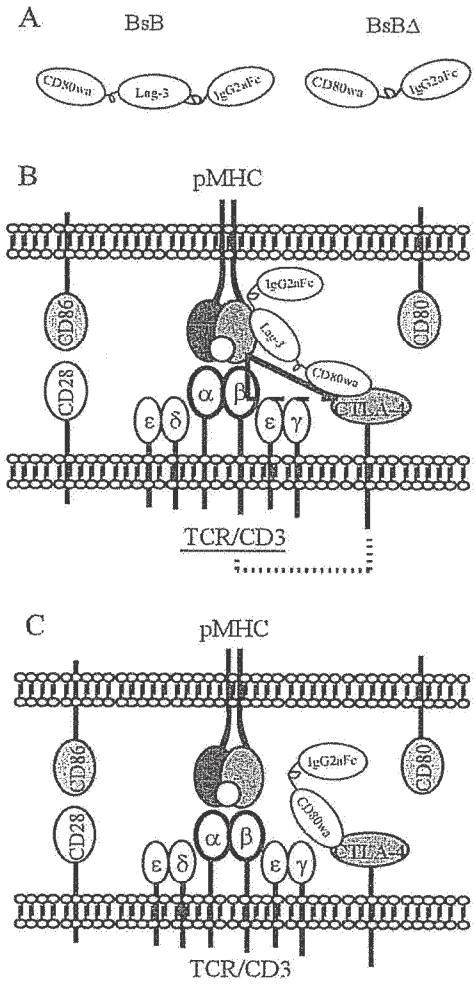

A
BsB
BsBΔ
CD80wa
Lag-3
IgG2aFc
CD80wa
IgG2aFc
B
pMHC
IgG2aFc
Lag-3
CD80wa
CTLA-4
CD86
CD80
CD28
α
β
ε
δ
ε
γ
TCR/CD3
C
pMHC
IgG2aFc
CD80wa
CTLA-4
CD86
CD80
CD28
α
β
ε
δ
ε
γ
TCR/CD3

Figure 1

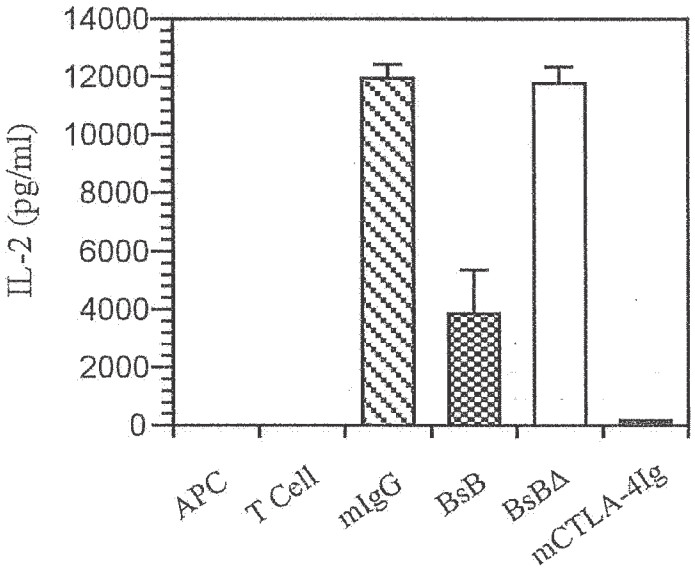
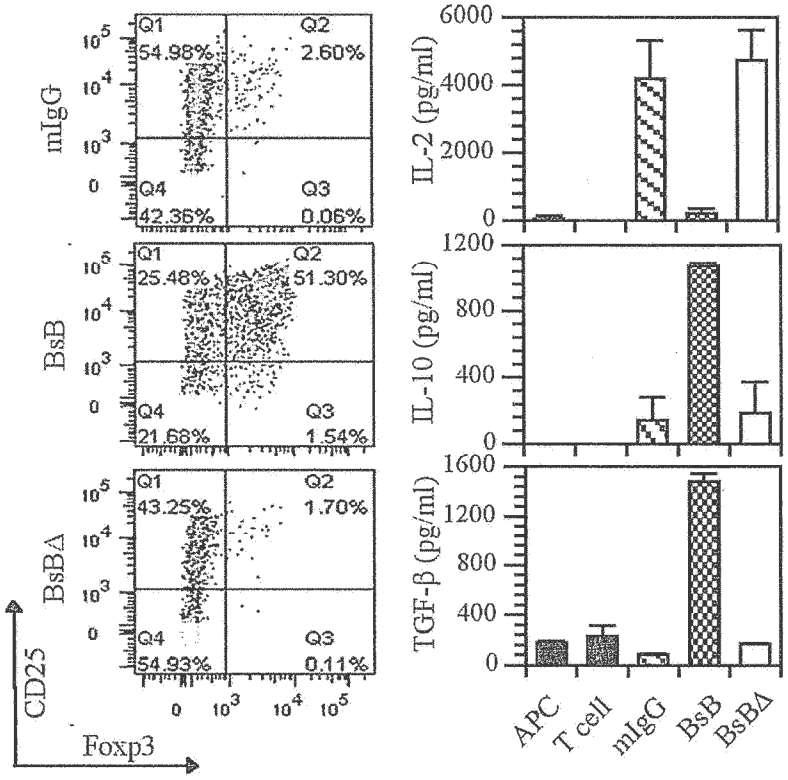

14000
12000
10000
8000
6000
4000
2000
0
IL-2 (pg/ml)
APC
T Cell
mIgG
BsB
BsBΔ
mCTLA-4Ig

Figure 2

A


mIgG
BsB
BsBΔ
Q1
Q2
Q3
Q4
54.98%
2.60%
42.36%
0.06%
25.48%
51.30%
21.68%
1.54%
43.25%
1.70%
54.93%
0.11%
CD25
Foxp3
IL-2 (pg/ml)
IL-10 (pg/ml)
TGF-β (pg/ml)
APC
T cell
mIgG
BsB
BsBΔ

B

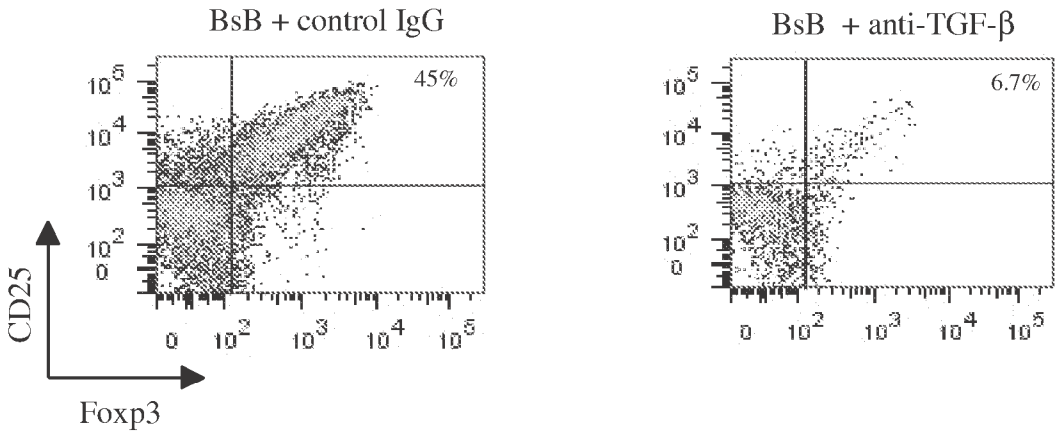

BsB + control IgG
45%
BsB + anti-TGF-β
6.7%
CD25
Foxp3

Figure 3

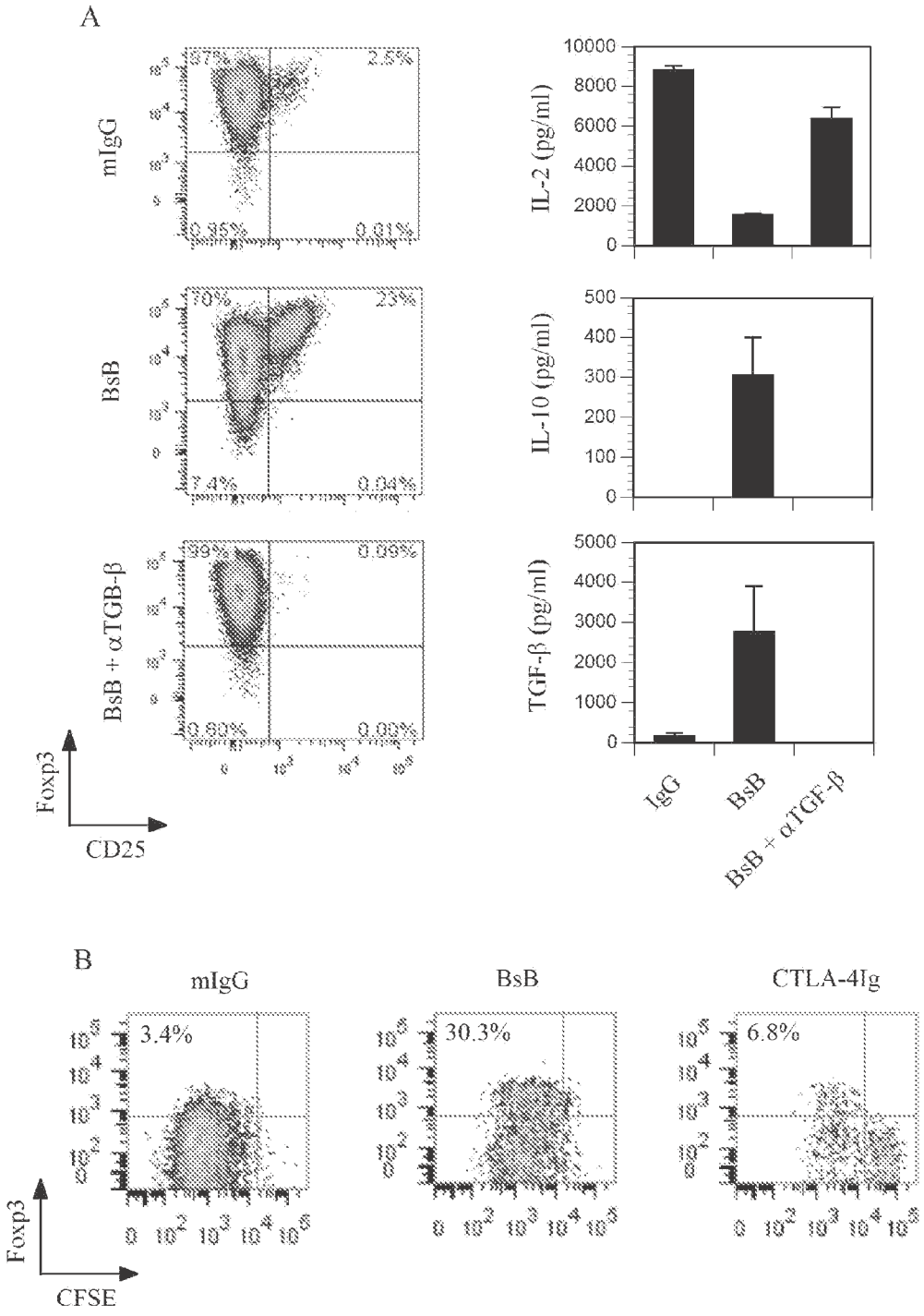

A
mIgG
BsB
BsB + αTGB-β
97%
2.5%
0.35%
0.01%
70%
23%
7.4%
0.04%
99%
0.09%
0.90%
0.00%
Foxp3
CD25
IL-2 (pg/ml)
IL-10 (pg/ml)
TGF-β (pg/ml)
IgG
BsB
BsB + αTGF-β
B
mIgG
BsB
CTLA-4Ig
3.4%
30.3%
6.8%
Foxp3
CFSE

Figure 4

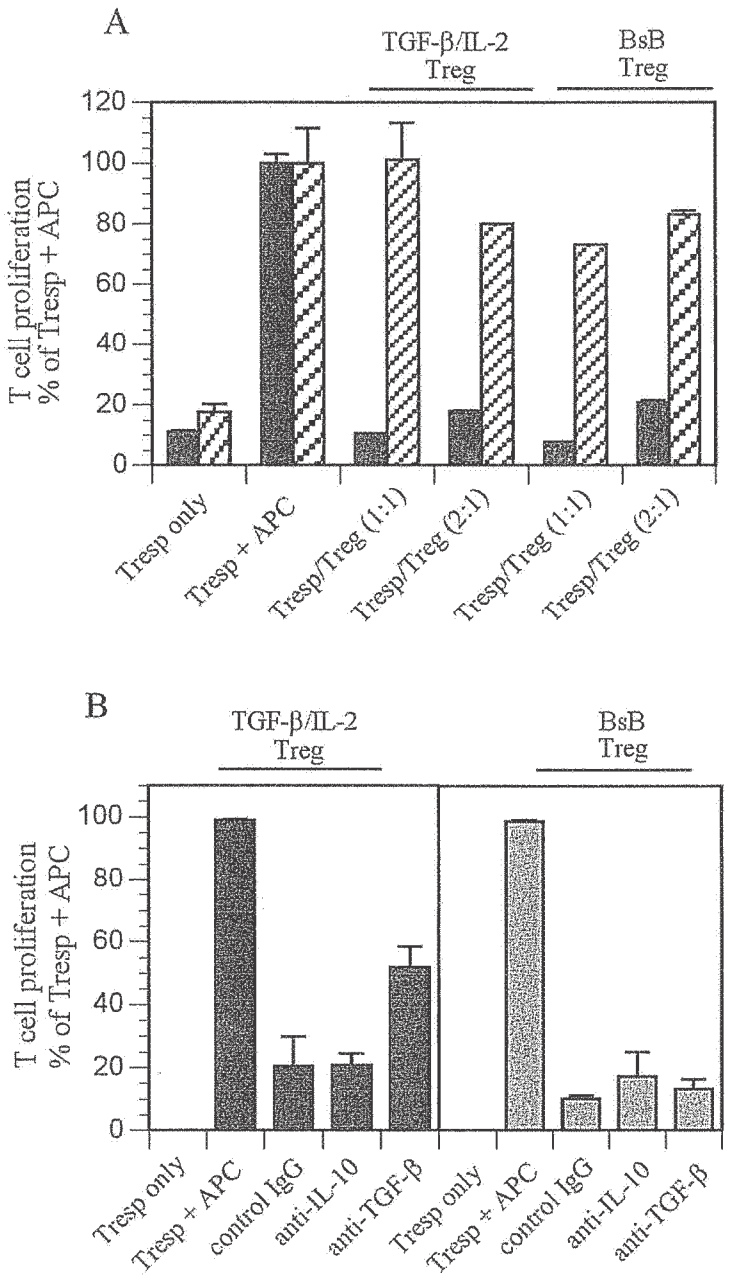

A
TGF-β/IL-2
Treg
BsB
Treg
T cell proliferation
% of Tresp + APC
120
100
80
60
40
20
0
Tresp only
Tresp + APC
Tresp/Treg (1:1)
Tresp/Treg (2:1)
Tresp/Treg (1:1)
Tresp/Treg (2:1)
B
TGF-β/IL-2
Treg
BsB
Treg
T cell proliferation
% of Tresp + APC
100
80
60
40
20
0
Tresp only
Tresp + APC
control IgG
anti-IL-10
anti-TGF-β
Tresp only
Tresp + APC
control IgG
anti-IL-10
anti-TGF-β

Figure 5

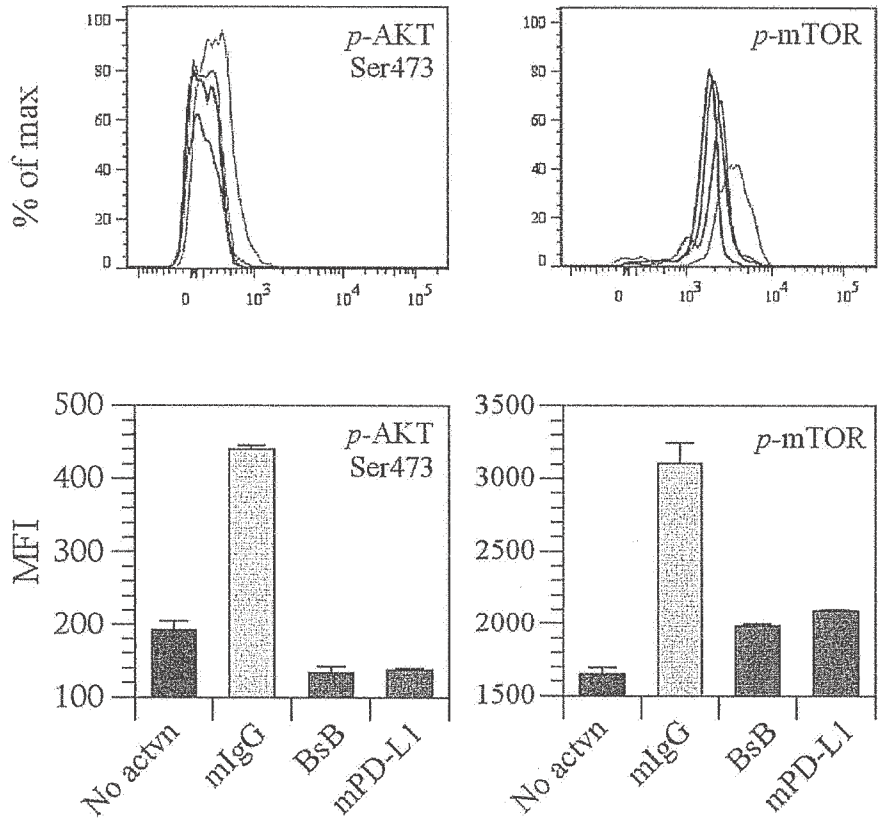


Figure 6

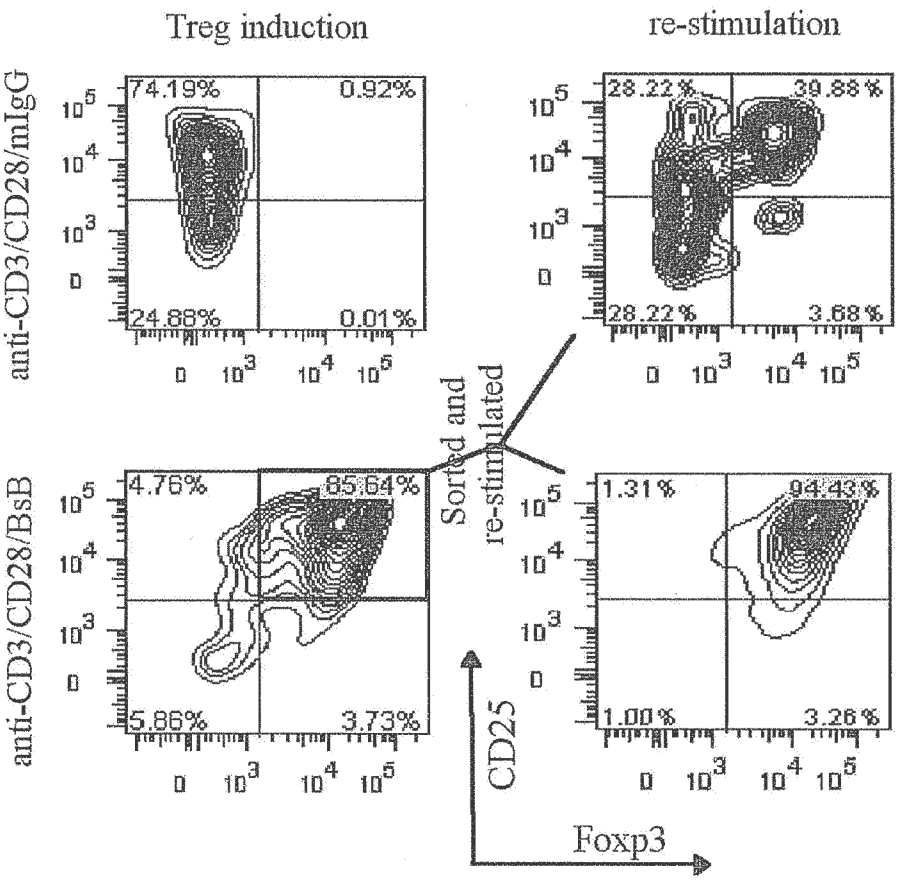
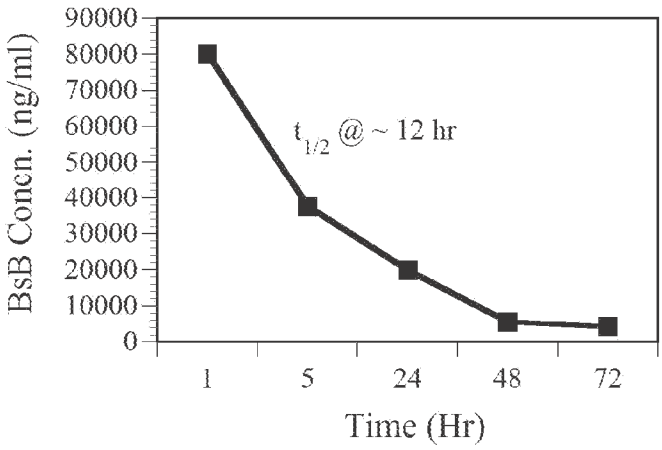

Treg induction
re-stimulation
anti-CD3/CD28/mIgG
anti-CD3/CD28/BsB
74.19%
0.92%
24.88%
0.01%
28.22%
39.88%
28.22%
3.68%
4.76%
85.64%
5.86%
3.73%
1.31%
94.43%
1.00%
3.26%
Sorted and re-stimulated
CD25
Foxp3

Figure 7

A


BsB Concn. (ng/ml)
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
$t_{1/2}$ @ ~ 12 hr
1
5
24
48
72
Time (Hr)

B

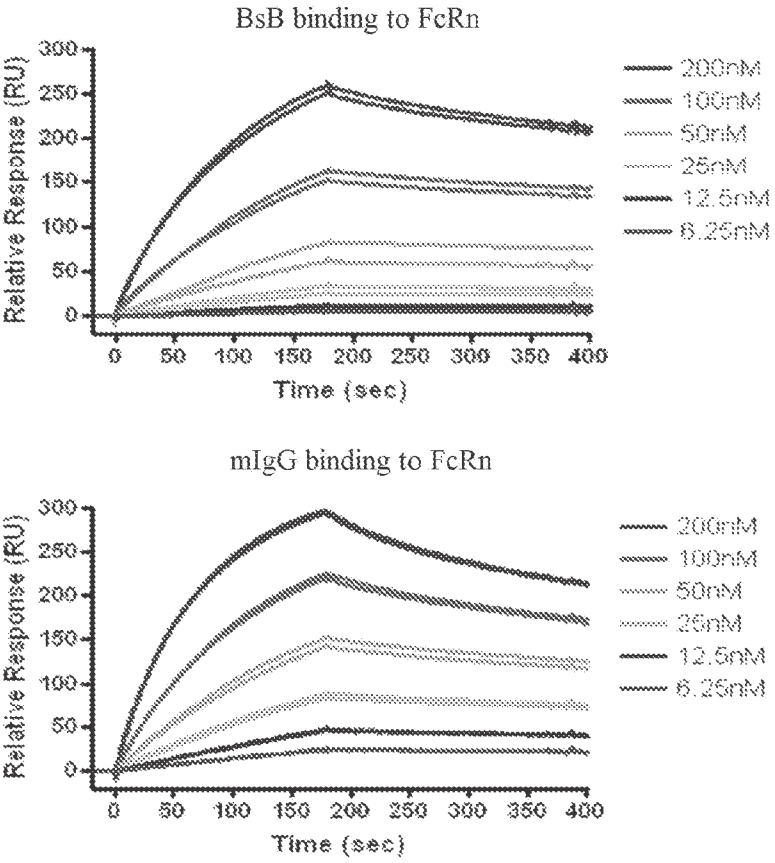
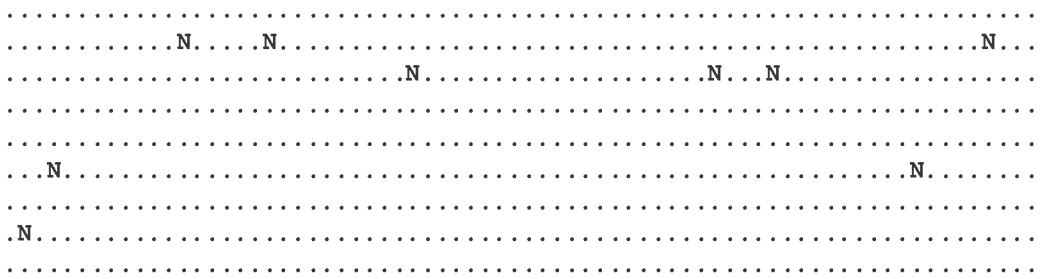

BsB binding to FcRn
Relative Response (RU)
300
250
200
150
100
50
0
0
50
100
150
200
250
300
350
400
Time (sec)
200nM
100nM
50nM
25nM
12.5nM
6.25nM
mIgG binding to FcRn
Relative Response (RU)
300
250
200
150
100
50
0
0
50
100
150
200
250
300
350
400
Time (sec)
200nM
100nM
50nM
25nM
12.5nM
6.25nM

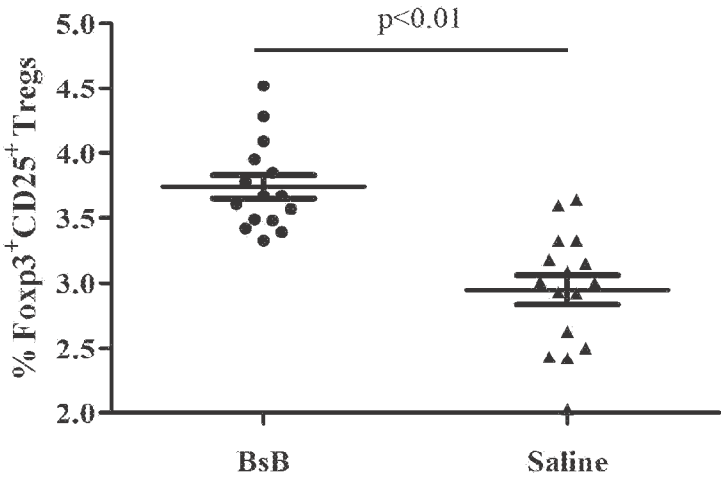
Figure 8



Sugars/BsB	Fuc	GlcNAc	Gal	Man	Sialic acid	Sialic acid/Gal ratio
Mol/Mol	8.0 ± 0.6	37.1 ± 2.2	28.5 ± 1.1	36.8±2.6	19.3 ± 0.7	0.68

Figure 9

A


p<0.01
5.0
4.5
4.0
3.5
3.0
2.5
2.0
% Foxp3+CD25+ Tregs
BsB
Saline

B

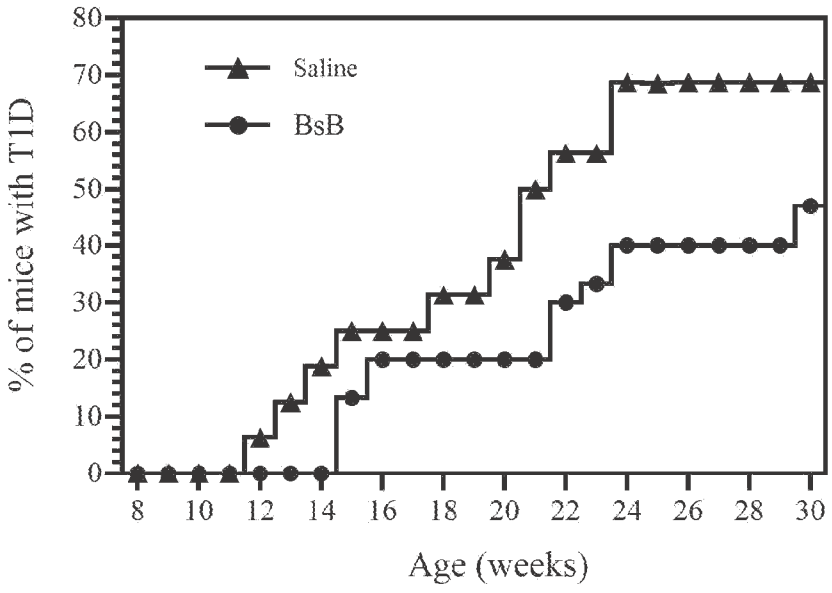
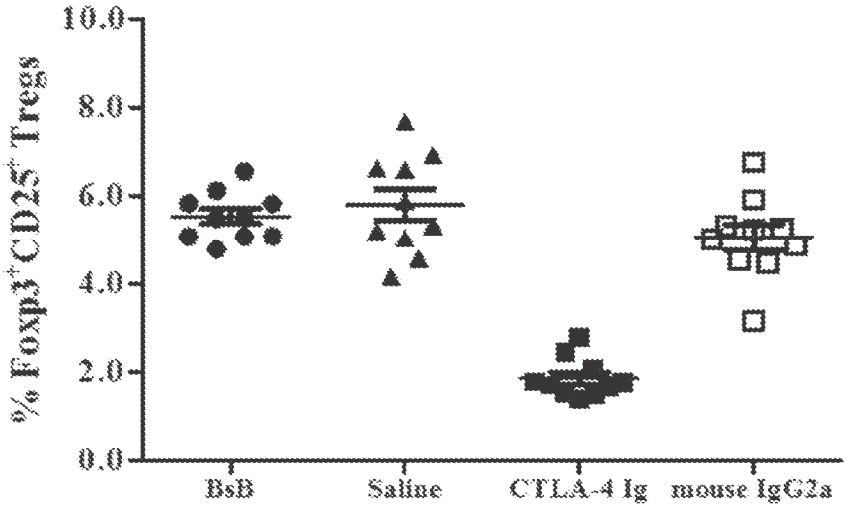

80
70
60
50
40
30
20
10
0
% of mice with T1D
Saline
BsB
8
10
12
14
16
18
20
22
24
26
28
30
Age (weeks)

Figure 10

A


% Foxp3+CD25+ Tregs
10.0
8.0
6.0
4.0
2.0
0.0
BsB
Saline
CTLA-4 Ig
mouse IgG2a

B

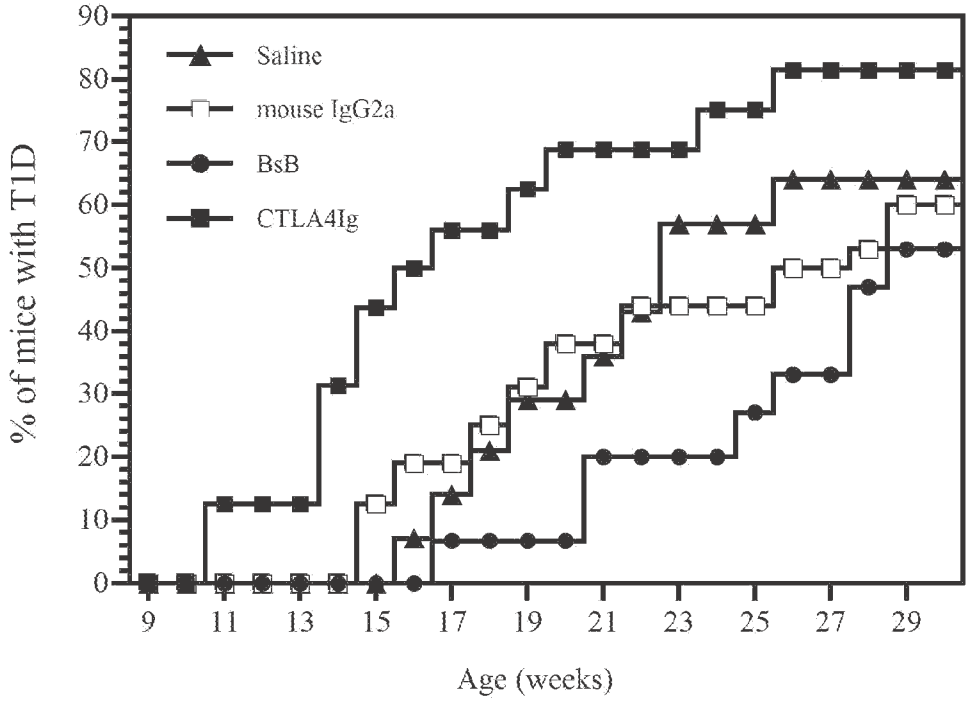
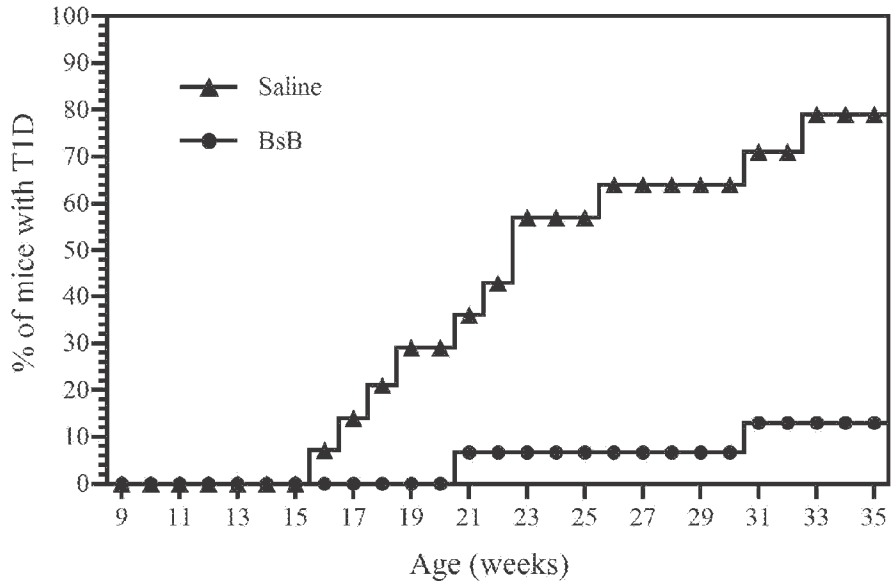

% of mice with T1D
90
80
70
60
50
40
30
20
10
0
9
11
13
15
17
19
21
23
25
27
29
Age (weeks)
Saline
mouse IgG2a
BsB
CTLA4Ig

Figure 11

A


100
90
80
70
60
50
40
30
20
10
0
% of mice with T1D
Saline
BsB
9
11
13
15
17
19
21
23
25
27
29
31
33
35
Age (weeks)

B

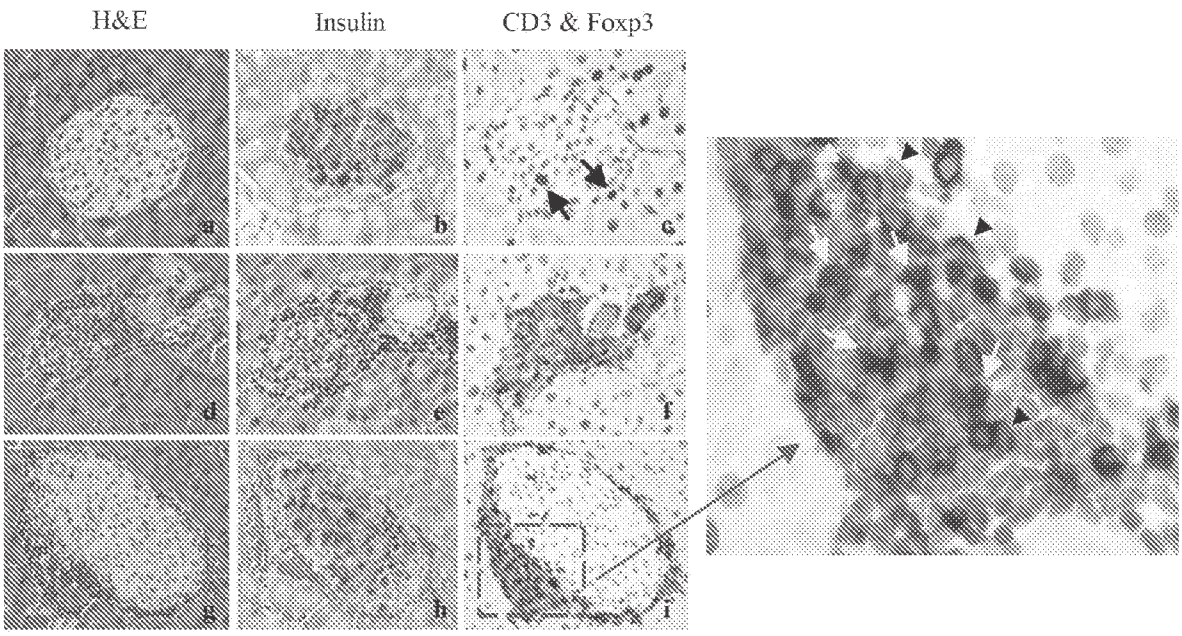

H&E
Insulin
CD3 & Foxp3
a
b
c
d
e
f
g
h
i

Figure 12