FIGURE 1A

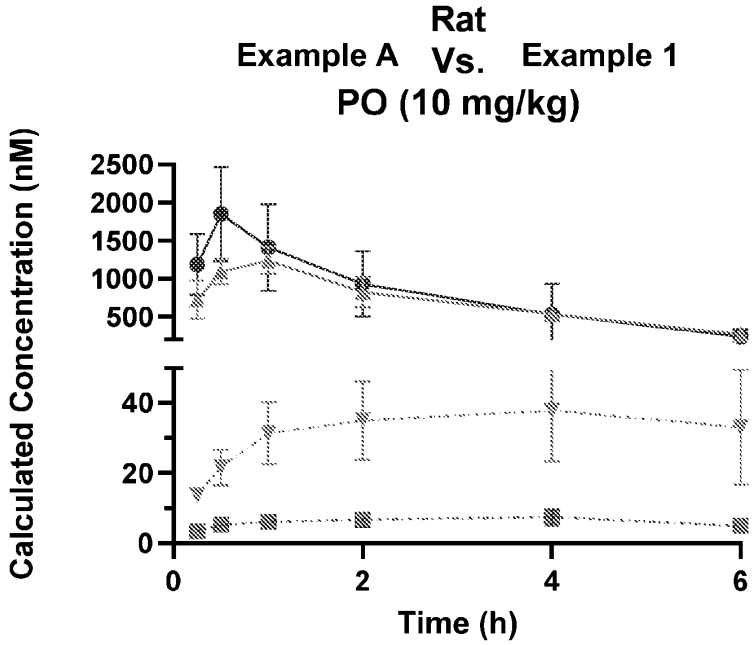


FIGURE 1B

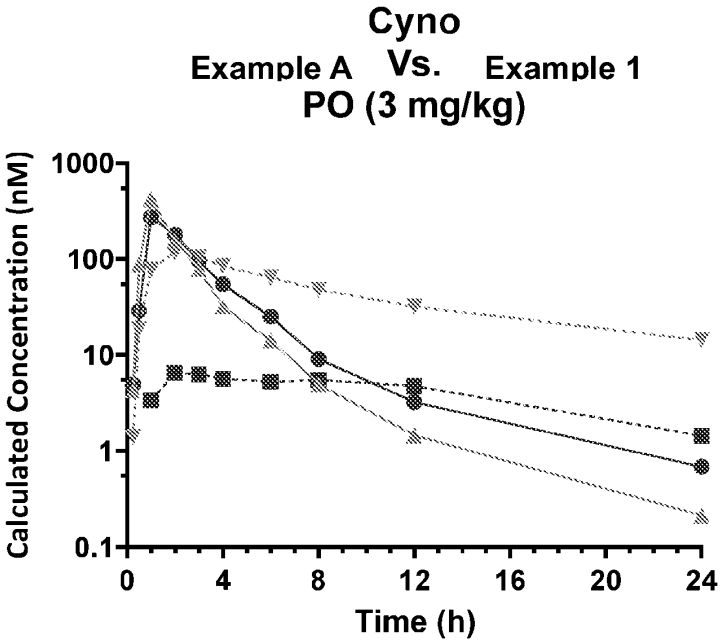


FIGURE 1C

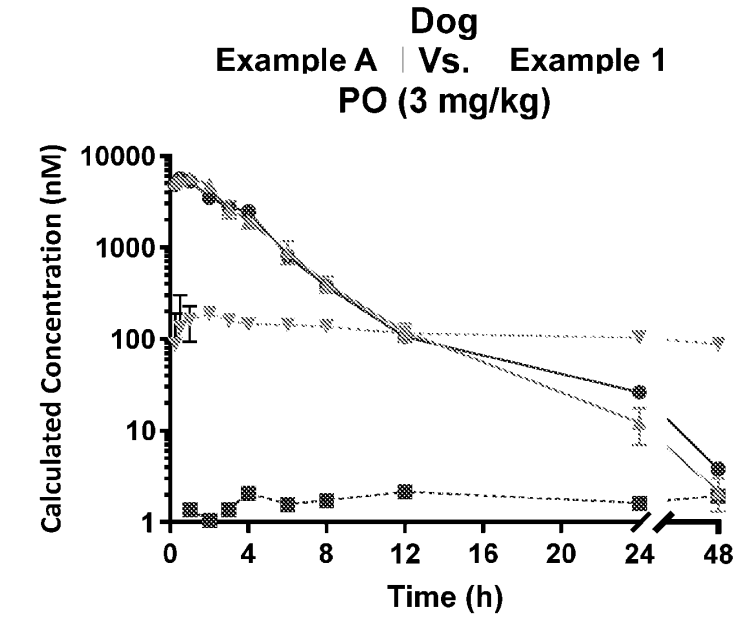

Dog
Example A Vs. Example 1
PO (3 mg/kg)
Calculated Concentration (nM)
10000
1000
100
10
1
0
4
8
12
16
20
24
48
Time (h)
Example A
Example 1
Diastereomer from Example A
Diastereomer from Example 1

FIGURE 2

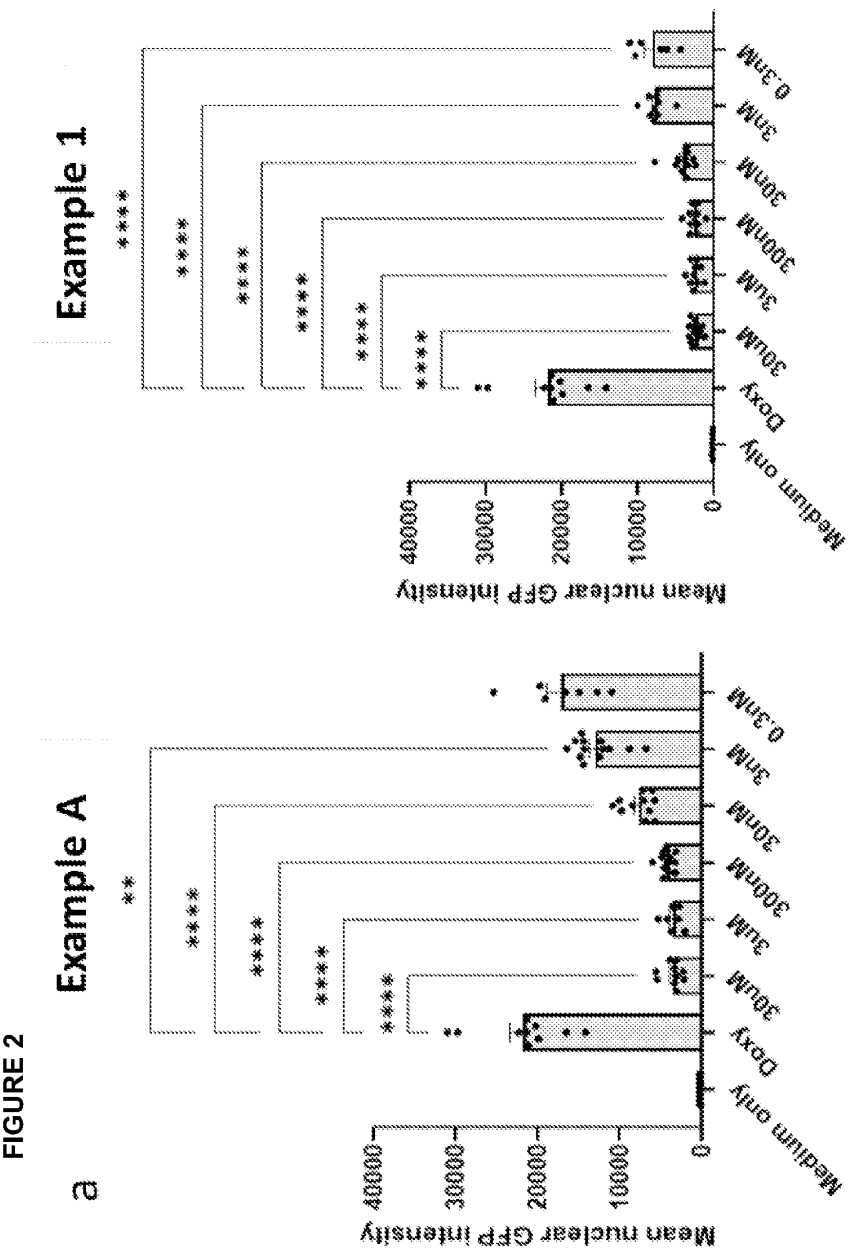
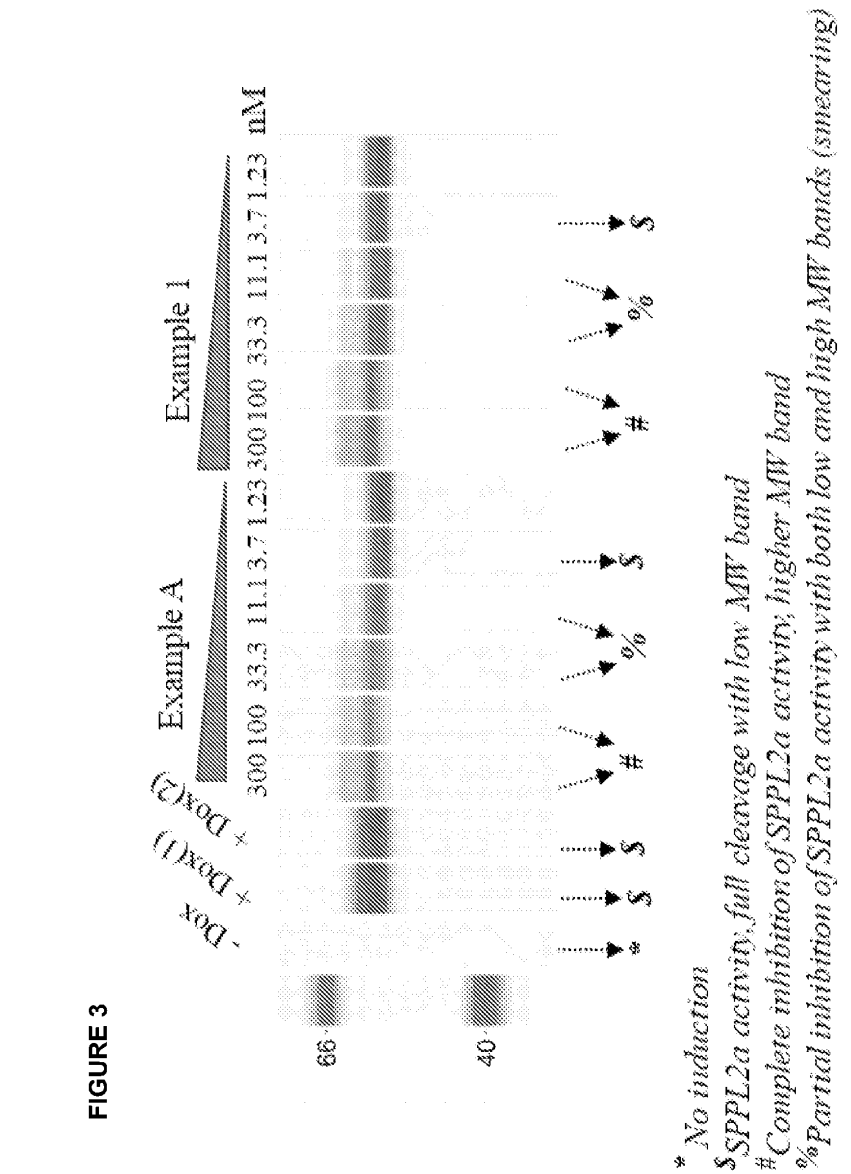

a
Example A
Mean nuclear GFP intensity
40000
30000
20000
10000
0
Medium only
Doxy
30uM
3uM
300nM
30nM
3nM
0.3nM
**
****
****
****
****
****
Example 1
Mean nuclear GFP intensity
40000
30000
20000
10000
0
Medium only
Doxy
30uM
3uM
300nM
30nM
3nM
0.3nM
**
****
****
****
****
****

FIGURE 3


- Dox
+ Dox(1)
+ Dox(2)
Example A
Example 1
300 100 33.3 11.1 3.7 1.23 300 100 33.3 11.1 3.7 1.23 nM
66
40
* $ $ # % $ # % $
* No induction
$SPPL2a activity, full cleavage with low MW band
#Complete inhibition of SPPL2a activity, higher MW band
%Partial inhibition of SPPL2a activity with both low and high MW bands (smearing)

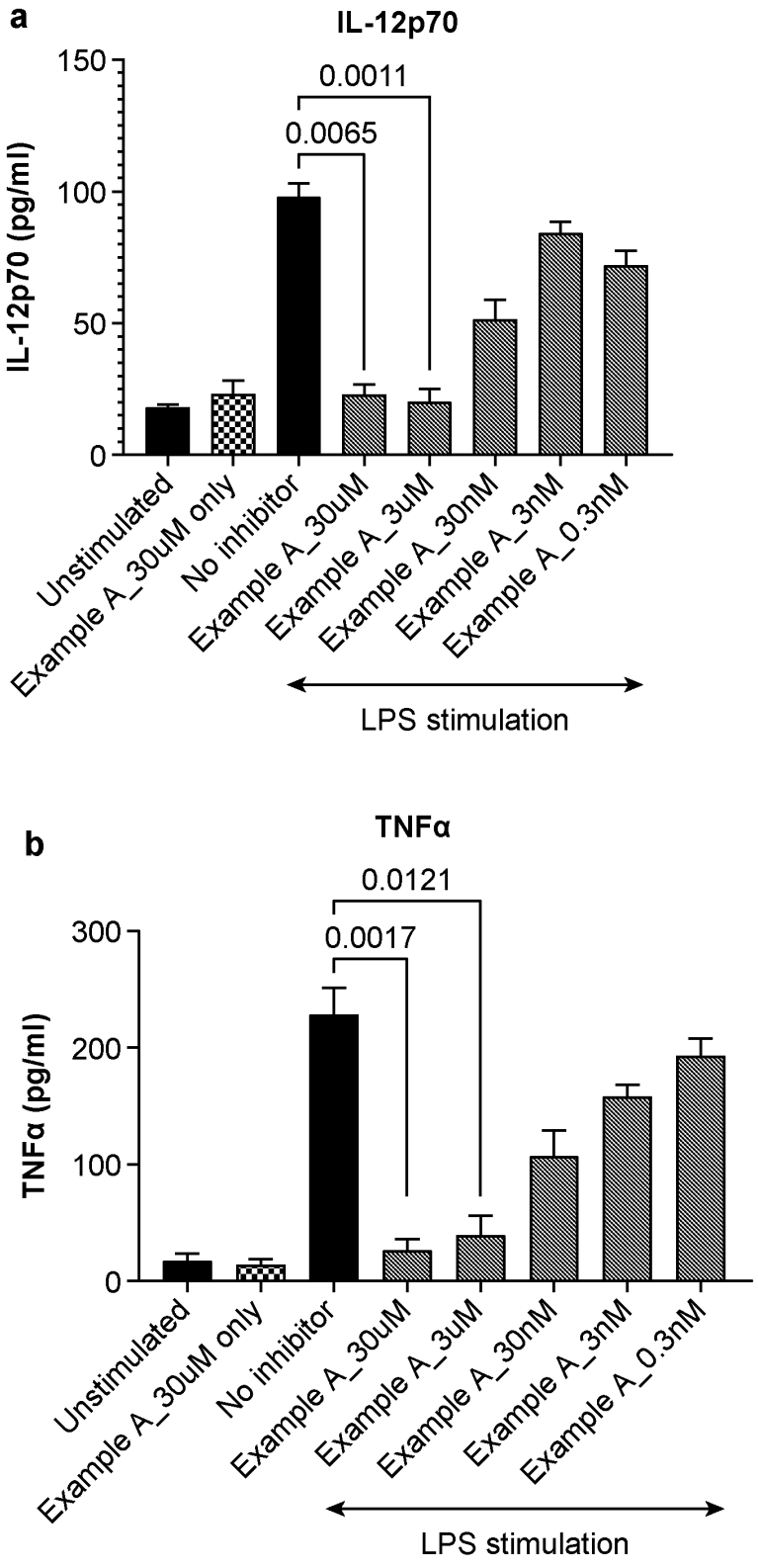

a
IL-12p70
IL-12p70 (pg/ml)
150
100
50
0
0.0011
0.0065
Unstimulated
Example A_30uM only
No inhibitor
Example A_30uM
Example A_3uM
Example A_30nM
Example A_3nM
Example A_0.3nM
LPS stimulation
b
TNFα
TNFα (pg/ml)
300
200
100
0
0.0121
0.0017
Unstimulated
Example A_30uM only
No inhibitor
Example A_30uM
Example A_3uM
Example A_30nM
Example A_3nM
Example A_0.3nM
LPS stimulation

FIG. 4

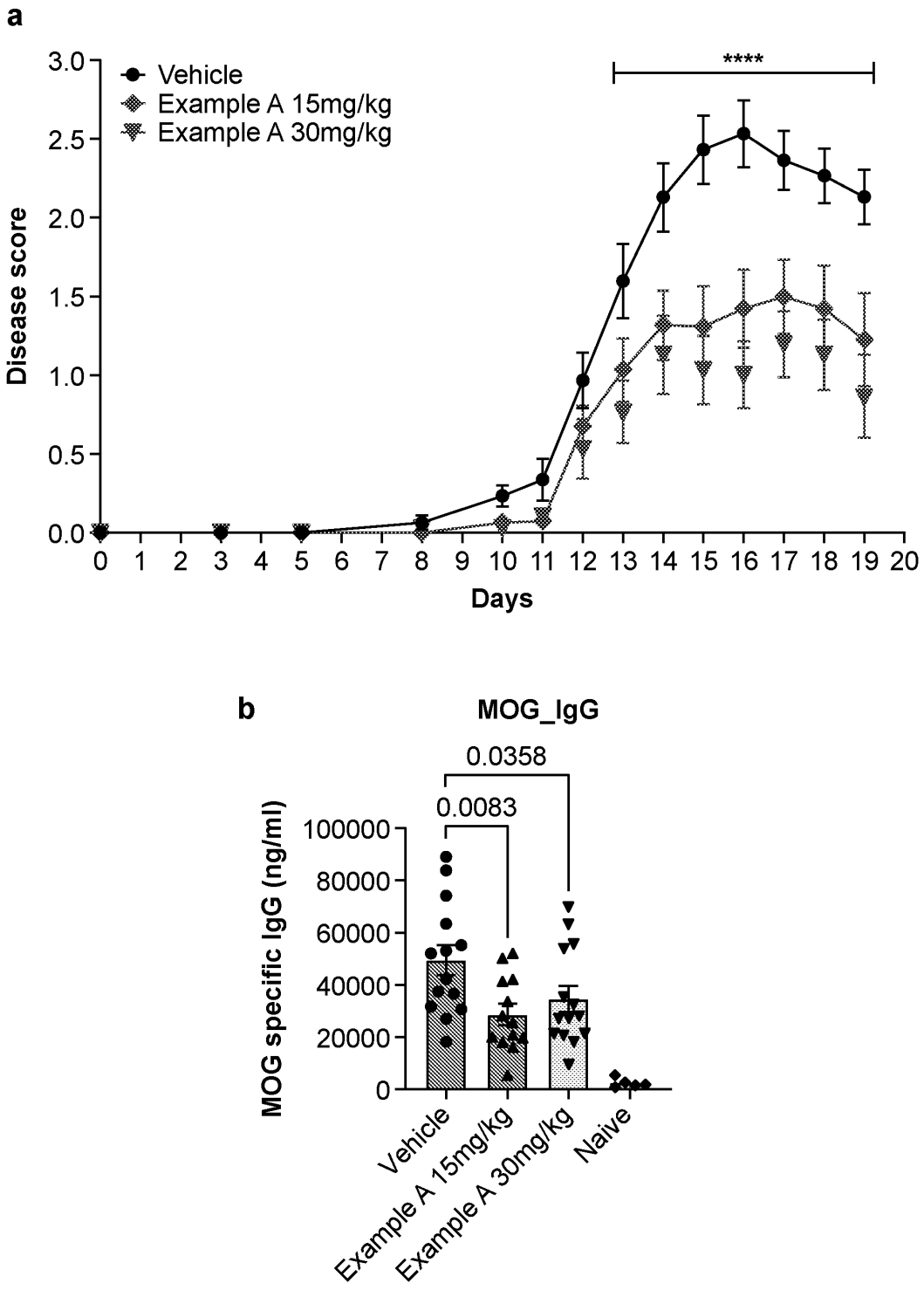

a
Vehicle
Example A 15mg/kg
Example A 30mg/kg
****
Disease score
Days
b
MOG_IgG
0.0358
0.0083
MOG specific IgG (ng/ml)
Vehicle
Example A 15mg/kg
Example A 30mg/kg
Naive

FIG. 5

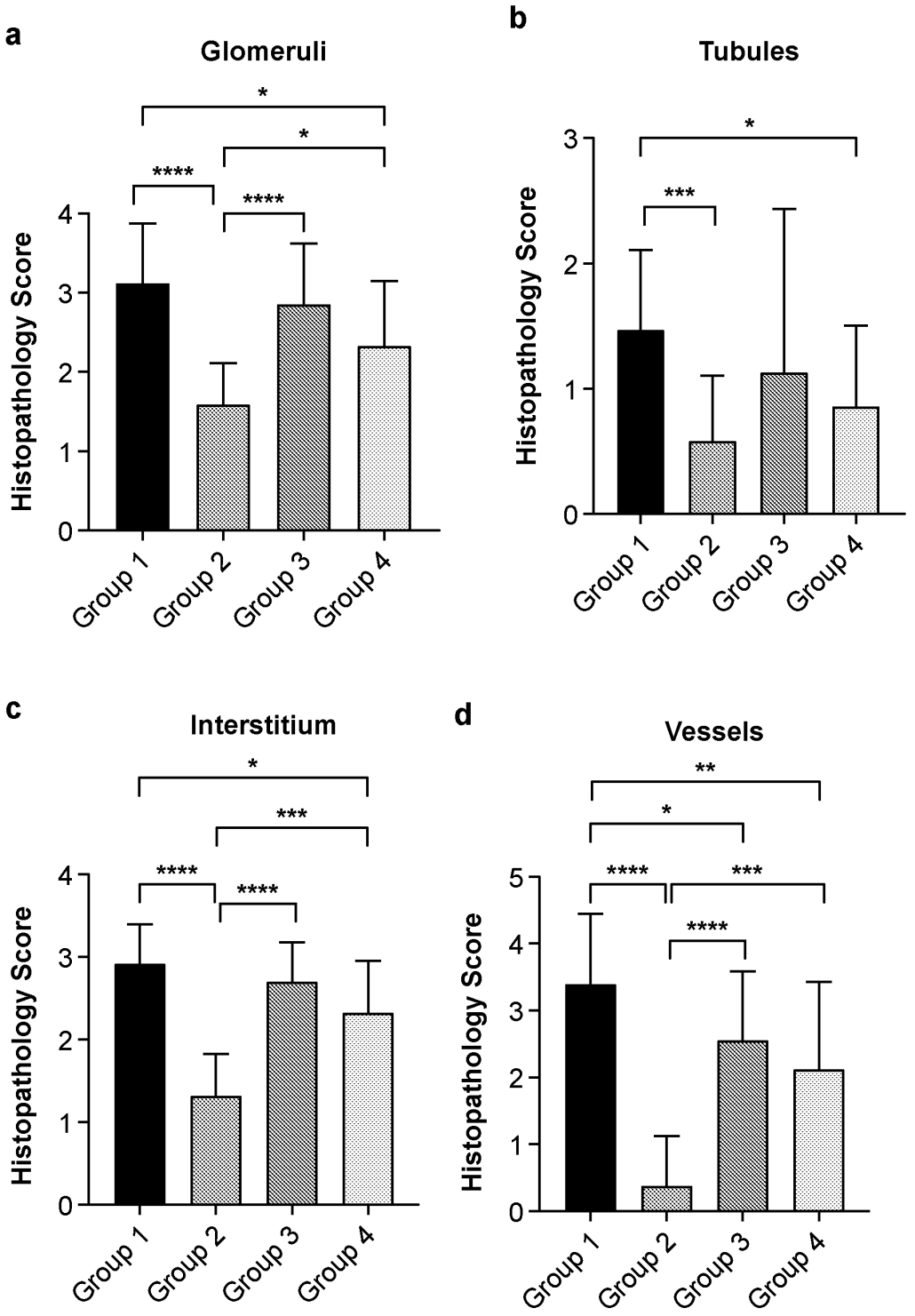

a
Glomeruli
Histopathology Score
0
1
2
3
4
*
*
****
****
Group 1
Group 2
Group 3
Group 4
b
Tubules
Histopathology Score
0
1
2
3
*
***
Group 1
Group 2
Group 3
Group 4
c
Interstitium
Histopathology Score
0
1
2
3
4
*
***
****
****
Group 1
Group 2
Group 3
Group 4
d
Vessels
Histopathology Score
0
1
2
3
4
5
**
*
****
***
****
Group 1
Group 2
Group 3
Group 4

FIG. 6

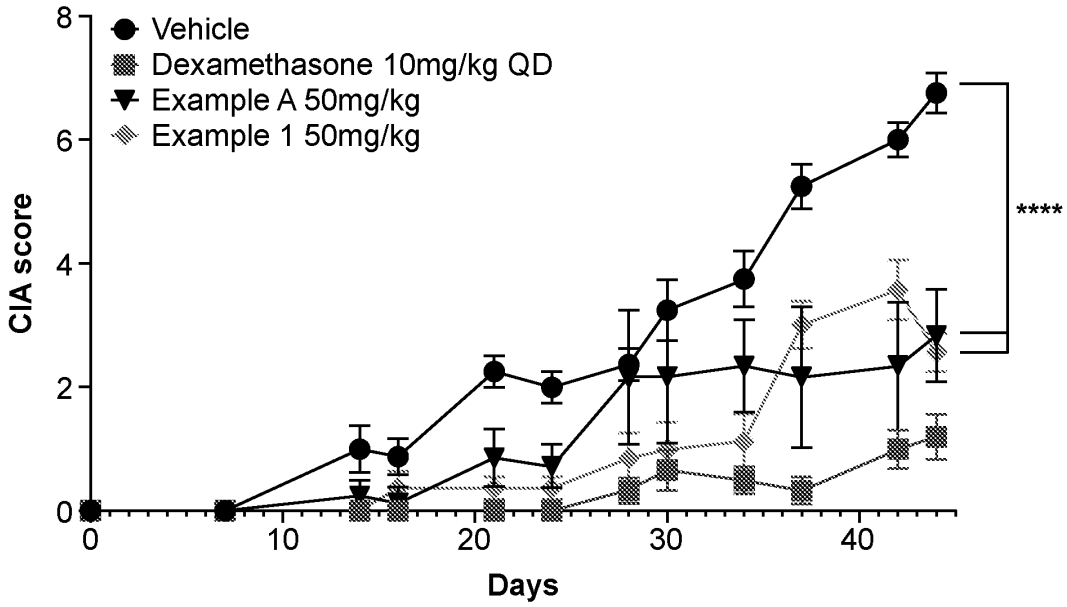

Vehicle
Dexamethasone 10mg/kg QD
Example A 50mg/kg
Example 1 50mg/kg
CIA score
Days
0
2
4
6
8
0
10
20
30
40
****

FIG. 7