

FIG. 1

		Proliferating CD4+ T Cells (%)								Inhibition of Proliferation (%)							
		Donor	3	4	5	7	9	10	11	3	4	5	7	9	10	11	
No Activation																	
			0.07	0.1	0.6	0.1	0.1	0.4	0.7								
anti-CD3			0.72	0.8	0.6	1.4	2.6	2.5	6.3								
anti-CD3 + MAdCAM			24.8	12.3	27.5	41.8	67.8	67.4	87.2								
anti-CD3 + MAdCAM + 1uM Cmpd. A			0.2	0.2	0.5	0.5	0.5	0.3	1.9	102	104	100	102	103	103	105	
anti-CD3 + MAdCAM + 1uM NEG			22.3	11.6	26.3					10.1	6.3	4.7					
anti-CD3 + MAdCAM + Vedo			0.4	0.3	0.7					101	104	100					

FIG. 2

	Non-proliferating CD4+ T Cells (%)					Proliferating CD4+ T Cells (%)				
	Donor	3	4	5		3	4	5		
anti-CD3										
	CD45RO-	57.58	46.3	60.8		NA	NA	NA		
	CD45RO+	42.4	53.7	38.6		NA	NA	NA		
	Memory/Naïve	0.7	1.2	0.6		NA	NA	NA		
anti-CD3 + MAdCAM										
	CD45RO-	50.2	38.3	53.0		31.9	19.9	27.0		
	CD45RO+	49.8	61.7	47.0		68.1	80.1	73.0		
	Memory/Naïve	1.0	1.6	0.9		2.1	4.0	2.7		

FIG. 3

A.	Divided CD4 ⁺ T-Cells					
	A	B	C	D	E	
% $\beta 7^{+}$	98.9	94.5	99.9	99.9	99.7	
$\beta 7$ MFI-1	5,692	5,549	4,299	3,671	5,441	
$\beta 7$ MFI-2	7,312	7,137	5,773	5,628	7,641	
$\beta 7$ MFI-3	7,742	7,537	6,599	6,973	9,699	
$\beta 7$ MFI-4	6,807	6,990	6,949	8,038	11,141	

B.	$\beta 7$ MFI	Undivided $\beta 7^{+}CD4^{+}$ T-Cells				
		A	B	C	D	E
0 nM Cmpd. A		873	1735	1132	1250	1242
1 μ M Cmpd. A		816	945	906	787	493
Percent Change		-6.5%	-46%	-20%	-37%	-60%

FIG. 4

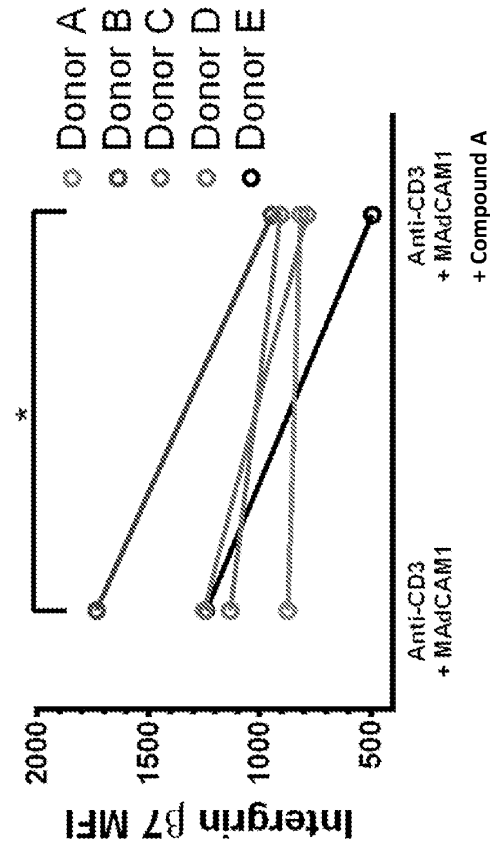
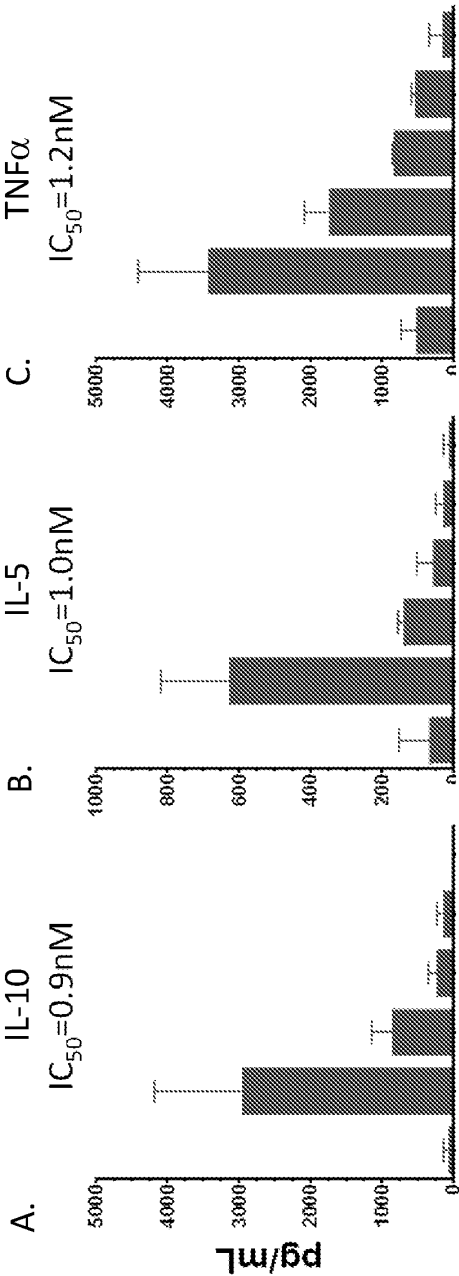


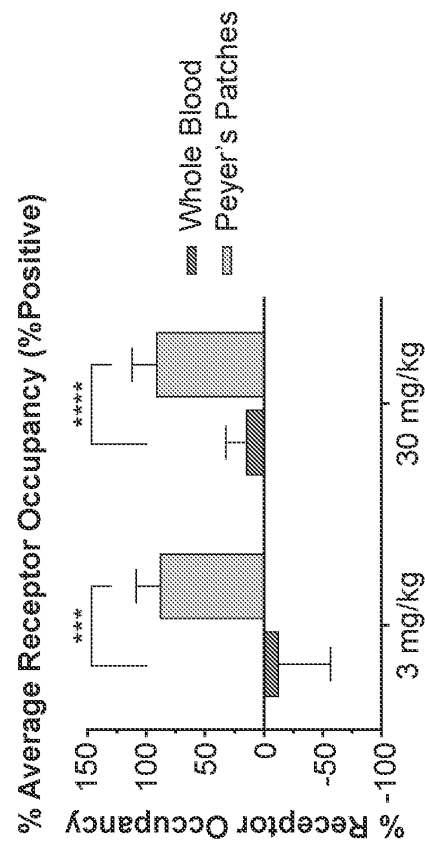
FIG. 6



Anti-CD3	+	+	+	+	+	+
MAdCAM1	-	+	+	+	+	+
Cmd. A (nM)	-	-	0.97	3.9	15.6	1000

	+	+	+	+	+	+
	-	+	+	+	+	+
	-	-	0.97	3.9	15.6	1000

	+	+	+	+	+	+
	-	+	+	+	+	+
	-	-	0.97	3.9	15.6	1000



Statistical analysis performed using an unpaired t-test.
: $p < 0.001$, *: $p < 0.0001$.

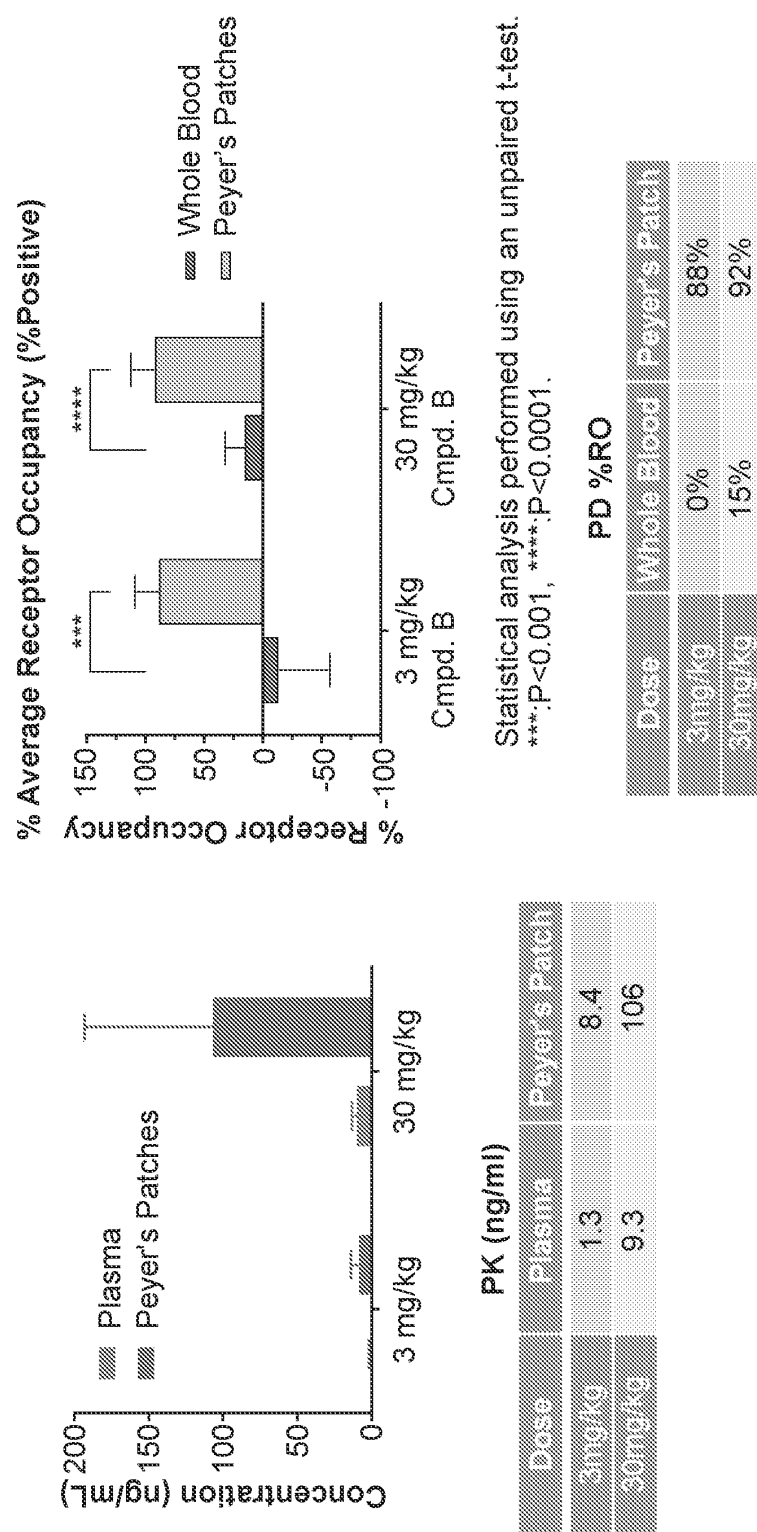
Dose	Whole Blood	Peyer's Patch
3mg/kg	0%	88%
30mg/kg	15%	92%

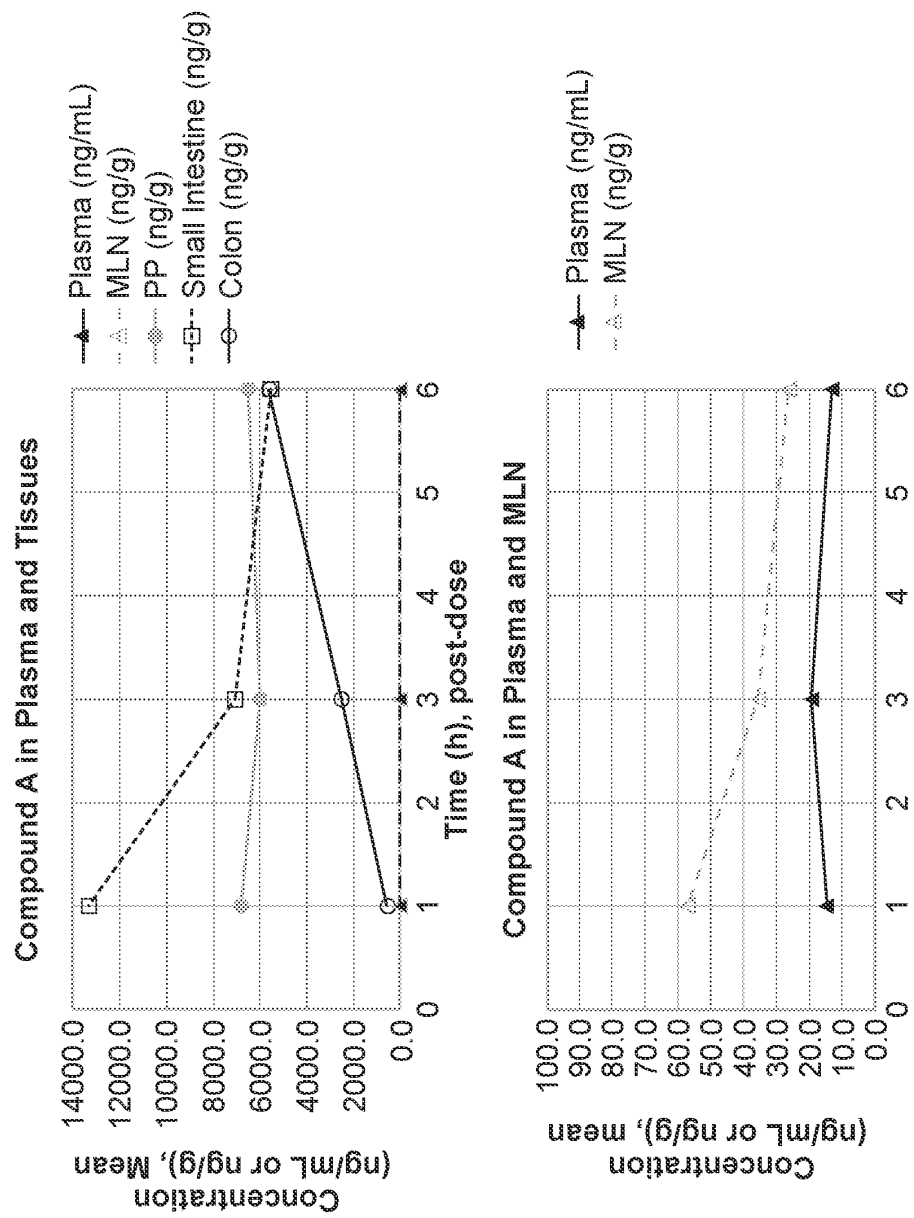
FIG. 7

FIG. 8

Receptor Occupancy – Individual Animals												
Whole Blood							Peyer's Patches					
Dose	#1	#2	#3	#4	#5	#6	#1	#2	#3	#4	#5	#6
3 mg/kg	-76.878	49.7714	7.05421	6.40105	-18.615	-44.415	88.7	100	47.3	93.5	100	100
30 mg/kg	15.872	9.66688	35.4017	15.872	-13.325	28.4781	50.9	100	100	100	100	100

AUC ₀₋₂₄ (hr·%)			
Dose (mg)	Day	T=24 hours	AUC ₀₋₂₄ (hr·%)
100	56	24	971
300	80	44	1467
1000	96	76	1957





Note that the lower panel represents data from the upper panel plotted with an expanded scale.
Data shown as Mean, N=4 per time point.

FIG. 10

FIG. 11

Table 7: PK Parameters for Cmpd. A following Single PO Dose Administration at 30 mg/kg in Mouse

Tissue	Dose mg/kg	t _{max} hour	C _{max} ng/mL or ng/g	AUC h*ng/mL
Plasma	30	3.00	19.0	95.4
MLN	30	1.00	56.9	276
PP	30	1.00	6790	37900
Small Intestine	30	1.00	13500	48600
Colon	30	6.00	5580	15700

MLN, mesenteric lymph node; PP, Peyer's patch.

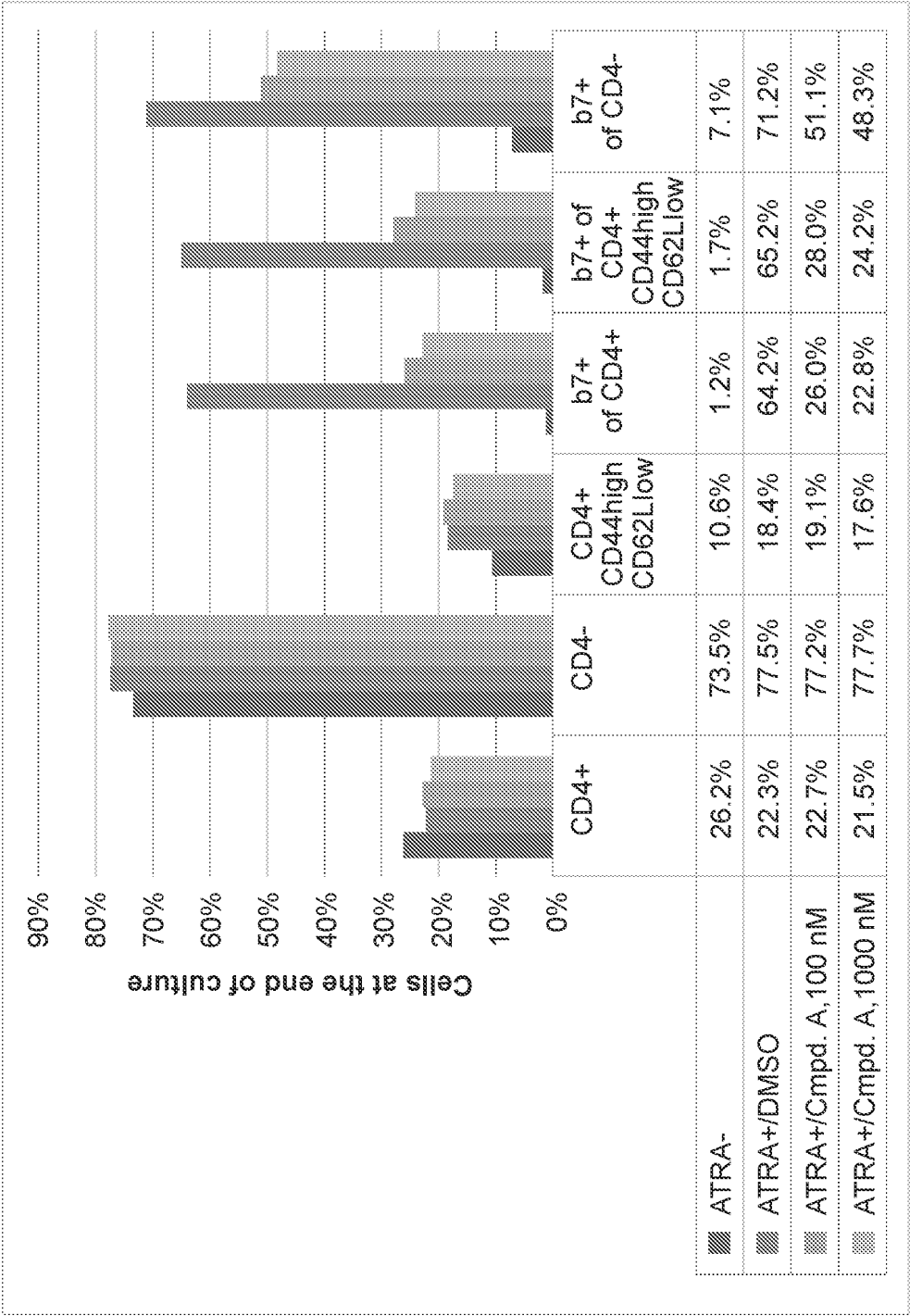


FIG. 12

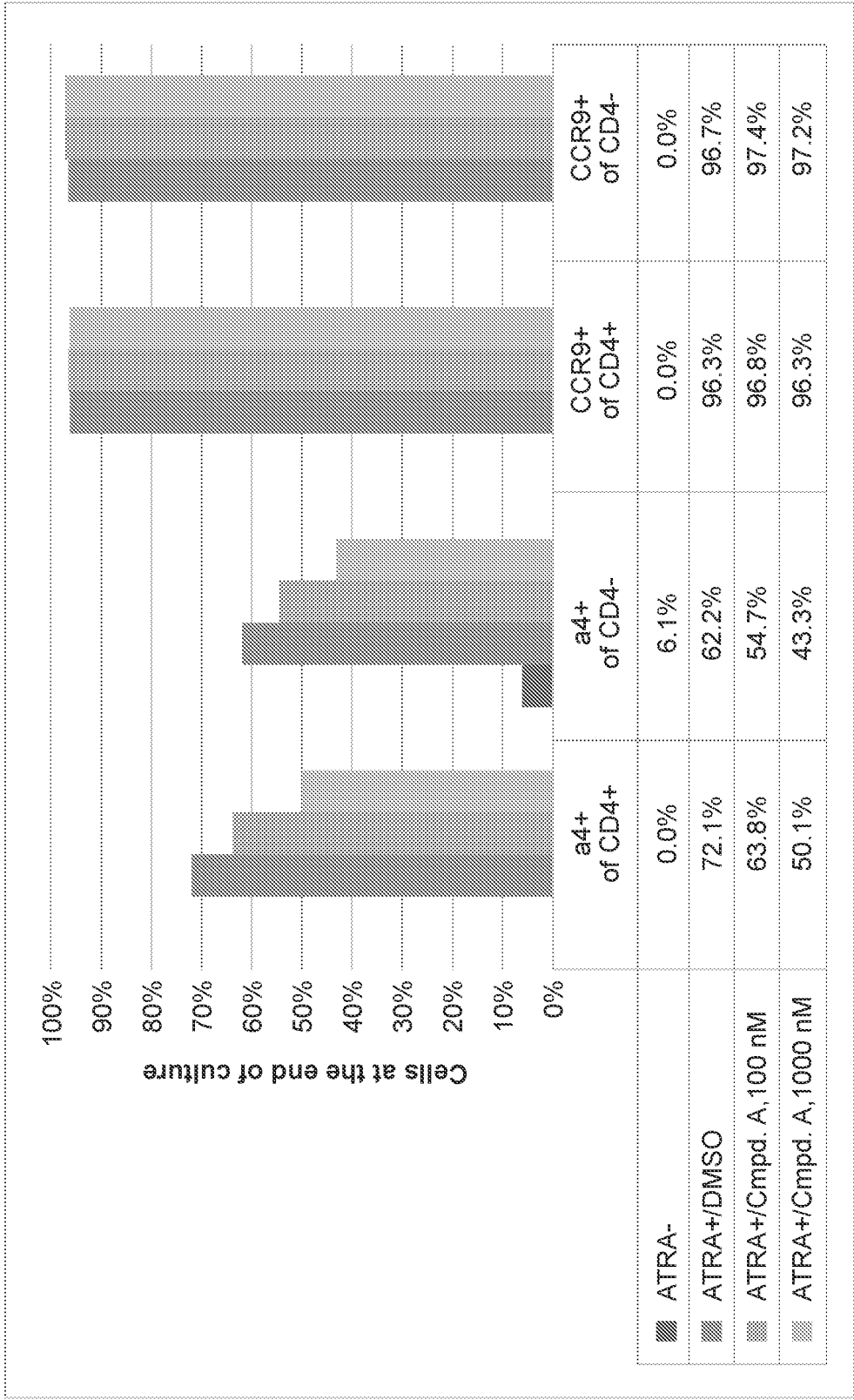


FIG. 13

FIG. 14

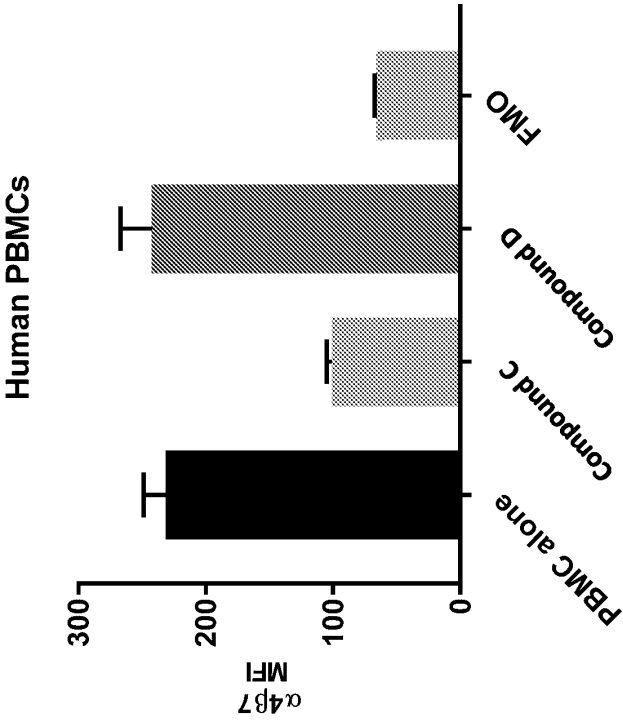


FIG. 15

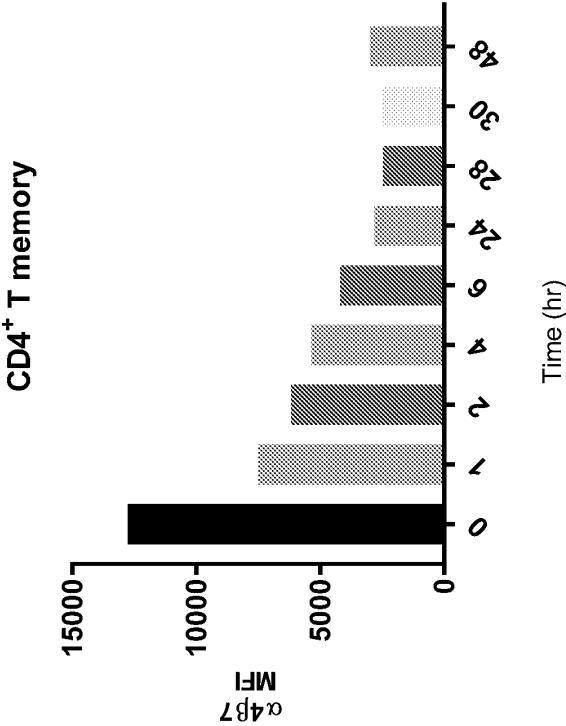


FIG. 16

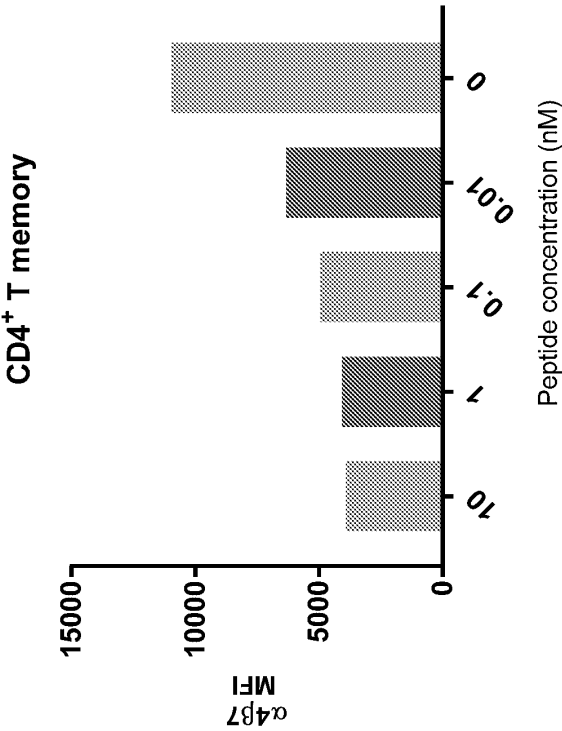


FIG. 17

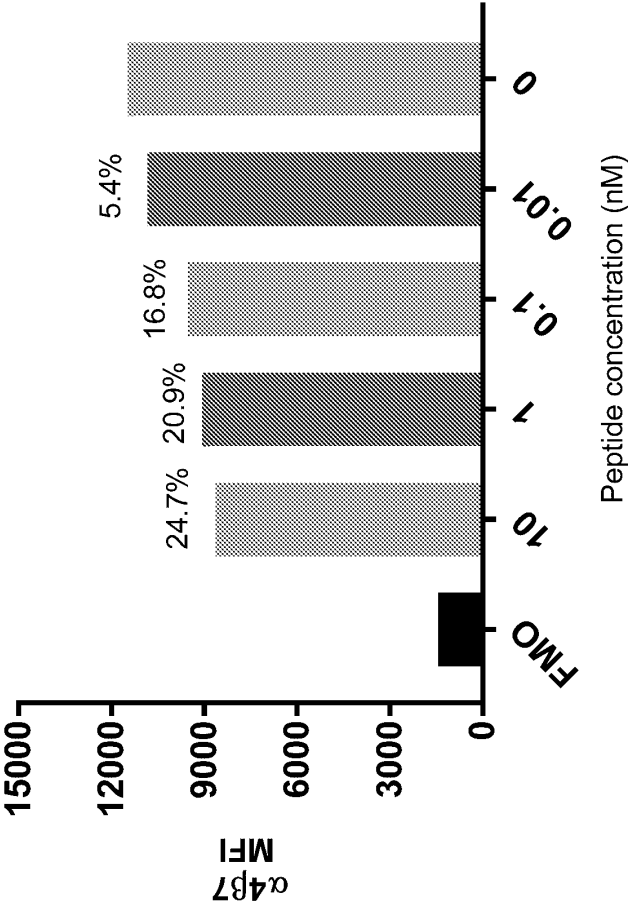


FIG. 18

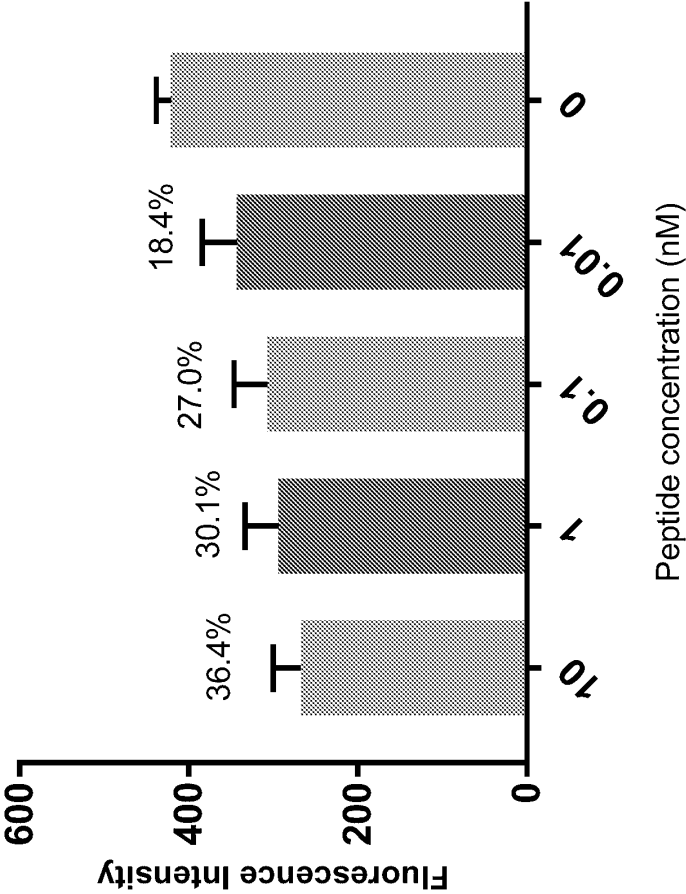


FIG. 19

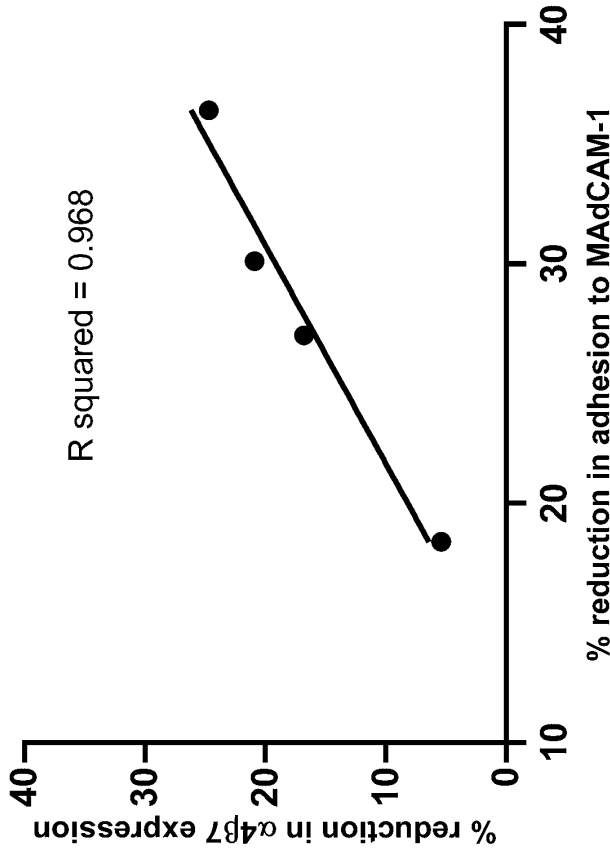


FIG. 20

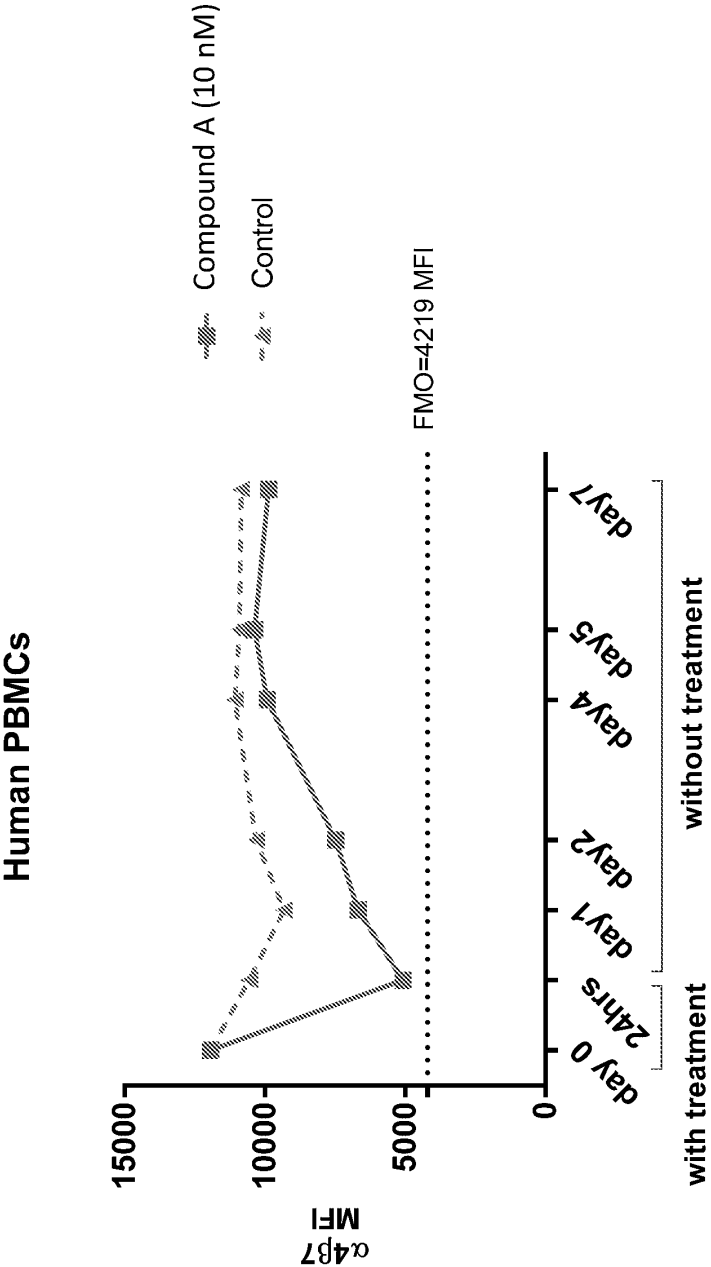


FIG. 21

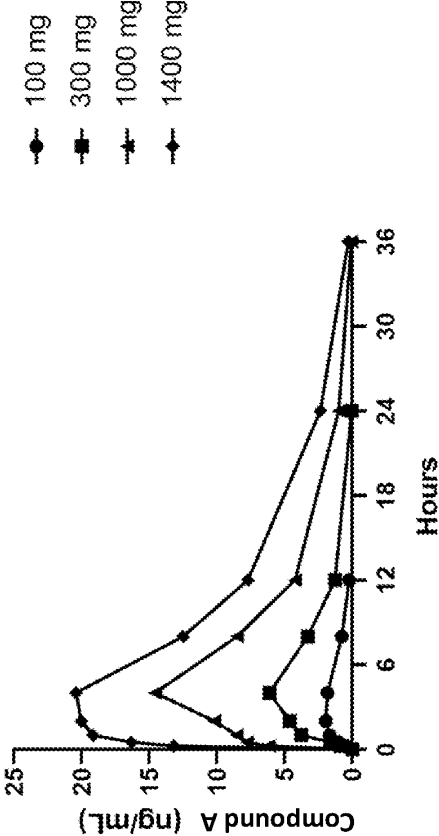


FIG. 22

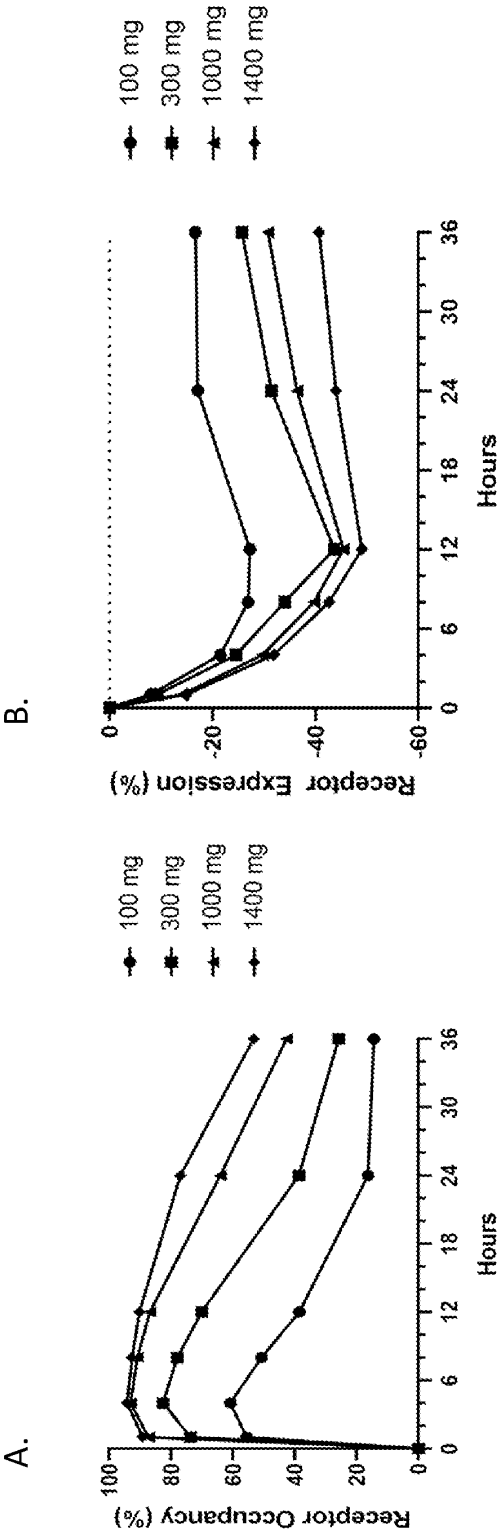


FIG. 23

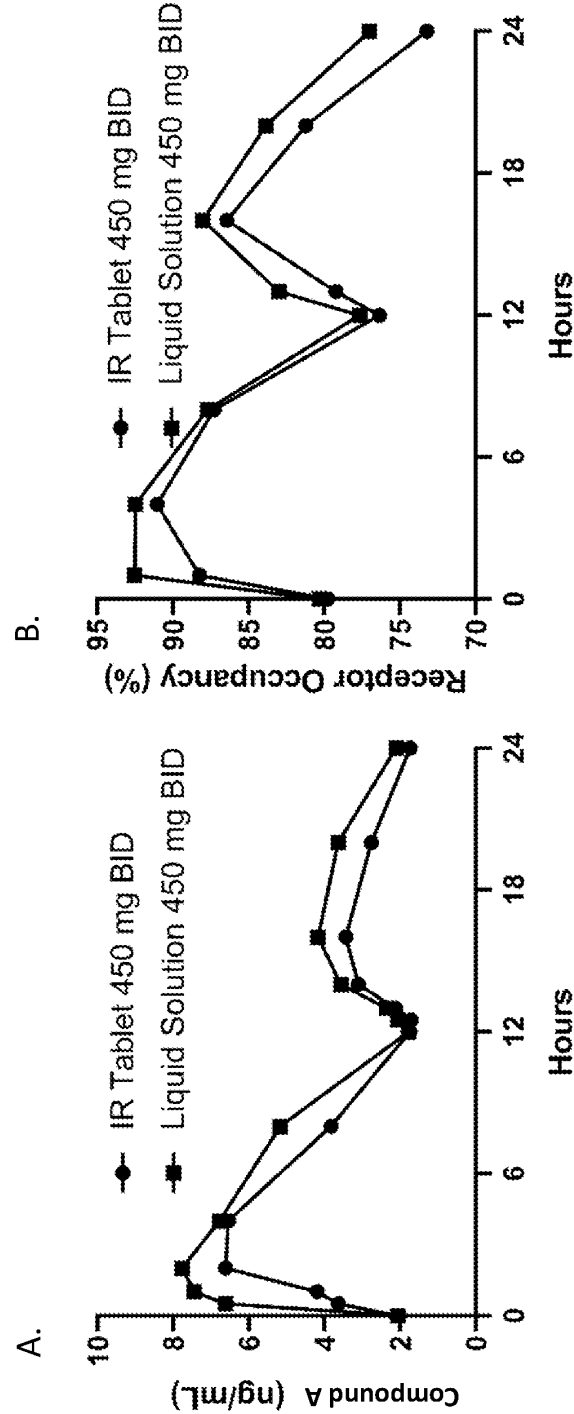
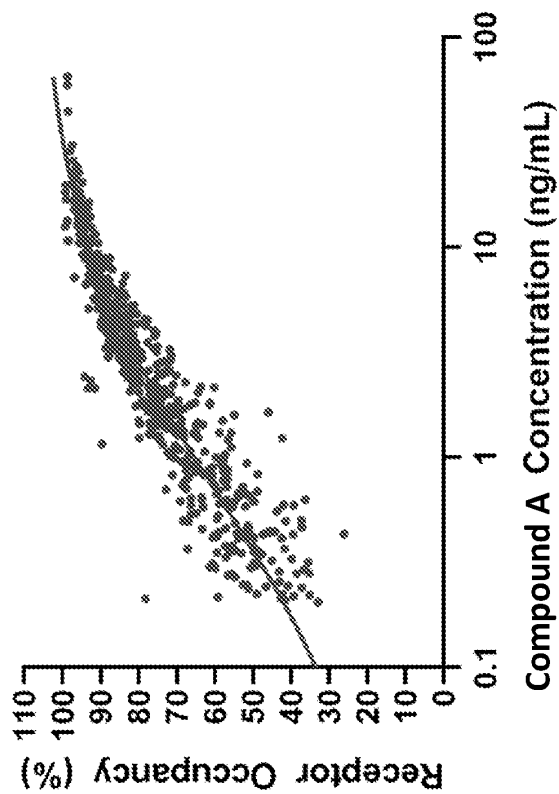


FIG. 24



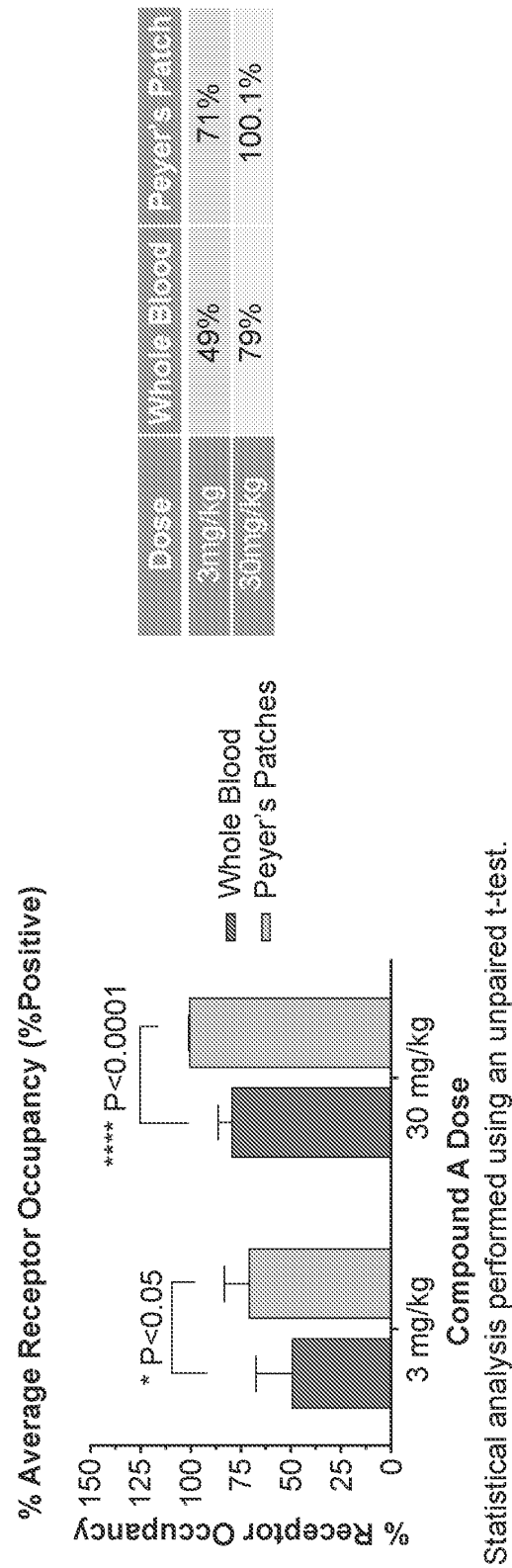


FIG. 25

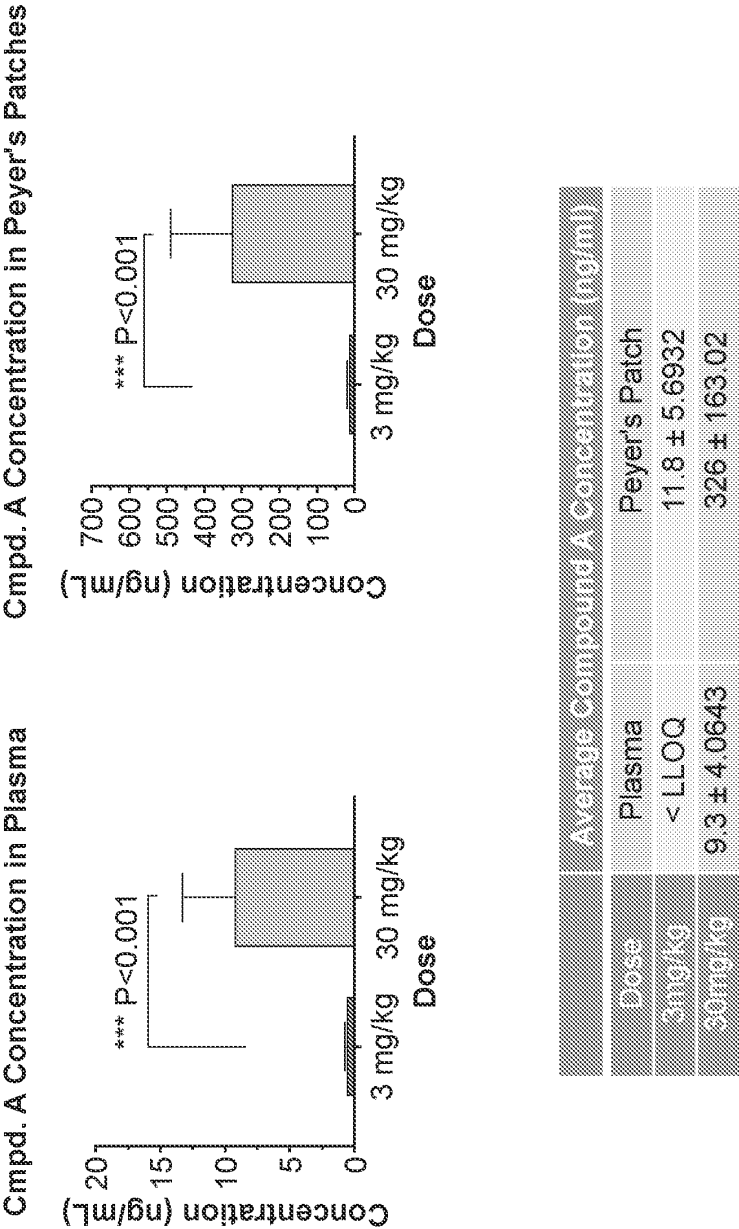


FIG. 26

FIG. 27

Receptor Occupancy -- Individual Animals													
		Whole Blood						Peyer's Patches					
Dose		#1	#2	#3	#4	#5	#6	#1	#2	#3	#4	#5	#6
3 mg/kg		54.08	46.65	41.64	3.31	76.47	27.91	56.79	74.54	55.13	75.3	87.98	74.21
30 mg/kg		81.97	85.3	66.14	80.78	83.04	79.6	100.89	100.63	100.63	100.99	100.16	100.99

%RO = (1-(%positive test sample / %positive median vehicle control))*100