FIG. 1

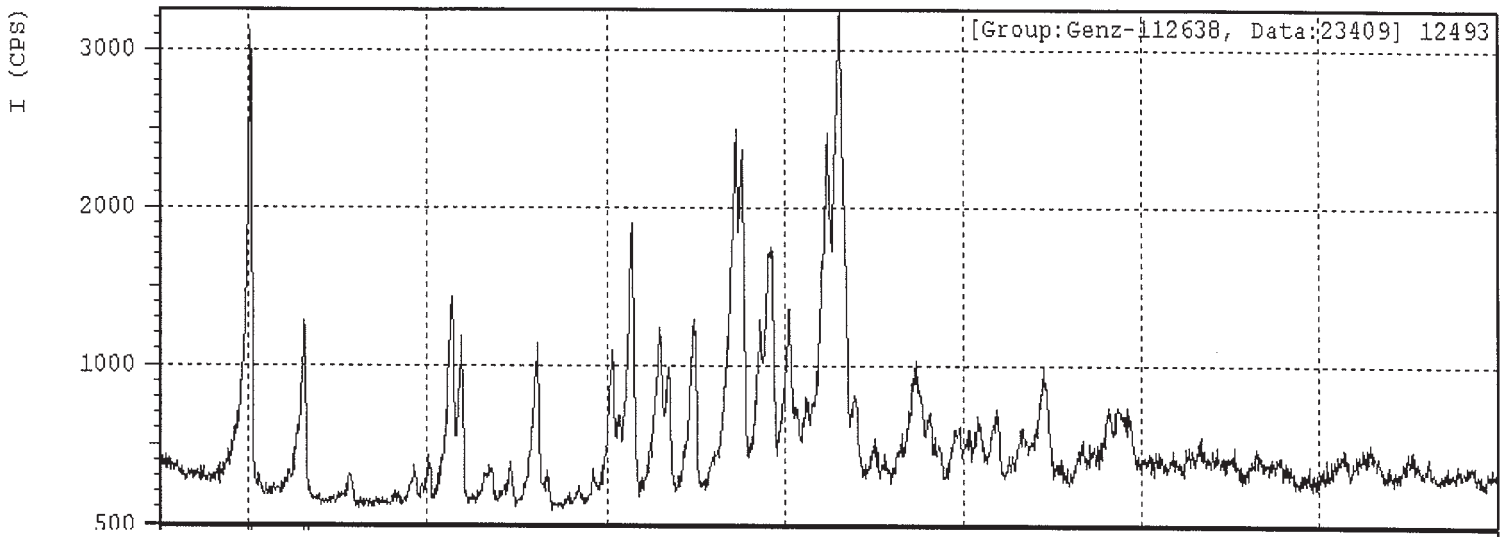


FIG. 2

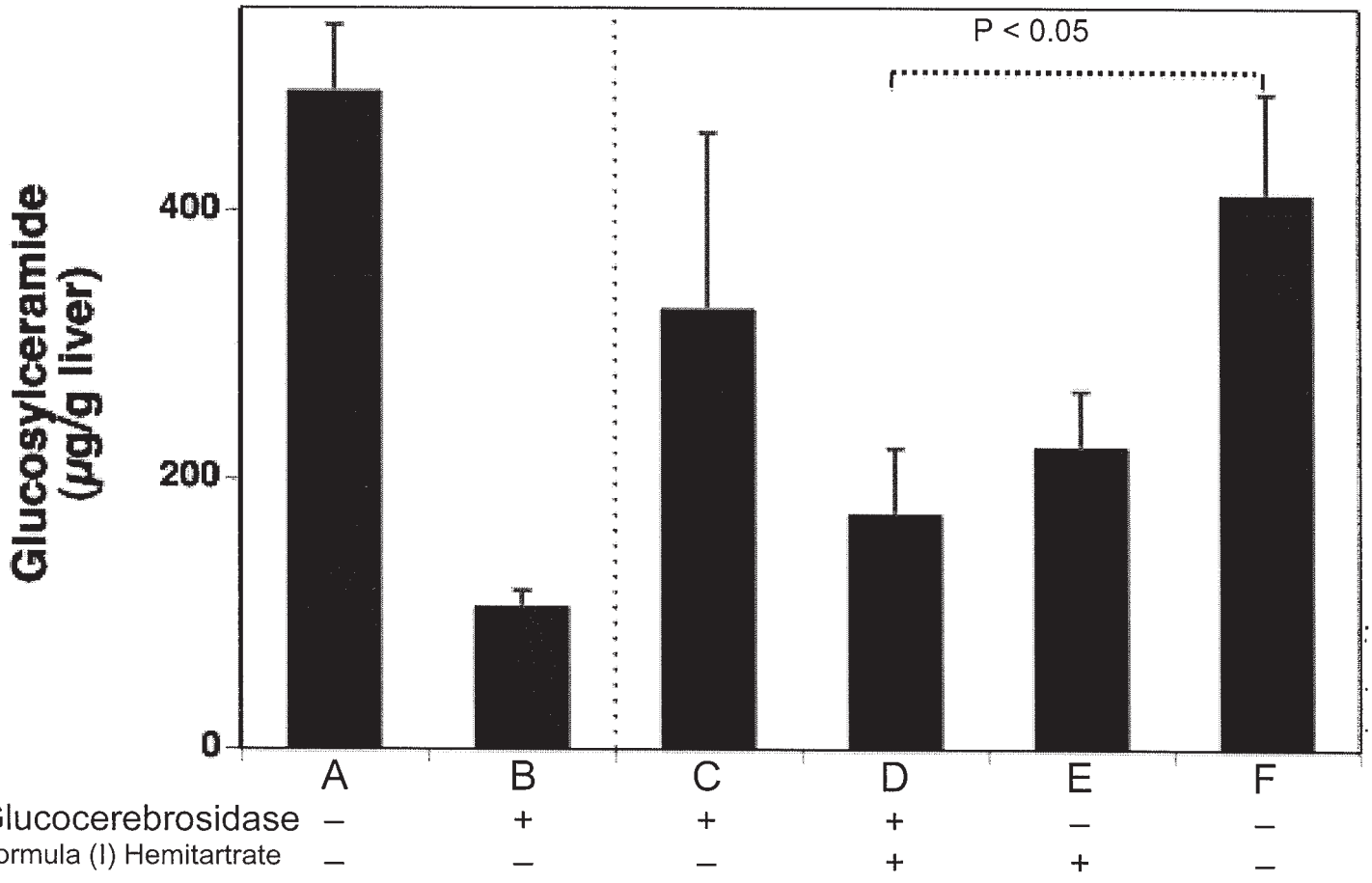

Glucosylceramide (μg/g liver)
400
200
0
P < 0.05
A
B
C
D
E
F
Glucocerebrosidase – + + + – –
Formula (I) Hemitartrate – – – + + –

FIG. 3

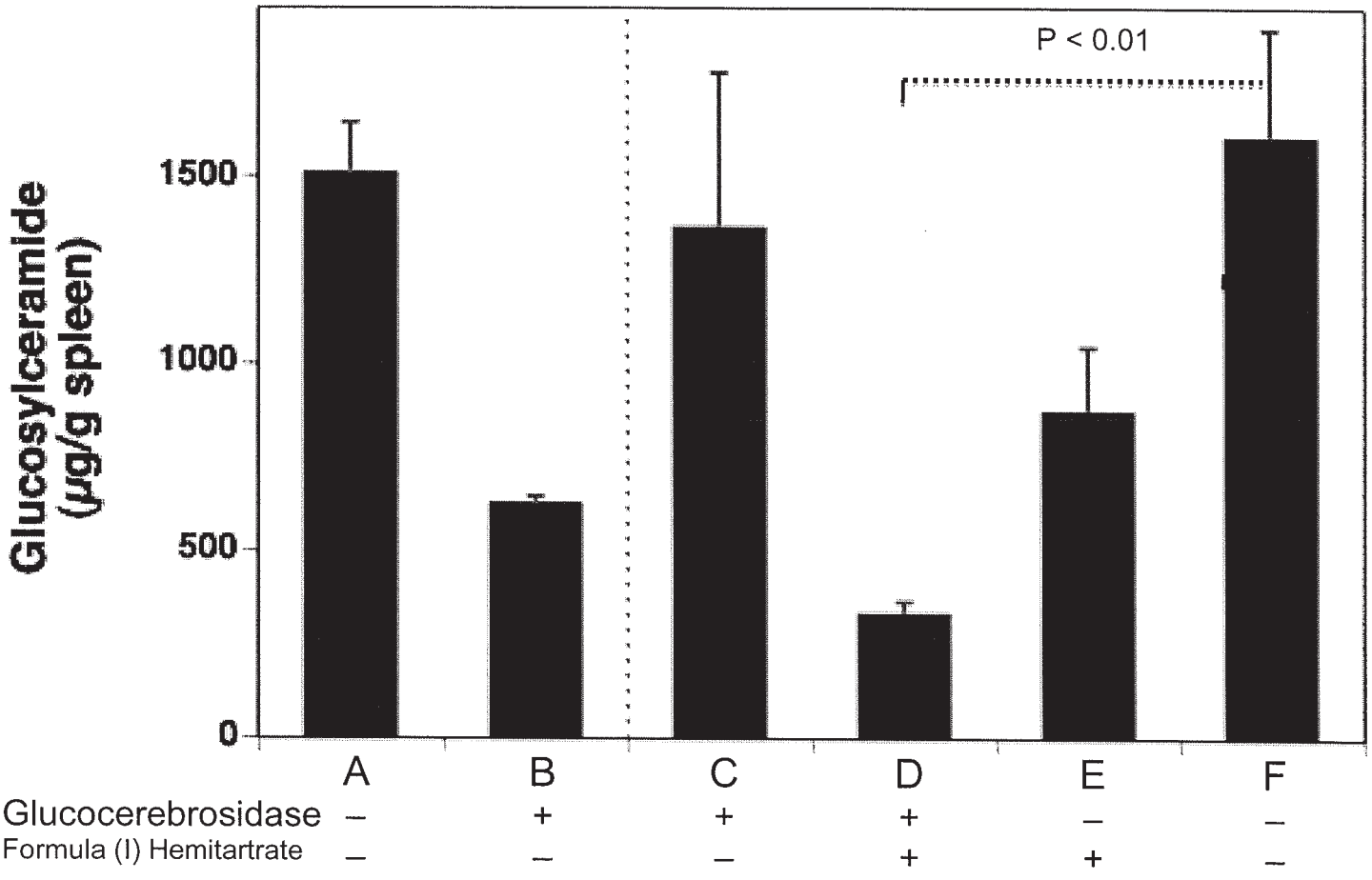

P < 0.01
Glucosylceramide (μg/g spleen)
1500
1000
500
0
A
B
C
D
E
F
Glucocerebrosidase – + + + – –
Formula (I) Hemitartrate – – – + + –

FIG 4.

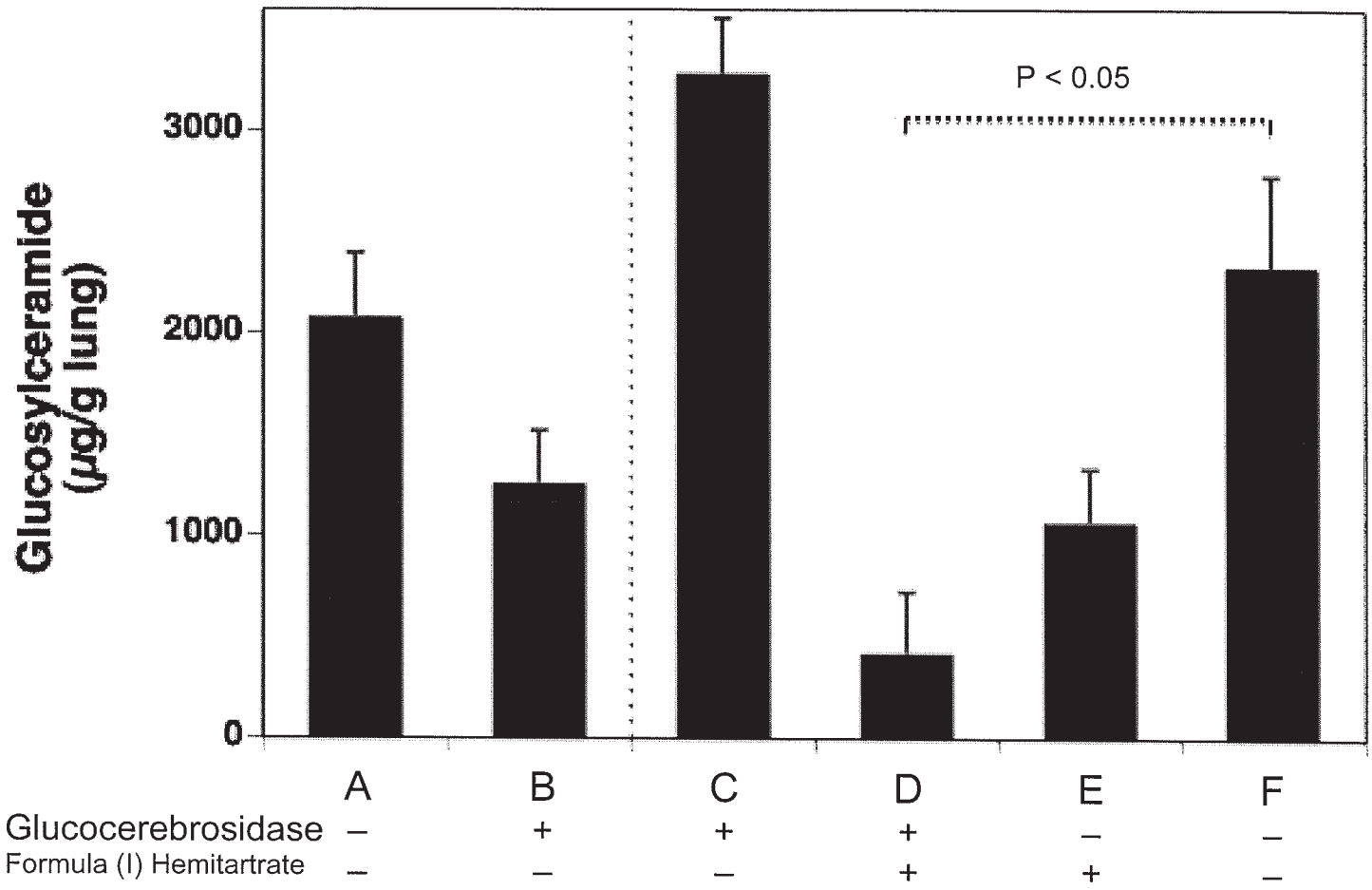
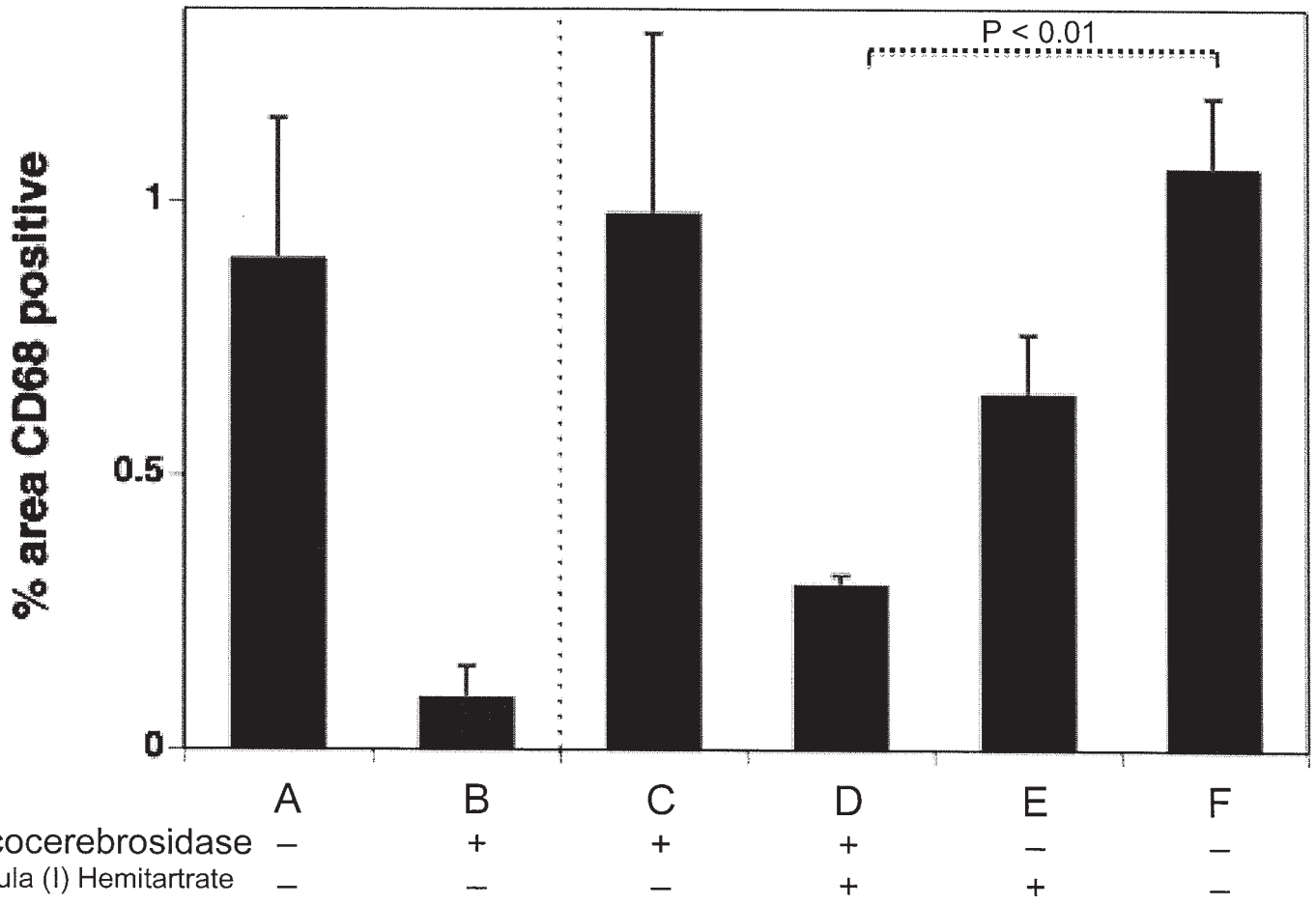

Glucosylceramide (μg/g lung)
3000
2000
1000
0
P < 0.05
A
B
C
D
E
F
Glucocerebrosidase – + + + – –
Formula (I) Hemitartrate – – – + + –

FIG. 5


% area CD68 positive
1
0.5
0
P < 0.01
A
B
C
D
E
F
Glucocerebrosidase – + + + – –
Formula (I) Hemitartrate – – – + + –

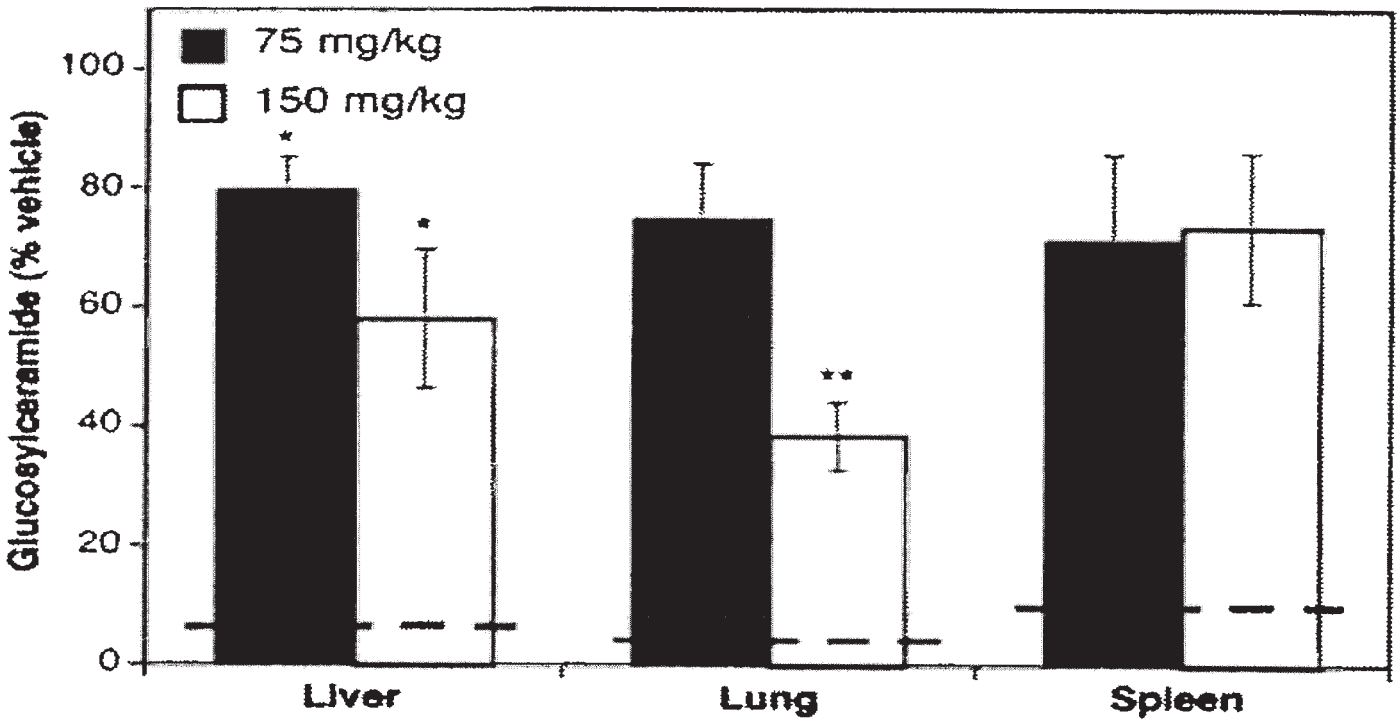
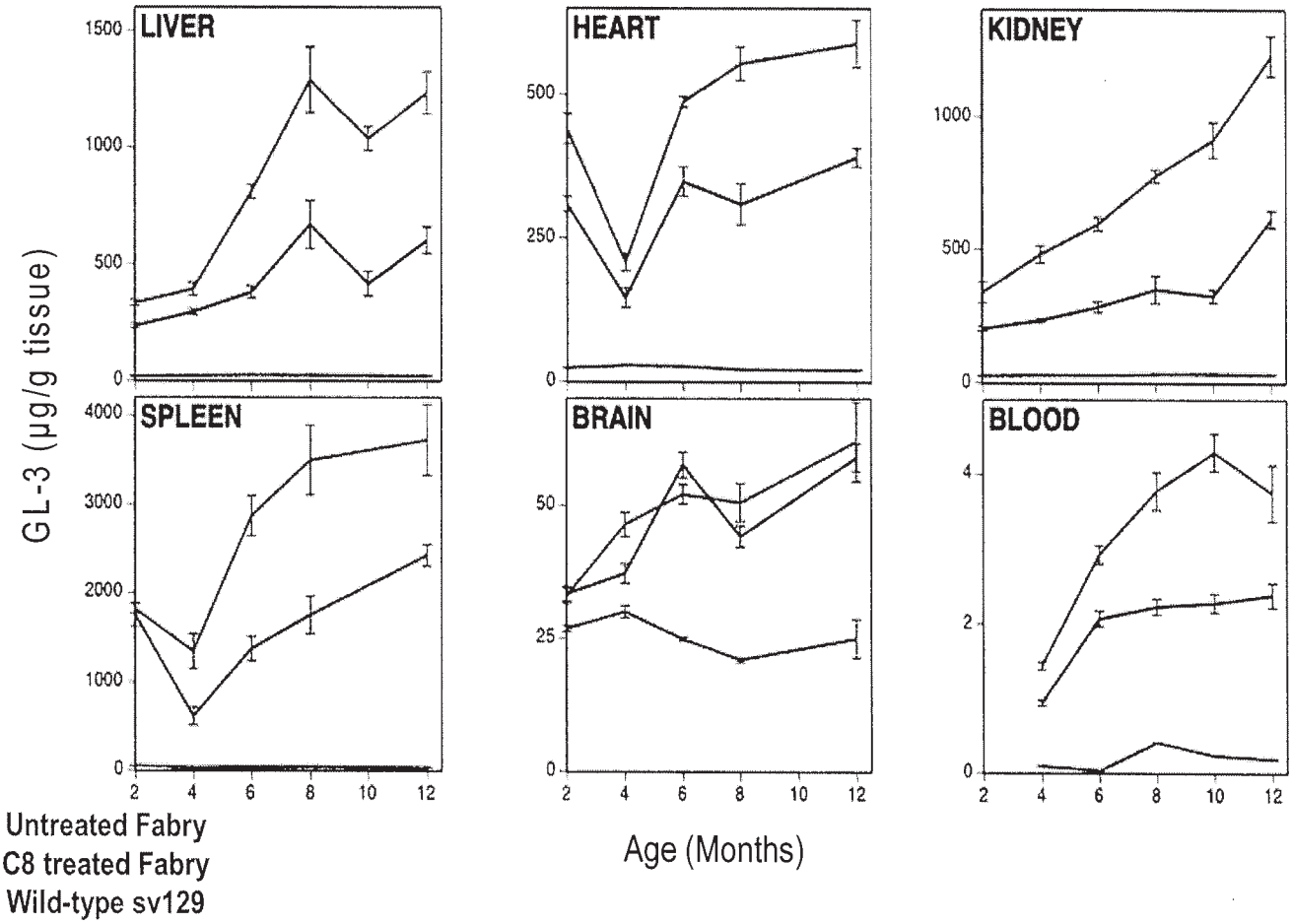

75 mg/kg
150 mg/kg
Glucosylceramide (% vehicle)
100
80
60
40
20
0
*
*
**
Liver
Lung
Spleen

FIG. 6

FIG. 7

Formula (I) Hemitartrate inhibits the extent of GL-3 accumulation in Fabry mice



WO 2011/066352 PCT/US2010/057952

FIG. 8

Formula (I) Hemitartrate delays onset and progression of peripheral neuropathy in Fabry mice

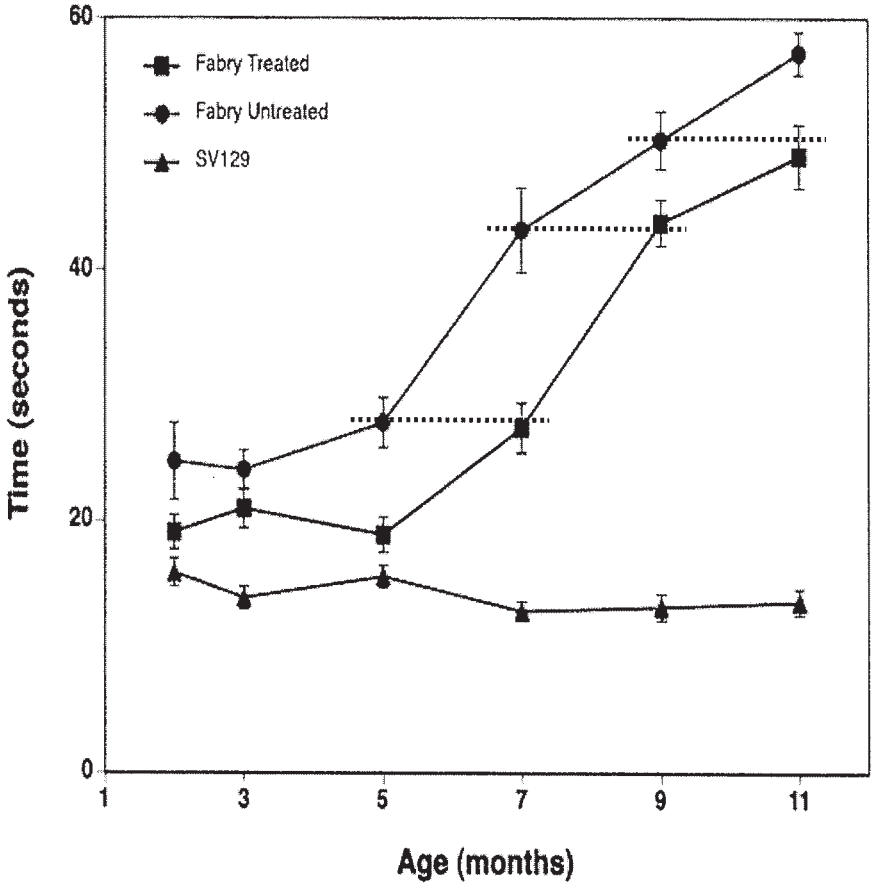
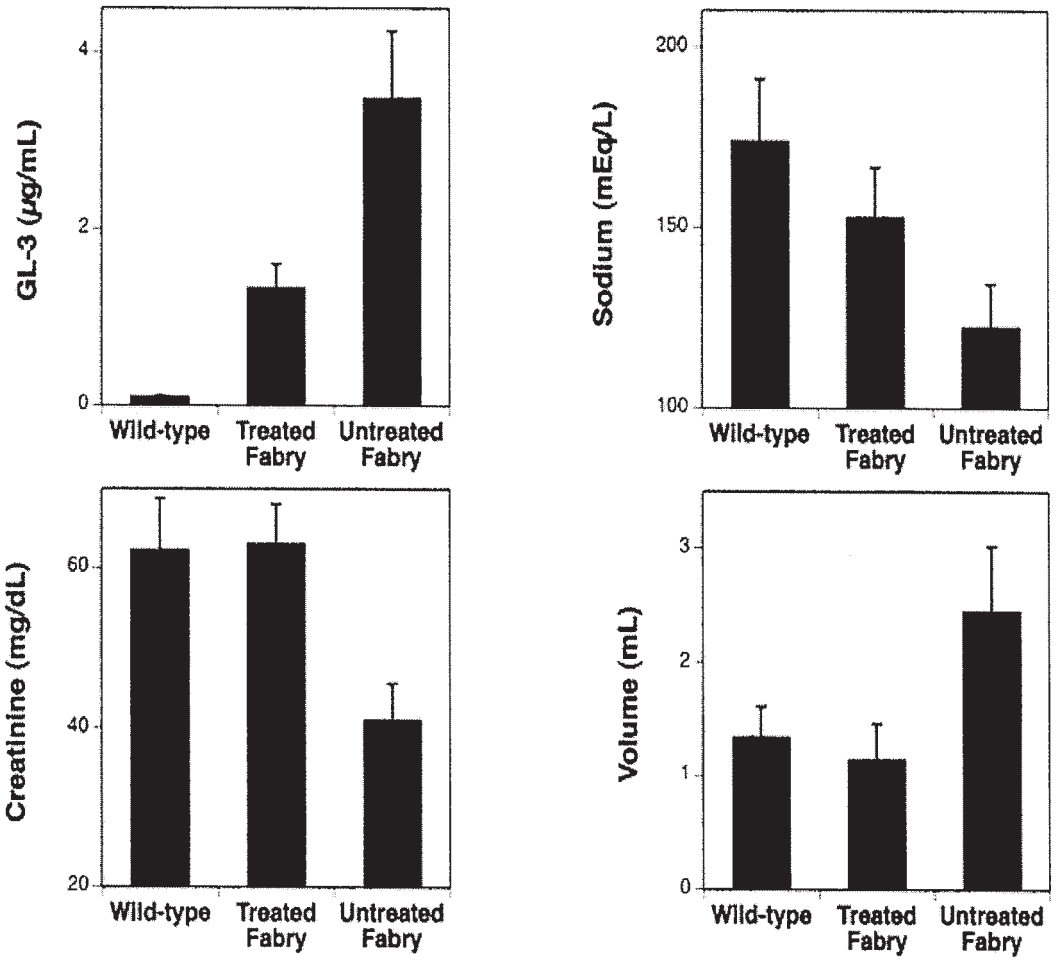


FIG. 9

Treatment of Fabry mice with Formula (I) Hemitartrate improves some markers of kidney function



12-month timepoint

FIG. 10

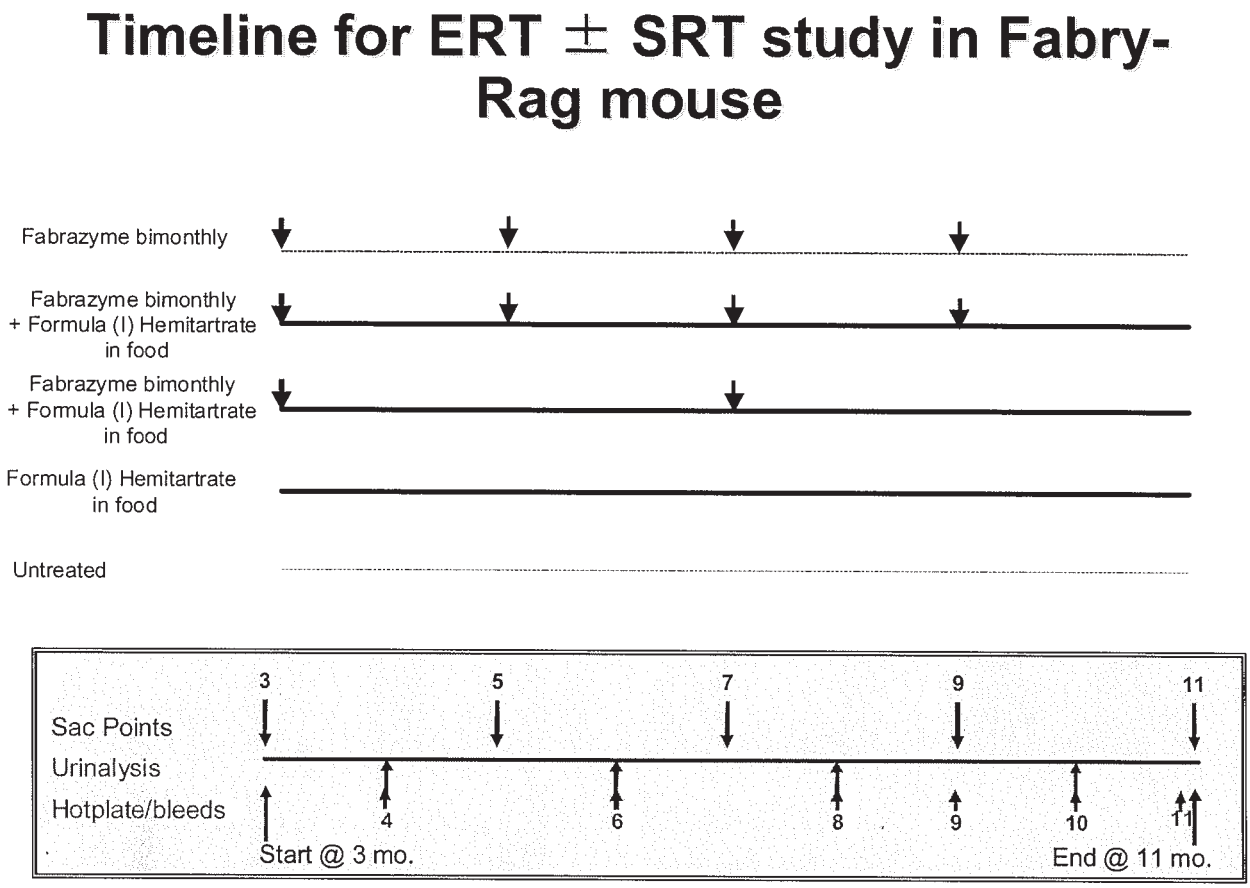

Timeline for ERT ± SRT study in Fabry-Rag mouse
Fabrazyme bimonthly
Fabrazyme bimonthly + Formula (I) Hemitartrate in food
Fabrazyme bimonthly + Formula (I) Hemitartrate in food
Formula (I) Hemitartrate in food
Untreated
3
5
7
9
11
Sac Points
Urinalysis
Hotplate/bleeds
4
6
8
9
10
11
Start @ 3 mo.
End @ 11 mo.

FIG. 11


ERT but not SRT reduces blood GL-3 levels in Fabry-Rag mice
GL-3 (ng/mL blood)
3000
2000
1000
0
3
5
7
9
11
Age (months)
Fab2
Fab2+C8
Fab4+C8
C8
Untreated
WT

FIG. 12

Combination ERT/SRT is most effective at reducing GL-3 levels in Fabry-Rag mice liver & kidney

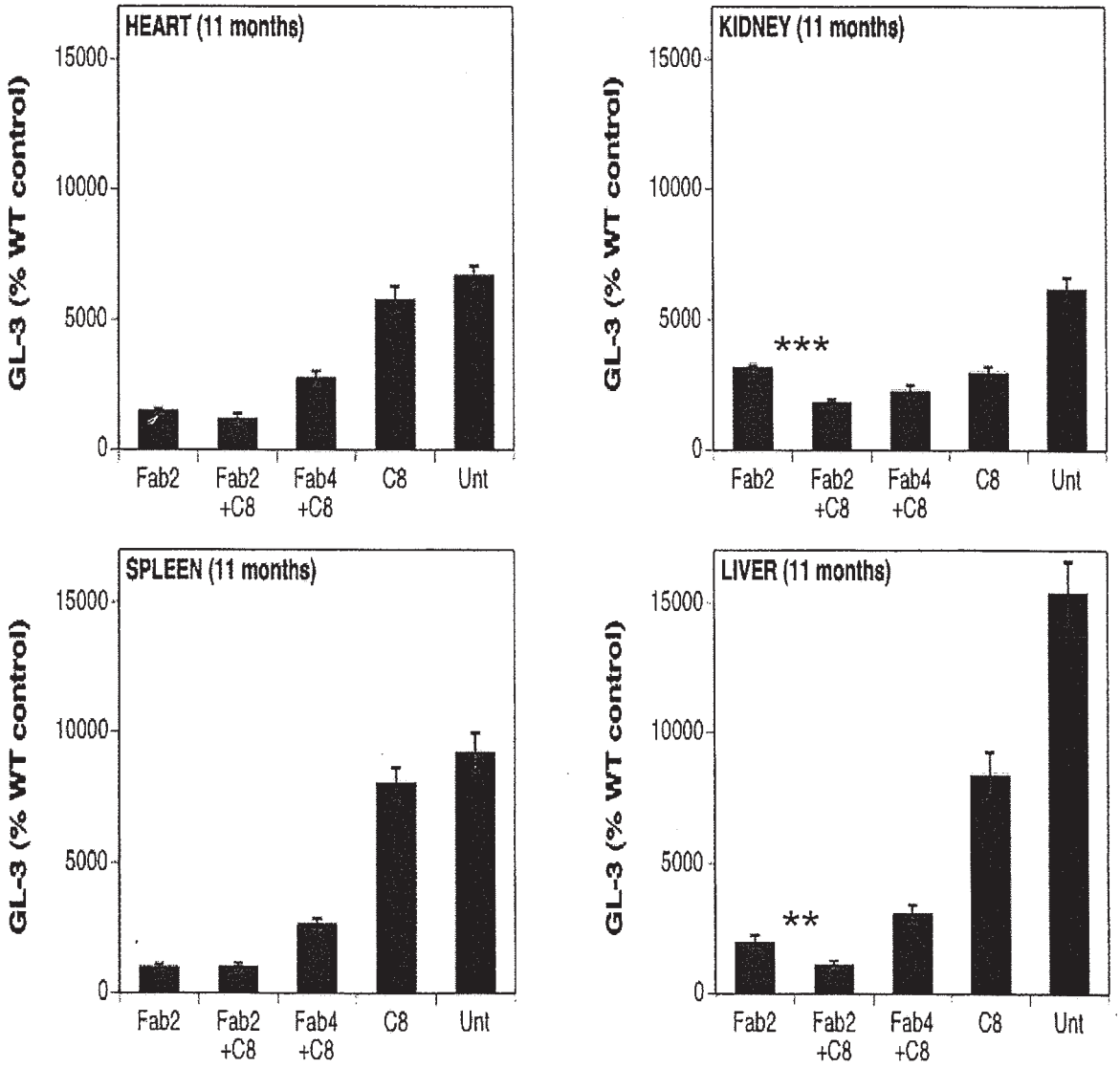


FIG. 13

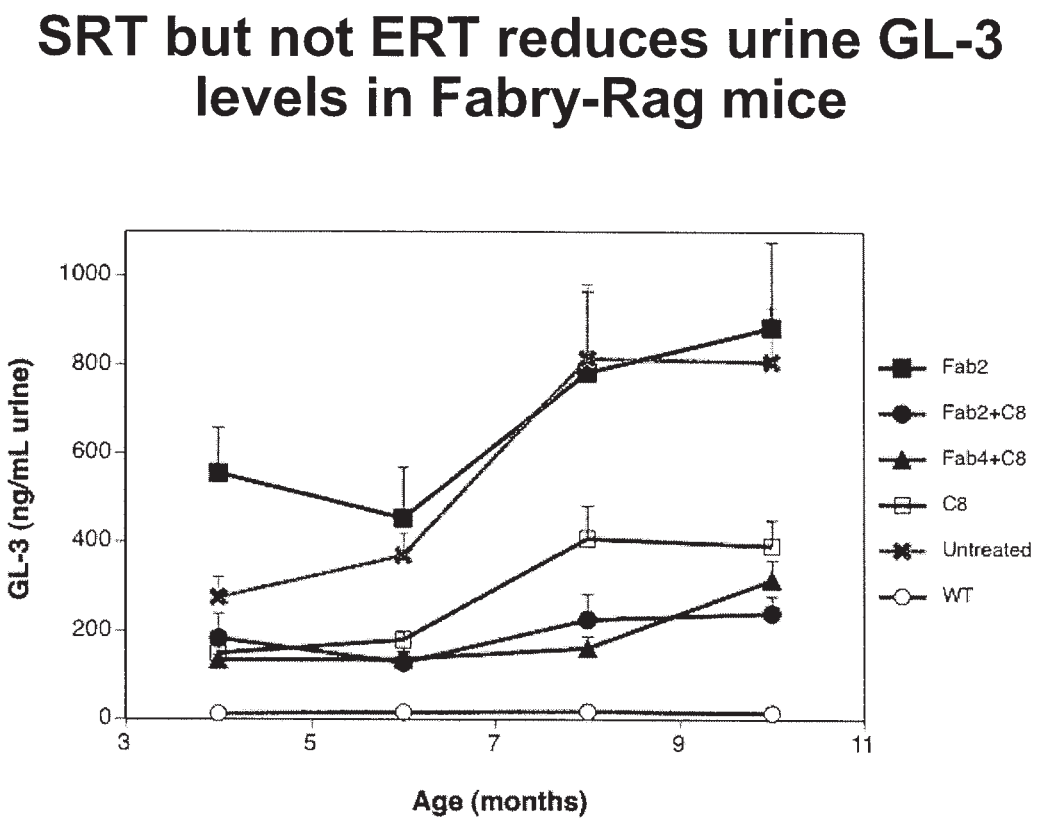

SRT but not ERT reduces urine GL-3 levels in Fabry-Rag mice
GL-3 (ng/mL urine)
1000
800
600
400
200
0
3
5
7
9
11
Age (months)
Fab2
Fab2+C8
Fab4+C8
C8
Untreated
WT

FIG. 14

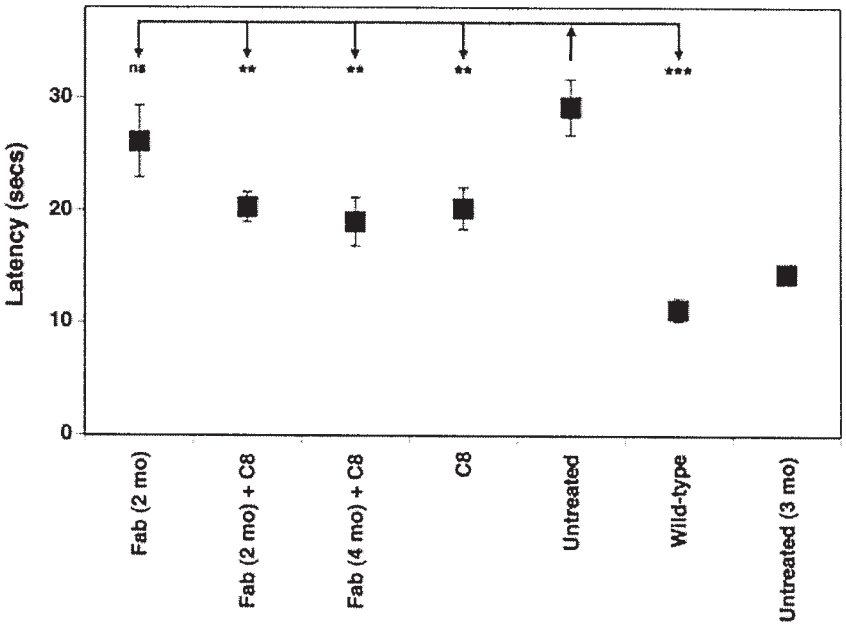
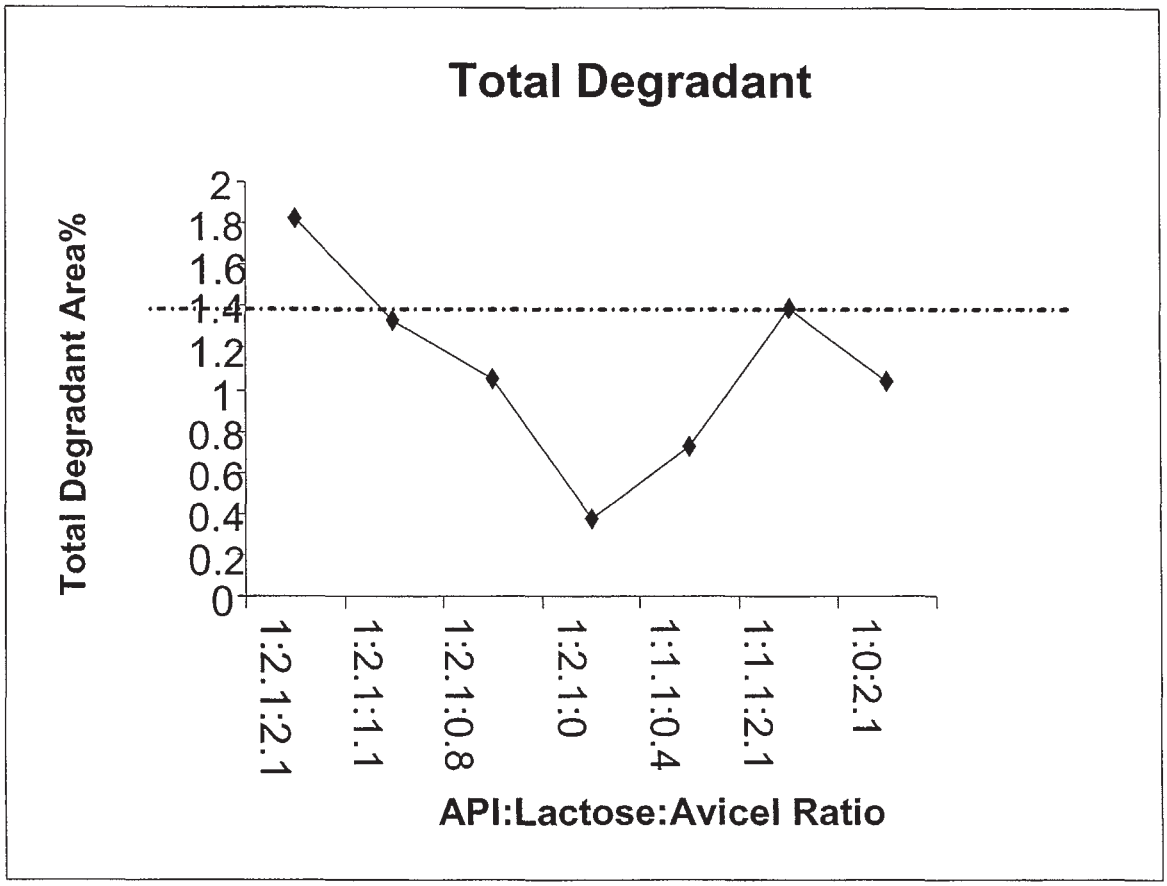

SRT but not ERT delays onset of heat-insensitivity in Fabry-Rag mice (11 months)
Latency (secs)
0
10
20
30
ns
**
**
**
**
***
Fab (2 mo)
Fab (2 mo) + C8
Fab (4 mo) + C8
C8
Untreated
Wild-type
Untreated (3 mo)

FIG 15


Total Degradant
Total Degradant Area%
2
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
0
1:2.1:2.1
1:2.1:1.1
1:2.1:0.8
1:2.1:0
1:1.1:0.4
1:1.1:2.1
1:0:2.1
API:Lactose:Avicel Ratio