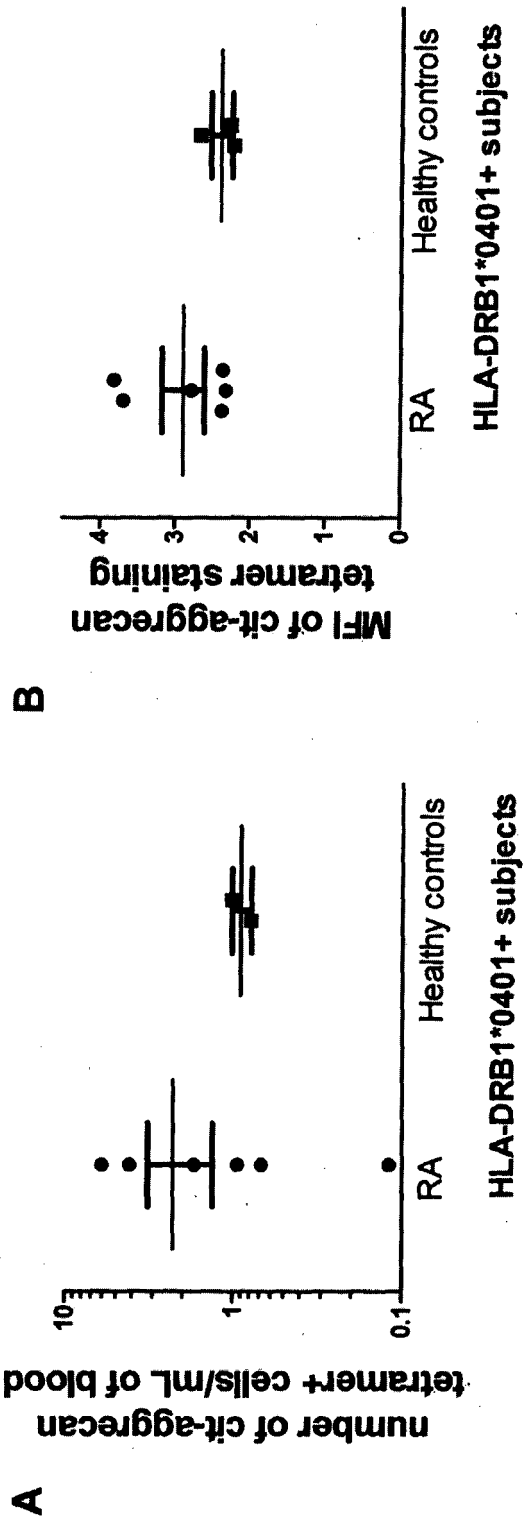

A
number of cit-aggrecan tetramer+ cells/mL of blood
10
1
0.1
RA
Healthy controls
HLA-DRB1*0401+ subjects
B
MFI of cit-aggrecan tetramer staining
4
3
2
1
0
RA
Healthy controls
HLA-DRB1*0401+ subjects

FIGURE 10