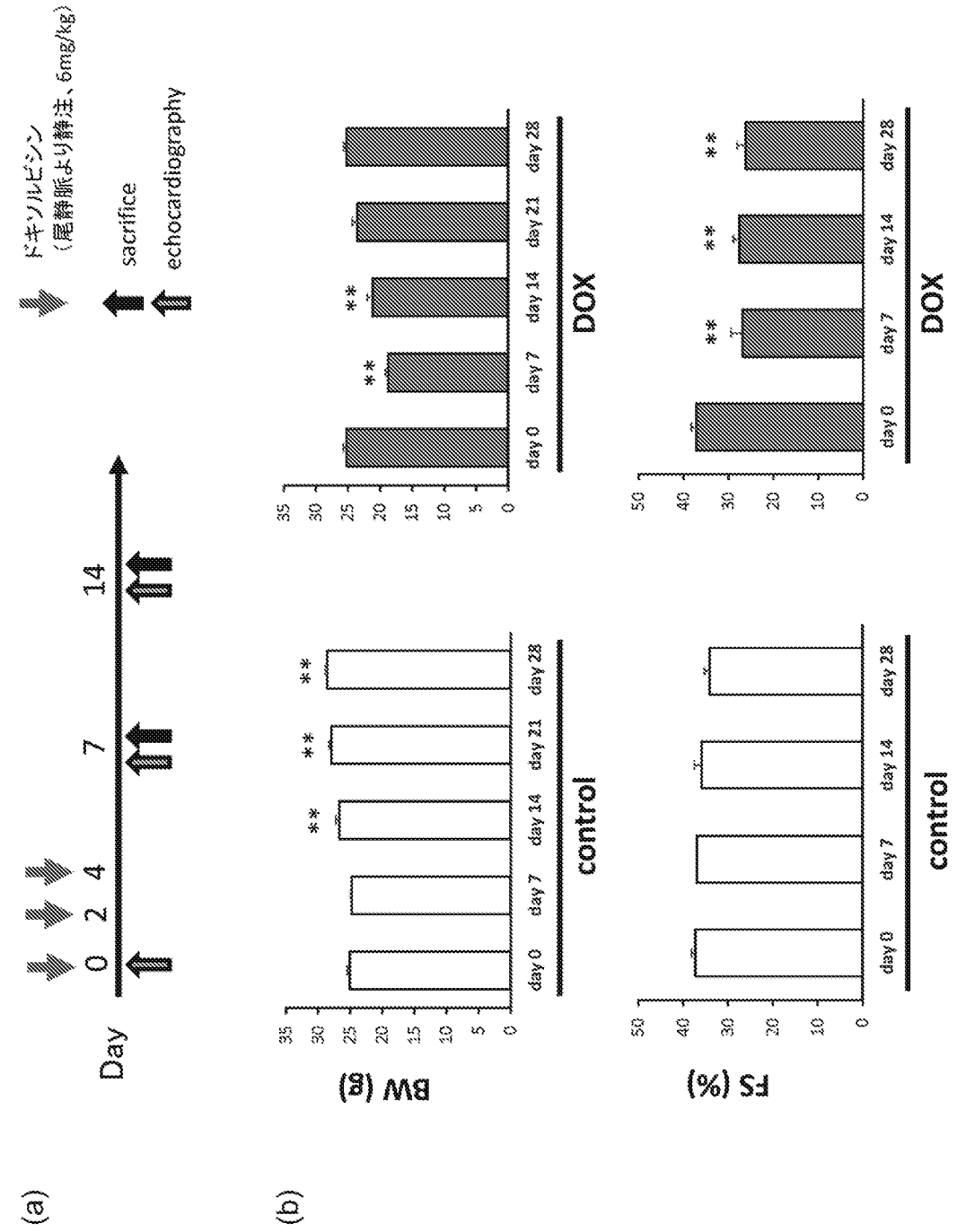
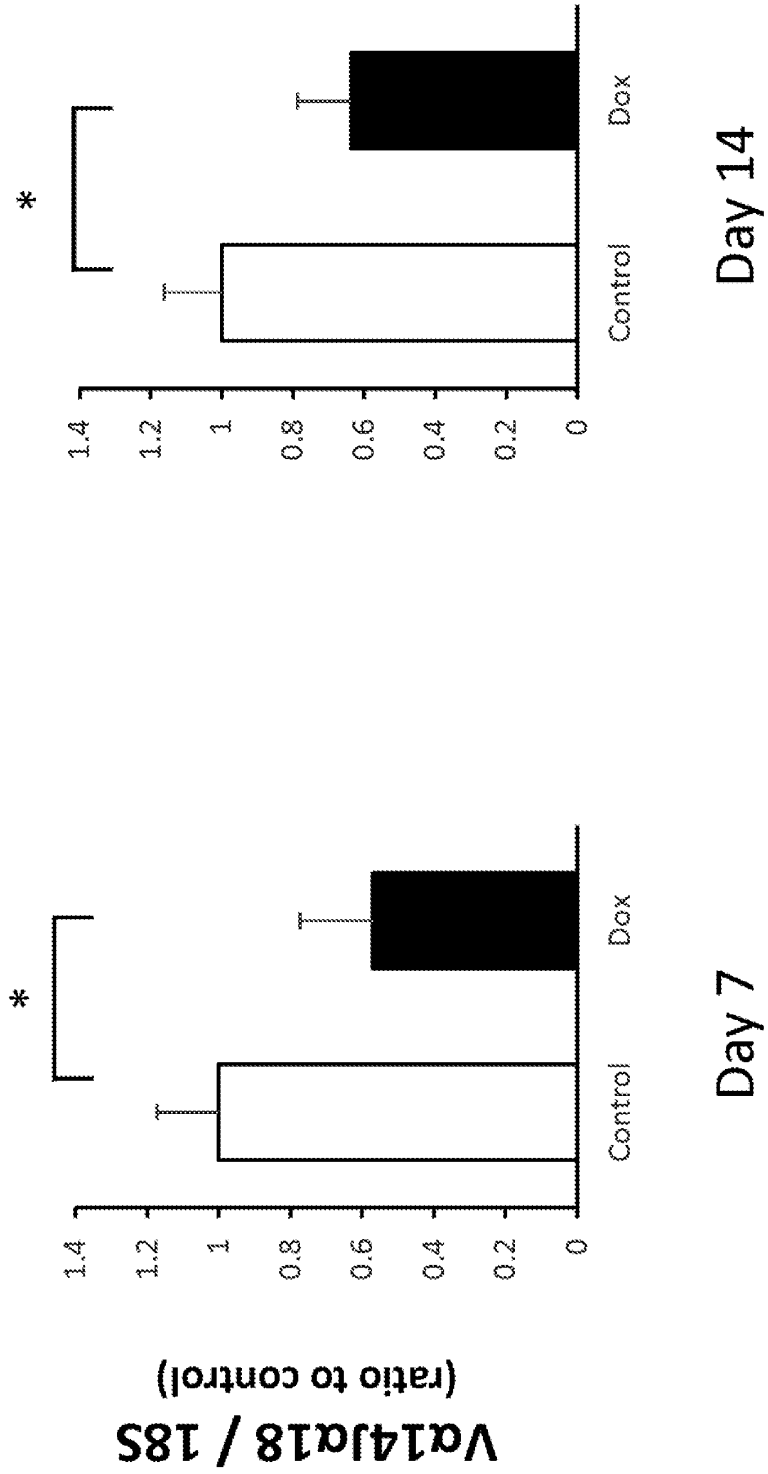
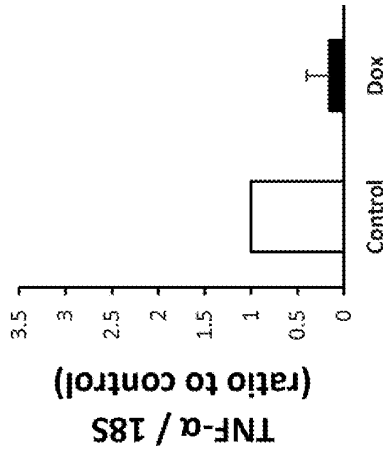
[図1]

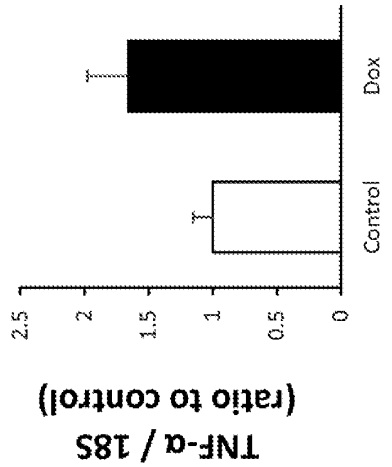

(a)
ドキソルビシン
（尾静脈より静注、6mg/kg）
sacrifice
echocardiography
Day
0
2
4
7
14
(b)
BW (g)
FS (%)
control
DOX
day 0
day 7
day 14
day 21
day 28
**

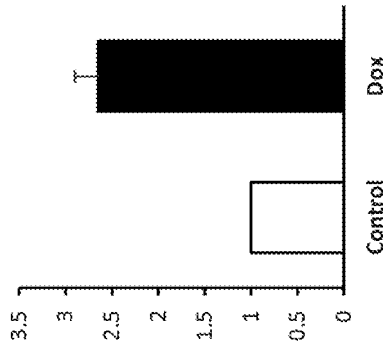
[図2]

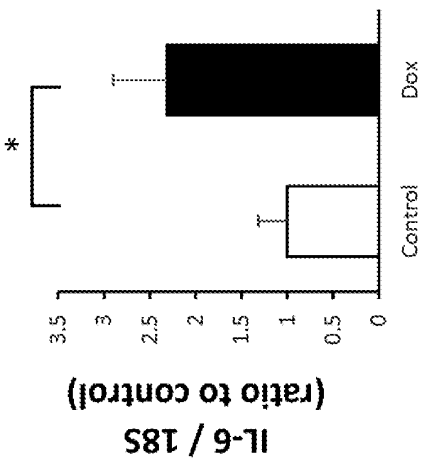

Vα14Jα18 / 18S
(ratio to control)
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Control
Dox
*
Day 7
Day 14

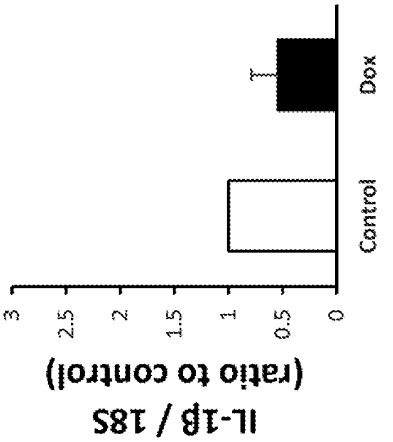
[図3]

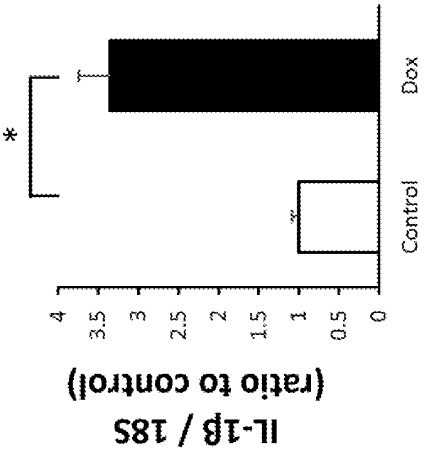

TNF-α / 18S
(ratio to control)
3.5
3
2.5
2
1.5
1
0.5
0
Control
Dox


TNF-α / 18S
(ratio to control)
2.5
2
1.5
1
0.5
0
Control
Dox

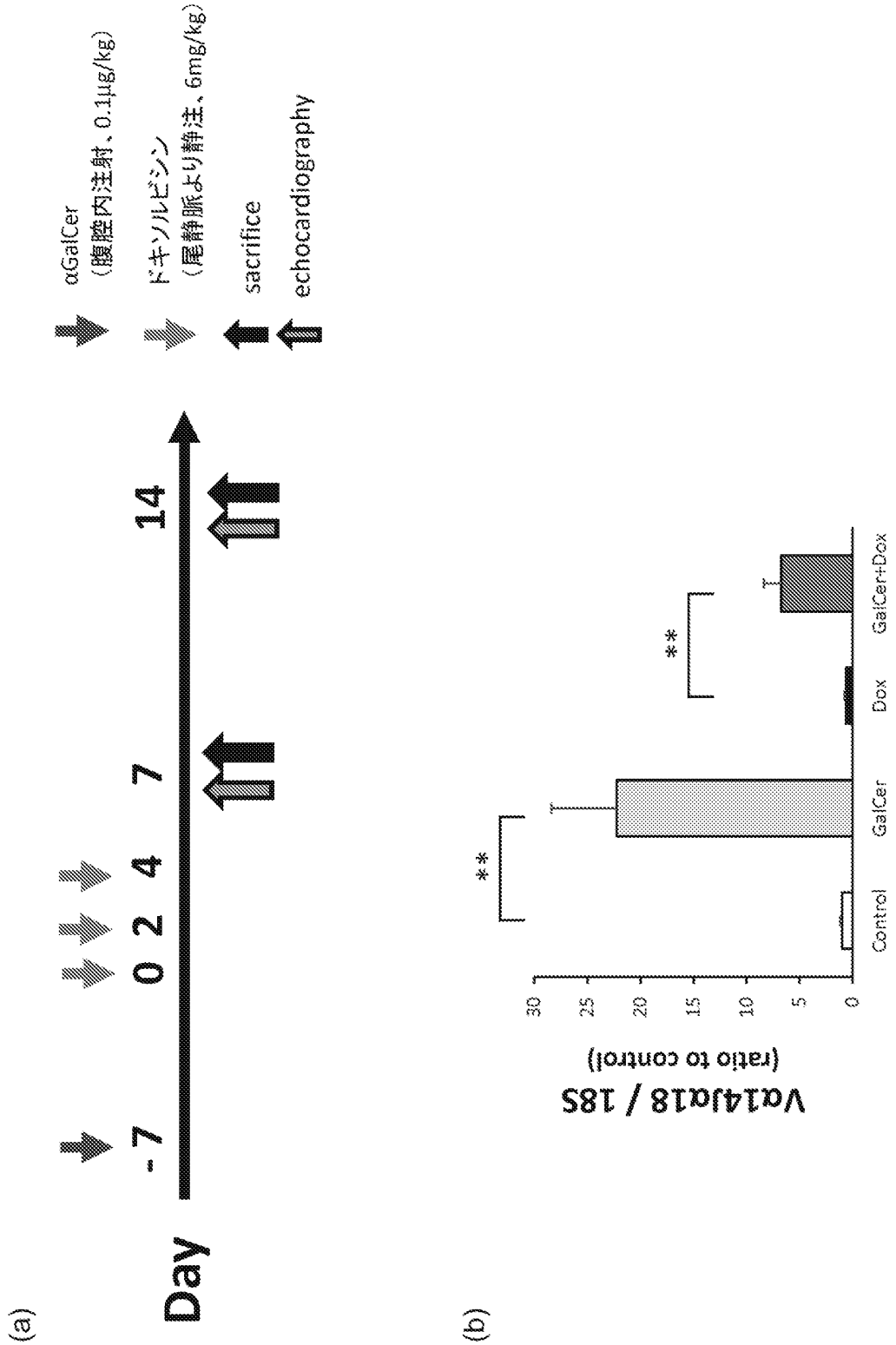

IL-6 / 18S
(ratio to control)
3.5
3
2.5
2
1.5
1
0.5
0
Control
Dox


IL-6 / 18S
(ratio to control)
*
3.5
3
2.5
2
1.5
1
0.5
0
Control
Dox

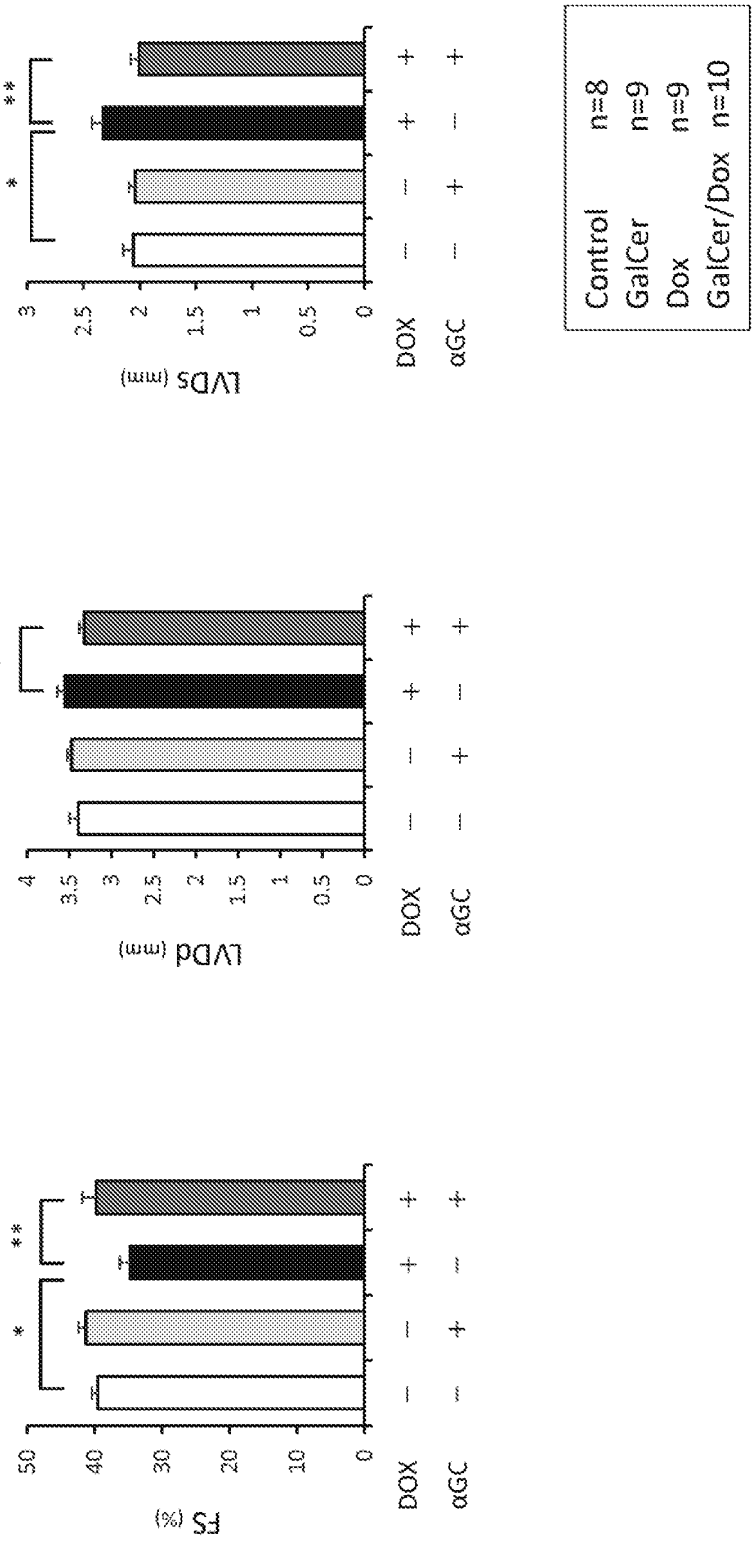

IL-1β / 18S
(ratio to control)
3
2.5
2
1.5
1
0.5
0
Control
Dox


IL-1β / 18S
(ratio to control)
*
4
3.5
3
2.5
2
1.5
1
0.5
0
Control
Dox

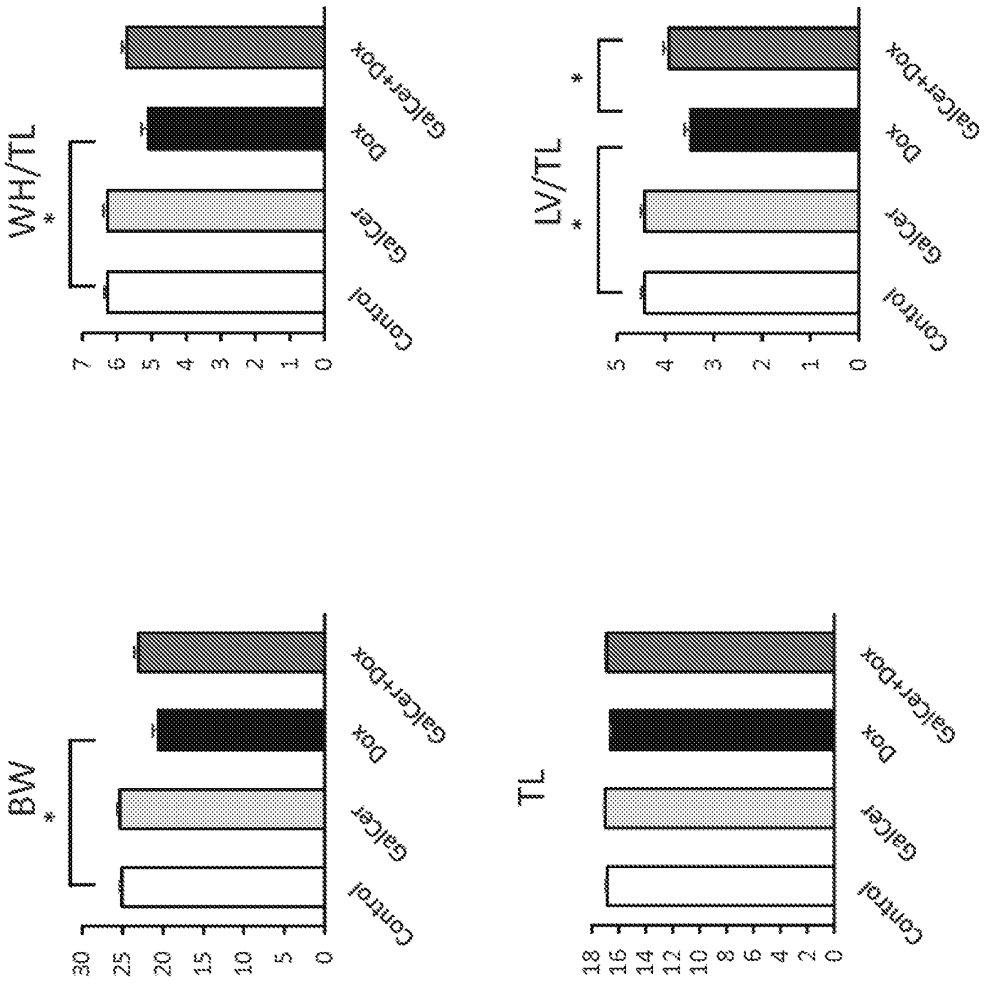
[図4]


(a)
Day
-7
0
2
4
7
14
αGalCer
（腹腔内注射、0.1μg/kg）
ドキソルビシン
（尾静脈より静注、6mg/kg）
sacrifice
echocardiography
(b)
Vα14Jα18 / 18S
(ratio to control)
30
25
20
15
10
5
0
**
**
Control
GalCer
Dox
GalCer+Dox

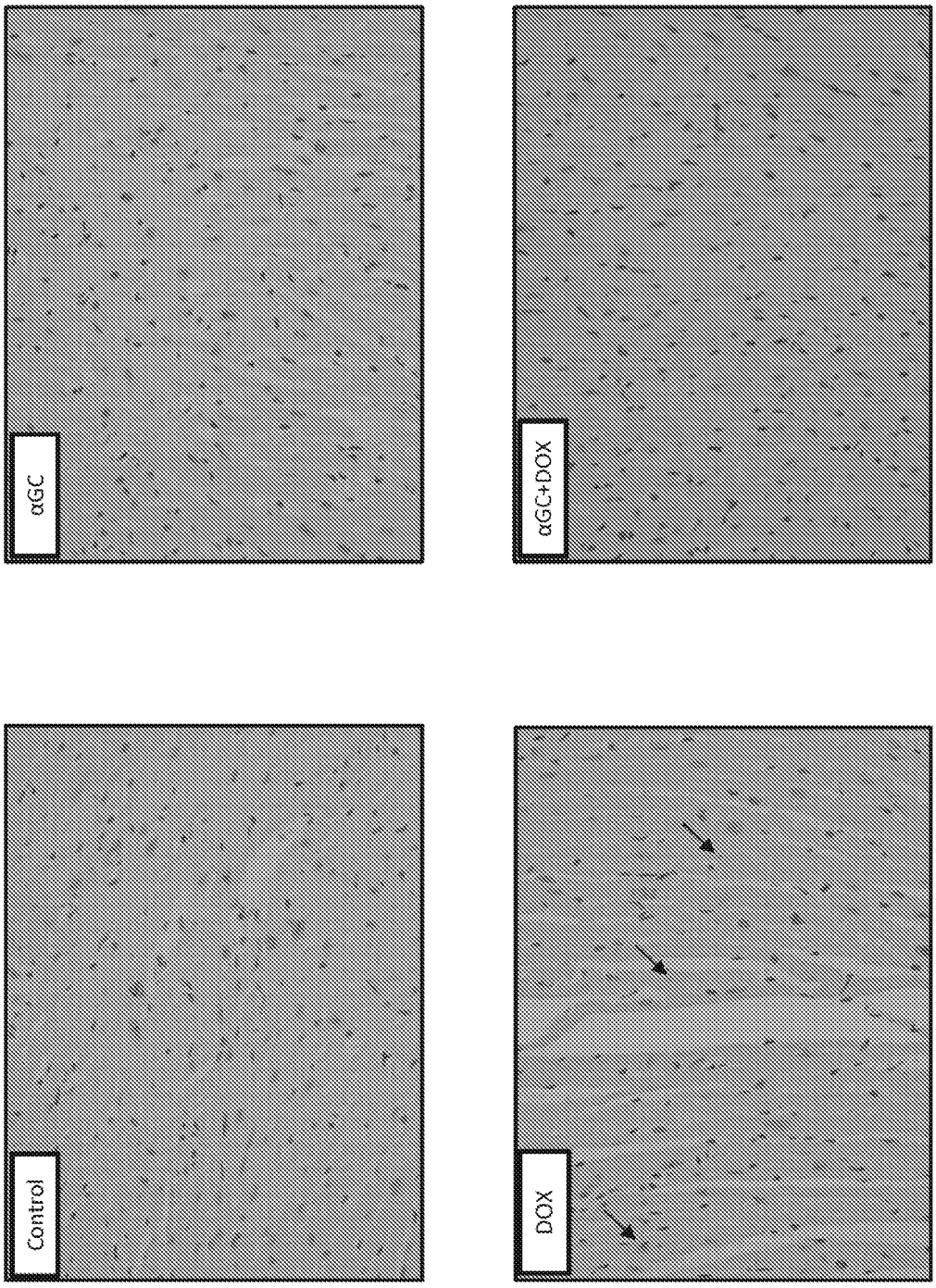
[図5]


Control n=8
GalCer n=9
Dox n=9
GalCer/Dox n=10
LVDs (mm)
LVDd (mm)
FS (%)
DOX
αGC
*
**

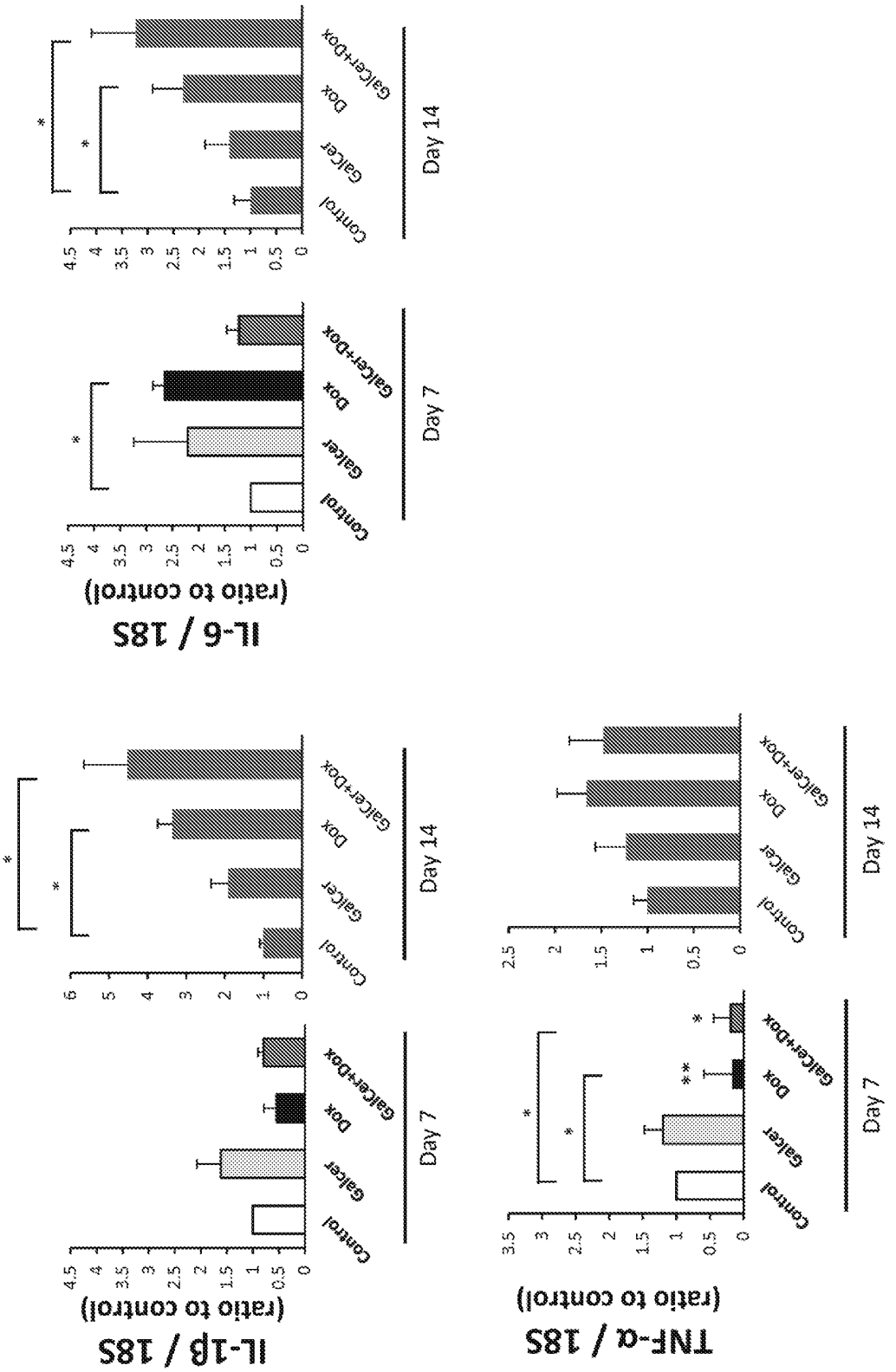
[図6]


BW
*
0
5
10
15
20
25
30
Control
Galcer
Dox
Galcer+Dox
TL
0
2
4
6
8
10
12
14
16
18
Control
Galcer
Dox
Galcer+Dox
LV/TL
*
0
1
2
3
4
5
Control
Galcer
Dox
Galcer+Dox
WH/TL
*
0
1
2
3
4
5
6
7
Control
Galcer
Dox
Galcer+Dox

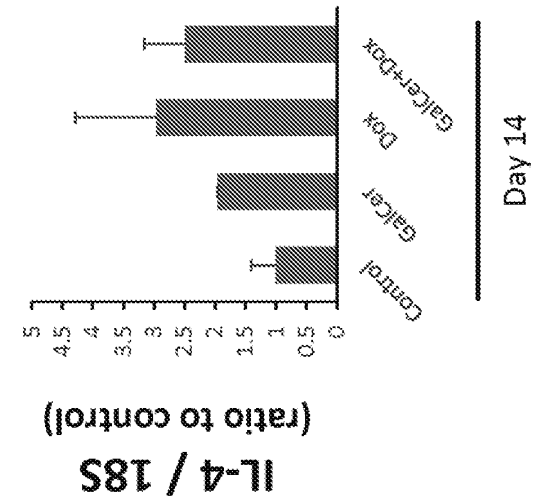
[図7]

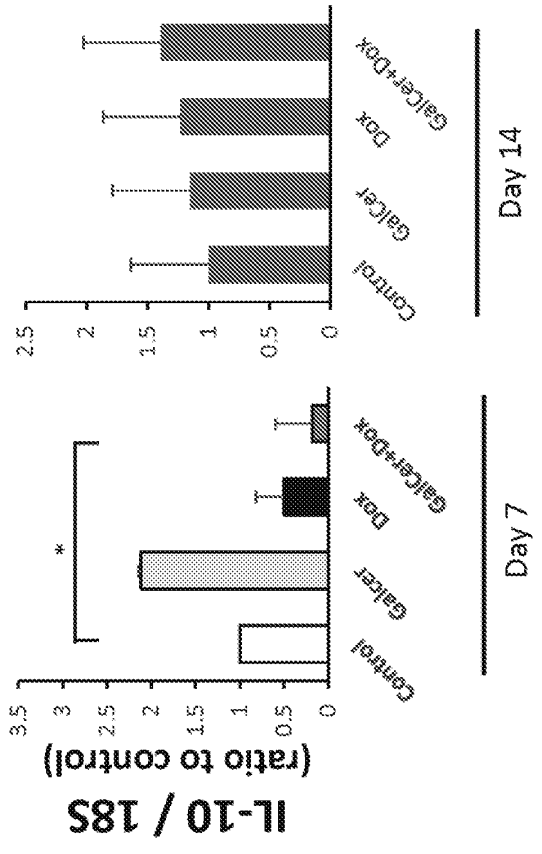


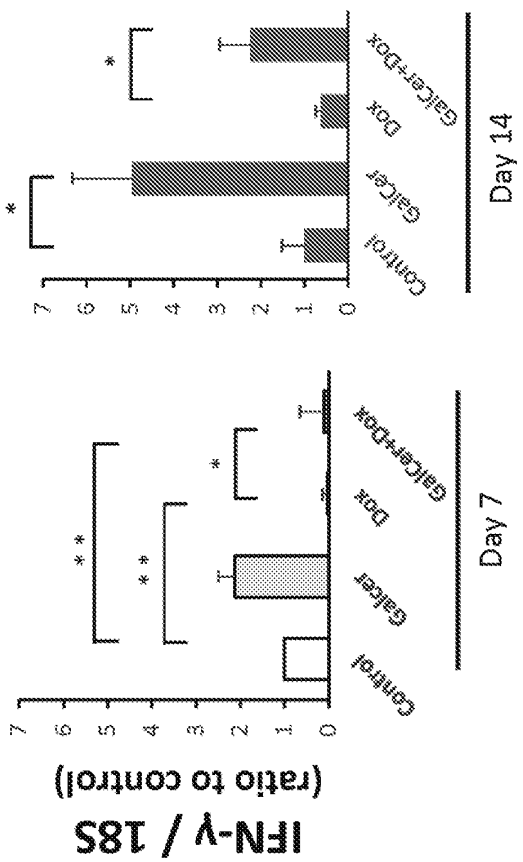
[図8]


IL-6 / 18S
(ratio to control)
Day 7
Day 14
Control
Galcer
Dox
Galcer+Dox
IL-1β / 18S
(ratio to control)
TNF-α / 18S
(ratio to control)

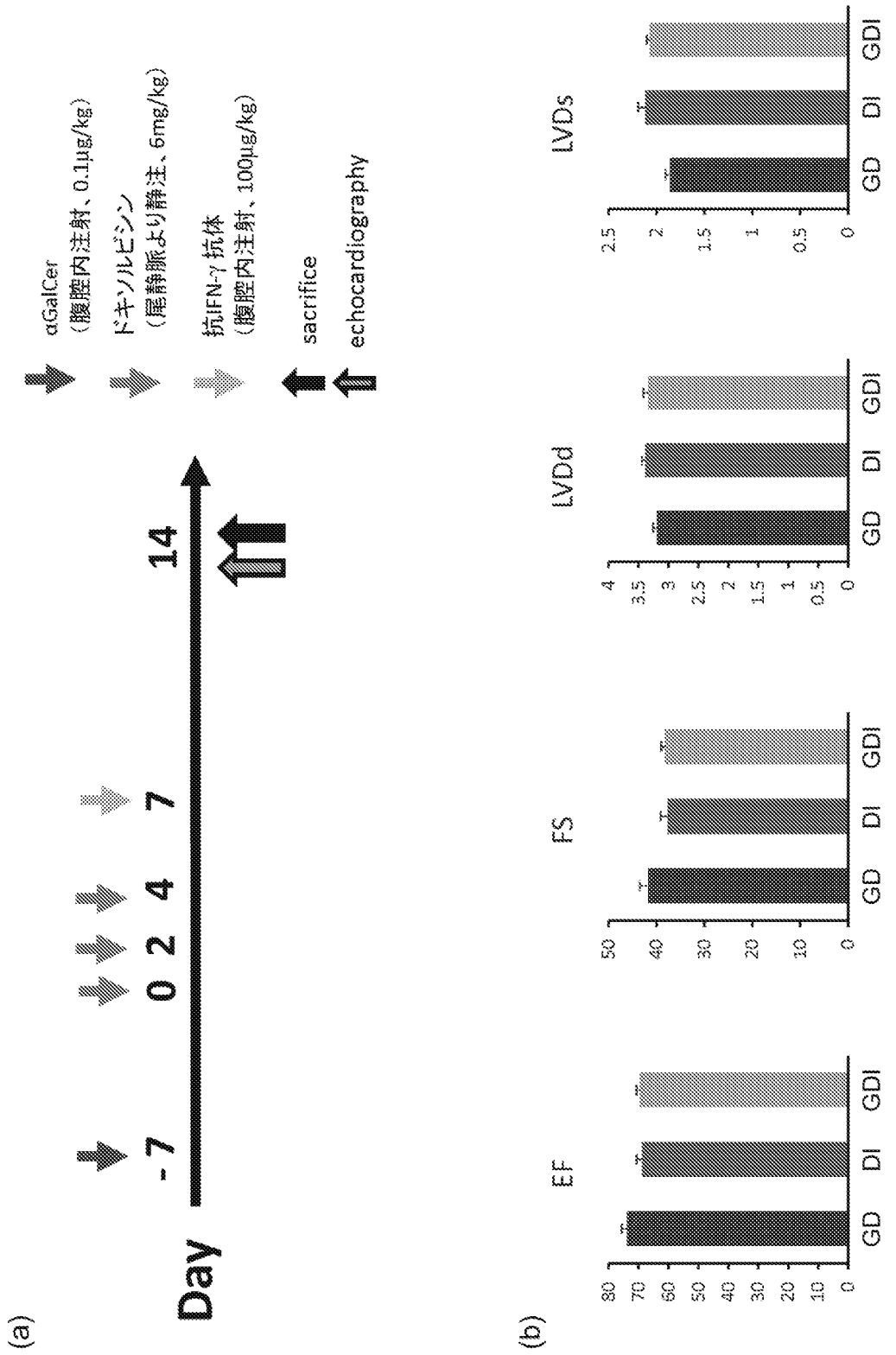
[図9]


IL-4 / 18S
(ratio to control)
Day 14
Control
Galcer
Dox
Galcer+Dox

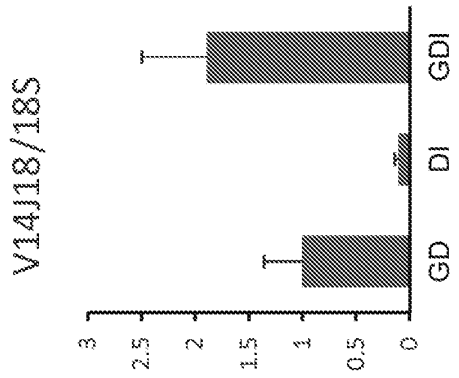

IL-10 / 18S
(ratio to control)
Day 7
Day 14
Control
Galcer
Dox
Galcer+Dox

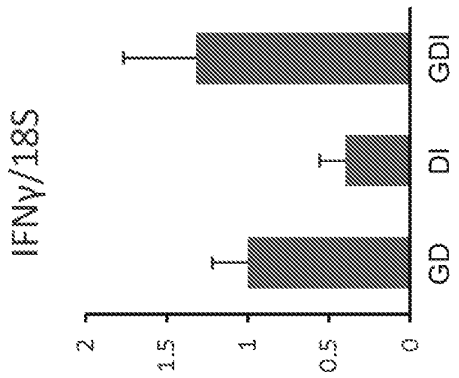

IFN-γ / 18S
(ratio to control)
Day 7
Day 14
Control
Galcer
Dox
Galcer+Dox

[図10]

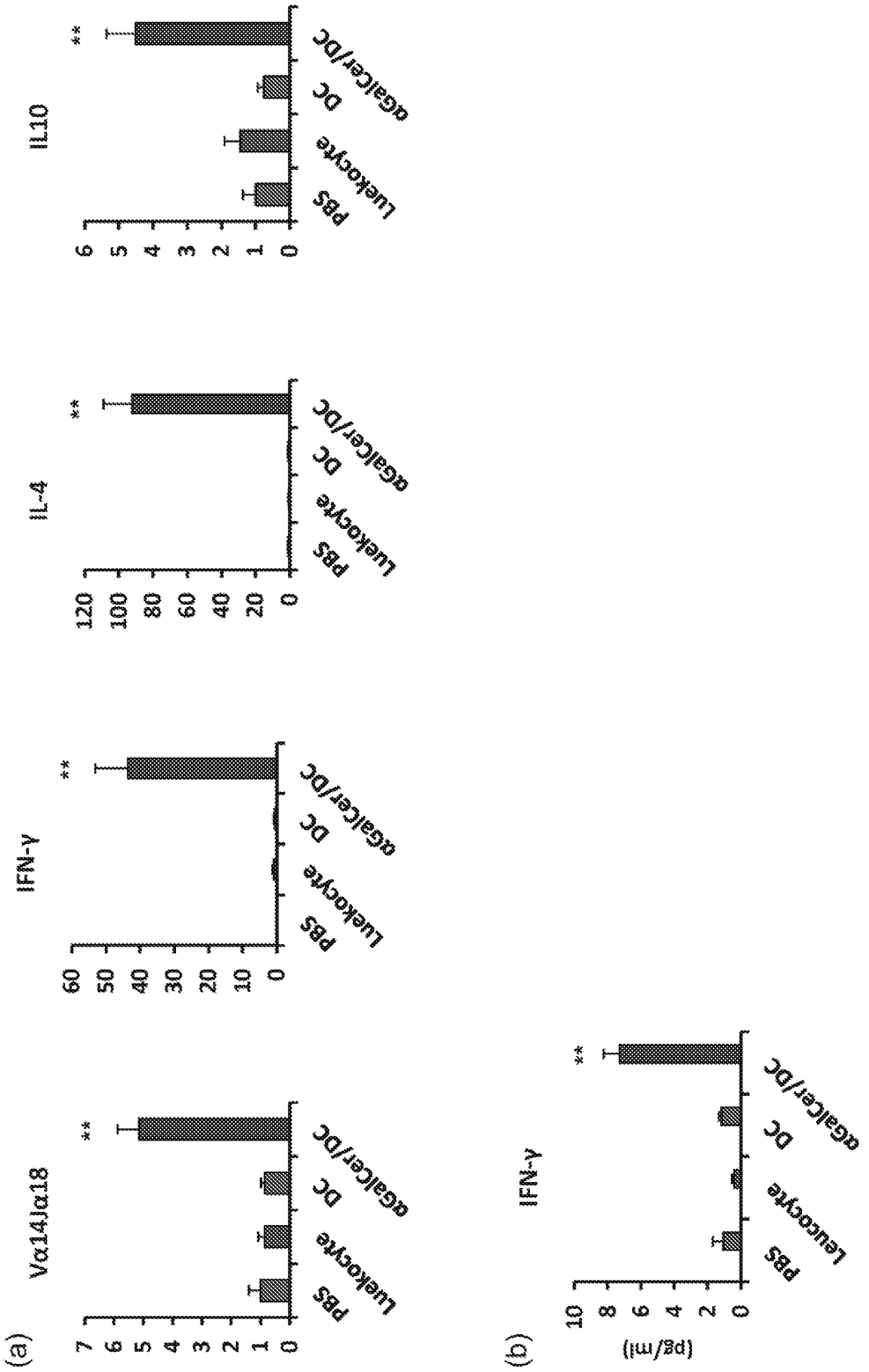

(a)
Day
-7
0
2
4
7
14
αGalCer
（腹腔内注射、0.1μg/kg）
ドキソルビシン
（尾静脈より静注、6mg/kg）
抗IFN-γ抗体
（腹腔内注射、100μg/kg）
sacrifice
echocardiography
(b)
EF
FS
LVDd
LVDs
GD
DI
GDI

[図11]

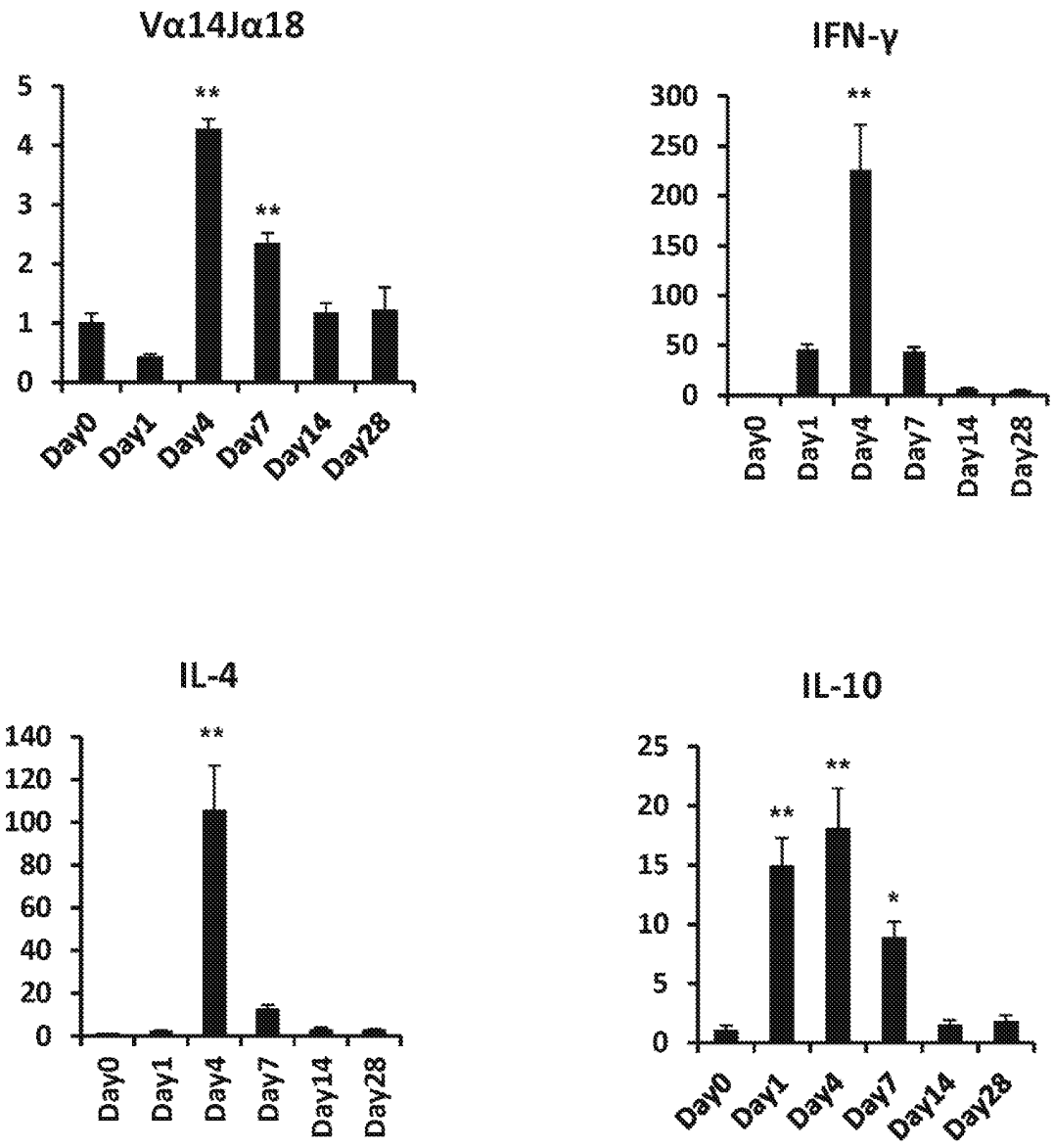




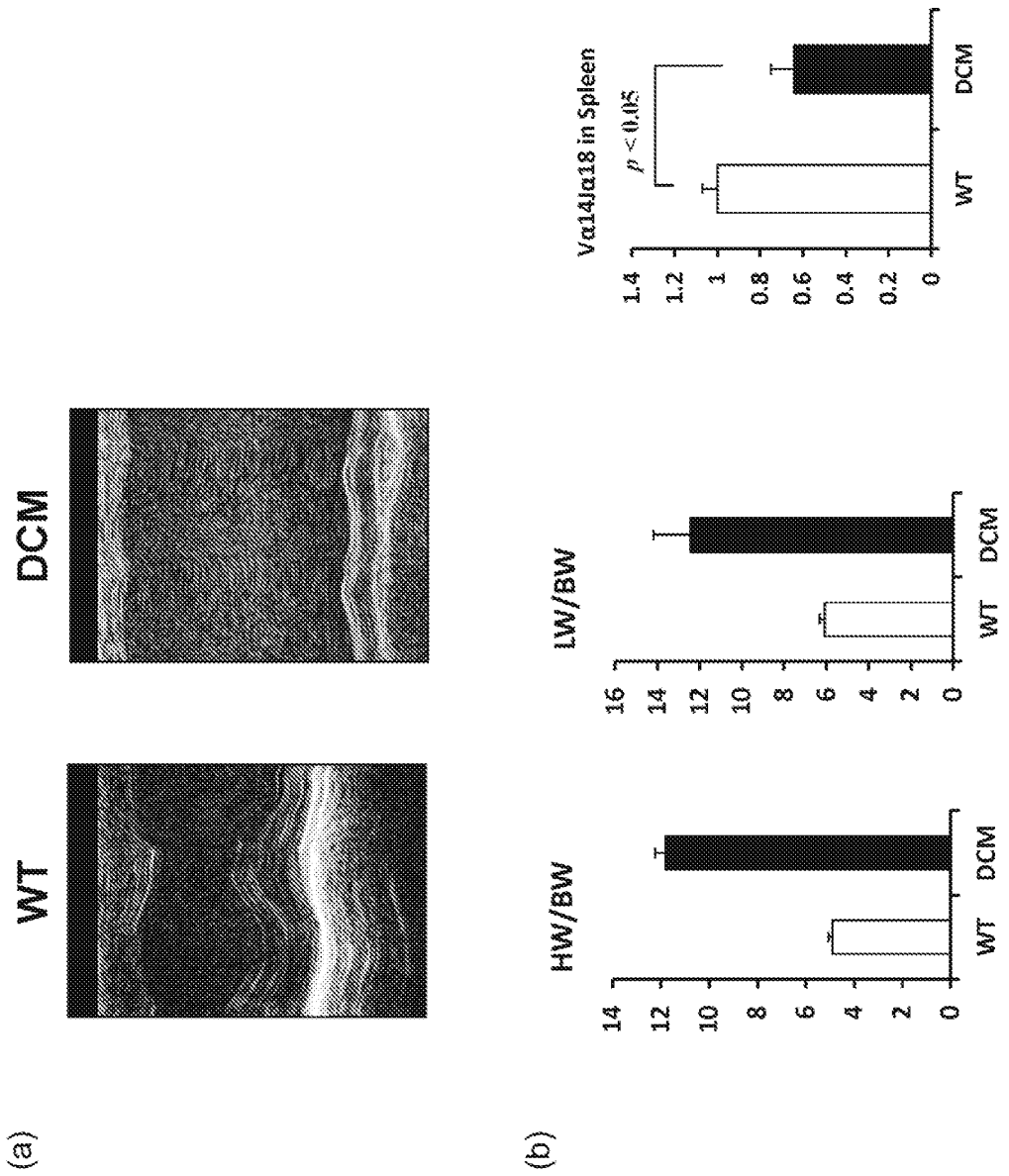
[図12]


(a)
Vα14Jα18
IFN-γ
IL-4
IL10
PBS
Leukocyte
DC
αGalCer/DC
**
(b)
IFN-γ
(pg/ml)
PBS
Leucocyte
DC
αGalCer/DC
**

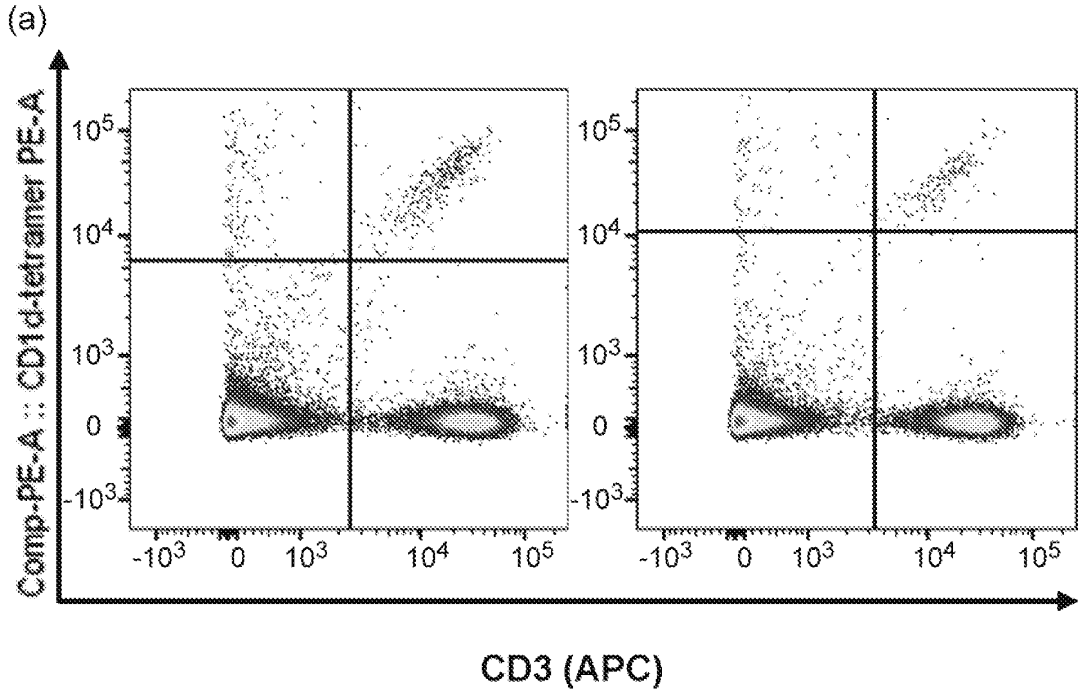
[図13]

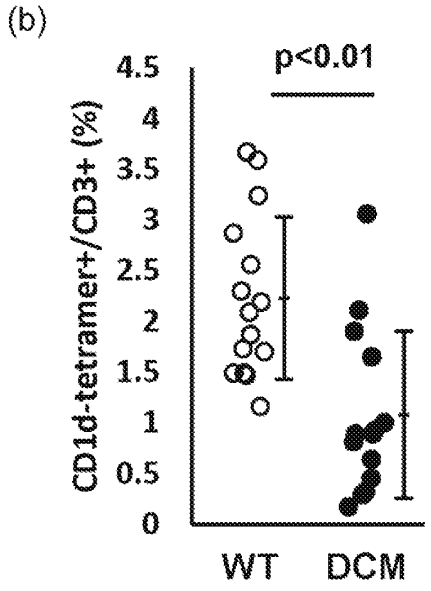

Vα14Jα18
5
4
3
2
1
0
**
**
Day0
Day1
Day4
Day7
Day14
Day28
IFN-γ
300
250
200
150
100
50
0
**
Day0
Day1
Day4
Day7
Day14
Day28
IL-4
140
120
100
80
60
40
20
0
**
Day0
Day1
Day4
Day7
Day14
Day28
IL-10
25
20
15
10
5
0
**
**
*
Day0
Day1
Day4
Day7
Day14
Day28

[図14]

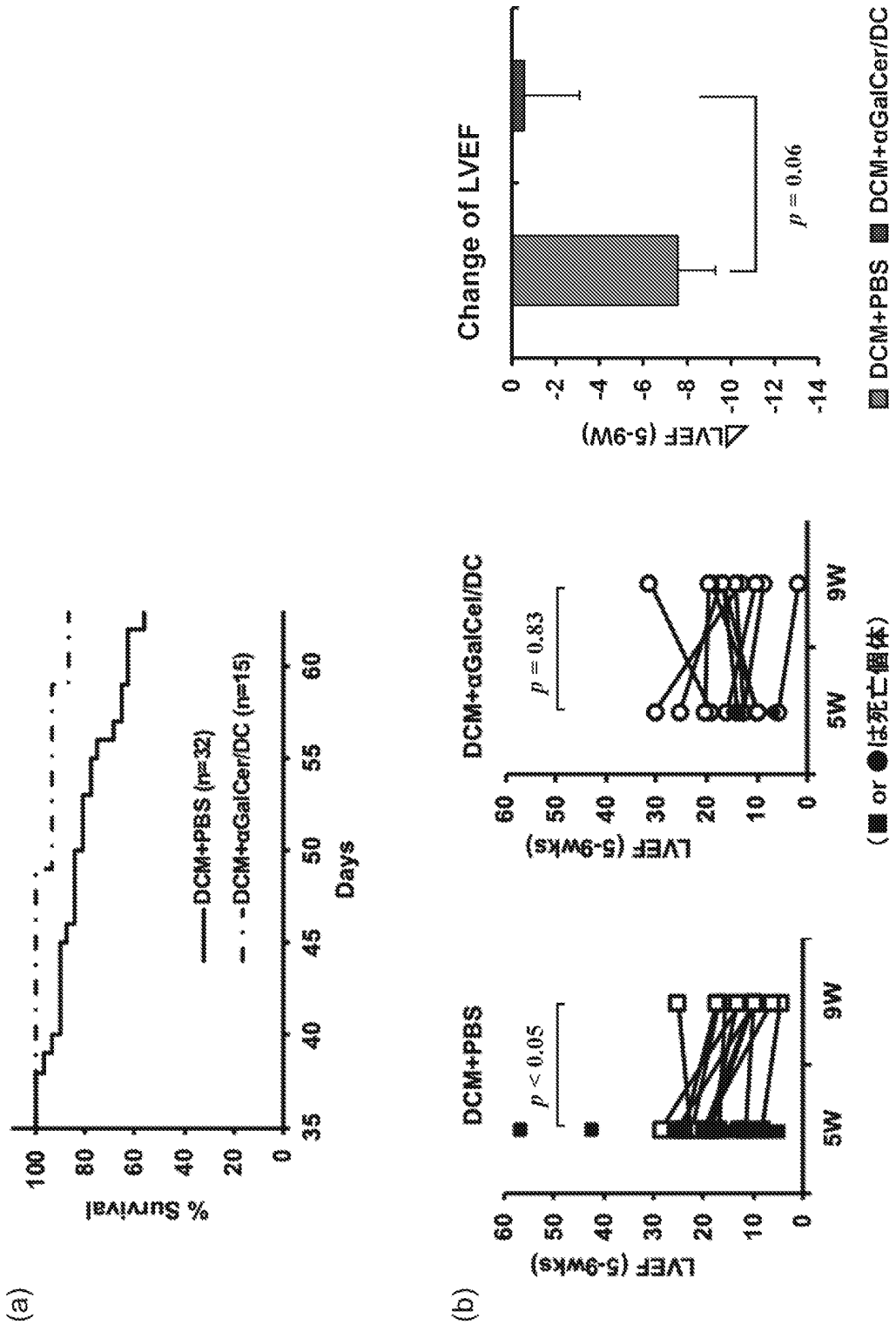


[図15]

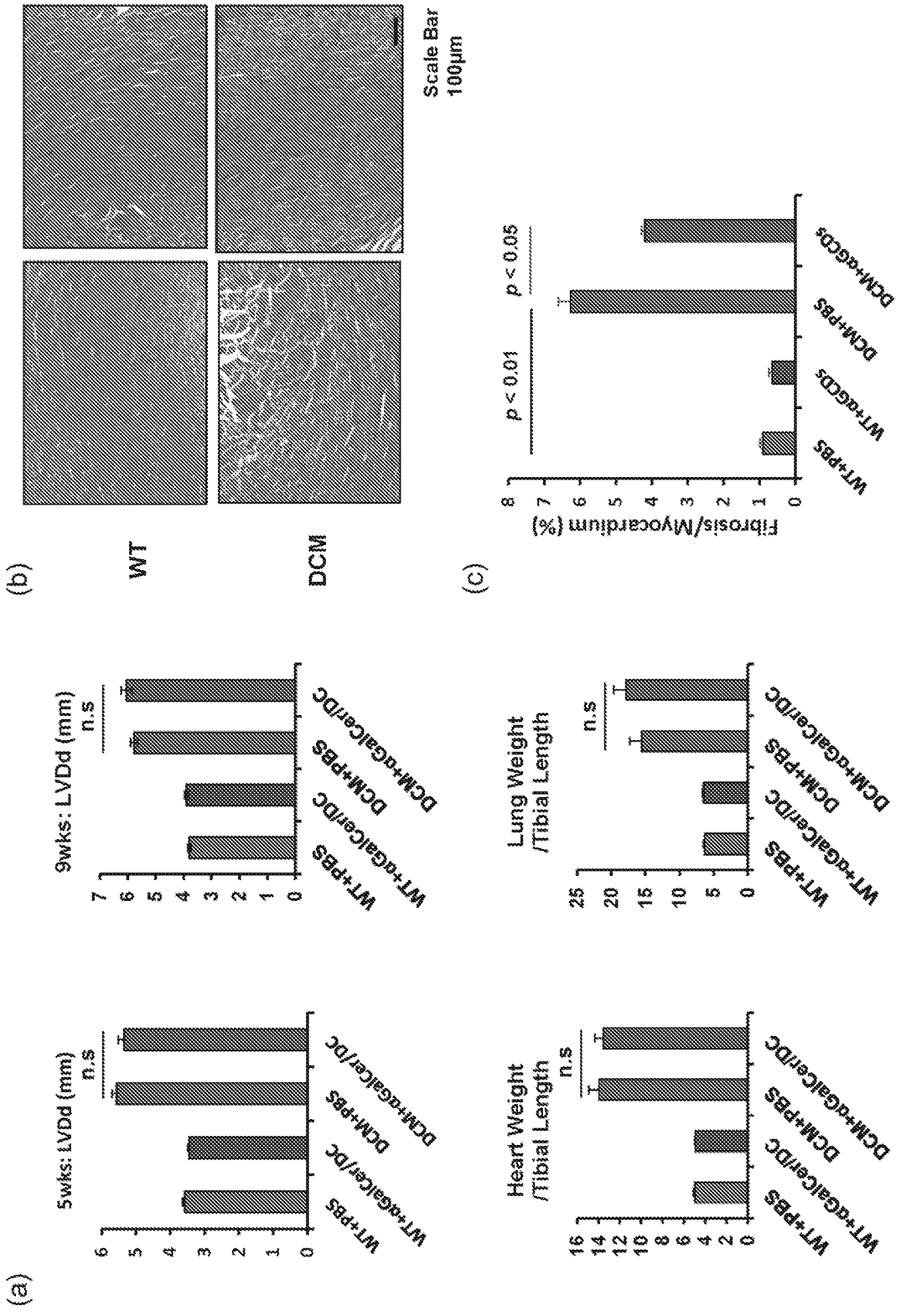

(a)
Comp-PE-A :: CD1d-tetramer PE-A
10^5
10^4
10^3
0
-10^3
-10^3 0 10^3 10^4 10^5
CD3 (APC)


(b)
p<0.01
CD1d-tetramer+/CD3+ (%)
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
WT
DCM

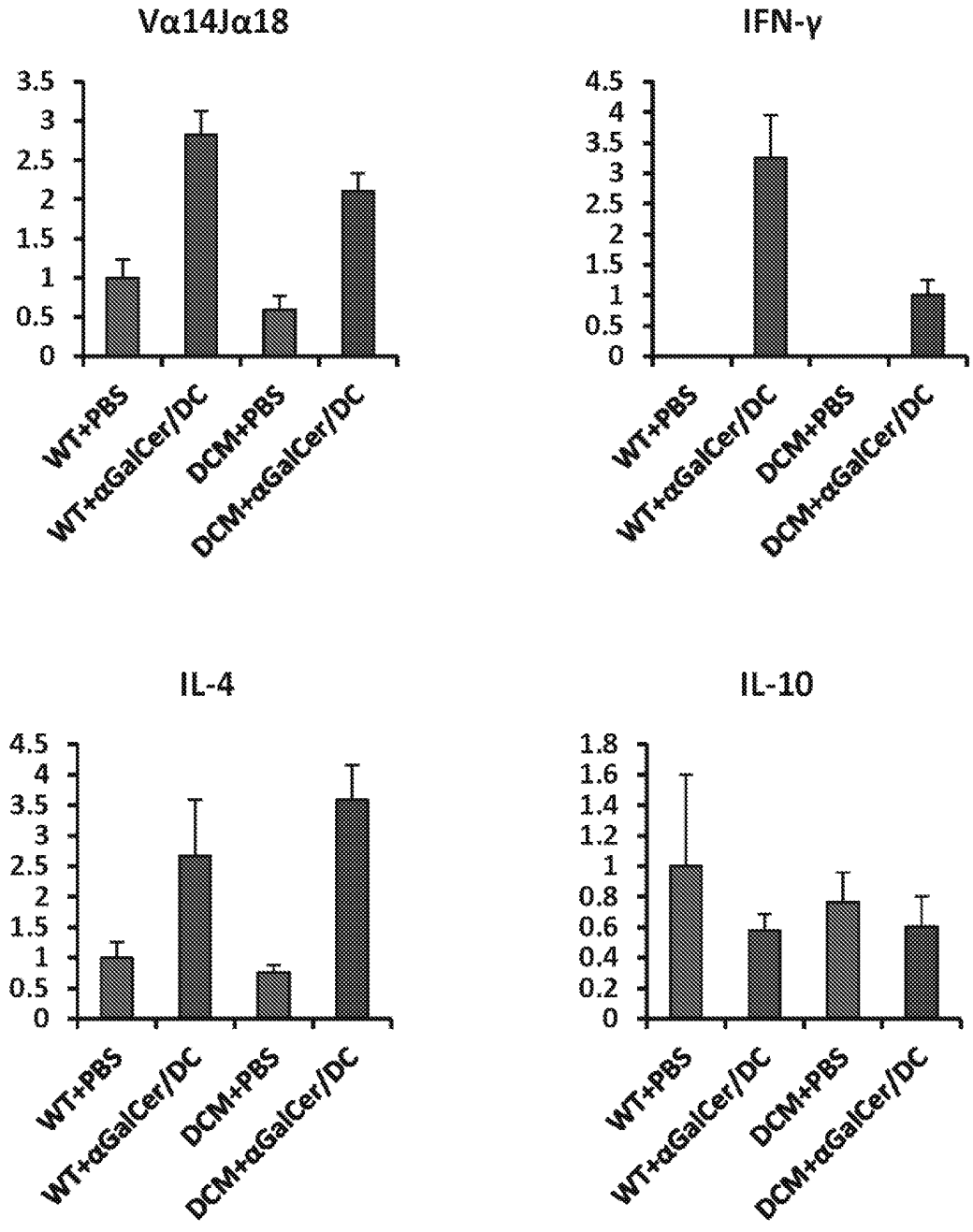
[図16]


(a)
% Survival
100
80
60
40
20
0
35
40
45
50
55
60
Days
DCM+PBS (n=32)
DCM+αGalCer/DC (n=15)
(b)
DCM+PBS
p < 0.05
LVEF (5-9wks)
5W
9W
DCM+αGalCel/DC
p = 0.83
(■ or ●は死亡個体)
Change of LVEF
p = 0.06
ΔLVEF (5-9W)
DCM+PBS
DCM+αGalCer/DC

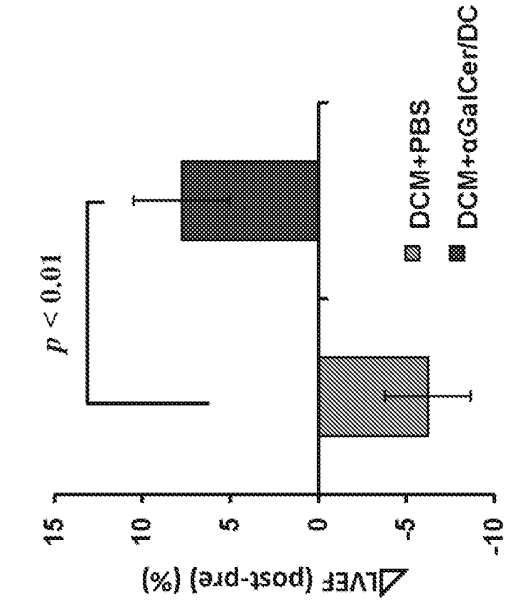
[図17]

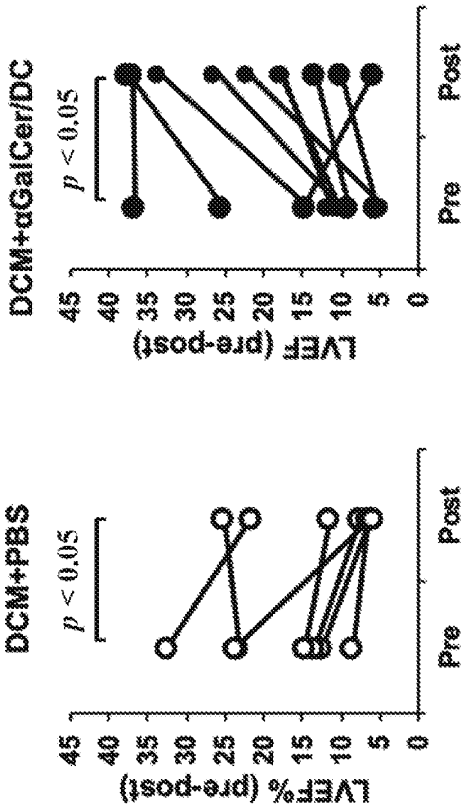

(a)
5wks: LVDd (mm)
n.s
WT+PBS
WT+αGalCer/DC
DCM+PBS
DCM+αGalCer/DC
9wks: LVDd (mm)
n.s
Heart Weight /Tibial Length
n.s
Lung Weight /Tibial Length
n.s
(b)
WT
DCM
Scale Bar 100μm
(c)
p < 0.01
p < 0.05
Fibrosis/Myocardium (%)
WT+PBS
WT+αGCDs
DCM+PBS
DCM+αGCDs

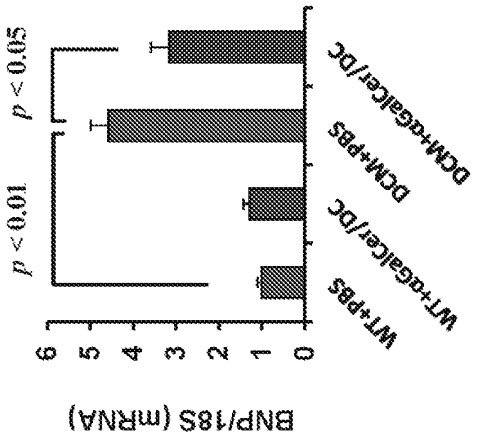
[図18]


Vα14Jα18
3.5
3
2.5
2
1.5
1
0.5
0
WT+PBS
WT+αGalCer/DC
DCM+PBS
DCM+αGalCer/DC
IFN-γ
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
WT+PBS
WT+αGalCer/DC
DCM+PBS
DCM+αGalCer/DC
IL-4
4.5
4
3.5
3
2.5
2
1.5
1
0.5
0
WT+PBS
WT+αGalCer/DC
DCM+PBS
DCM+αGalCer/DC
IL-10
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
WT+PBS
WT+αGalCer/DC
DCM+PBS
DCM+αGalCer/DC

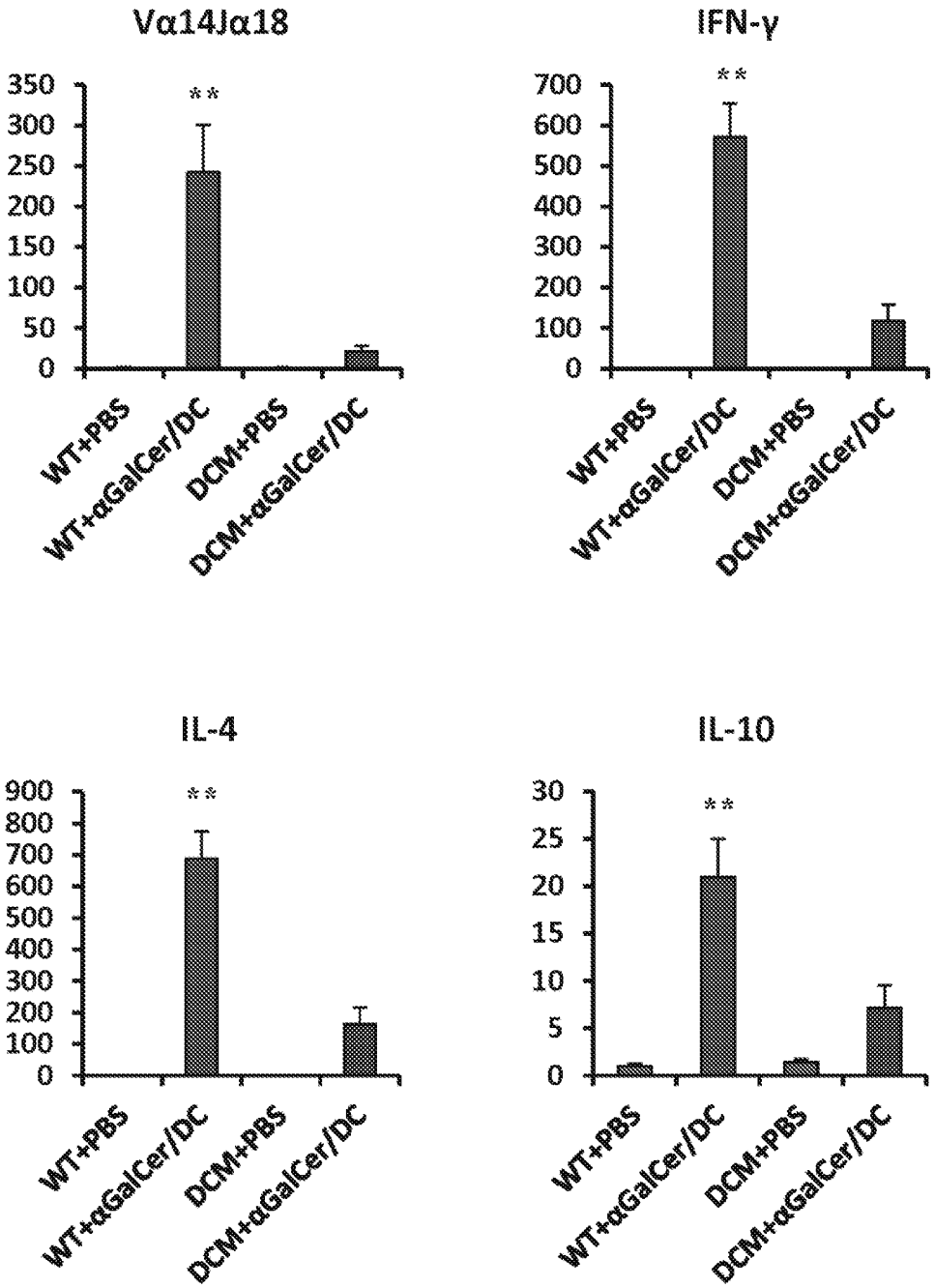
[図19]


ΔLVEF (post-pre) (%)
15
10
5
0
-5
-10
p < 0.01
DCM+PBS
DCM+αGalCer/DC

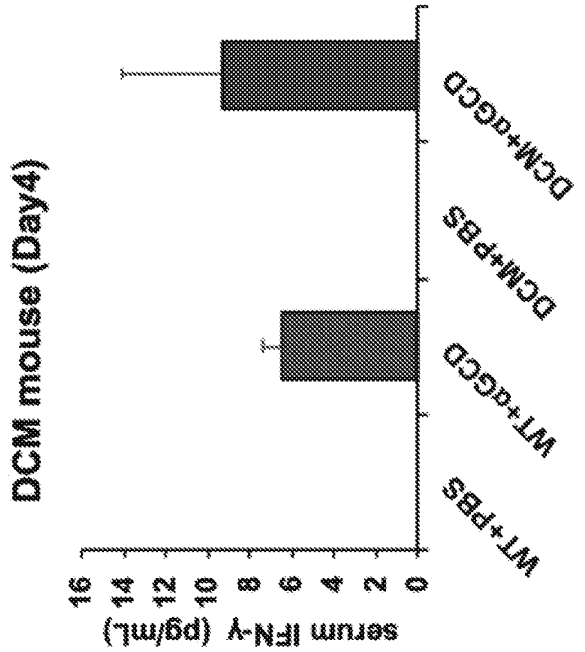

LVEF% (pre-post)
45
40
35
30
25
20
15
10
5
0
DCM+PBS
p < 0.05
Pre
Post
LVEF (pre-post)
DCM+αGalCer/DC
p < 0.05
Pre
Post

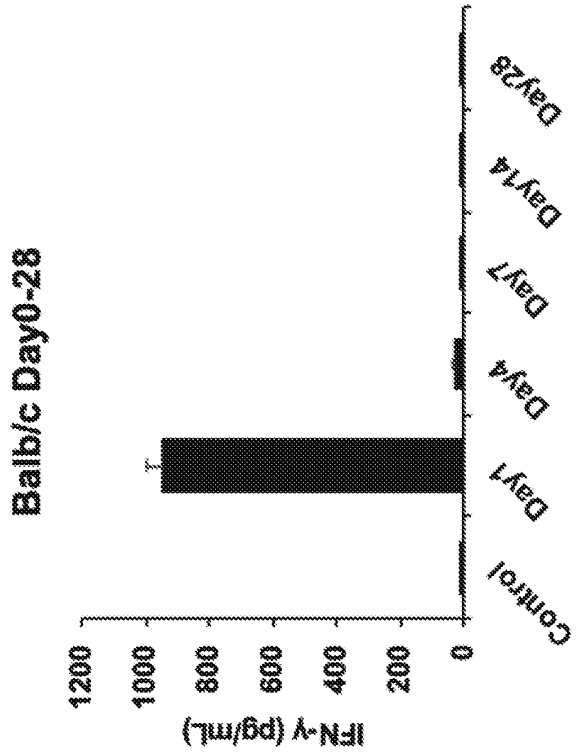

BNP/18S (mRNA)
6
5
4
3
2
1
0
p < 0.01
p < 0.05
WT+PBS
WT+αGalCer/DC
DCM+PBS
DCM+αGalCer/DC

[図20]


Vα14Jα18
350
300
250
200
150
100
50
0
**
WT+PBS
WT+αGalCer/DC
DCM+PBS
DCM+αGalCer/DC
IFN-γ
700
600
500
400
300
200
100
0
**
WT+PBS
WT+αGalCer/DC
DCM+PBS
DCM+αGalCer/DC
IL-4
900
800
700
600
500
400
300
200
100
0
**
WT+PBS
WT+αGalCer/DC
DCM+PBS
DCM+αGalCer/DC
IL-10
30
25
20
15
10
5
0
**
WT+PBS
WT+αGalCer/DC
DCM+PBS
DCM+αGalCer/DC

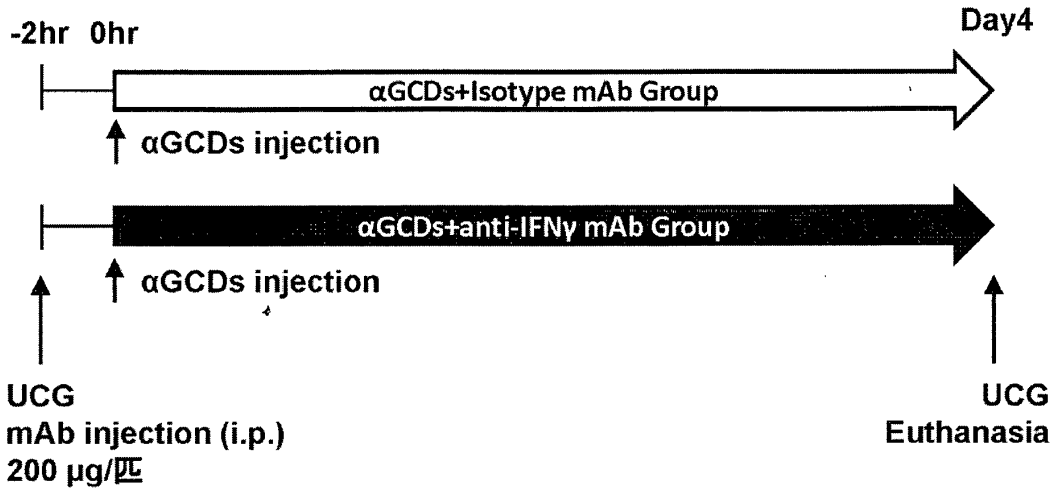
[図21]


DCM mouse (Day4)
serum IFN-γ (pg/mL)
0
2
4
6
8
10
12
14
16
WT+PBS
WT+αGCD
DCM+PBS
DCM+αGCD

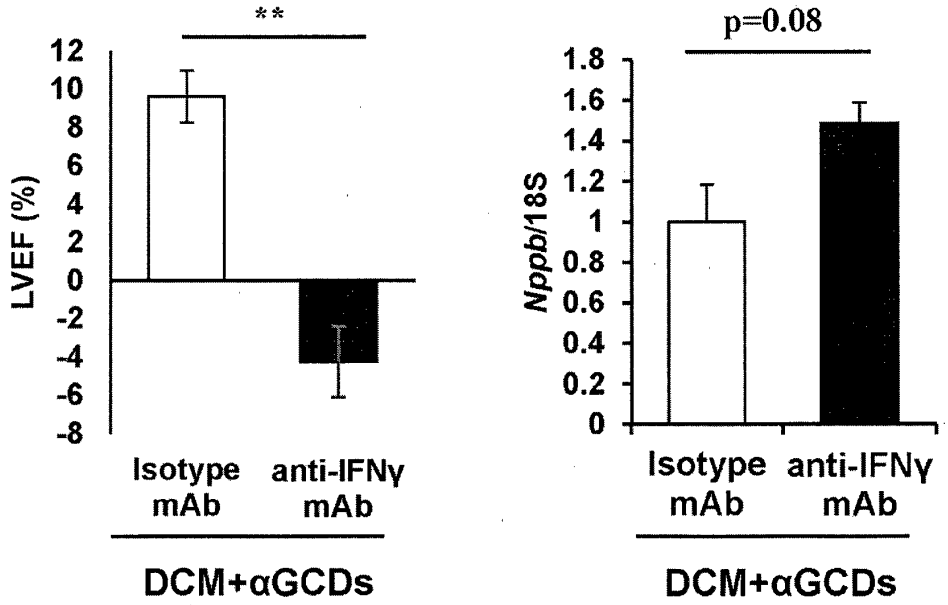

Balb/c Day0-28
IFN-γ (pg/mL)
0
200
400
600
800
1000
1200
Control
Day1
Day4
Day7
Day14
Day28

[図 22]

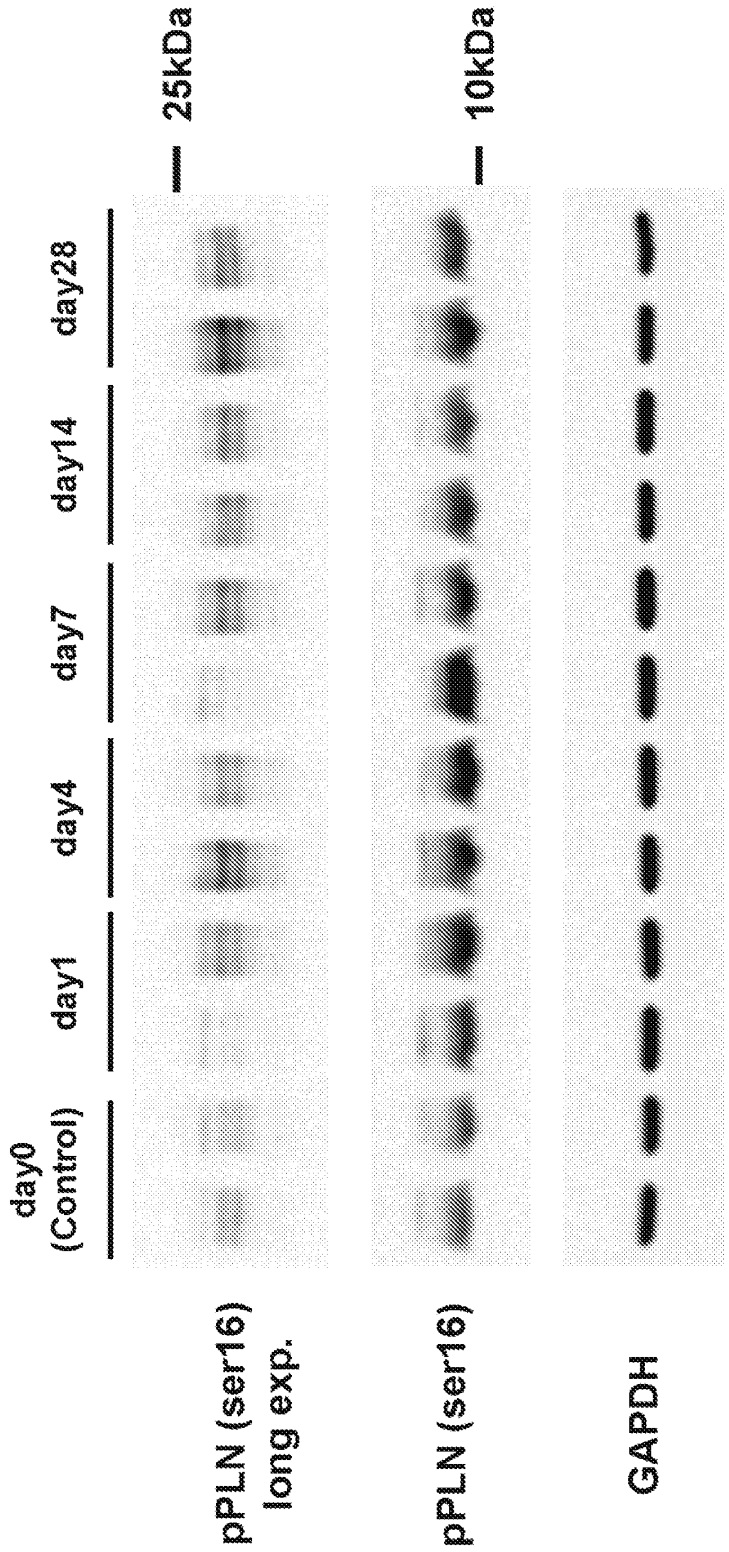
(a)


-2hr 0hr
Day4
αGCDs+Isotype mAb Group
αGCDs injection
αGCDs+anti-IFNγ mAb Group
αGCDs injection
UCG
mAb injection (i.p.)
200 μg/匹
UCG
Euthanasia

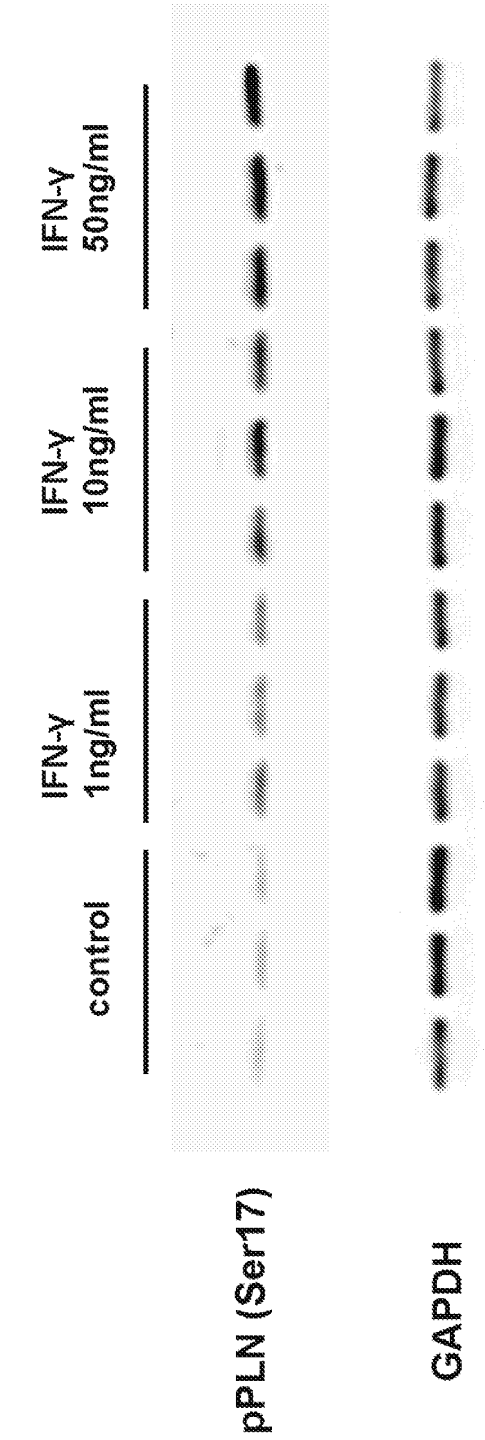
(b)


**
LVEF (%)
12
10
8
6
4
2
0
-2
-4
-6
-8
Isotype mAb
anti-IFNγ mAb
DCM+αGCDs
p=0.08
Nppb/18S
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Isotype mAb
anti-IFNγ mAb
DCM+αGCDs

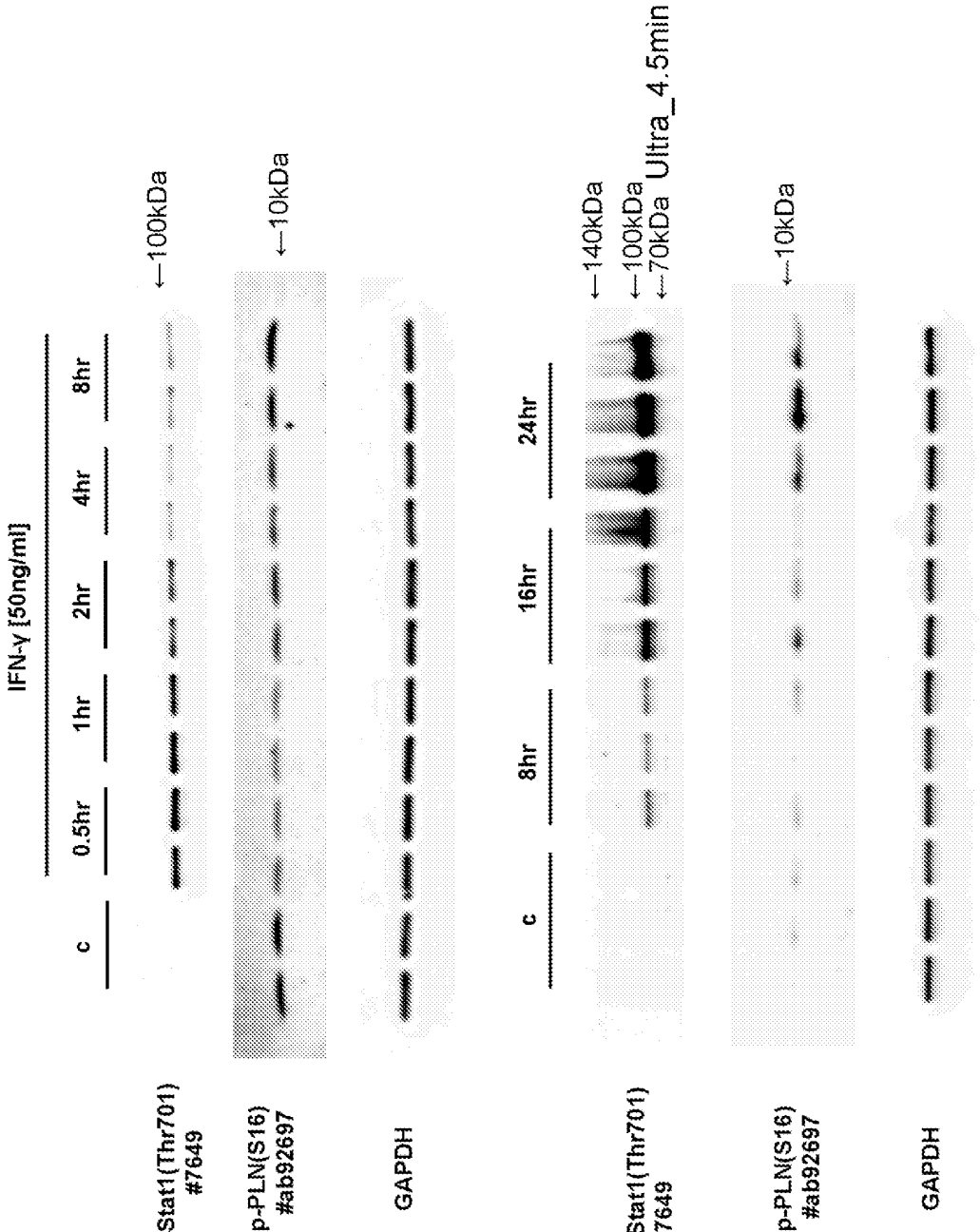
[図23]


day0 (Control)
day1
day4
day7
day14
day28
25kDa
10kDa
pPLN (ser16) long exp.
pPLN (ser16)
GAPDH

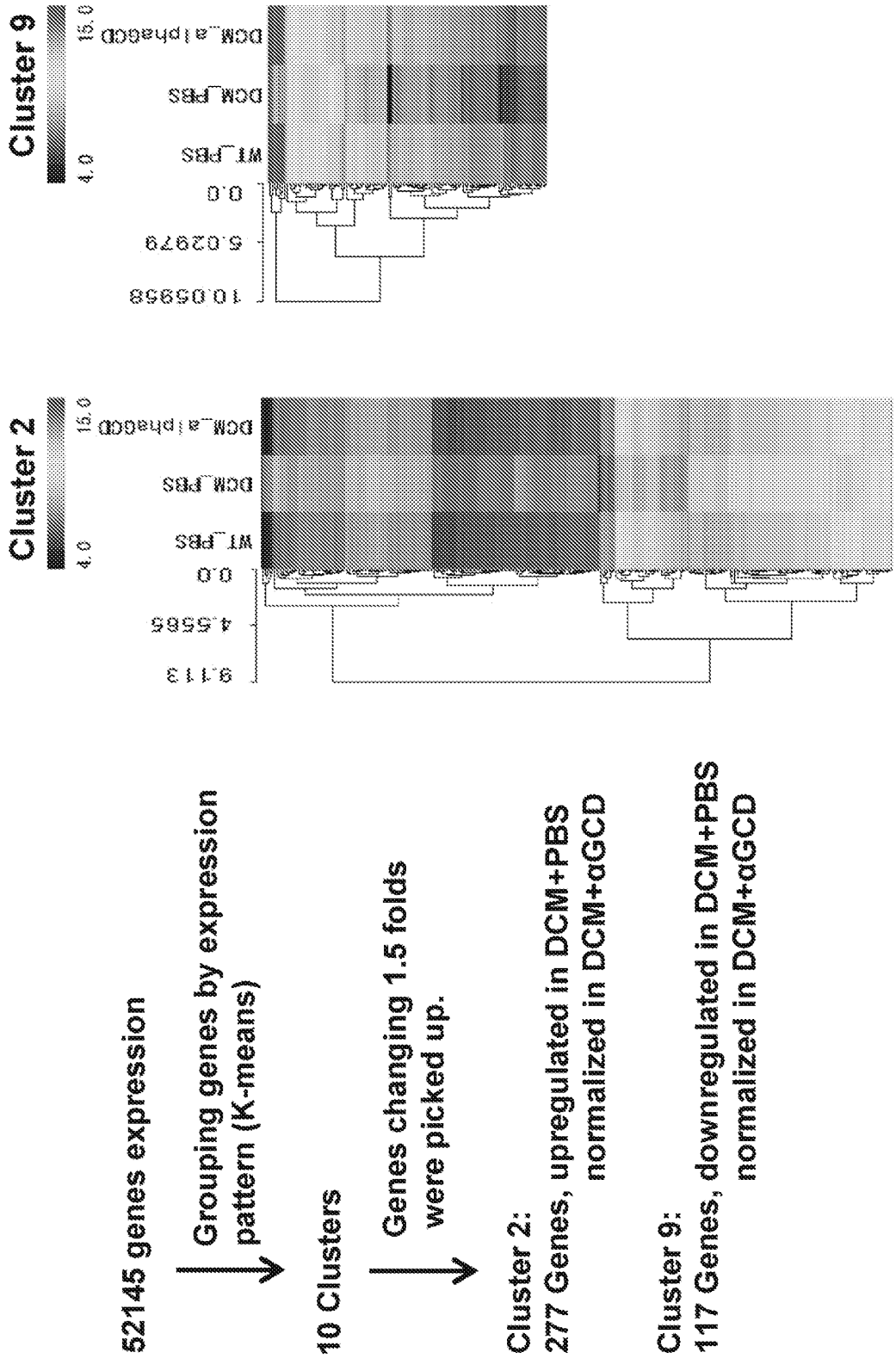
[図24]


control
IFN-γ 1ng/ml
IFN-γ 10ng/ml
IFN-γ 50ng/ml
pPLN (Ser17)
GAPDH

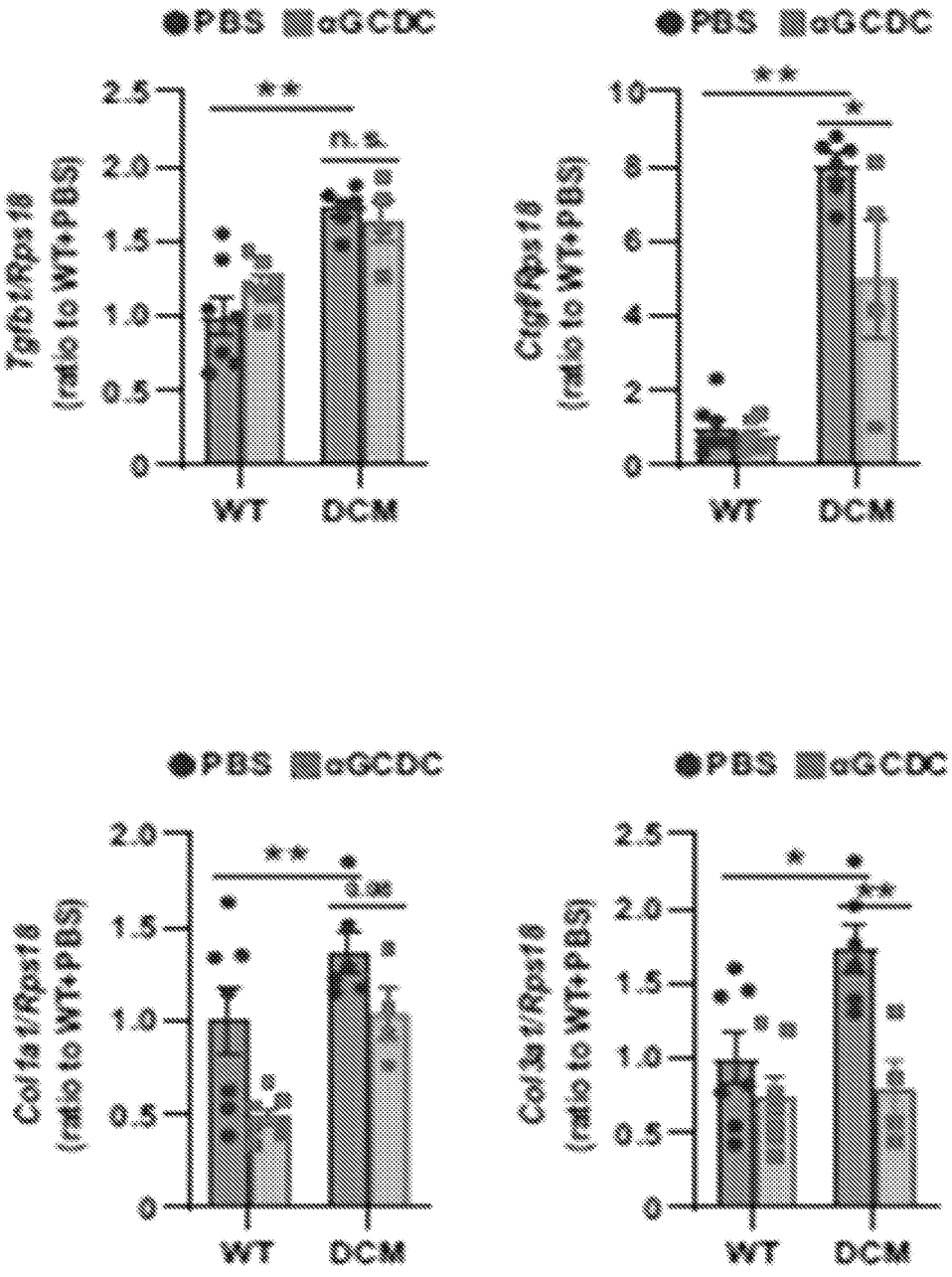
[図25]


IFN-γ [50ng/ml]
c
0.5hr
1hr
2hr
4hr
8hr
16hr
24hr
←100kDa
←10kDa
←140kDa
←100kDa
←70kDa
Ultra_4.5min
p-Stat1(Thr701) #7649
p-PLN(S16) #ab92697
GAPDH

[図26]

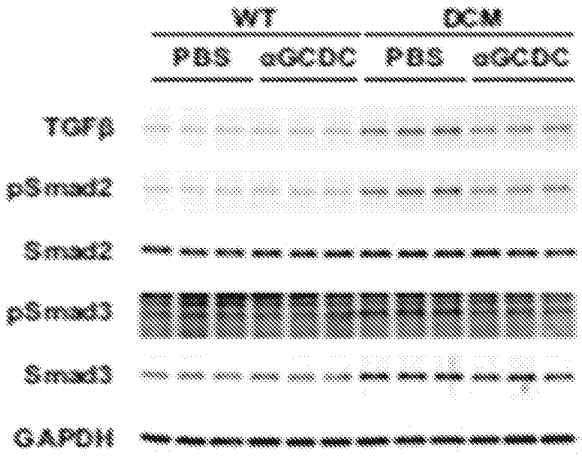

Cluster 9
16.0
4.0
DCM_αGCD
DCM_PBS
WT_PBS
0.0
5.02979
10.05958
Cluster 2
16.0
4.0
DCM_αGCD
DCM_PBS
WT_PBS
0.0
4.5565
9.113
52145 genes expression
Grouping genes by expression pattern (K-means)
10 Clusters
Genes changing 1.5 folds were picked up.
Cluster 2:
277 Genes, upregulated in DCM+PBS normalized in DCM+αGCD
Cluster 9:
117 Genes, downregulated in DCM+PBS normalized in DCM+αGCD

[図27]

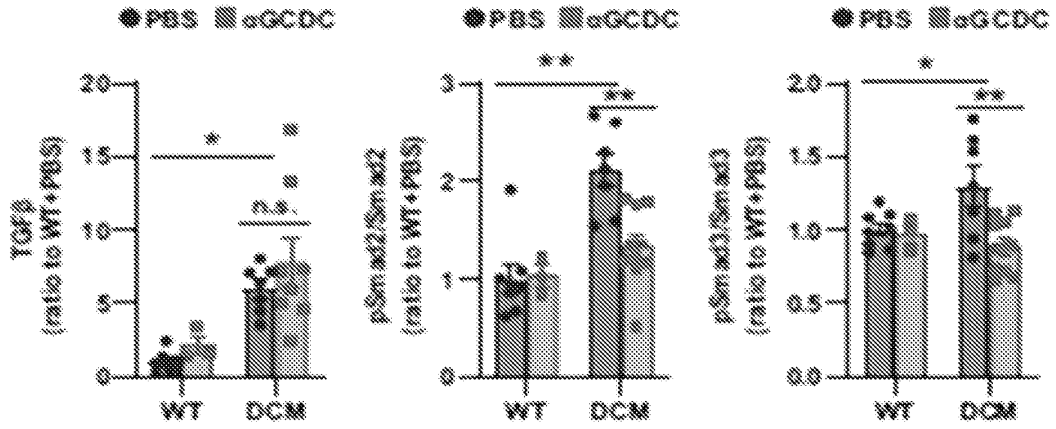

PBS
aGCDC
Tgfb1/Rps18 (ratio to WT+PBS)
Ctgf/Rps18 (ratio to WT+PBS)
Col1a1/Rps18 (ratio to WT+PBS)
Col3a1/Rps18 (ratio to WT+PBS)
WT
DCM
n.s.

[図28]

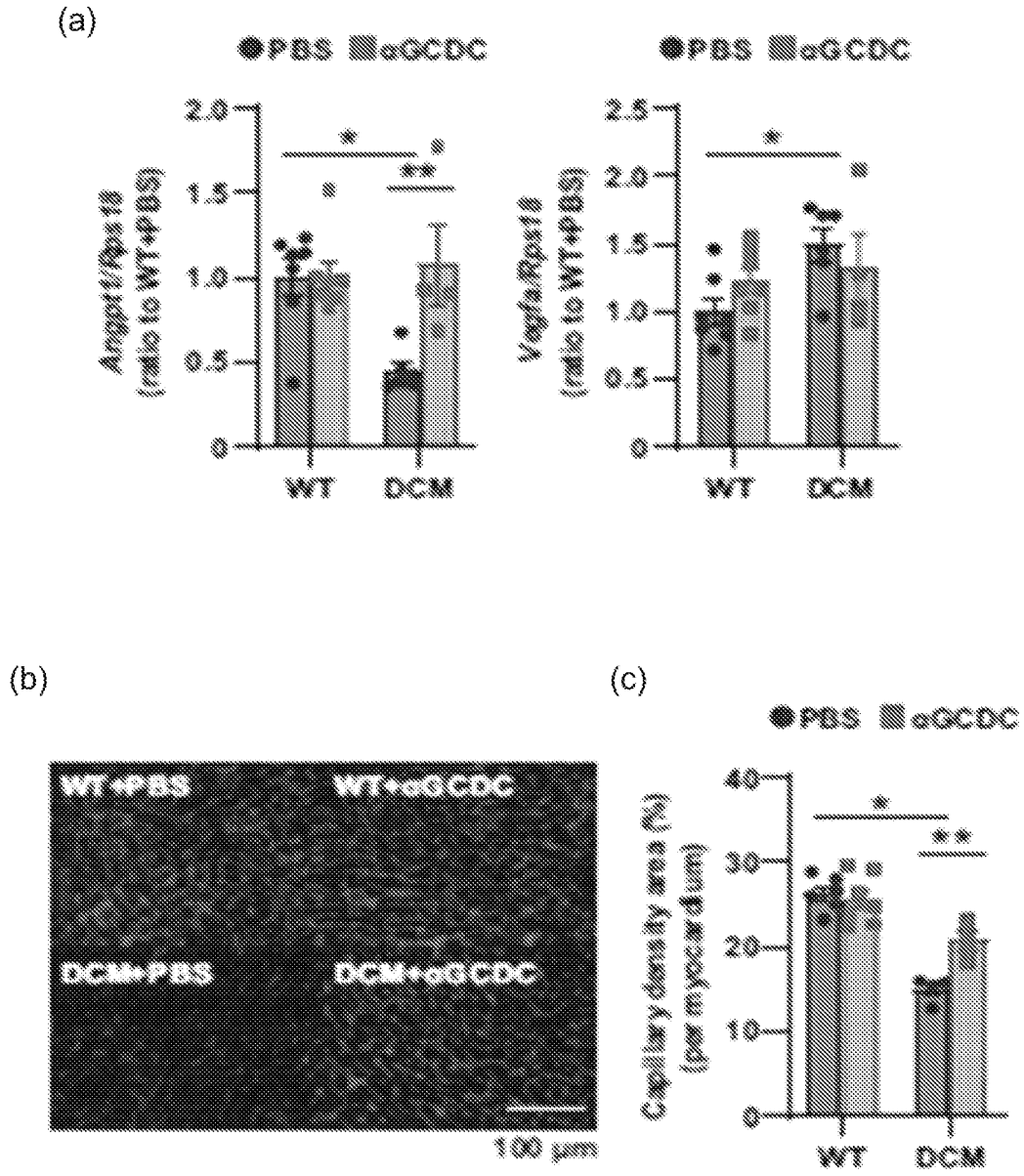
(a)


WT
DCM
PBS
αGCDC
PBS
αGCDC
TGFβ
pSmad2
Smad2
pSmad3
Smad3
GAPDH

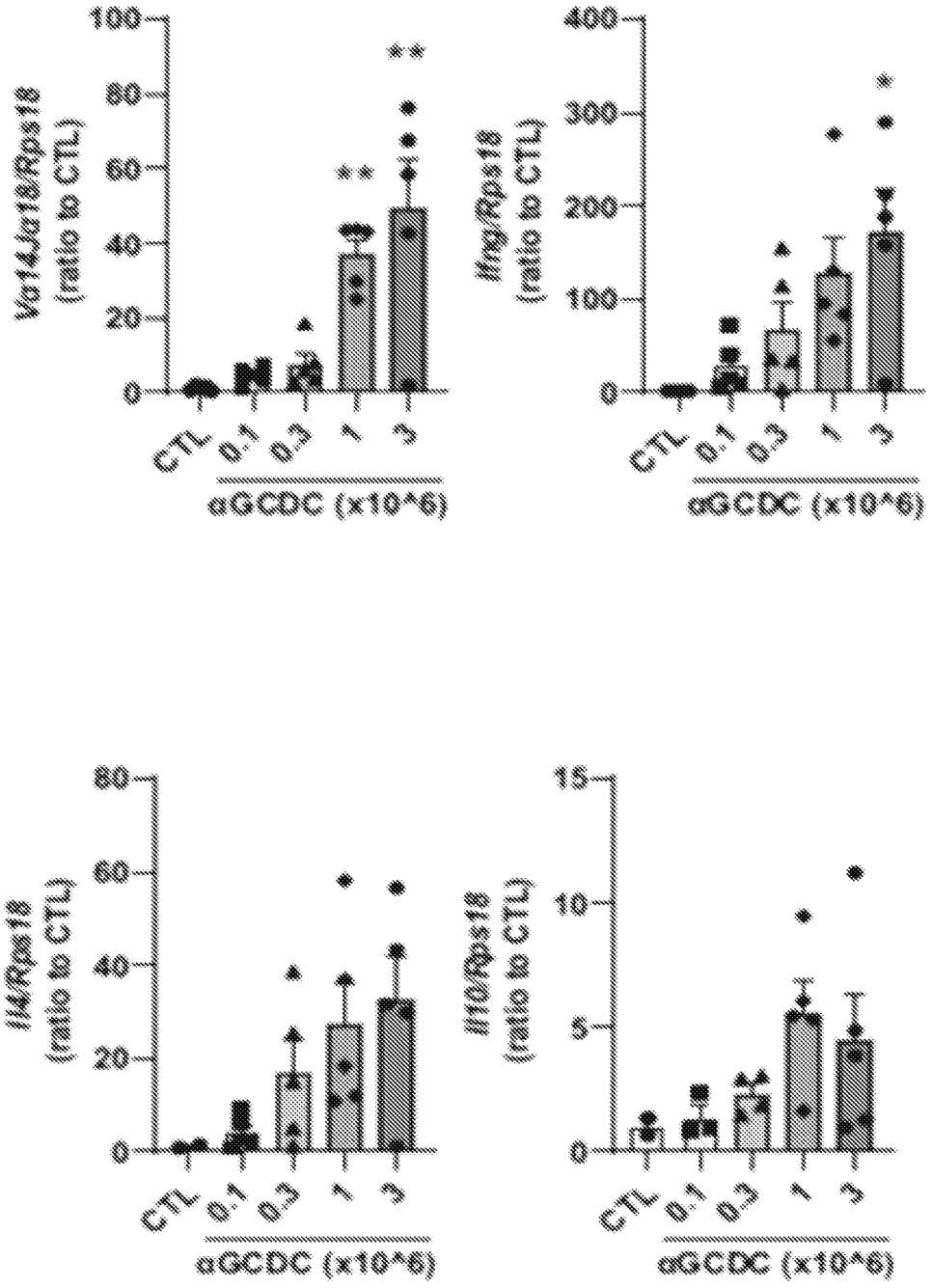
(b)


PBS
αGCDC
TGFβ (ratio to WT+PBS)
n.s.
WT
DCM
pSmad2/Smad2 (ratio to WT+PBS)
pSmad3/Smad3 (ratio to WT+PBS)

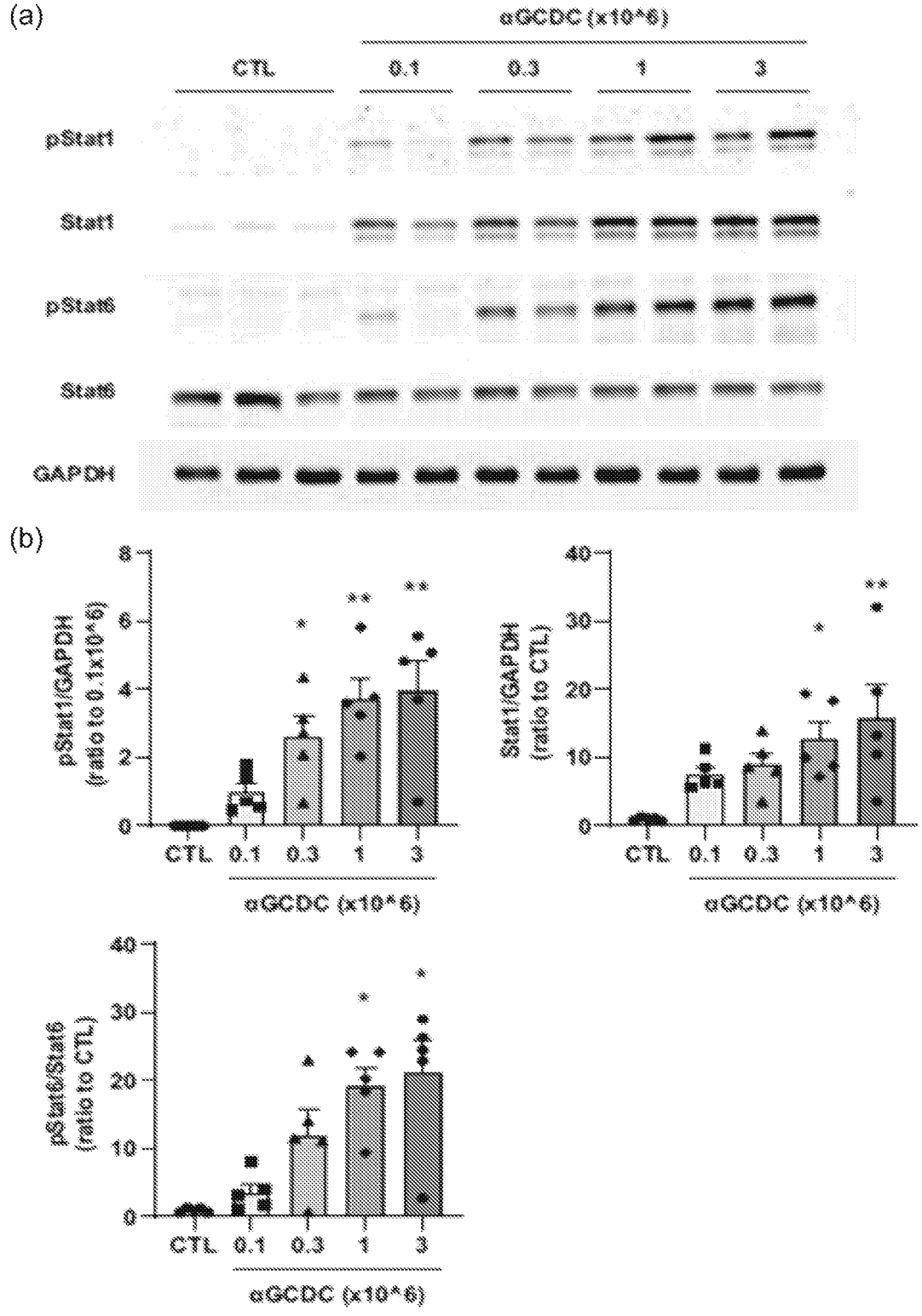
[図29]


(a)
PBS
αGCDC
Angpt1/Rps18
(ratio to WT+PBS)
2.0
1.5
1.0
0.5
0
*
**
WT
DCM
PBS
αGCDC
Vegfa/Rps18
(ratio to WT+PBS)
2.5
2.0
1.5
1.0
0.5
0
*
WT
DCM
(b)
WT+PBS
WT+αGCDC
DCM+PBS
DCM+αGCDC
100 μm
(c)
PBS
αGCDC
Capillary density area (%)
(per cycle area (μm))
40
30
20
10
0
*
**
WT
DCM

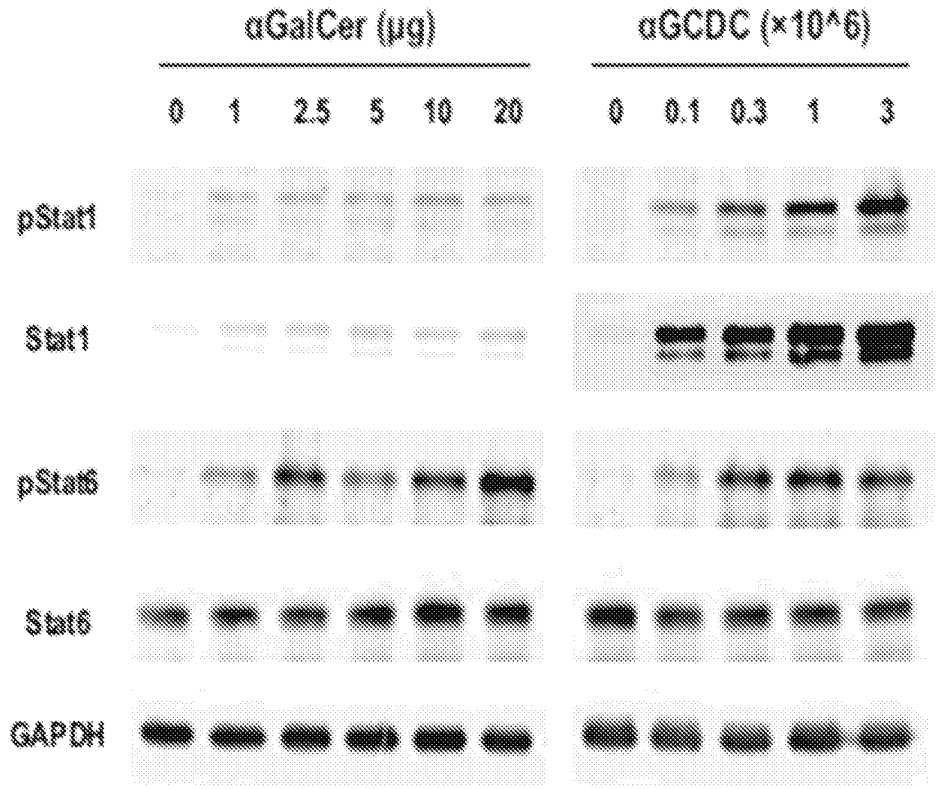
[図30]


Vα14Jα18/Rps18
(ratio to CTL)
100
80
60
40
20
0
**
**
CTL
0.1
0.3
1
3
αGCDC (×10^6)
Ifng/Rps18
(ratio to CTL)
400
300
200
100
0
*
CTL
0.1
0.3
1
3
αGCDC (×10^6)
Il4/Rps18
(ratio to CTL)
80
60
40
20
0
CTL
0.1
0.3
1
3
αGCDC (×10^6)
Il10/Rps18
(ratio to CTL)
15
10
5
0
CTL
0.1
0.3
1
3
αGCDC (×10^6)

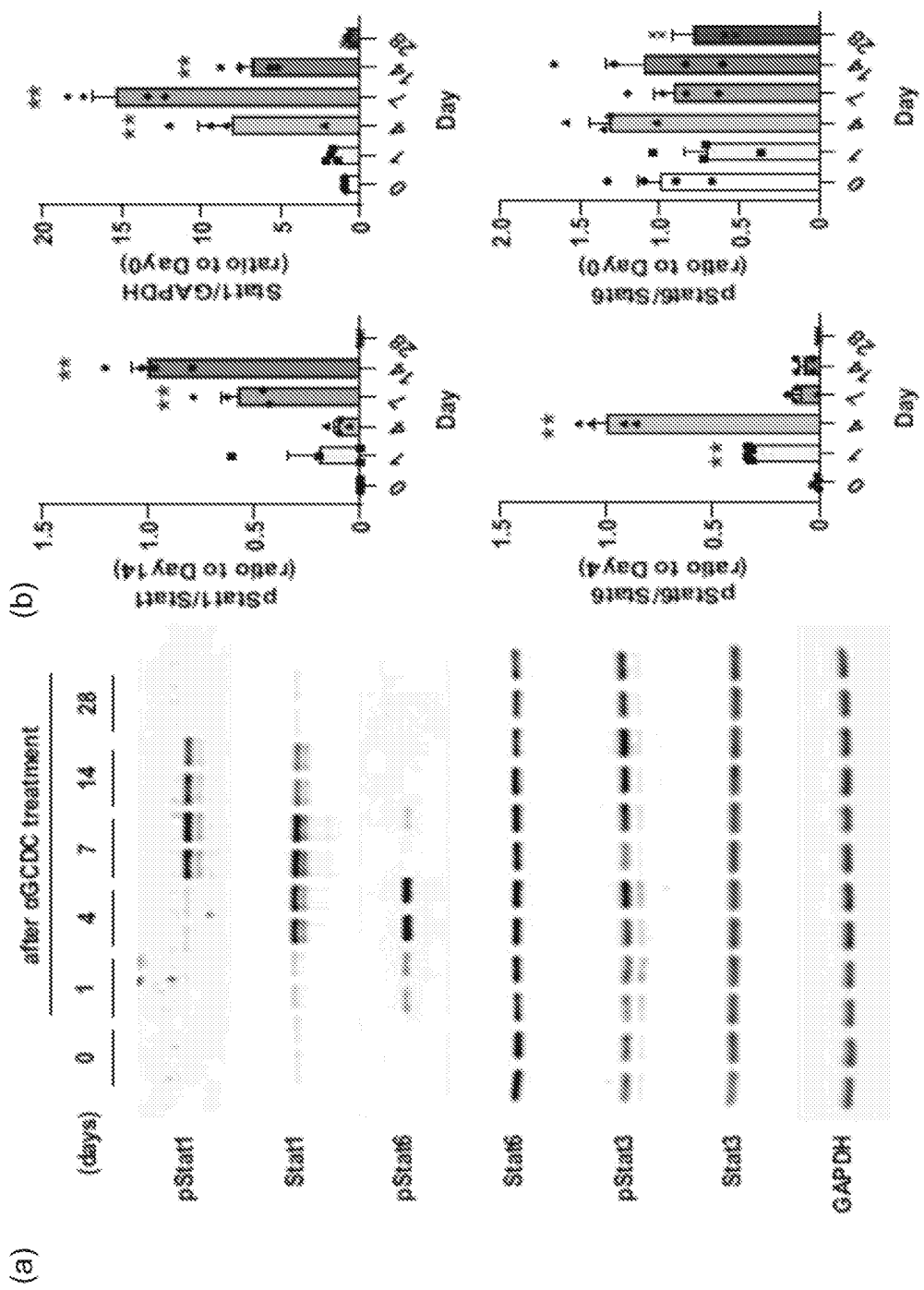
[図31]


(a)
αGCDC (x10^6)
CTL
0.1
0.3
1
3
pStat1
Stat1
pStat6
Stat6
GAPDH
(b)
pStat1/GAPDH (ratio to 0.1x10^6)
Stat1/GAPDH (ratio to CTL)
pStat6/Stat6 (ratio to CTL)
αGCDC (x10^6)

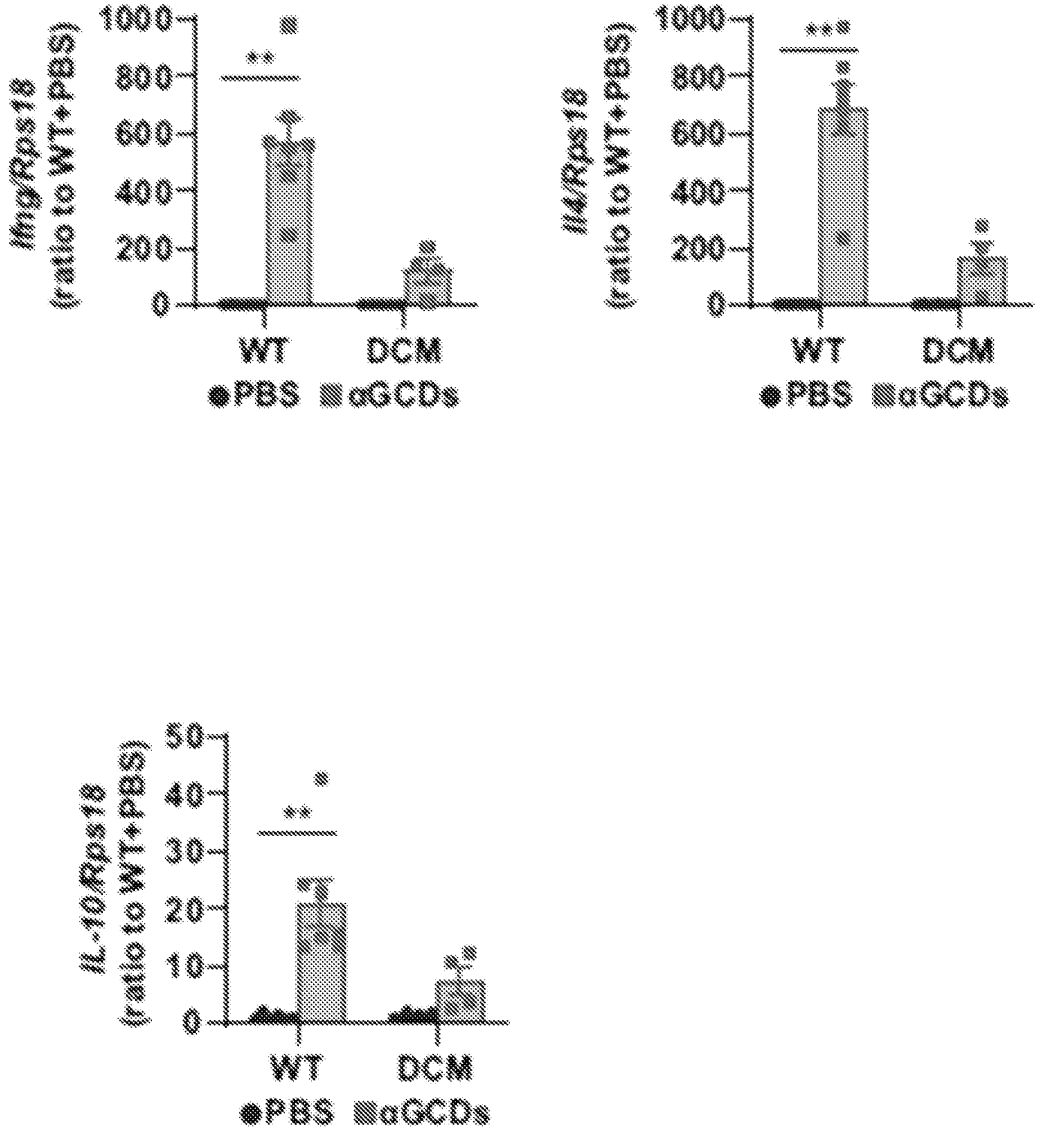
[図32]


αGalCer (μg)
αGCDC (×10^6)
0 1 2.5 5 10 20
0 0.1 0.3 1 3
pStat1
Stat1
pStat6
Stat6
GAPDH

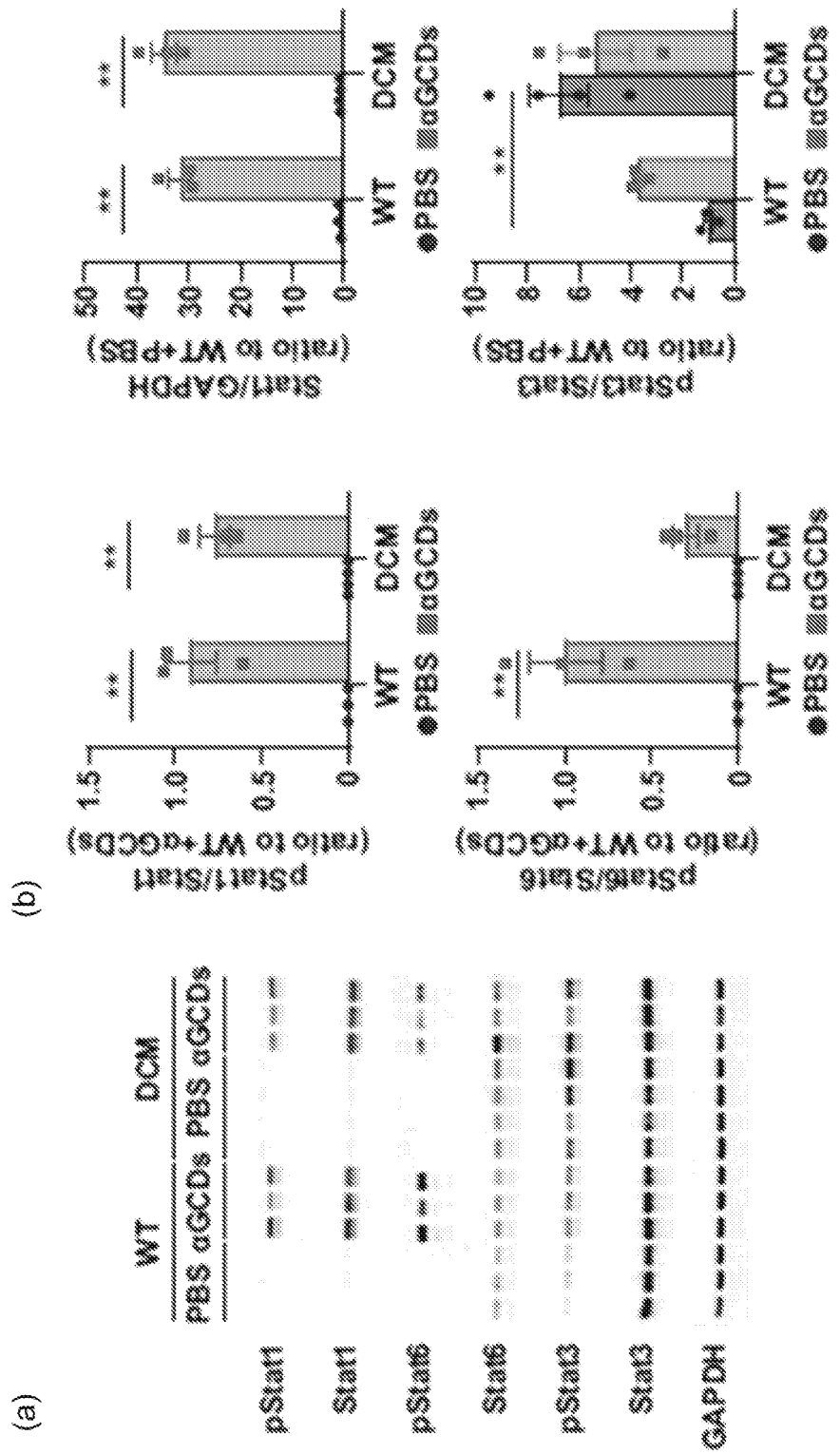
[図33]


(a)
after αGCDC treatment
(days)
0
1
4
7
14
28
pStat1
Stat1
pStat6
Stat6
pStat3
Stat3
GAPDH
(b)
pStat1/Stat1
(ratio to Day14)
pStat6/Stat6
(ratio to Day4)
Stat1/GAPDH
(ratio to Day0)
pStat6/Stat6
(ratio to Day0)
Day

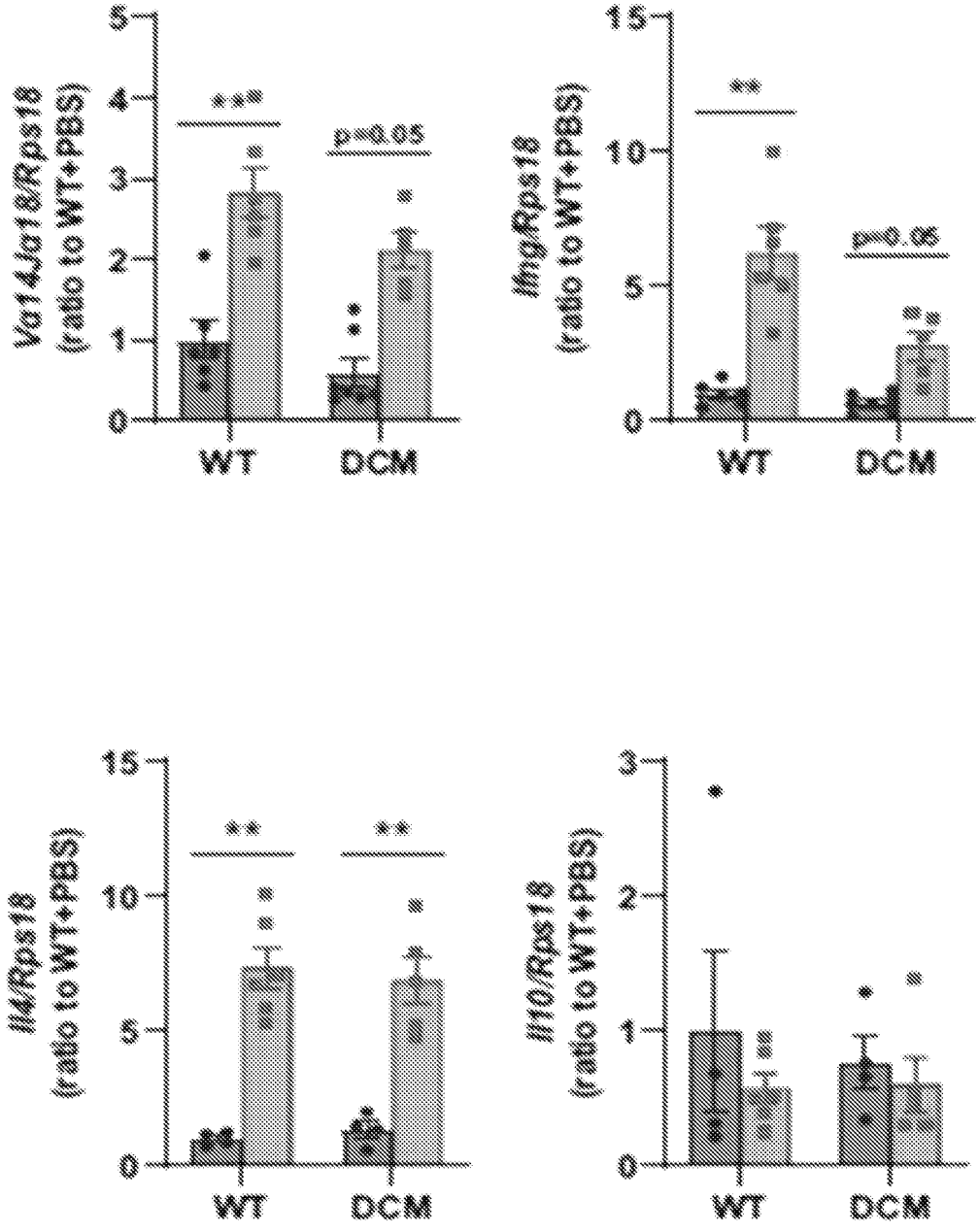
[図34]


Ifng/Rps18
(ratio to WT+PBS)
1000
800
600
400
200
0
**
WT
DCM
PBS
αGCDs
Il4/Rps18
(ratio to WT+PBS)
1000
800
600
400
200
0
***
WT
DCM
PBS
αGCDs
IL-10/Rps18
(ratio to WT+PBS)
50
40
30
20
10
0
**
WT
DCM
PBS
αGCDs

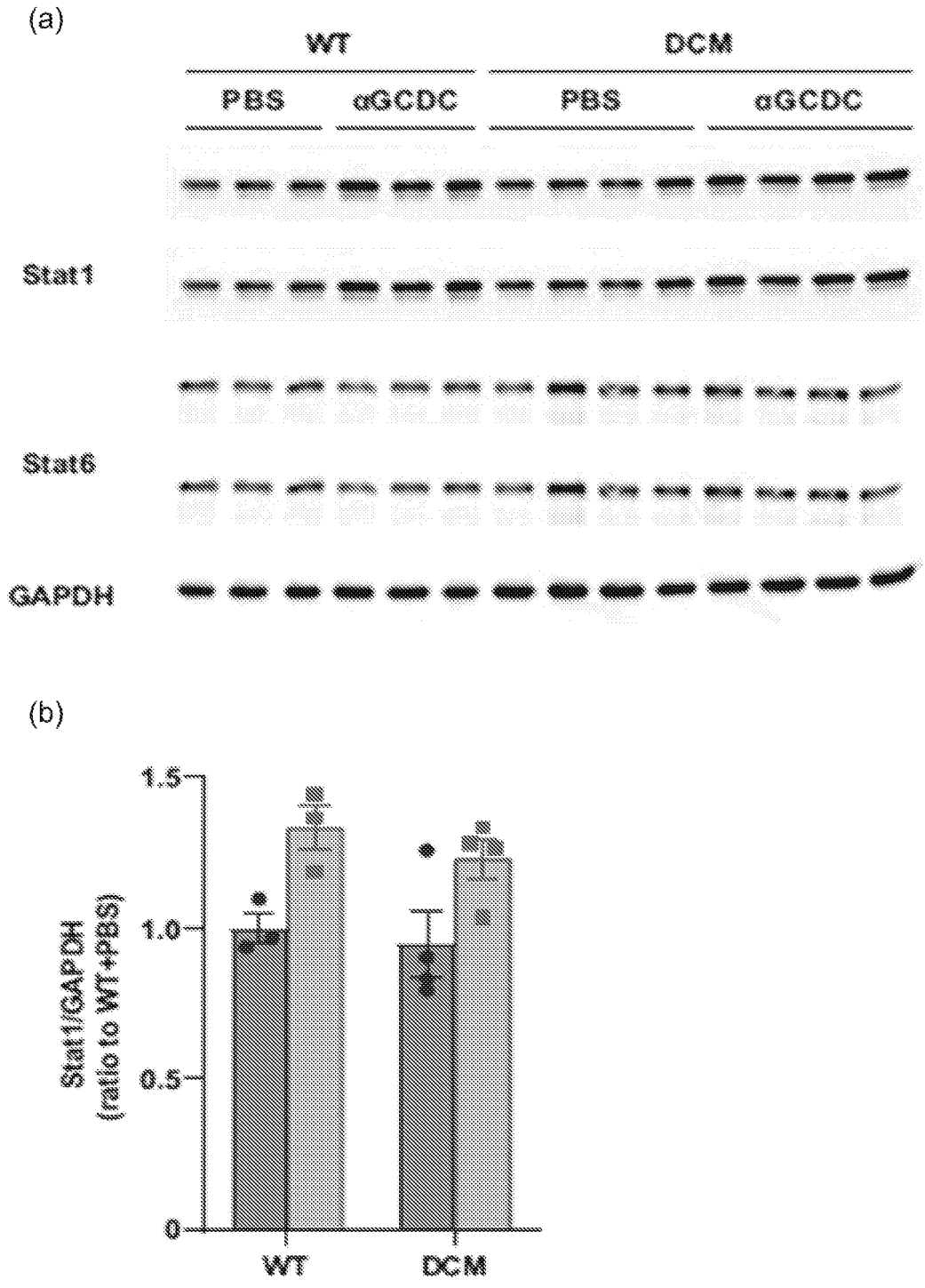
[図35]


(a)
WT
PBS
αGCDs
DCM
PBS
αGCDs
pStat1
Stat1
pStat6
Stat6
pStat3
Stat3
GAPDH
(b)
pStat1/Stat1 (ratio to WT+αGCDs)
pStat6/Stat6 (ratio to WT+αGCDs)
pStat3/Stat3 (ratio to WT+PBS)
Stat1/GAPDH (ratio to WT+PBS)
WT
DCM
PBS
αGCDs

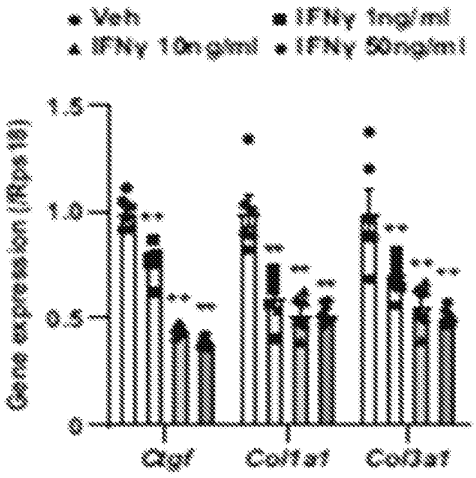
[図36]

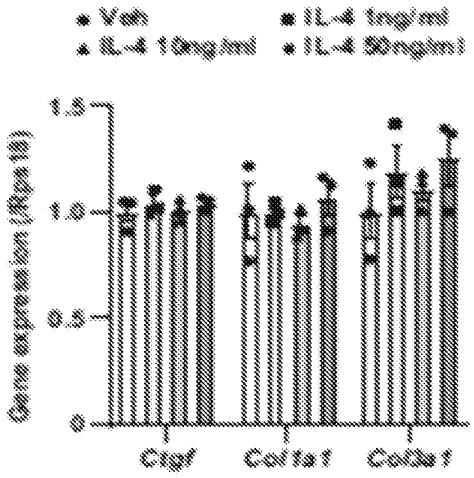

Va14Ja18/Rps18
(ratio to WT+PBS)
**
p=0.05
WT
DCM
Ifng/Rps18
(ratio to WT+PBS)
**
p=0.06
WT
DCM
Il4/Rps18
(ratio to WT+PBS)
**
**
WT
DCM
Il10/Rps18
(ratio to WT+PBS)
WT
DCM

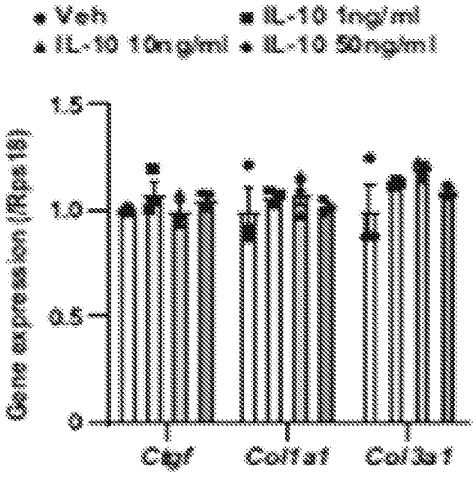
[図37]


(a)
WT
DCM
PBS
αGCDC
PBS
αGCDC
Stat1
Stat6
GAPDH
(b)
Stat1/GAPDH
(ratio to WT+PBS)
1.5
1.0
0.5
0
WT
DCM

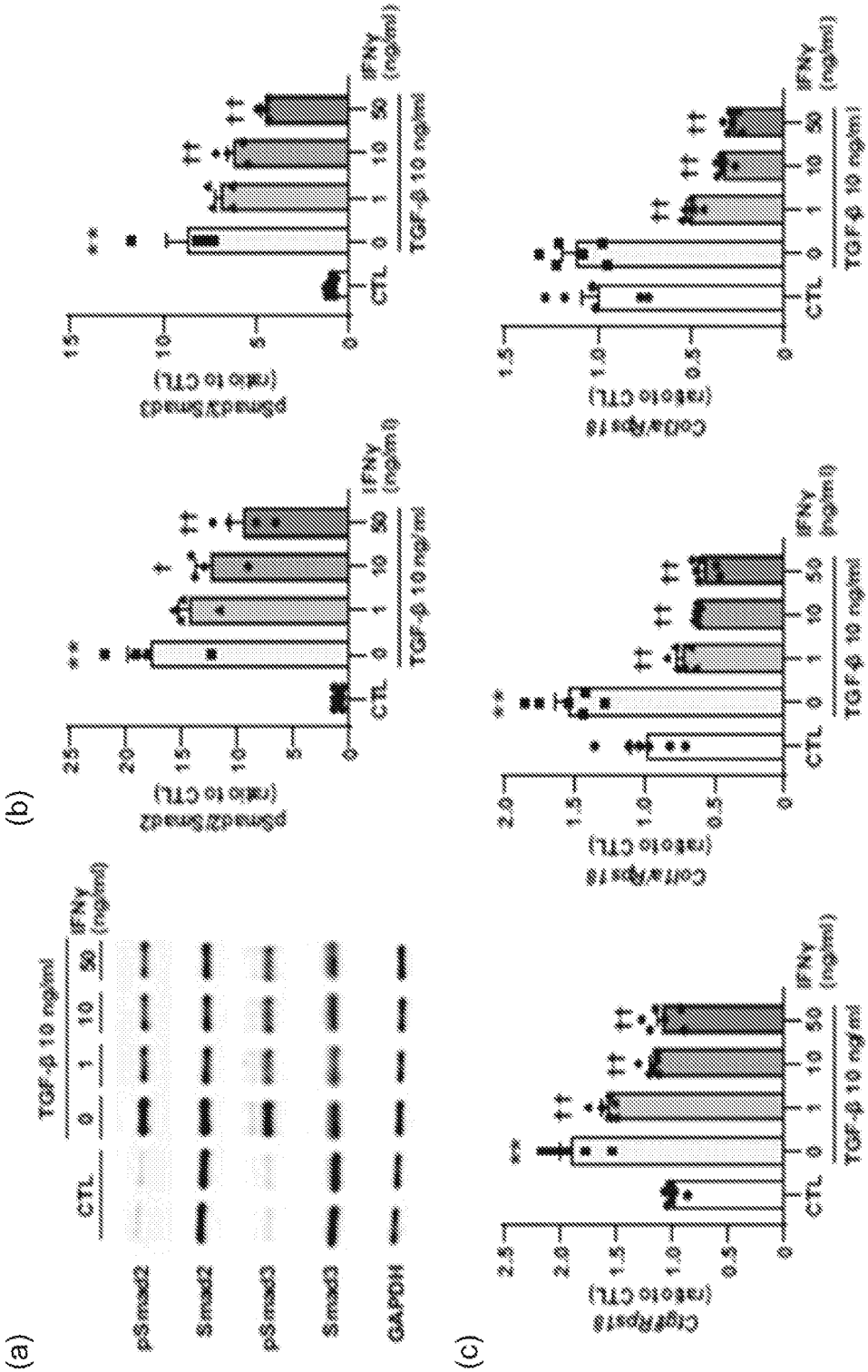
[図38]


Veh
IFNγ 1ng/ml
IFNγ 10ng/ml
IFNγ 50ng/ml
Gene expression (Rps18)
1.5
1.0
0.5
0
Ctgf
Col1a1
Col3a1

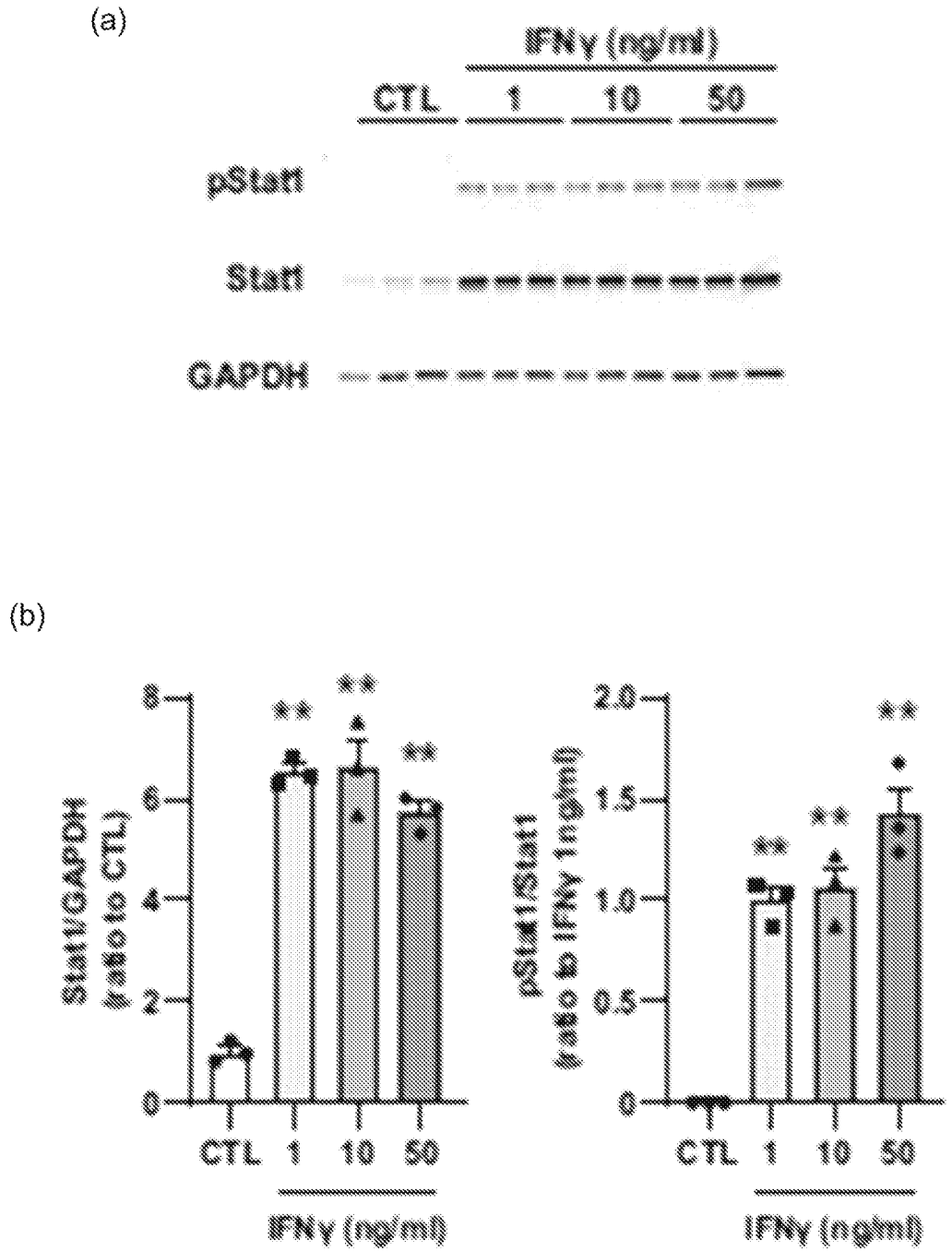

Veh
IL-4 1ng/ml
IL-4 10ng/ml
IL-4 50ng/ml
Gene expression (Rps18)
1.5
1.0
0.5
0
Ctgf
Col1a1
Col3a1


Veh
IL-10 1ng/ml
IL-10 10ng/ml
IL-10 50ng/ml
Gene expression (Rps18)
1.5
1.0
0.5
0
Ctgf
Col1a1
Col3a1

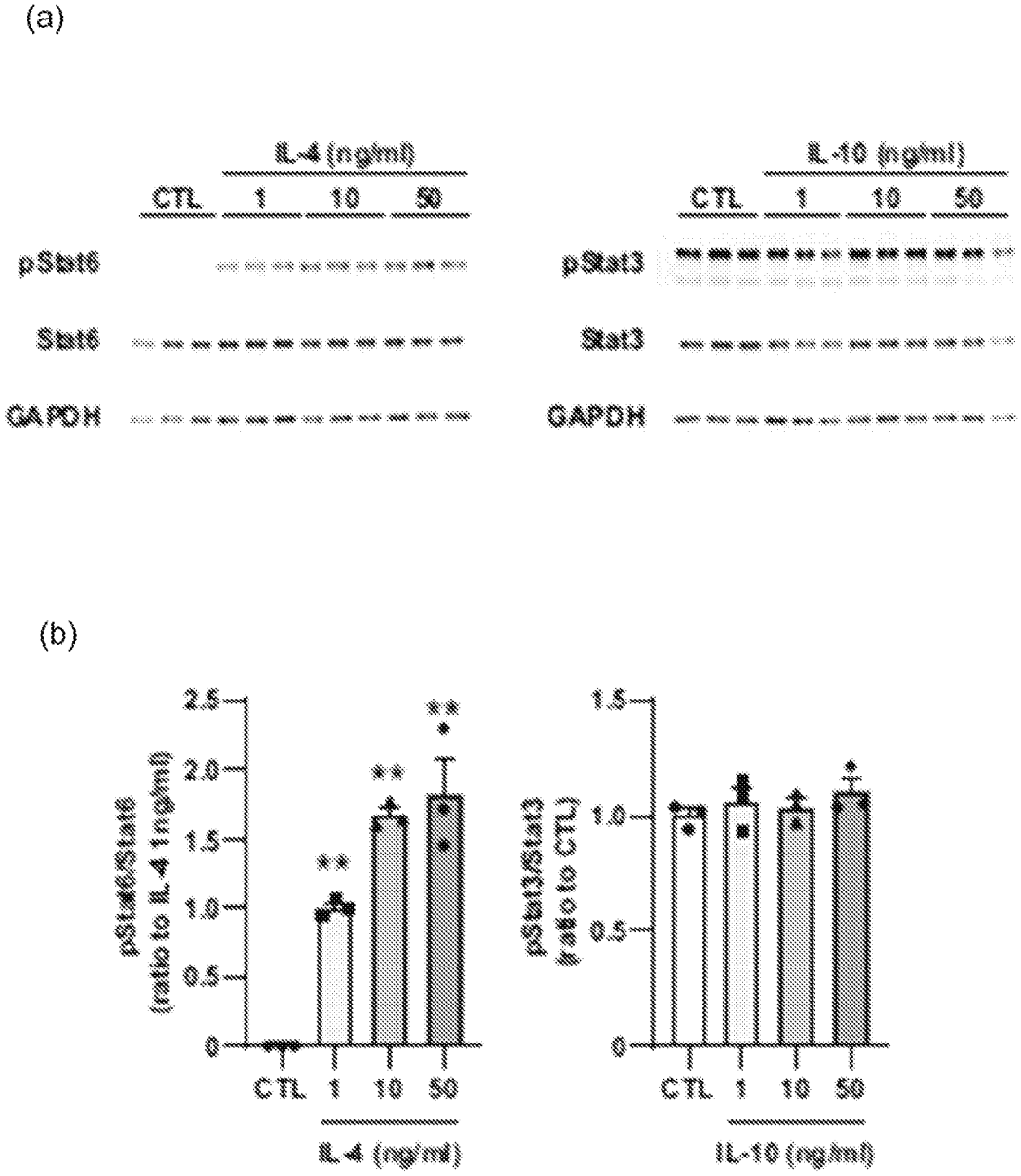
[図39]


(a)
CTL
TGF-β 10 ng/ml
IFNγ (ng/ml)
0
1
10
50
p-Smad2
Smad2
p-Smad3
Smad3
GAPDH
(b)
pSmad2/Smad2 (ratio to CTL)
pSmad3/Smad3 (ratio to CTL)
TGF-β 10 ng/ml
IFNγ (ng/ml)
(c)
Col1a/Rps18 (ratio to CTL)
Col3/Rps18 (ratio to CTL)

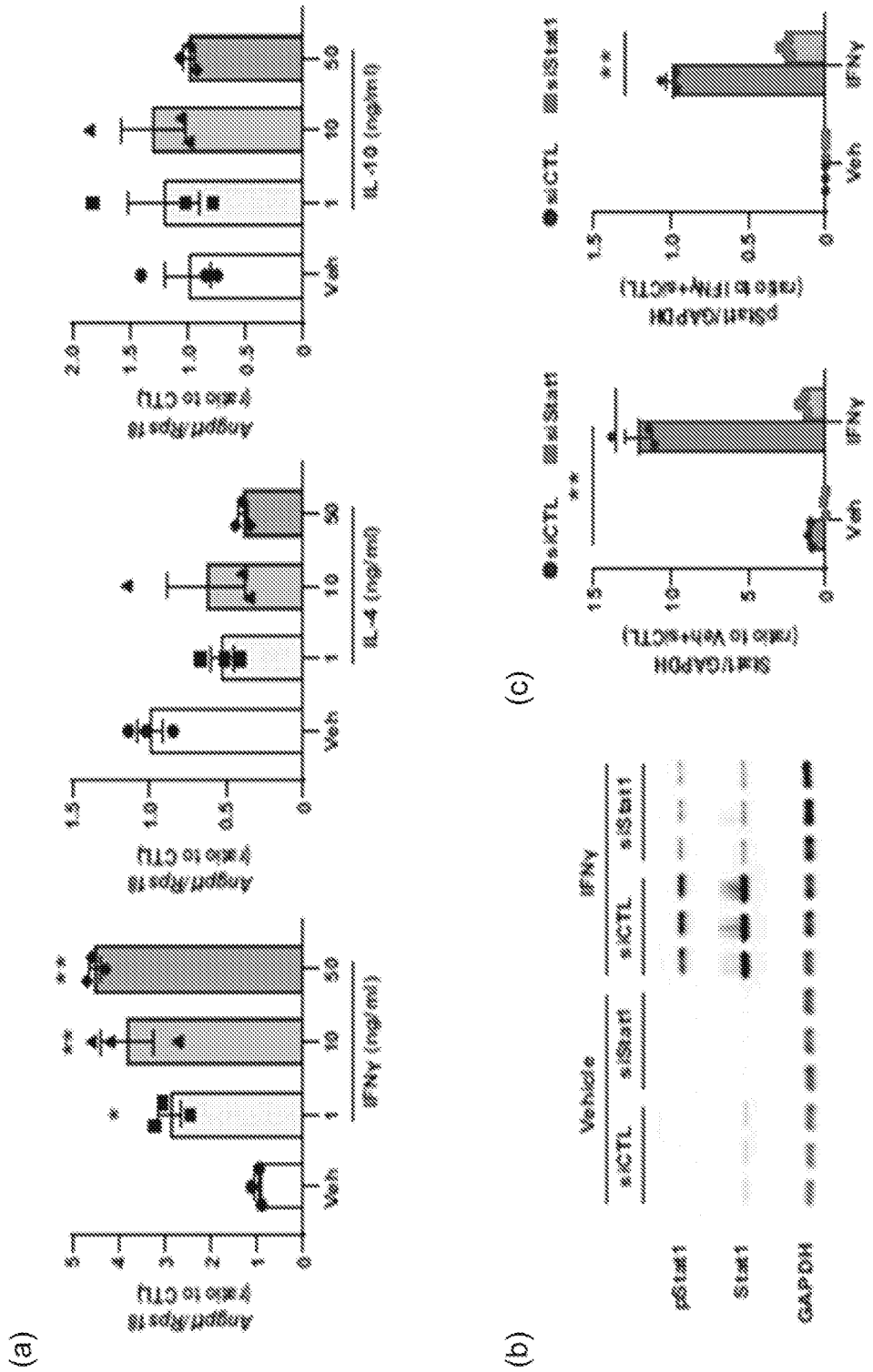
[図40]


(a)
IFNγ (ng/ml)
CTL
1
10
50
pStat1
Stat1
GAPDH
(b)
Stat1/GAPDH (ratio to CTL)
pStat1/Stat1 (ratio to IFNγ 1ng/ml)
CTL
1
10
50
IFNγ (ng/ml)

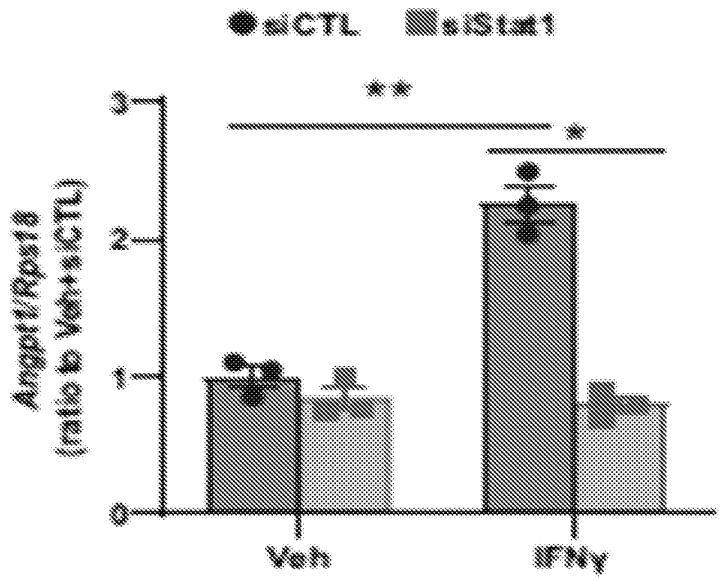
[図41]


(a)
IL-4 (ng/ml)
CTL
1
10
50
pStat6
Stat6
GAPDH
IL-10 (ng/ml)
CTL
1
10
50
pStat3
Stat3
GAPDH
(b)
pStat6/Stat6 (ratio to IL-4 1(ng/ml))
2.5
2.0
1.5
1.0
0.5
0
**
**
**
CTL
1
10
50
IL-4 (ng/ml)
pStat3/Stat3 (ratio to CTL)
1.5
1.0
0.5
0
CTL
1
10
50
IL-10 (ng/ml)

[図42]

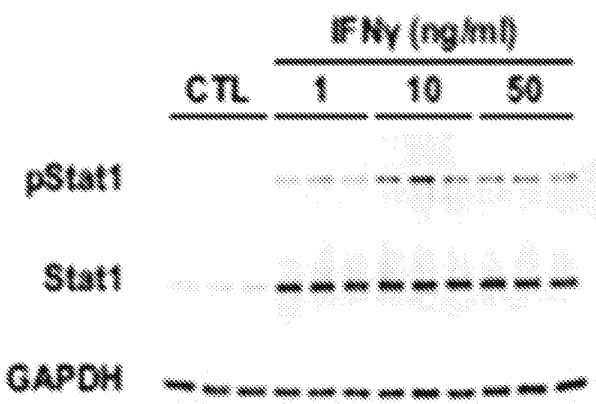

(a)
Angpt/Hprt fold
(ratio to CTL)
Veh
IFNγ (ng/ml)
IL-4 (ng/ml)
IL-10 (ng/ml)
(b)
Vehicle
IFNγ
siCTL
siStat1
pStat1
Stat1
GAPDH
(c)
siCTL
siStat1
Stat1/GAPDH
(ratio to Veh+siCTL)
pStat1/GAPDH
(ratio to IFNγ+siCTL)

[図43]

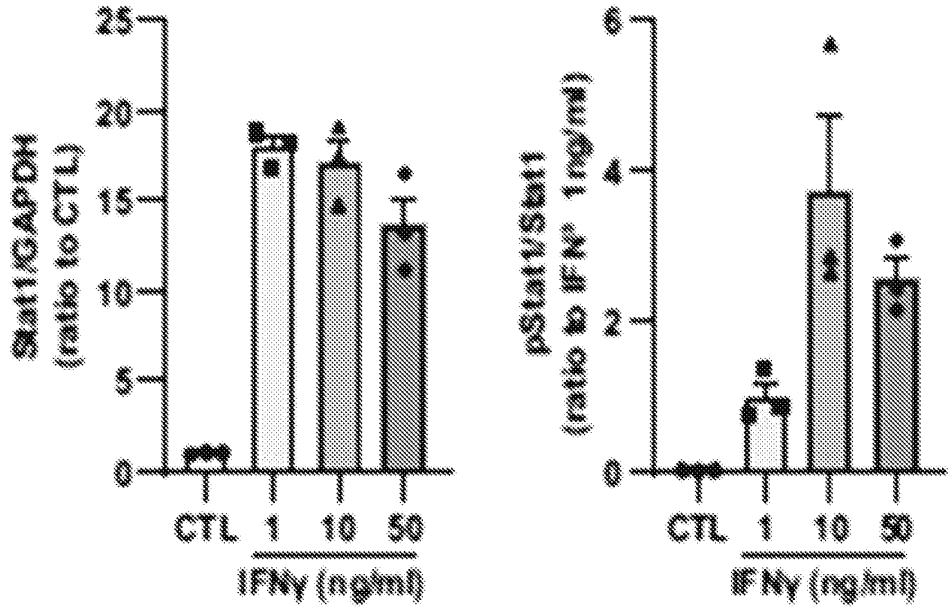

siCTL
siStat1
**
*
Angptl1/Rps18
(ratio to Veh+siCTL)
3
2
1
0
Veh
IFNγ

[図44]

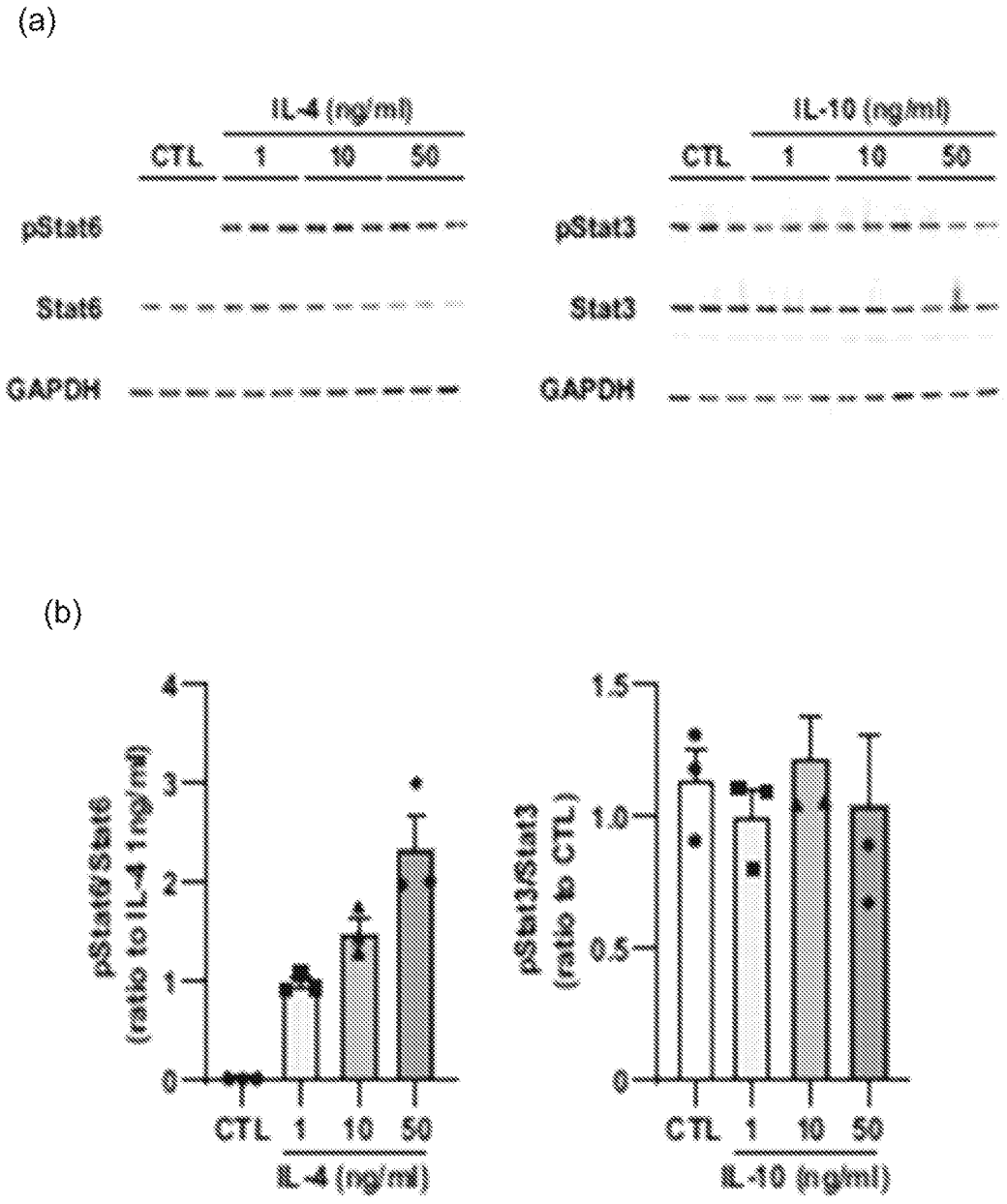
(a)


IFNγ (ng/ml)
CTL
1
10
50
pStat1
Stat1
GAPDH

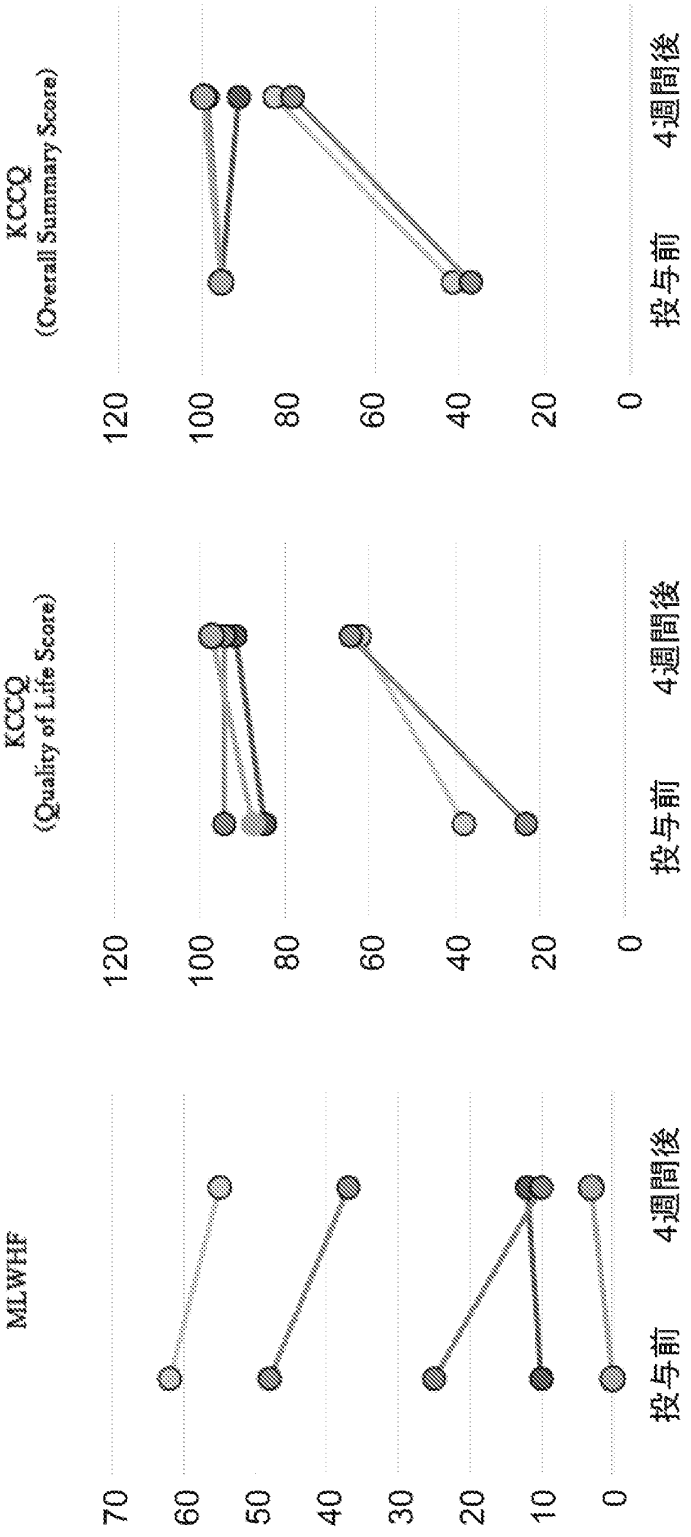
(b)


Stat1/GAPDH (ratio to CTL)
25
20
15
10
5
0
CTL
1
10
50
IFNγ (ng/ml)
pStat1/Stat1 (ratio to IFNγ 1ng/ml)
6
4
2
0
CTL
1
10
50
IFNγ (ng/ml)

[図45]


(a)
IL-4 (ng/ml)
CTL
1
10
50
pStat6
Stat6
GAPDH
IL-10 (ng/ml)
CTL
1
10
50
pStat3
Stat3
GAPDH
(b)
pStat6/Stat6 (ratio to IL-4 1 ng/ml)
0
1
2
3
4
CTL
1
10
50
IL-4 (ng/ml)
pStat3/Stat3 (ratio to CTL)
0
0.5
1.0
1.5
CTL
1
10
50
IL-10 (ng/ml)

[図46]


KCCQ
(Overall Summary Score)
120
100
80
60
40
20
0
投与前
4週間後
KCCQ
(Quality of Life Score)
120
100
80
60
40
20
0
投与前
4週間後
MLWHF
70
60
50
40
30
20
10
0
投与前
4週間後