

Figure 1**Protein Engineering to Modulate IL2-R Selectivity**

Name	Yield (mg/L)	Aggreg. (%)	T _m	LAL (EU/mg)	Format	Treg (fold expan.)	NK (fold expan.)	CD8 Teff (fold expan.)	IL-2R α β (EC ₅₀ vs. IL-2)	IL-2R β γ (EC ₅₀ vs. IL-2)
rhIL-2 (Proleukin)	N/A	N/A	N/A	N/A	Non-grafted	1.5	2.4	1.9	1	1
IgG-IL2R α 67A.H1	5.6	0.01	70.9/73.2	0.85	R38A in H1	1.5	1	3.6	0.03	90
IgG-IL2F71A.H1	8.9	1.6	70.6/72.9	0.16	F42A in H1	1.5	0.6	6.6	8	2
GFTX3b-IL2-H1	9.6	1.8	68.6	0.95	H1	1.5	0.8	2.1	1	0.3
GFTX3b-IL2-H2	8.6	1.6	67.4	0.76	H2	0.9	0.9	2.2	6	1
GFTX3b-IL2-H3	6.8	2.3	67	0.96	H3	1.1	1.2	1.3	250	3400
GFTX3b-IL2-L1	3.4	1.9	63.7/76.5	1.04	L1	0.9	0.5	2	1	0.5
GFTX3b-IL2-L2	-	-	-	-	L2	-	-	-	-	-
GFTX3b-IL2-L3	3.6	3.6	69.3	0.98	L3	1.5	0.7	4.1	4	4

Figure 2

IgG.IL2R67A.H1 has extended half-life compared to Proleukin® (IL-2)

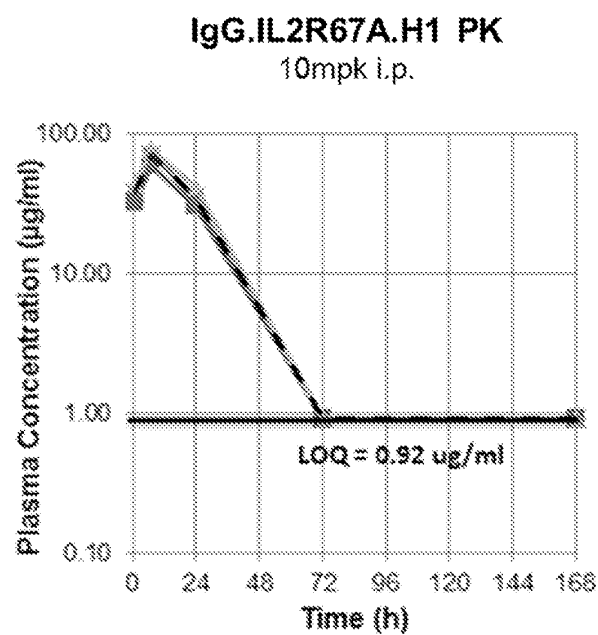


Figure 3A

IgG.IL2R67A.H1/IL-2Fc 100ug (~1nmol of IL-2 equivalent) 4.3mg per kg in 1 dose given on day 1
Proleukin 3.41 ug (1nmol of IL-2) 0.14mg per kg in 5 consecutive daily doses/week

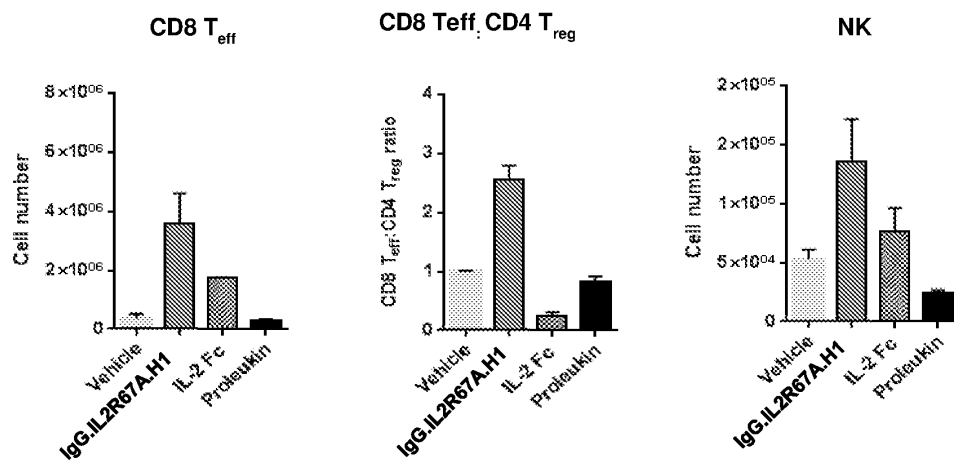
**Splenic populations
Day 4**

Figure 3B

IgG.IL2R67A.H1/IL-2Fc 100ug (~1nmol of IL-2 equivalent) 4.3mg per kg in 1 dose given on day 1
Proleukin 3.41 ug (1nmol of IL-2) 0.14mg per kg in 5 consecutive daily doses/week

**Splenic populations
Day 8**

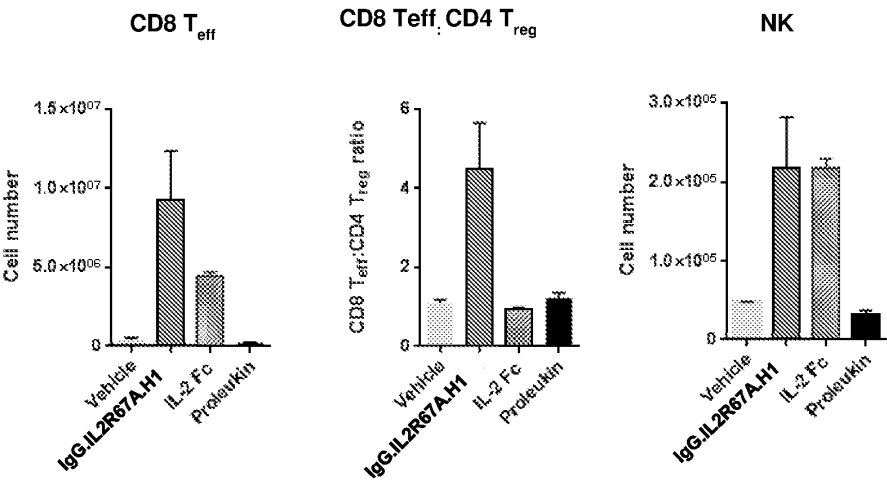


Figure 3C

IgG.IL2R67A.H1/IL-2Fc 100ug (~1nmol of IL-2 equivalent) 4.3mg per kg in 1 dose given on day 1
Proleukin 3.41 ug (1nmol of IL-2) 0.14mg per kg in 5 consecutive daily doses/week

**Splenic populations
Day 8**

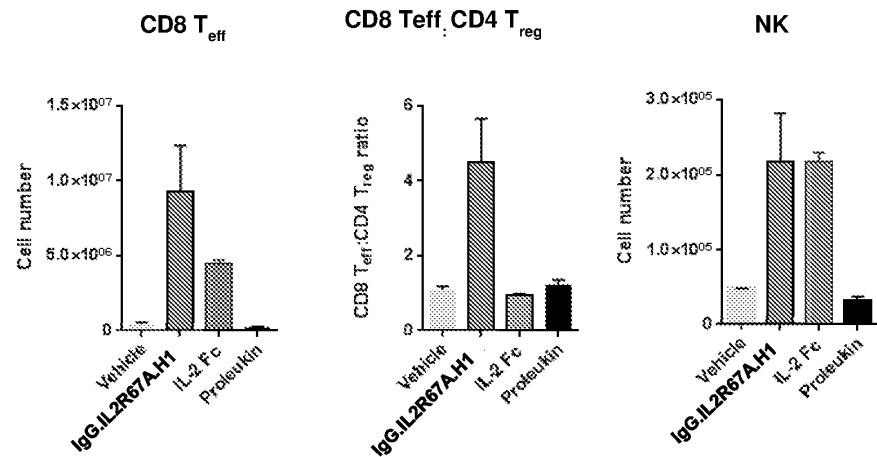


Figure 3D

IgG.IL2R67A.H1/IL-2Fc 500ug (5nmol) 21.7mg per kg in 1 dose given on day 1 Proleukin 17.04 ug (5nmol) 0.74mg per kg in 5 consecutive daily doses/week

**Splenic populations
Day 4**

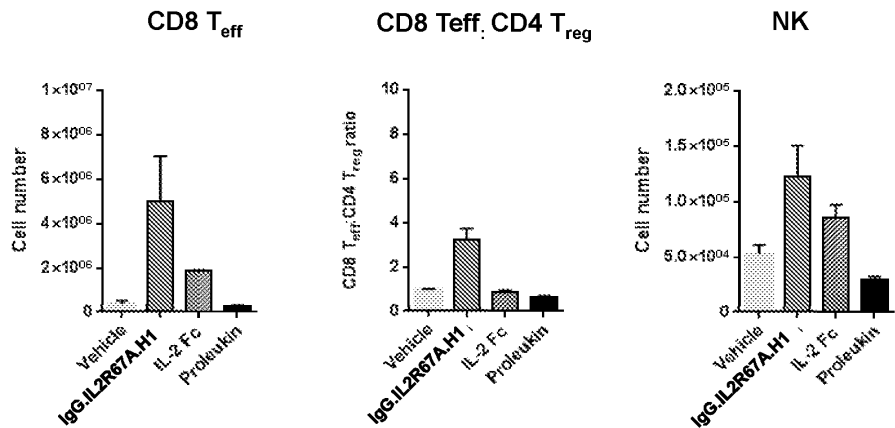


Figure 3E

IgG.IL2R67A.H1/IL-2Fc 500ug (5nmol) 21.7mg per kg in 1 dose given on day 1 Proleukin 17.04 ug (5nmol) 0.74mg per kg in 5 consecutive daily doses/week

**Splenic populations
Day 8**

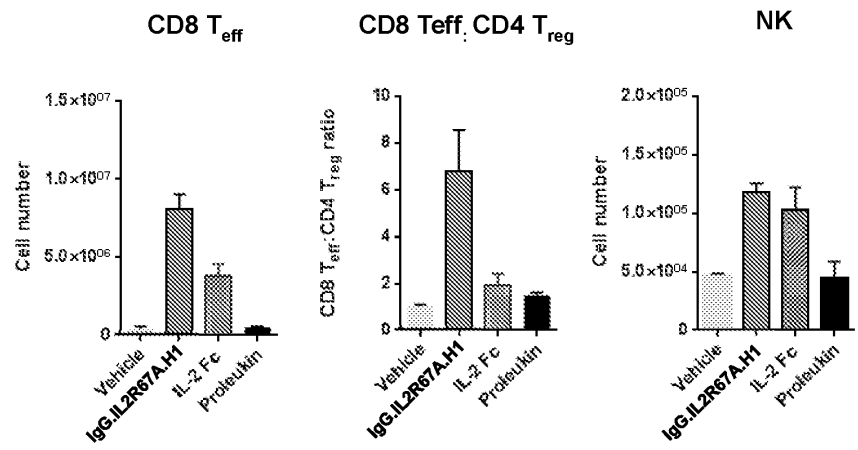


Figure 3F

IgG.IL2R67A.H1/IL-2Fc 500ug (5nmol) 21.7mg per kg in 1 dose given on day 1 Proleukin 17.04 ug (5nmol) 0.74mg per kg in 5 consecutive daily doses/week

**Splenic populations
Day 11**

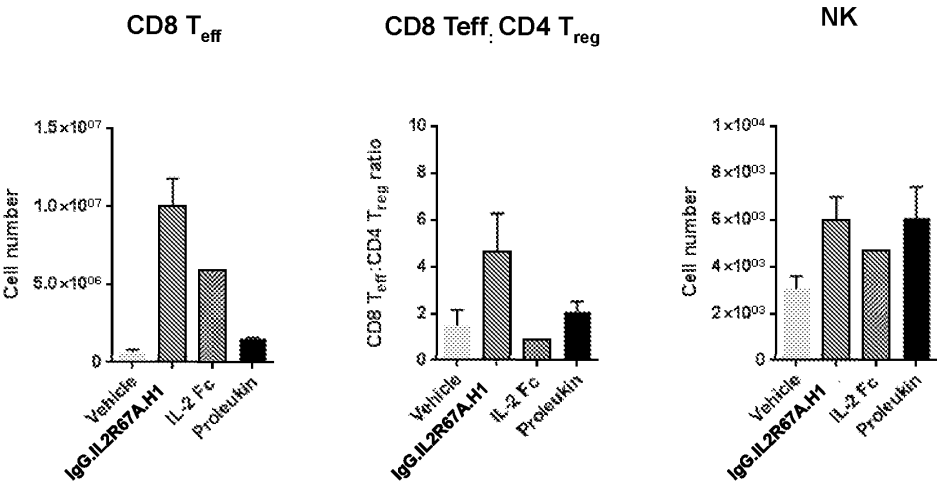


Figure 4A

IgG.IL2R67A.H1 selectively expands CD8 T_{eff}, better tolerated than Proleukin® in NOD Mice

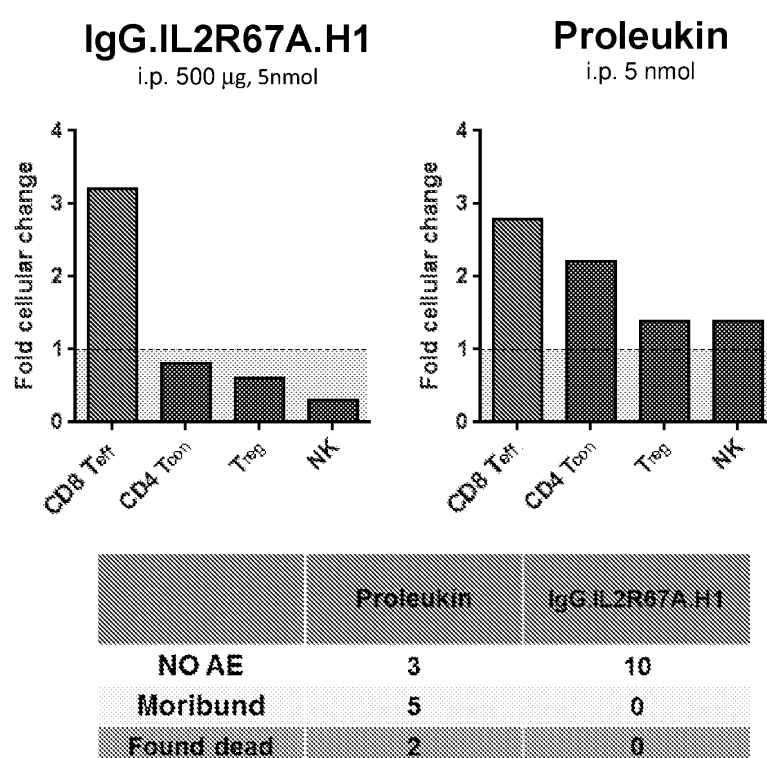


Figure 4B

IgG.IL2R67A.H1 selectively expands CD8 T_{eff} , better tolerated than Proleukin® in NOD Mice

**Fold cellular changes
in prediabetic mice**
(treatment vs. vehicle)

	Dose nmol IL-2-equiv per kg	IgG.IL2R67A.H1	IgG.IL2F71A.H1	IL-2 proleukin
CD8 T _{eff}	200	3.8	6.1	2.8
	40	1.7	2.2	0.9
T _{reg}	200	1.0	1.5	1.4
	40	0.9	1.2	1.1
CD4 T _{eff}	200	1.1	1.2	1.1
	40	1.0	1.1	0.8
NK	200	0.4	0.7	1.2
	40	0.4	0.6	0.9

Figure 5

IgG.IL2R67A.H1 shows single-agent efficacy in CT26 model

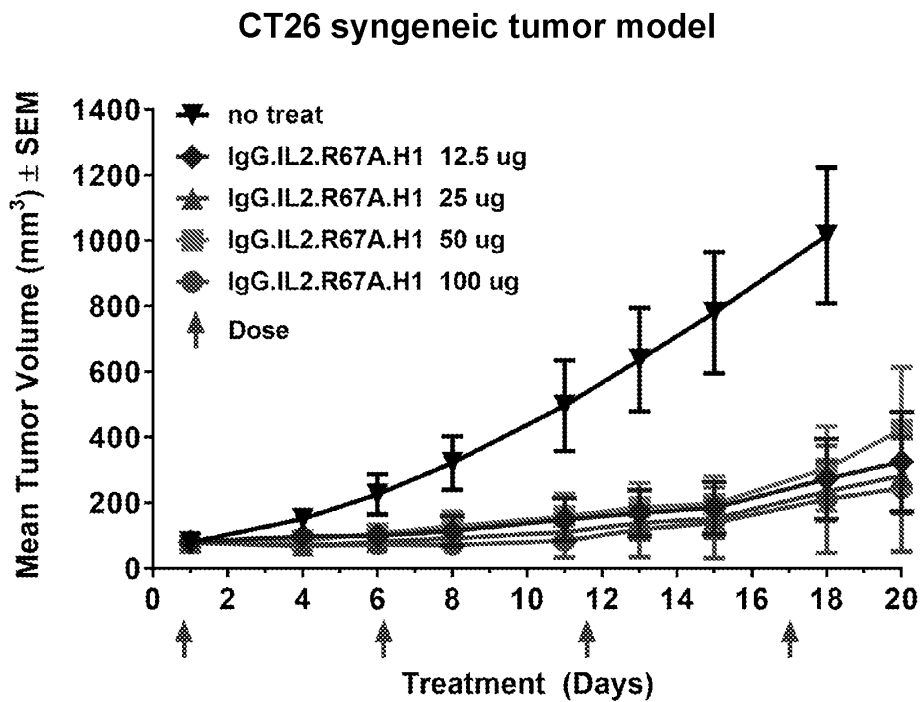


Figure 6

IgG.IL2R67A.H1 +/- TA99 shows efficacy in B16 model

Efficacy in B16 tumor model

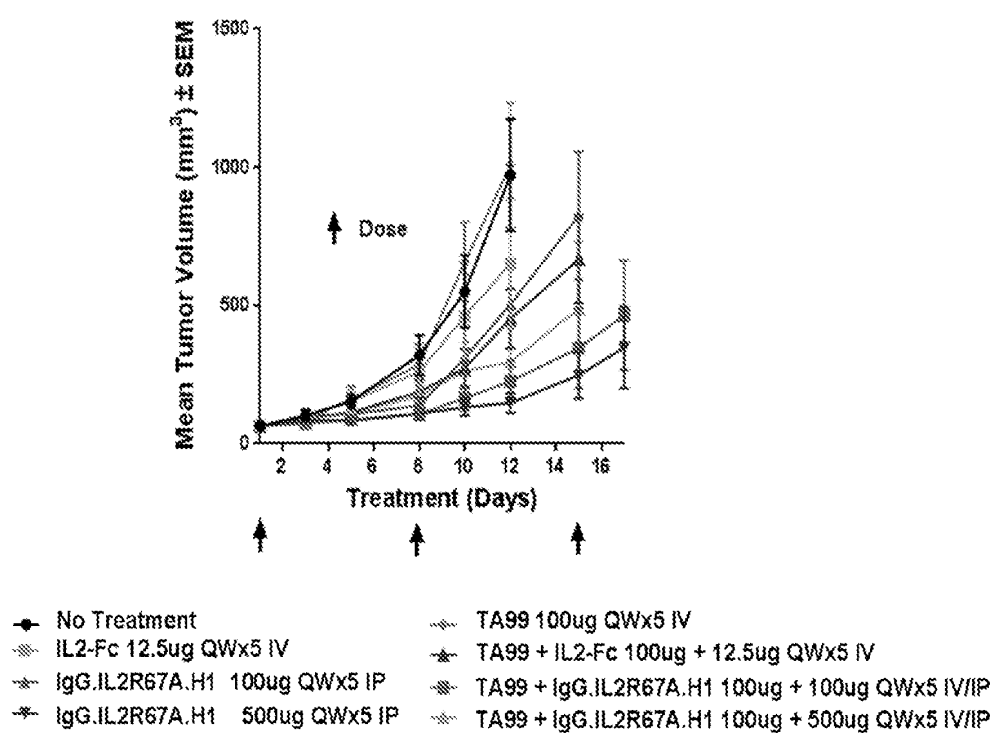


Figure 7

Activity of IL-2 Grafts in Human Cells

CD8 pSTAT5	Equimolar graft/IL-2 2nM	Fold pSTAT5			
		CD8	NK	T _{reg}	CD4
	Proleukin (IL-2)	102	71	30	300
	GFTX3b_IL-2-H1	98	83	37	347
	IgG.IL2R67A.H1	71	64	24	234
	IgG.IL2F71A.H1	36	34	11	70
	GFTX3b_IL-2-H2	20	28	13	142
	GFTX3b_IL-2D113A	4	12	15	118

Figure 8