

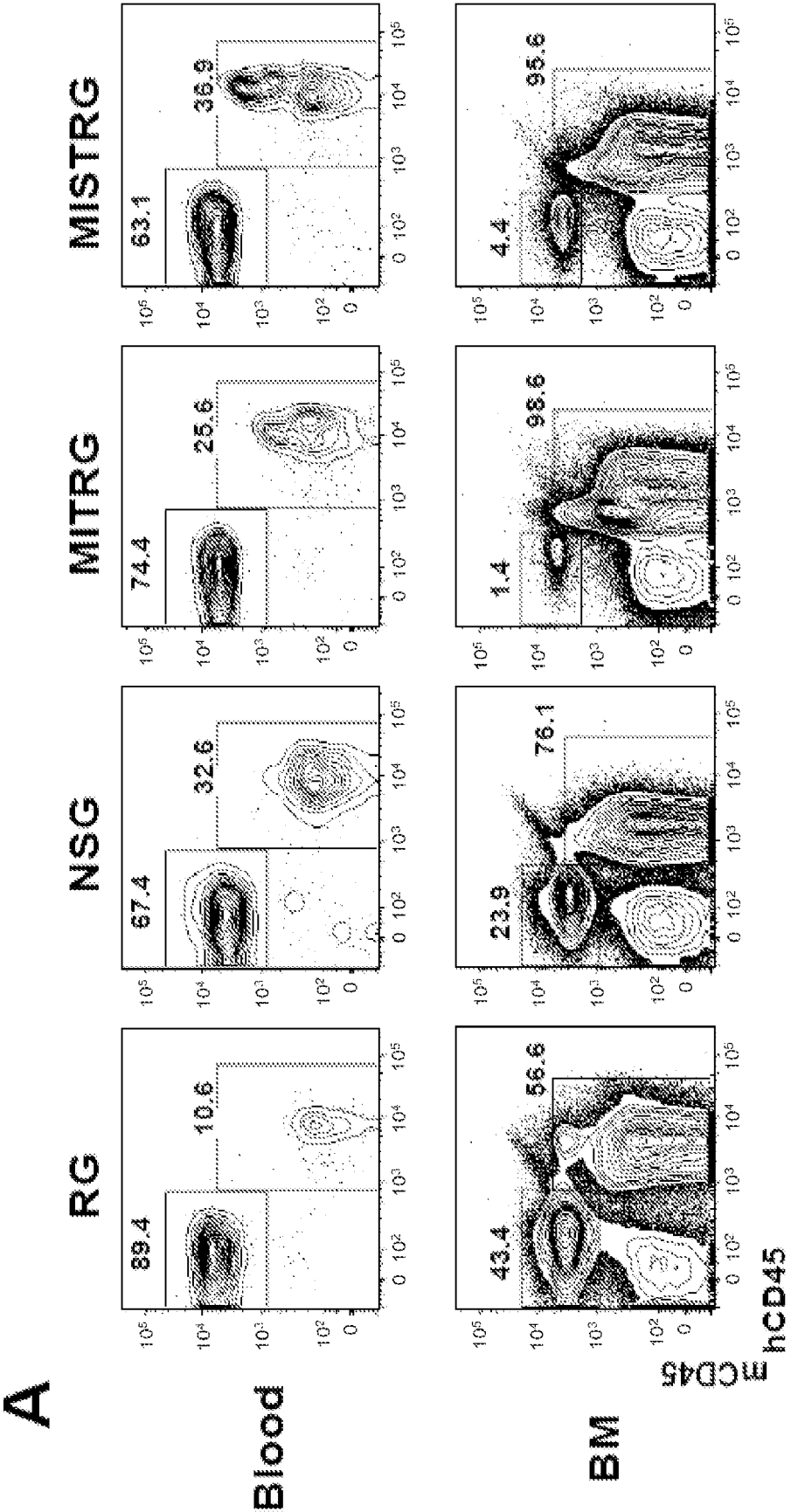


Figure 1A

2/36

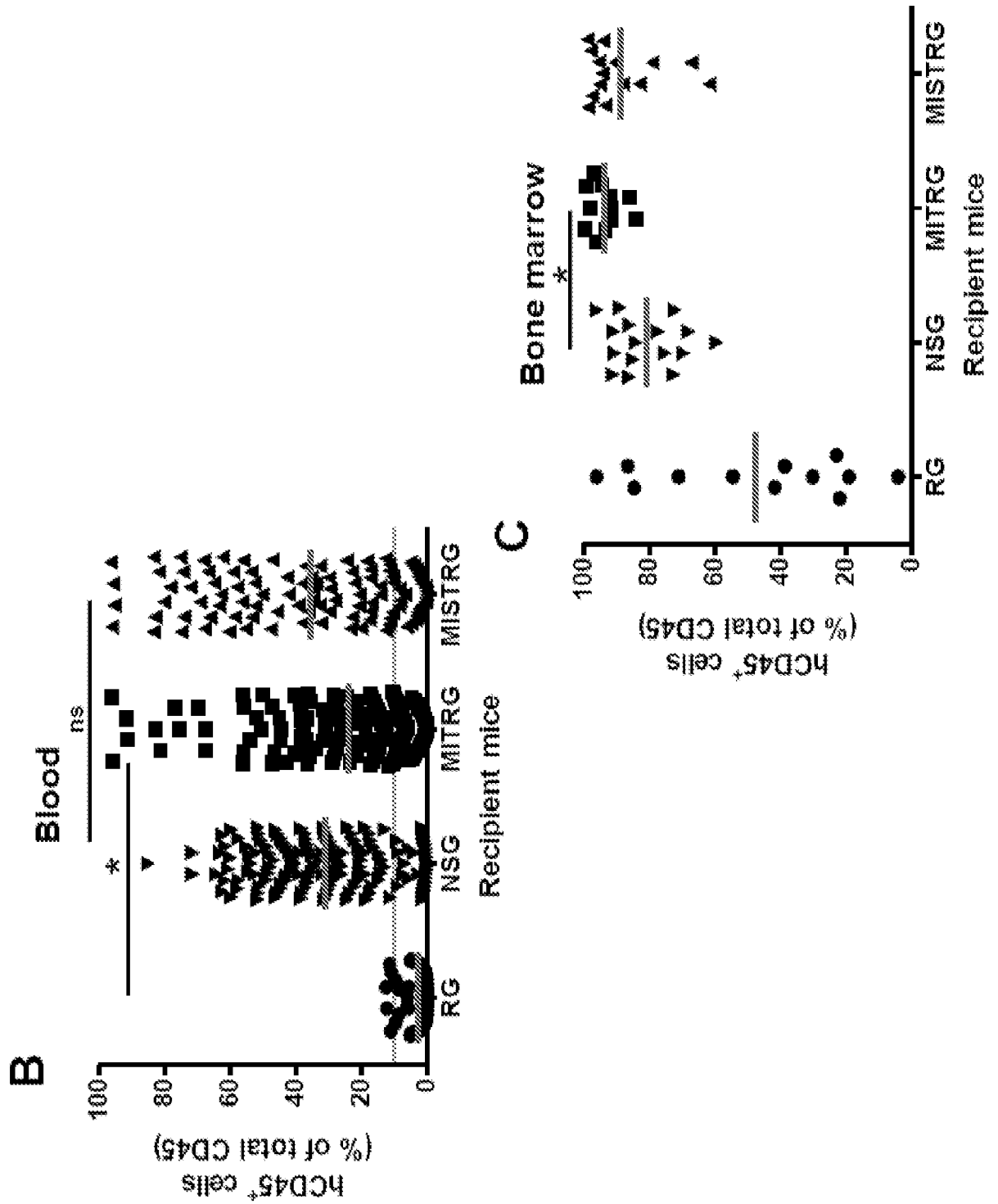


Figure 1B-1C

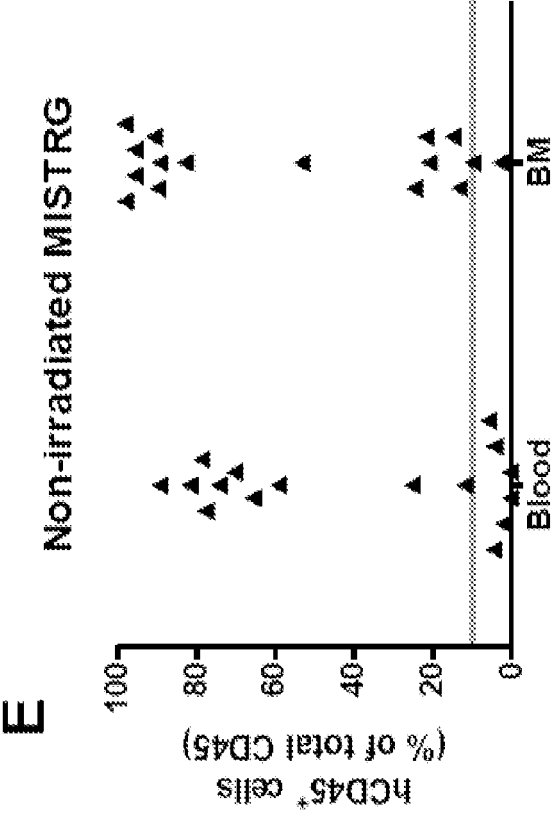
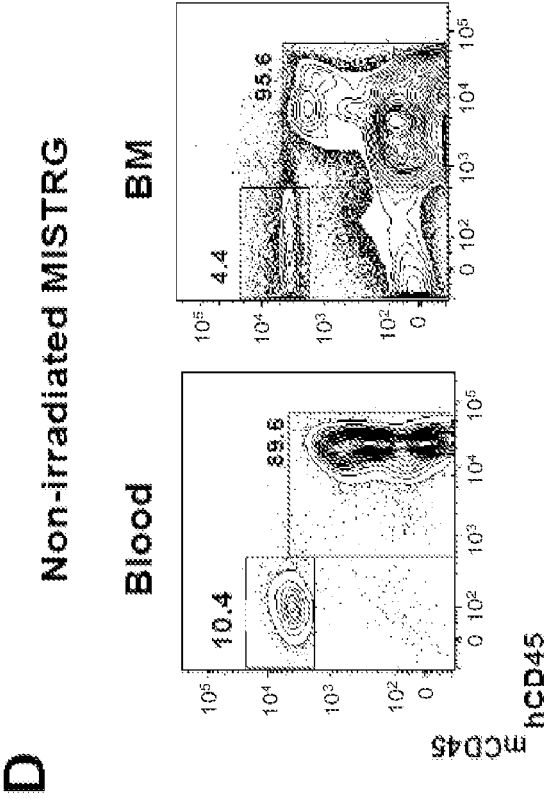


Figure 1D-1E

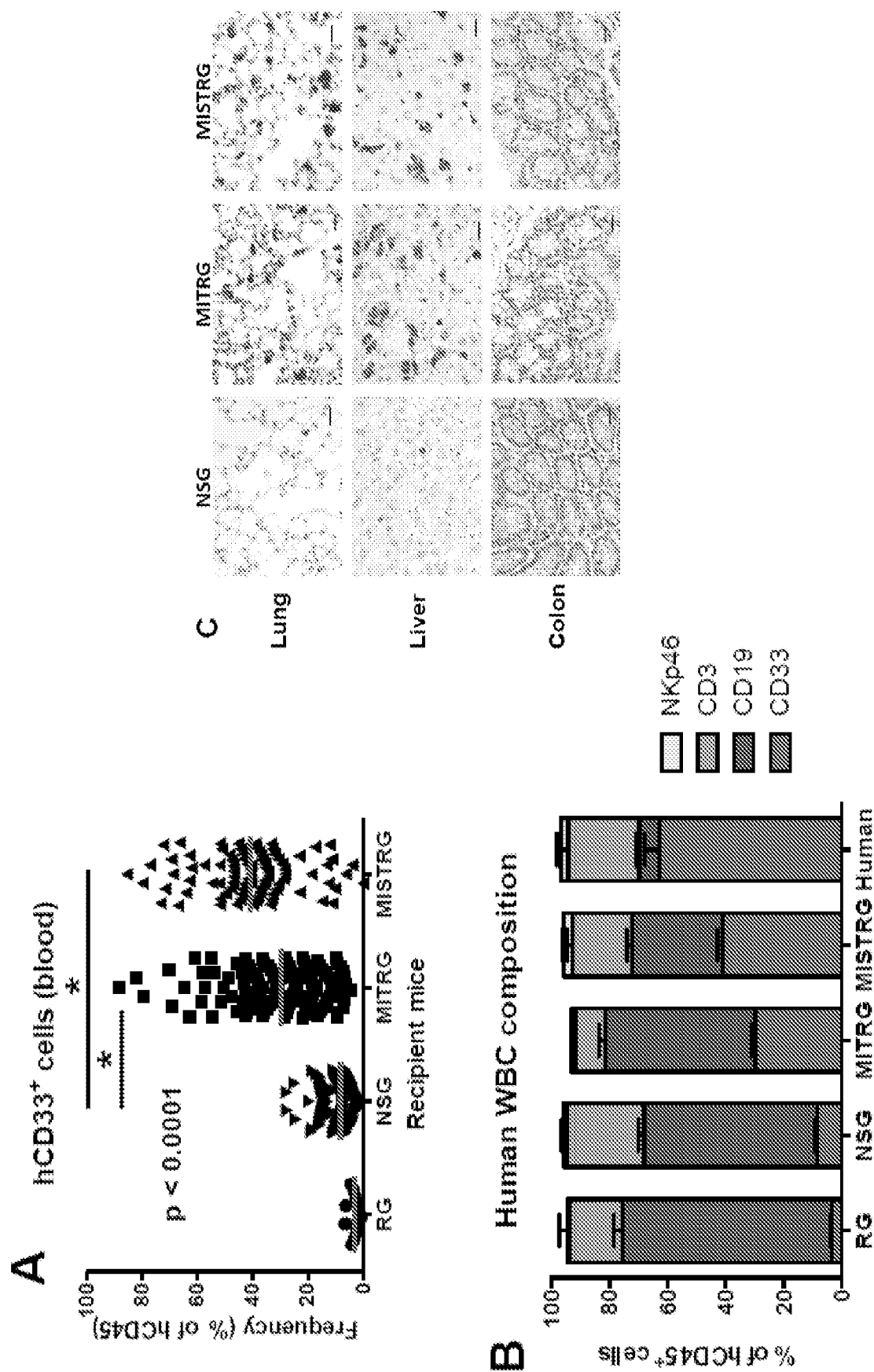


Figure 2A-2C

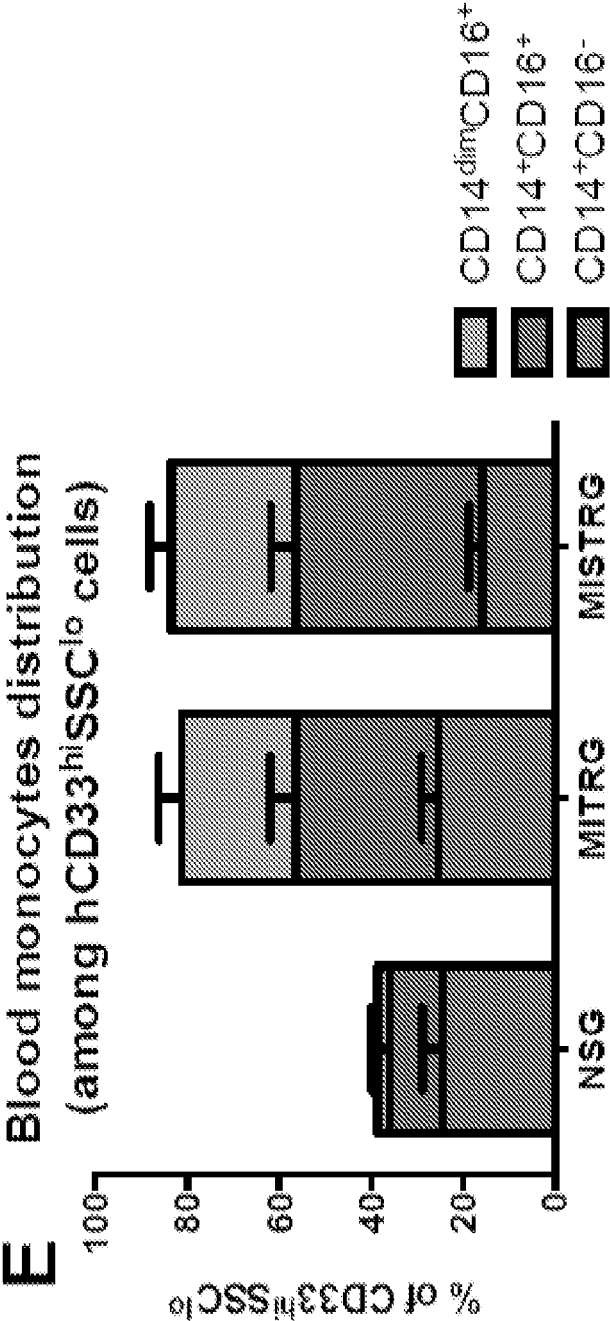
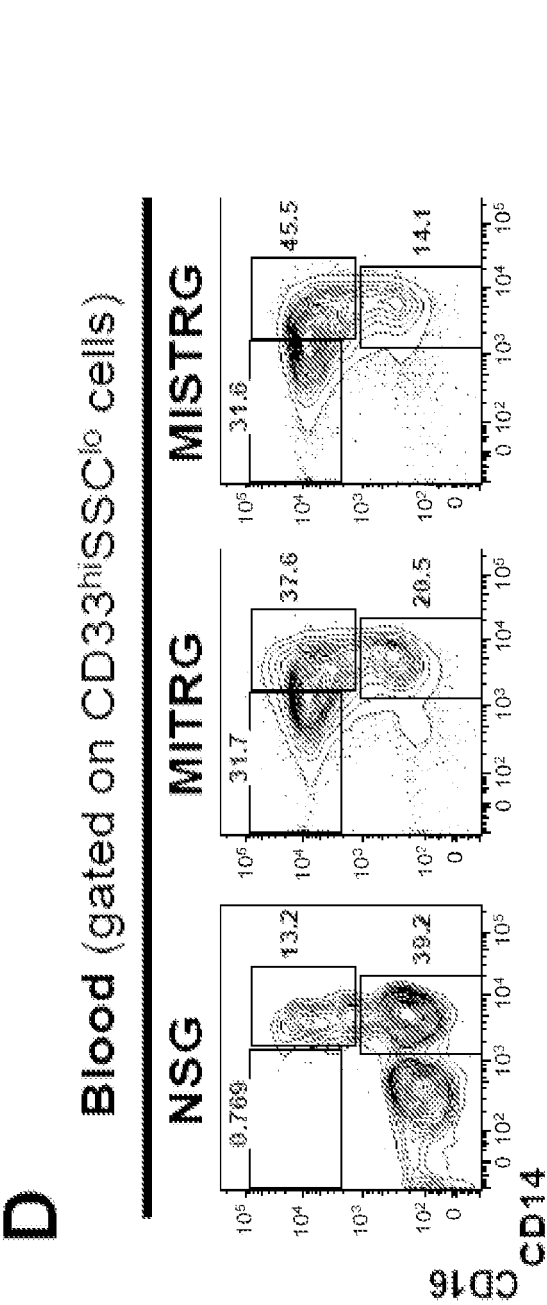
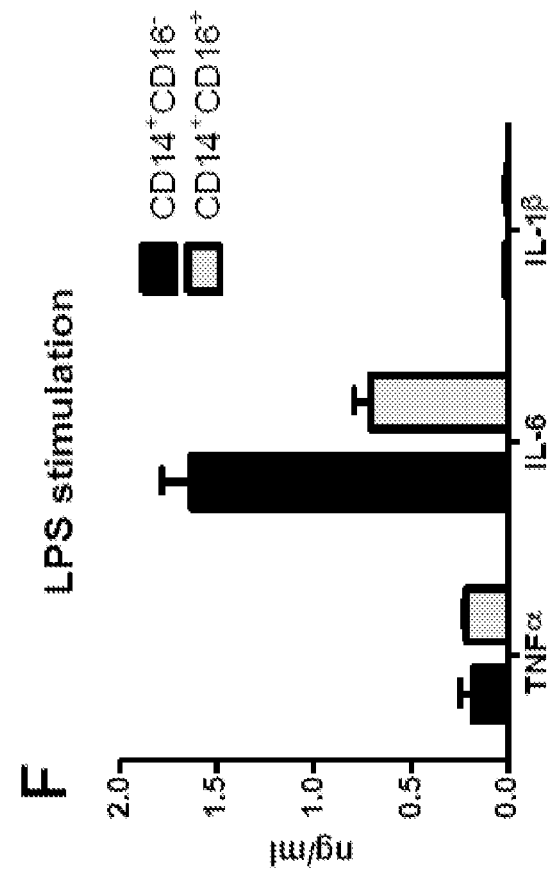
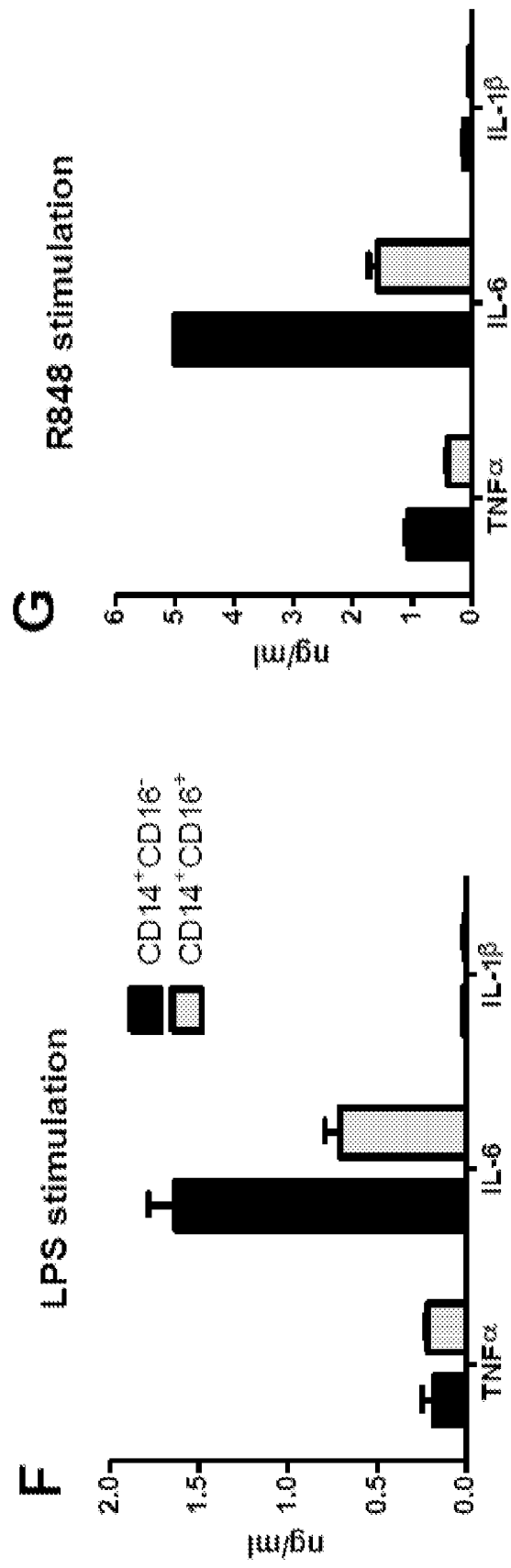


Figure 2D-2E



H *E. coli*-GFP phagocytosis

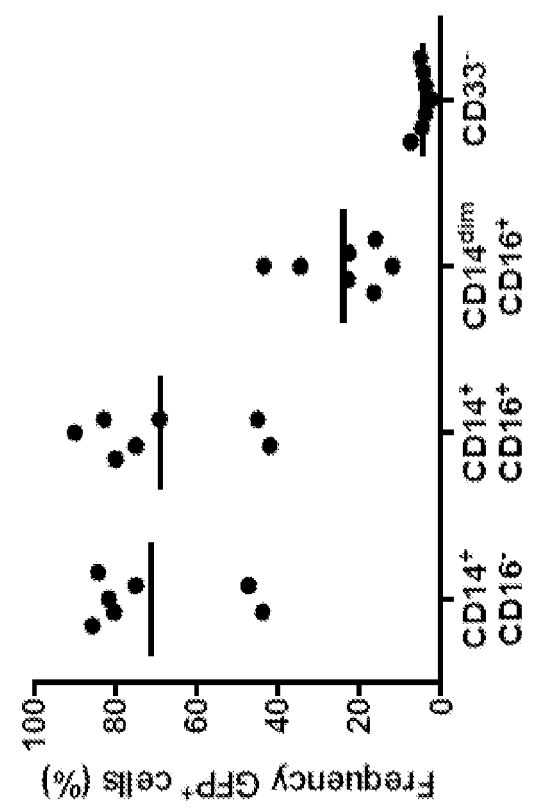
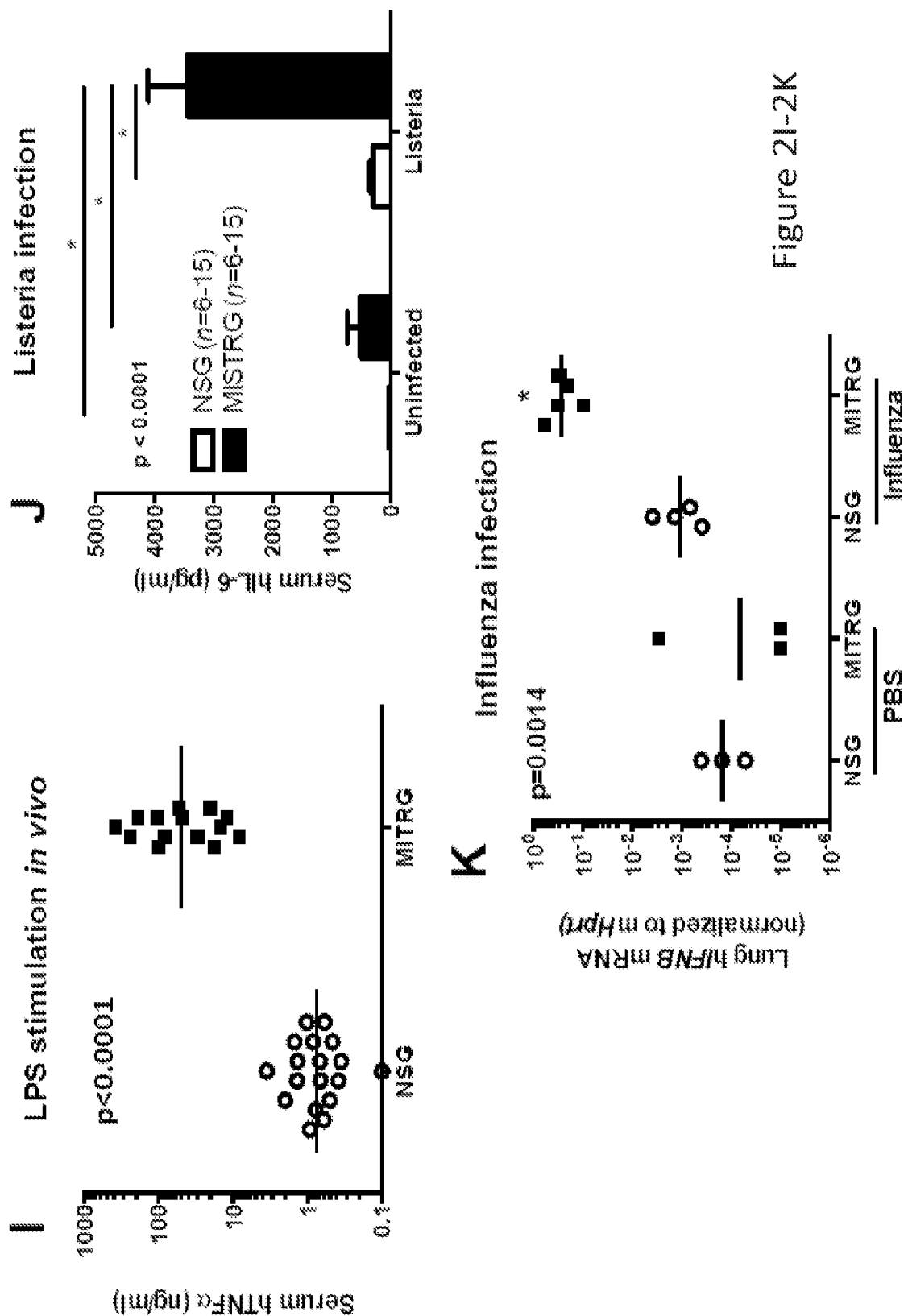


Figure 2F-2H



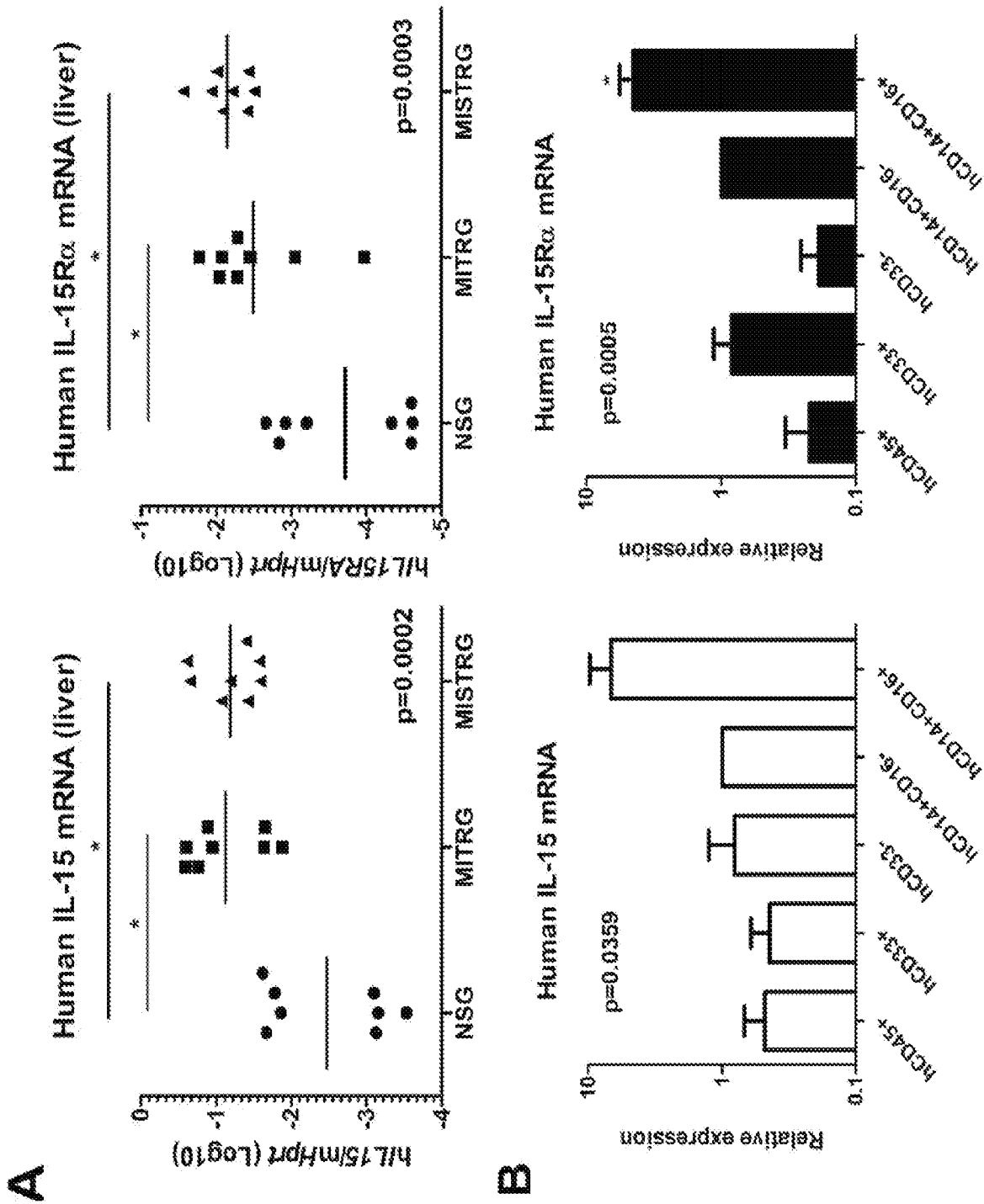


Figure 3A-3B

9/36

C

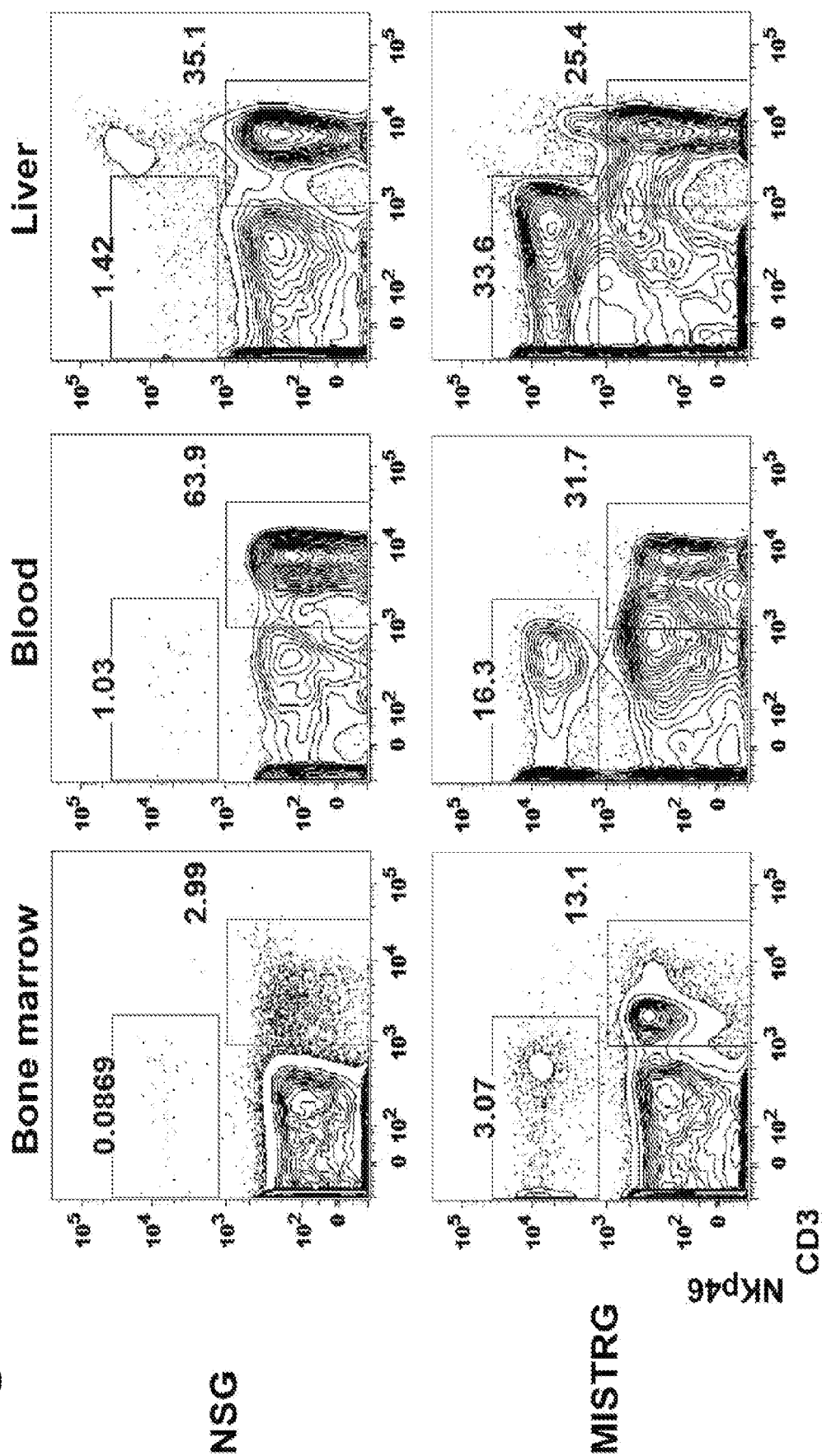


Figure 3C

10/36

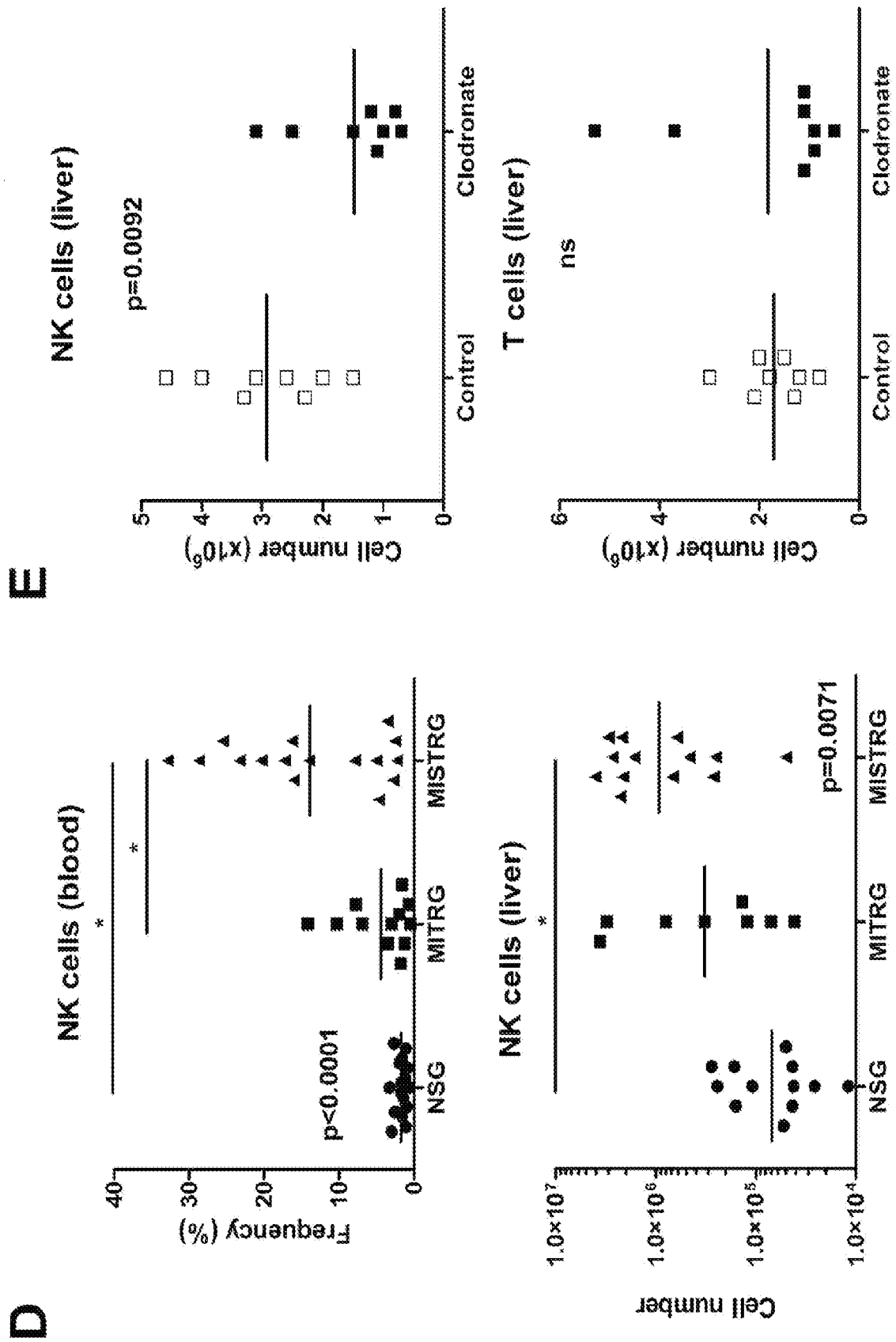


Figure 3D-3E

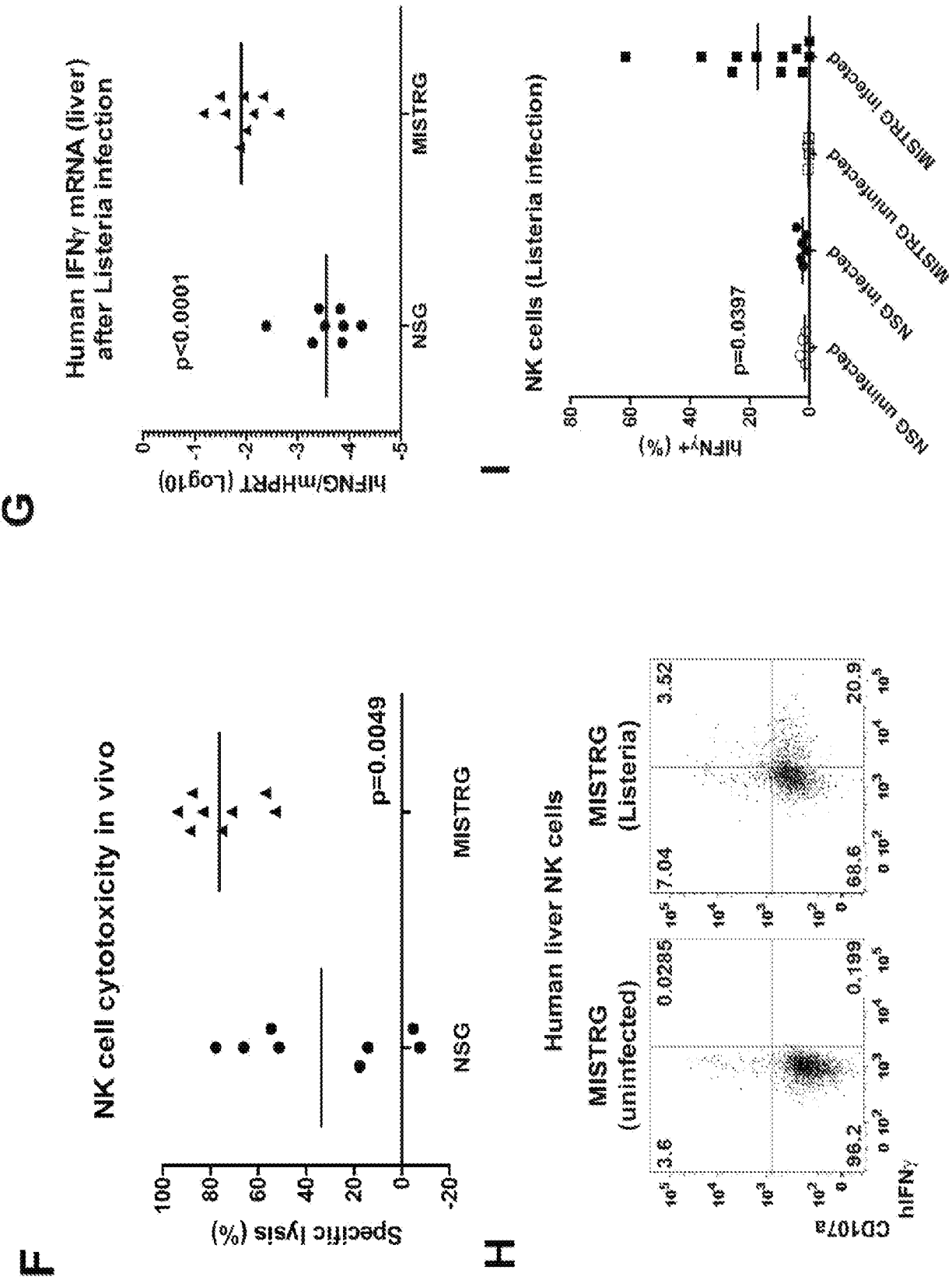


Figure 3F-3I

12/36

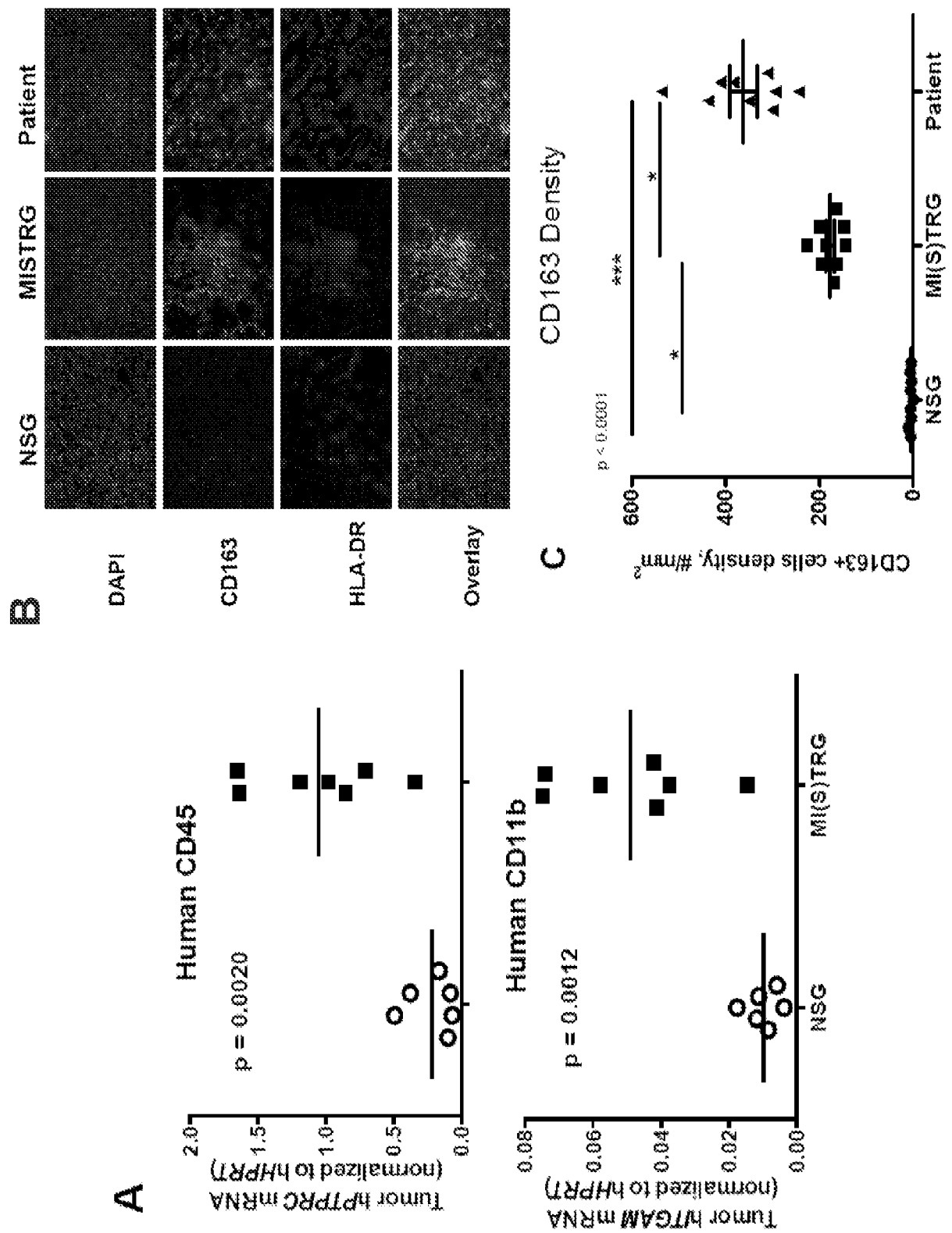


Figure 4A-4C

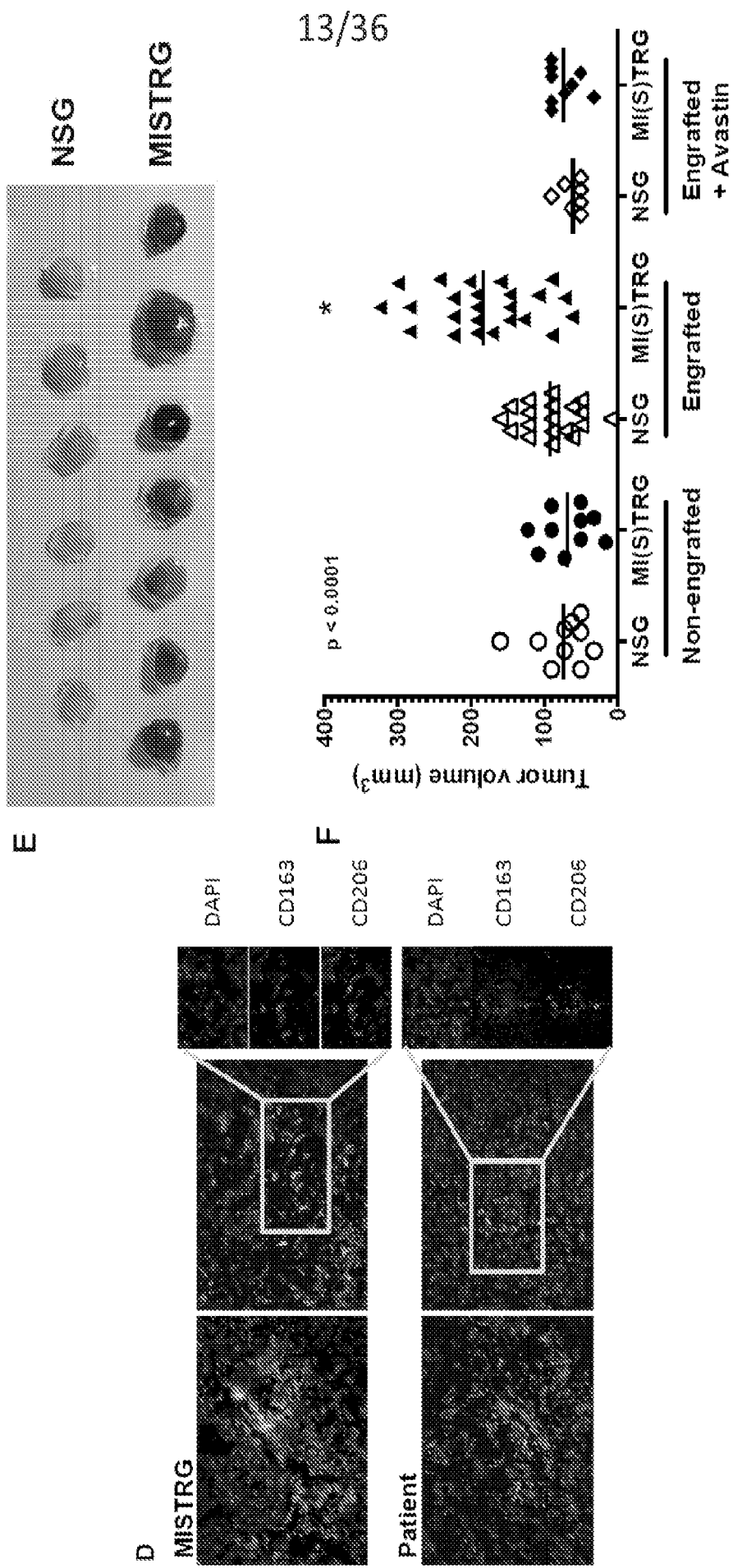


Figure 4D-4F

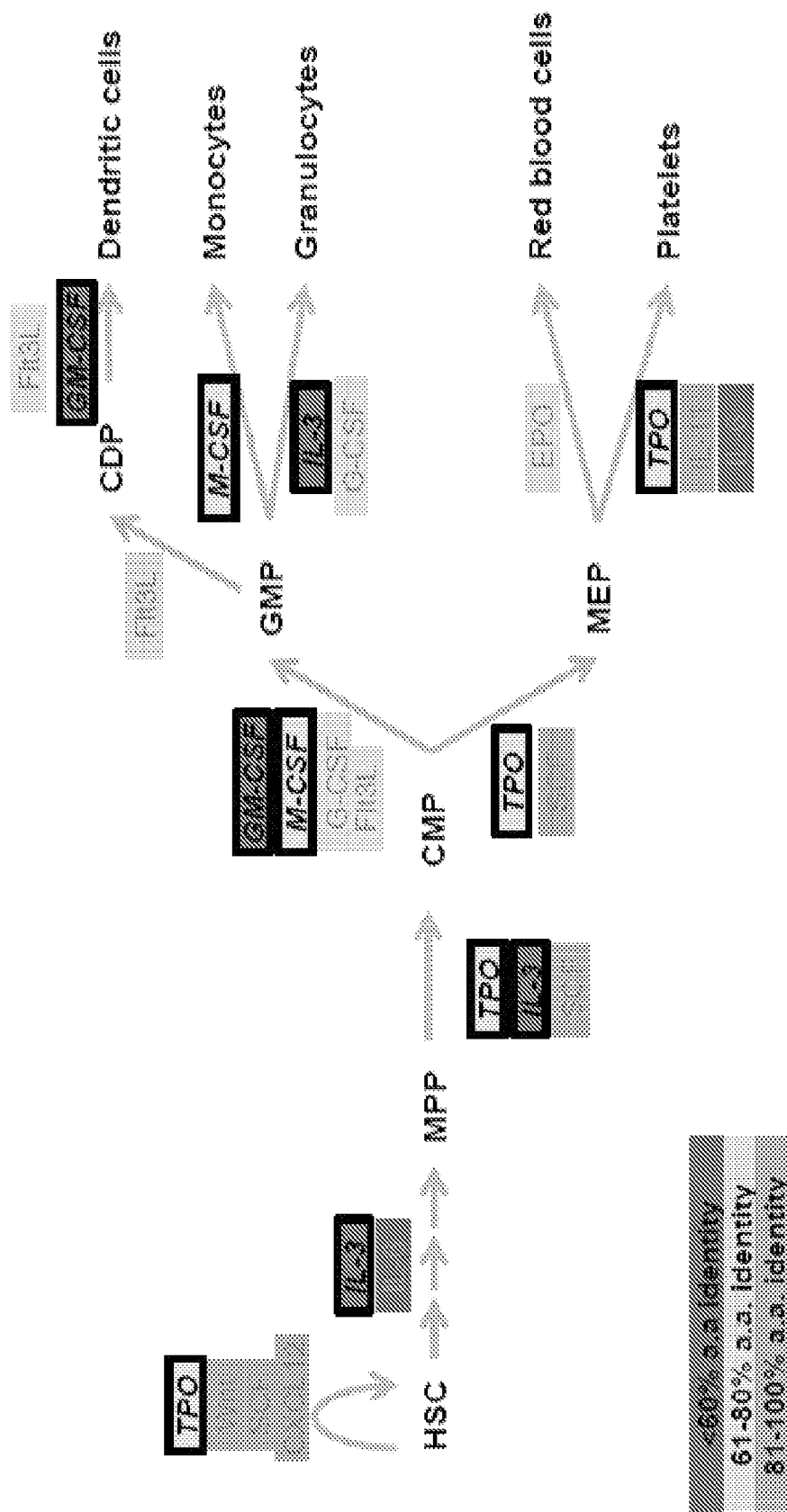
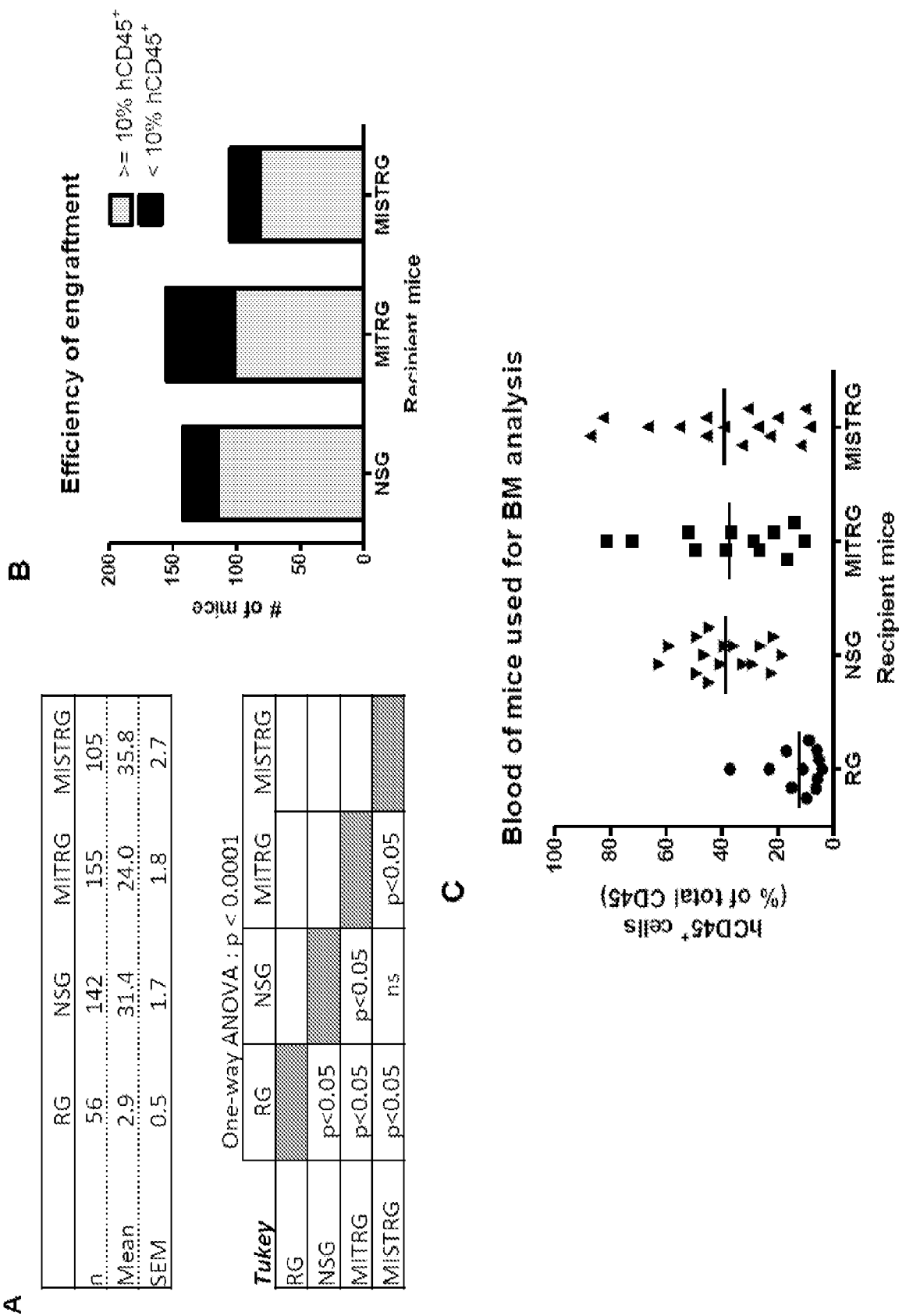


Figure 5



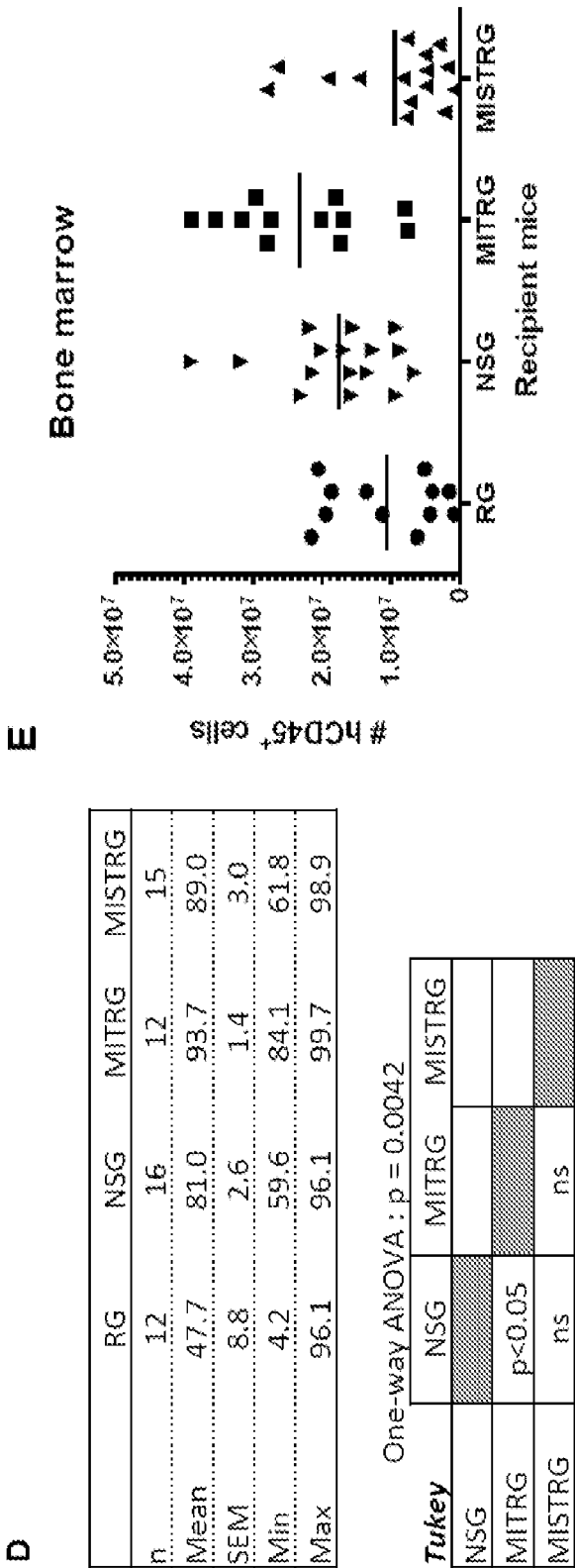


Figure 6D-6E

A

	RG	NSG	MITRG	MISTRG
n	20	122	129	88
Mean	3.5	8.5	29.8	40.9
SEM	0.4	0.5	1.5	1.9

One-way ANOVA : $p < 0.0001$

Tukey	RG	NSG	MITRG	MISTRG
RG				
NSG	ns			
MITRG	$p < 0.05$	$p < 0.05$		
MISTRG	$p < 0.05$	$p < 0.05$	$p < 0.05$	

C

	RG	NSG	MITRG	MISTRG
n	12	16	12	14
Mean	10.3	21.6	30.5	37.3
SEM	1.3	3.5	3.8	3.5

One-way ANOVA : $p < 0.0001$

Tukey	RG	NSG	MITRG	MISTRG
RG				
NSG	ns			
MITRG	$p < 0.05$	ns		
MISTRG	$p < 0.05$	$p < 0.05$	$p < 0.05$	

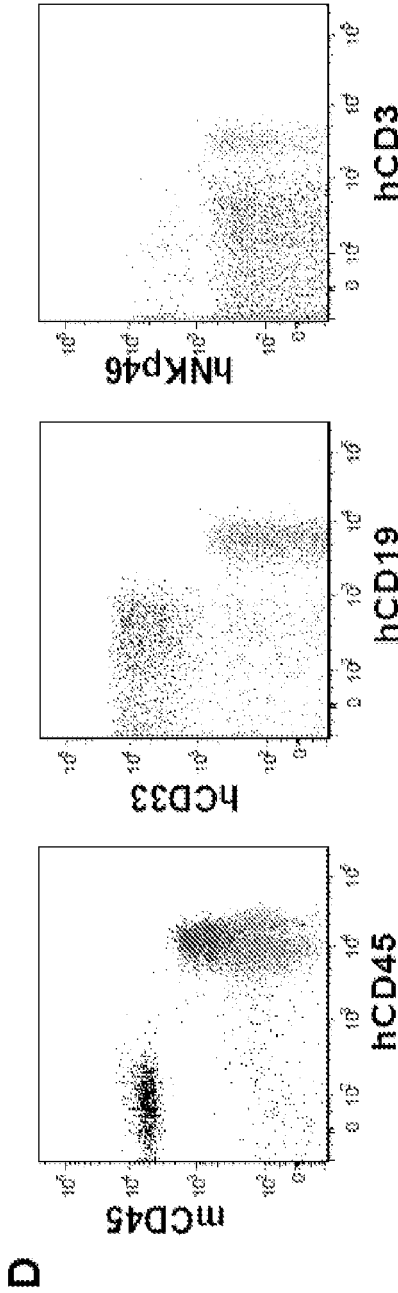
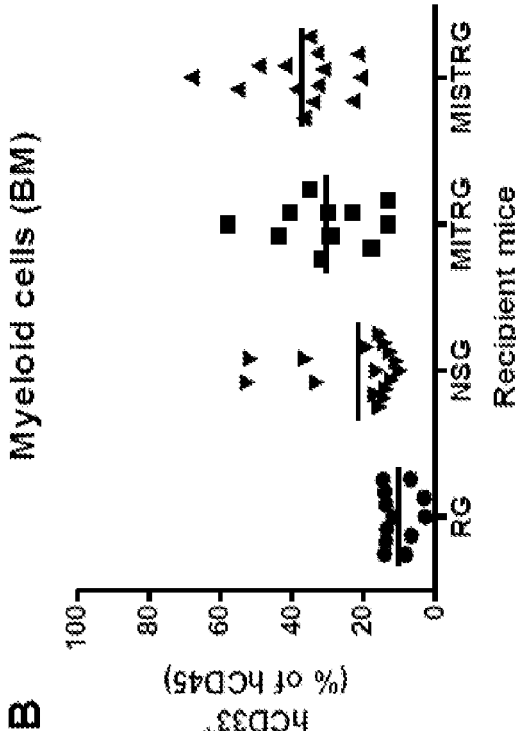
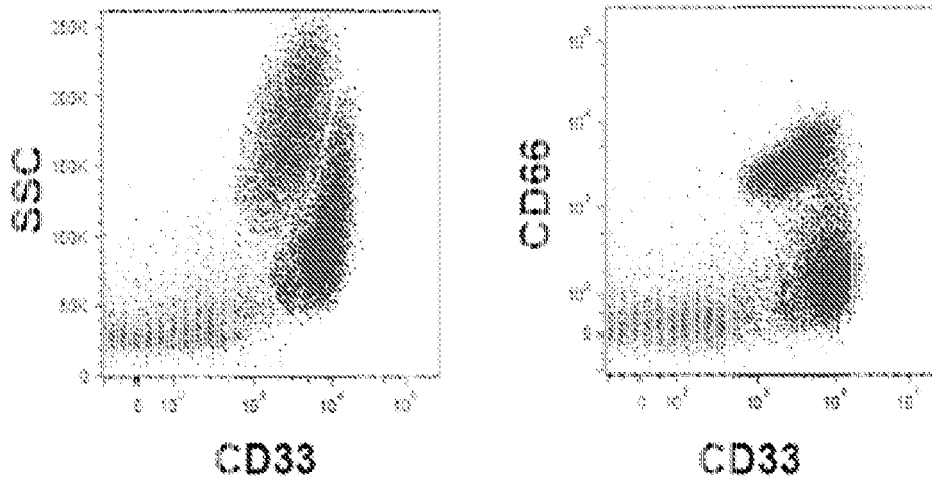


Figure 7A-7D

18/36

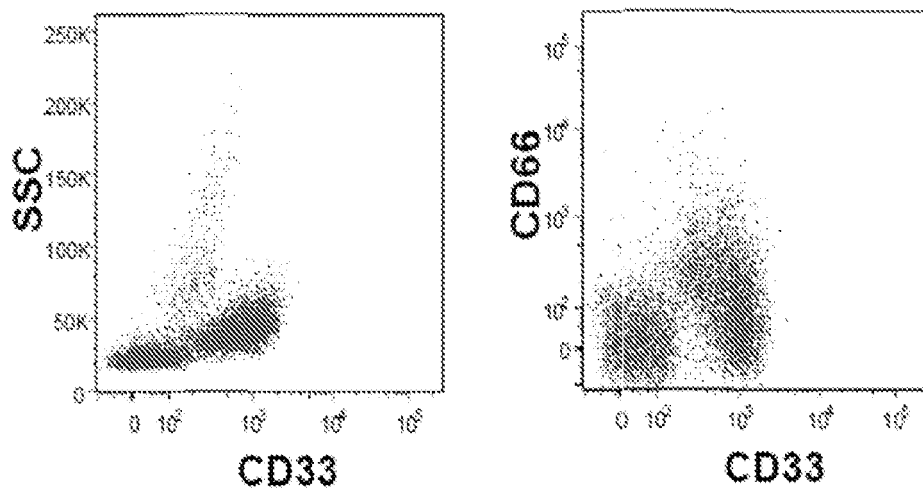
E

MISTRG BM (gated on hCD45⁺)



F

MISTRG blood (gated on hCD45⁺)



Human blood

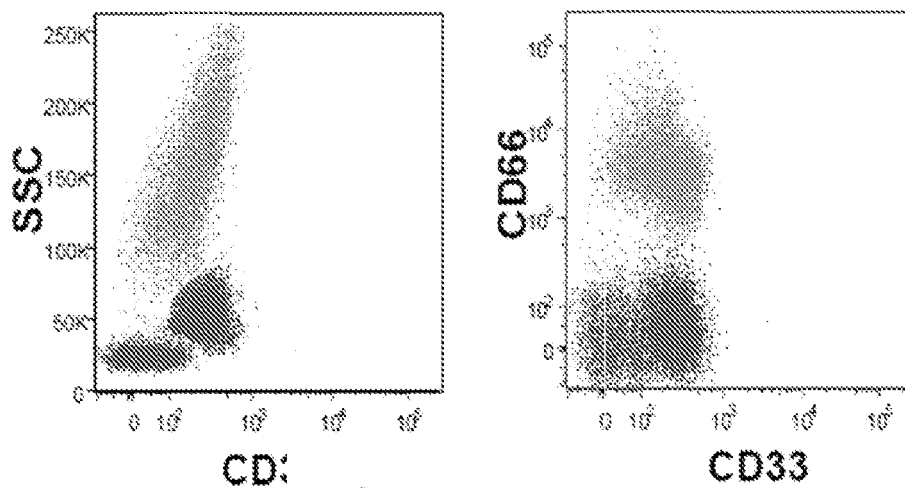


Figure 7E-7F

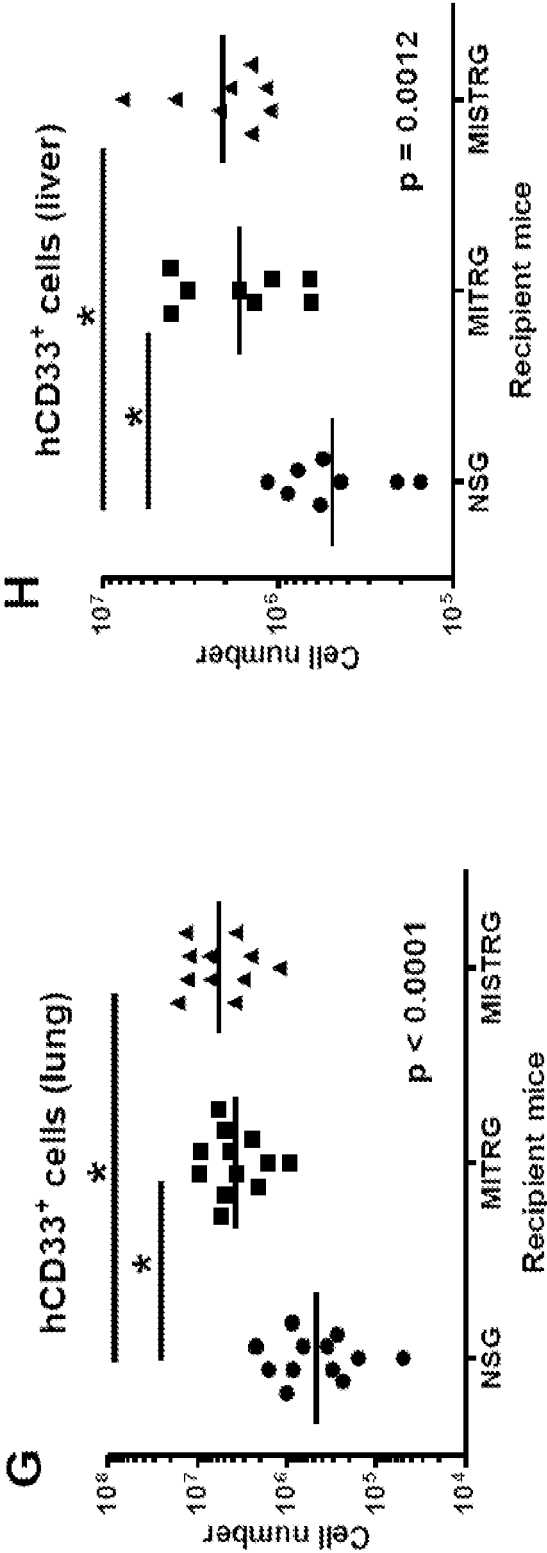


Figure 7G-7H

20/36

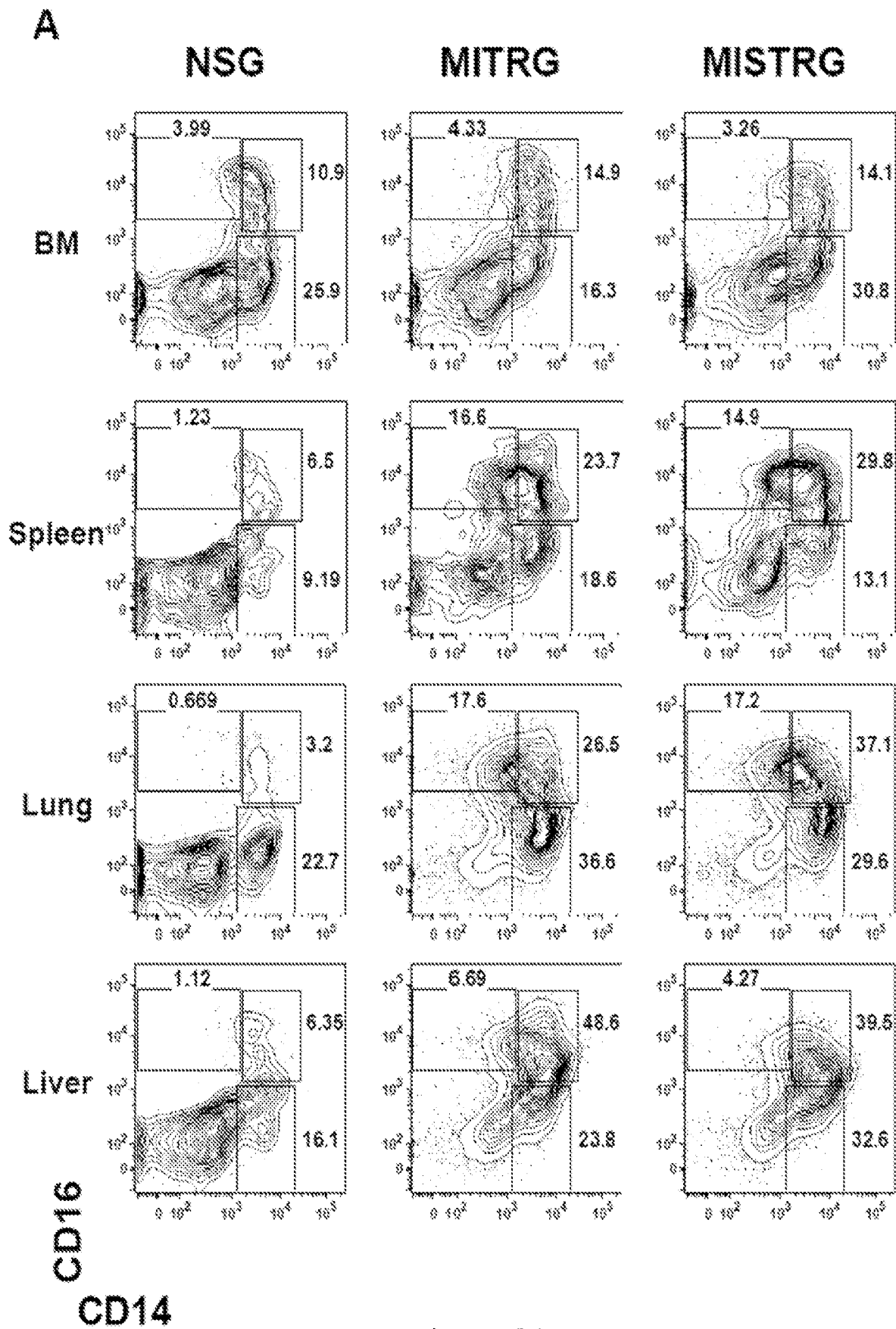


Figure 8A

21/36

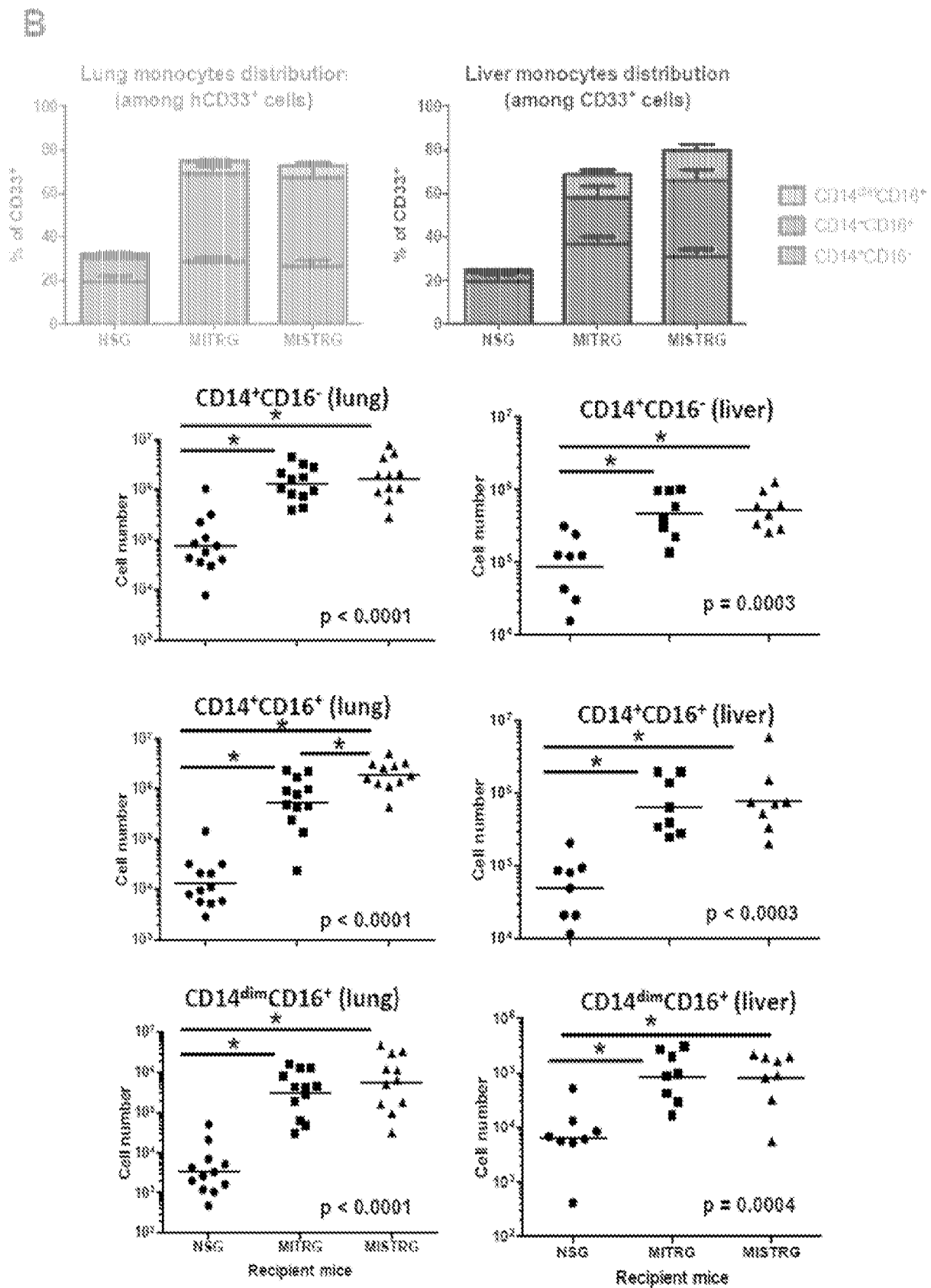


Figure 8B

22/36

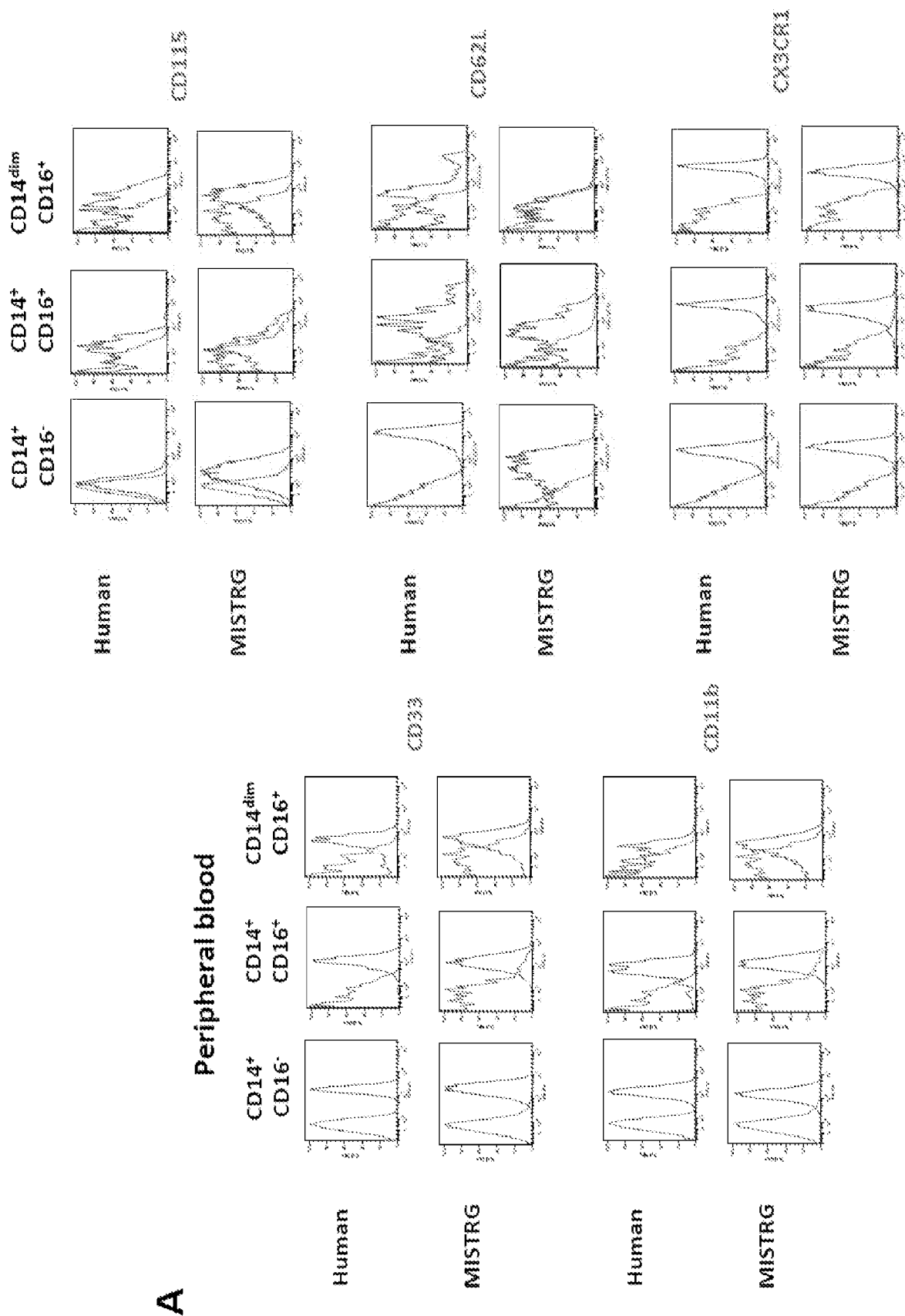


Figure 9A

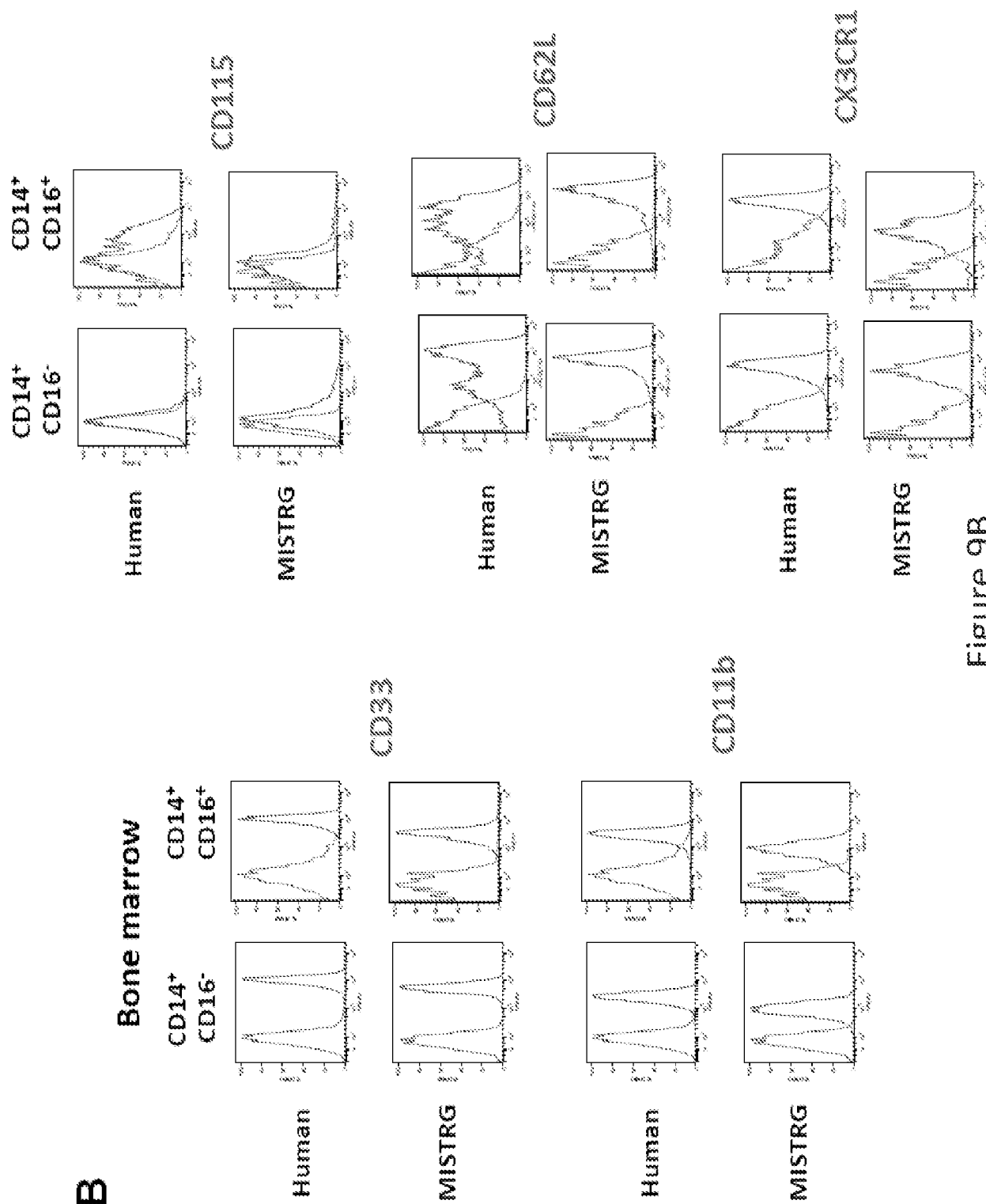


Figure 9B

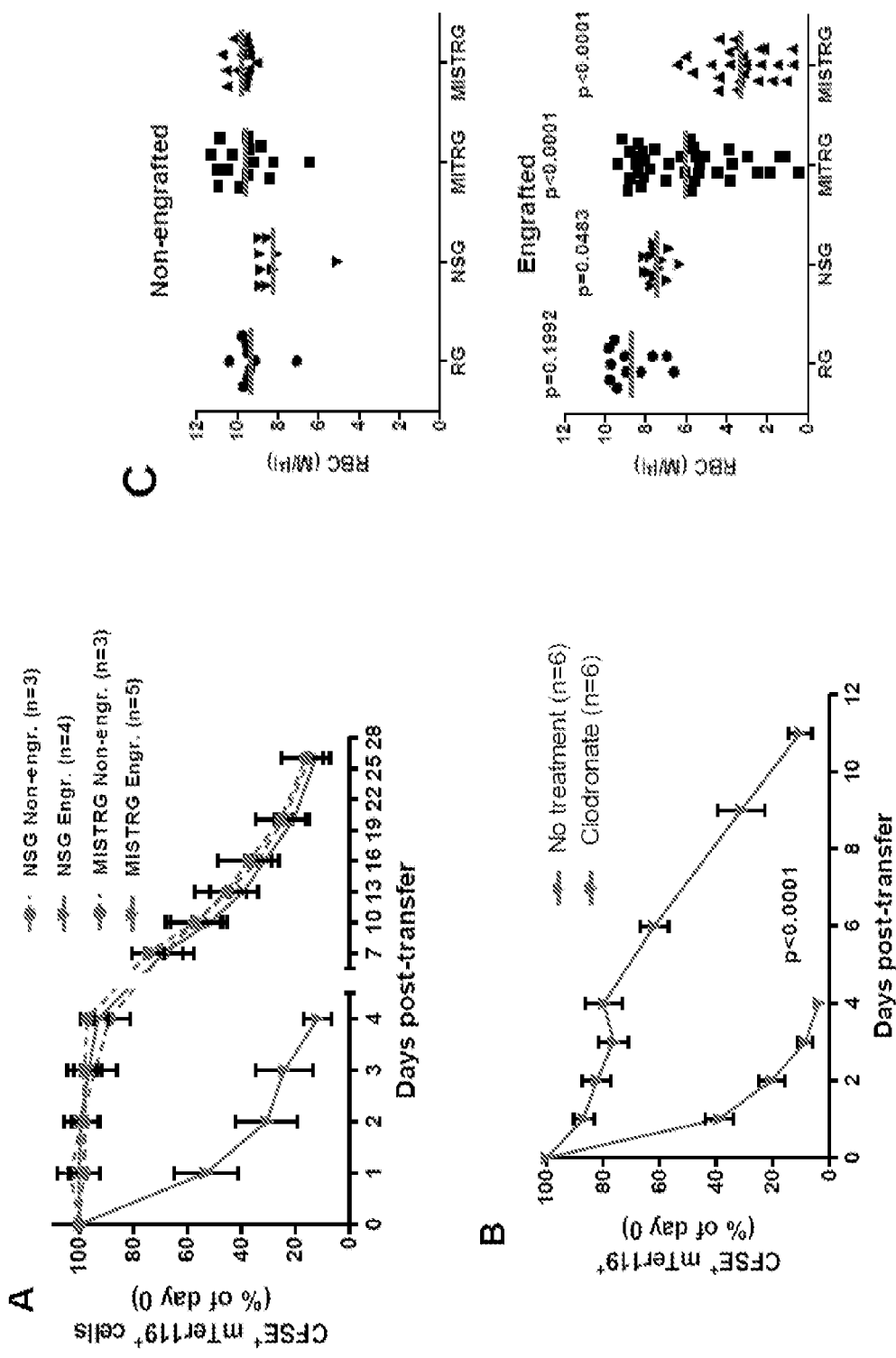


Figure 10A-10C

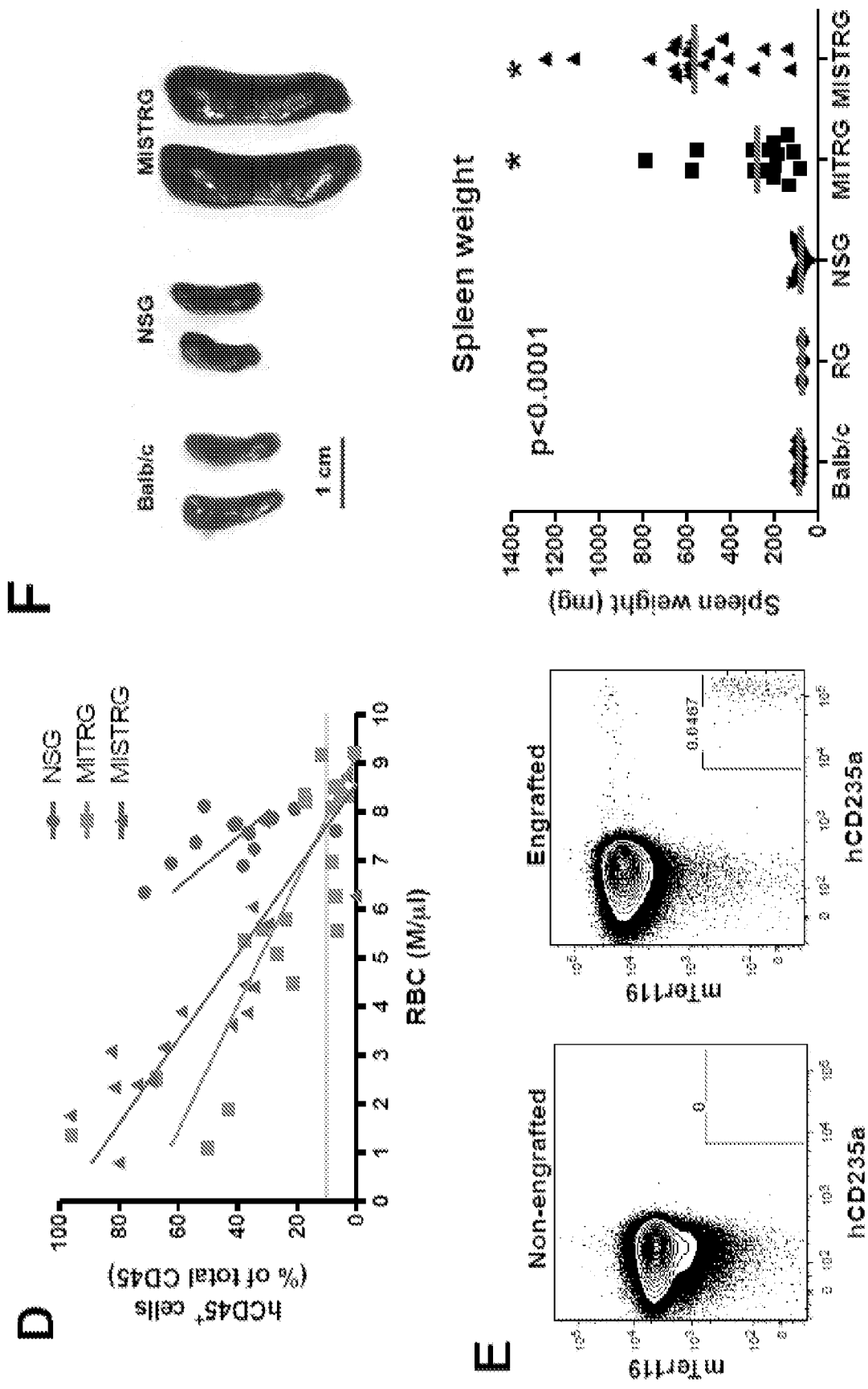


Figure 10D-10F

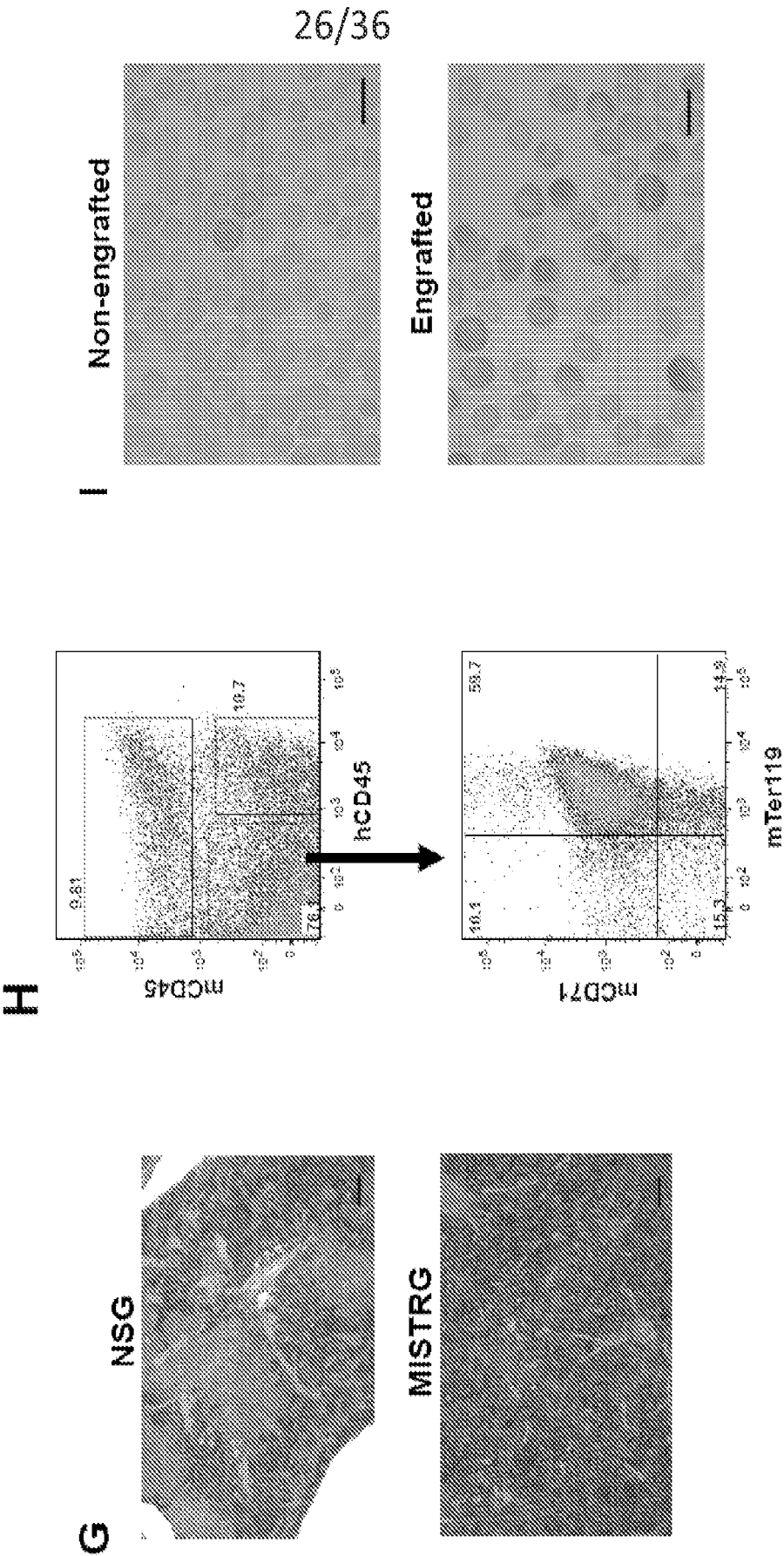


Figure 10G-10I

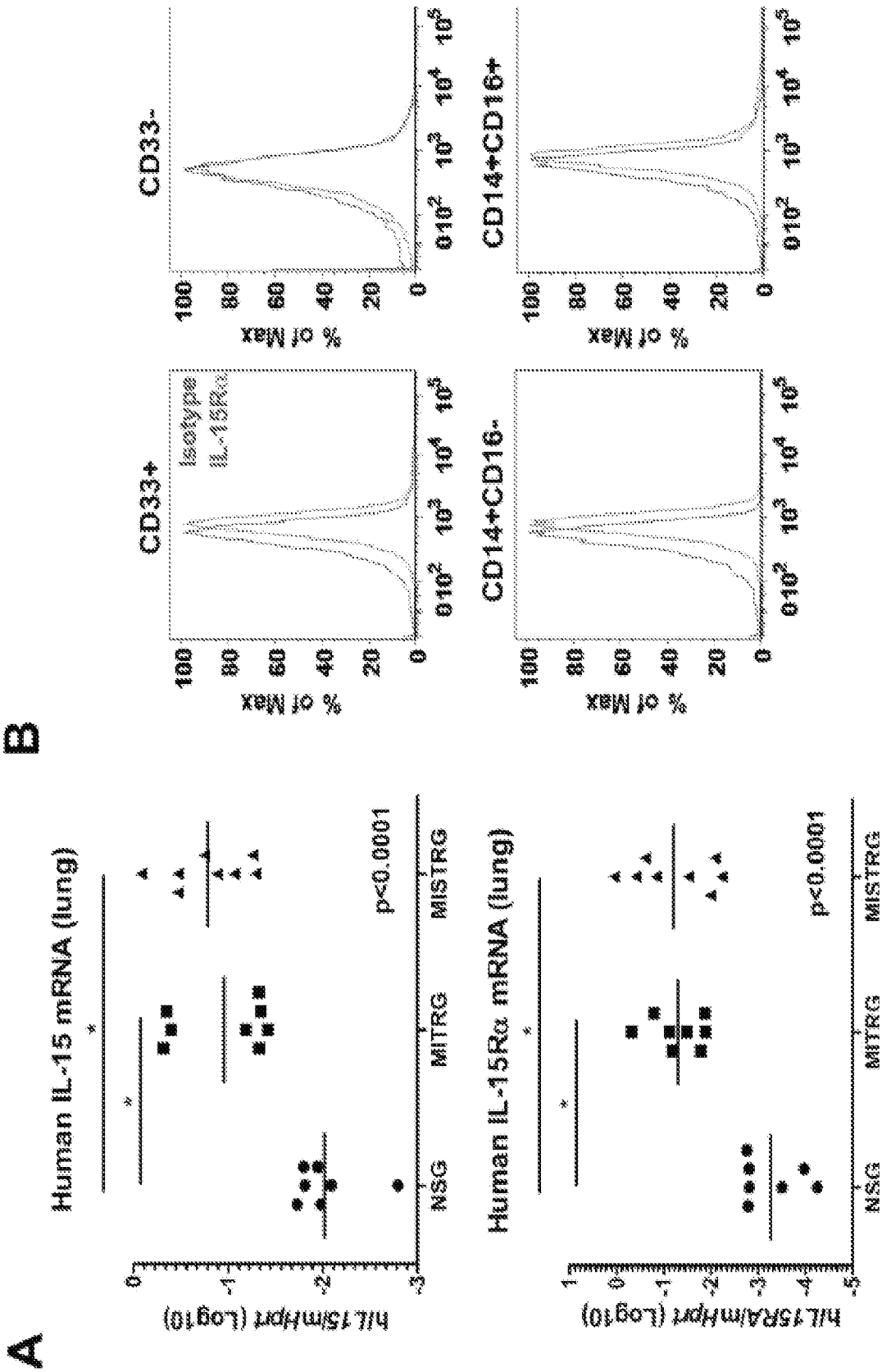


Figure 11

NK cells

A

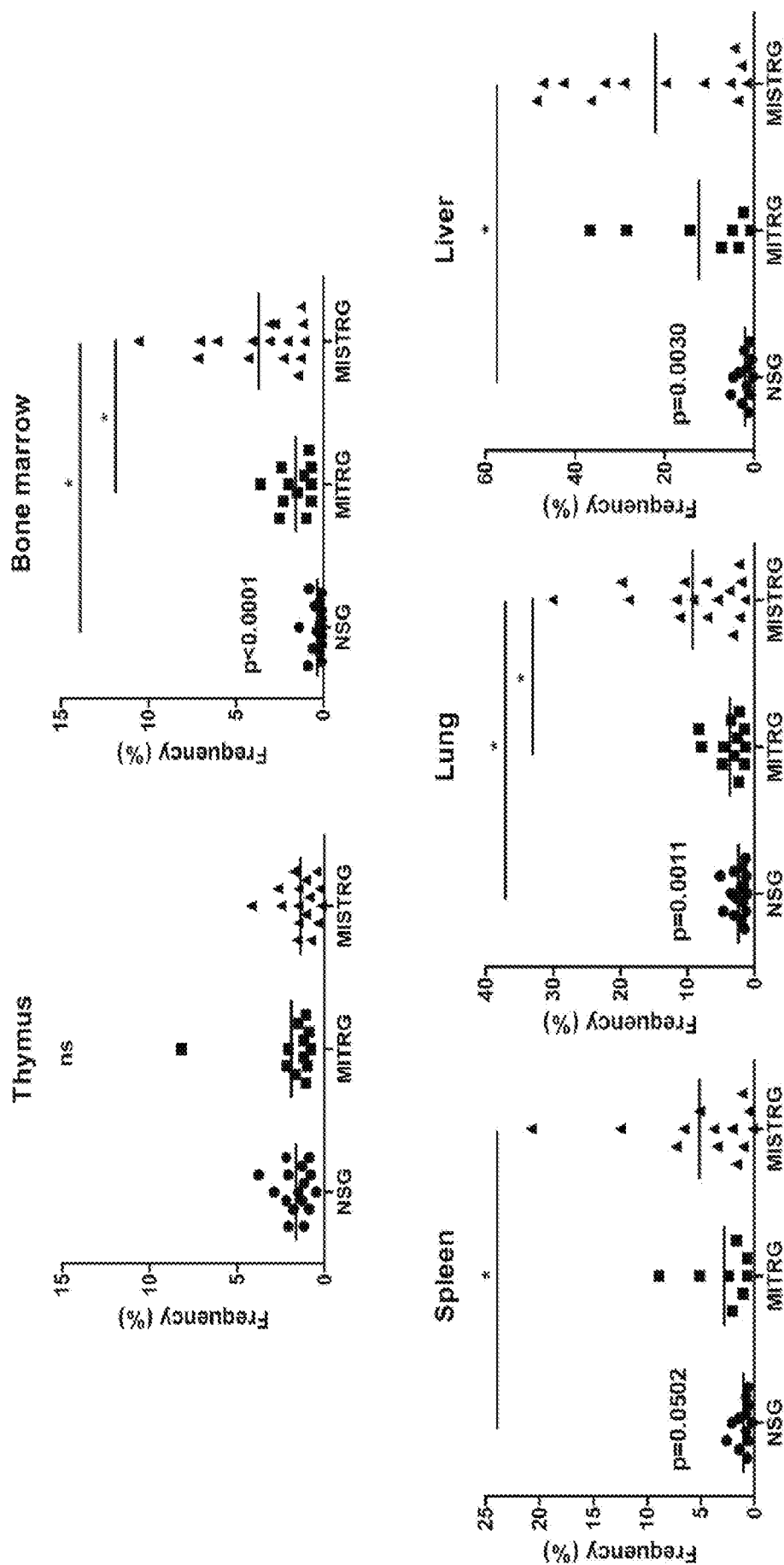


Figure 12A

B

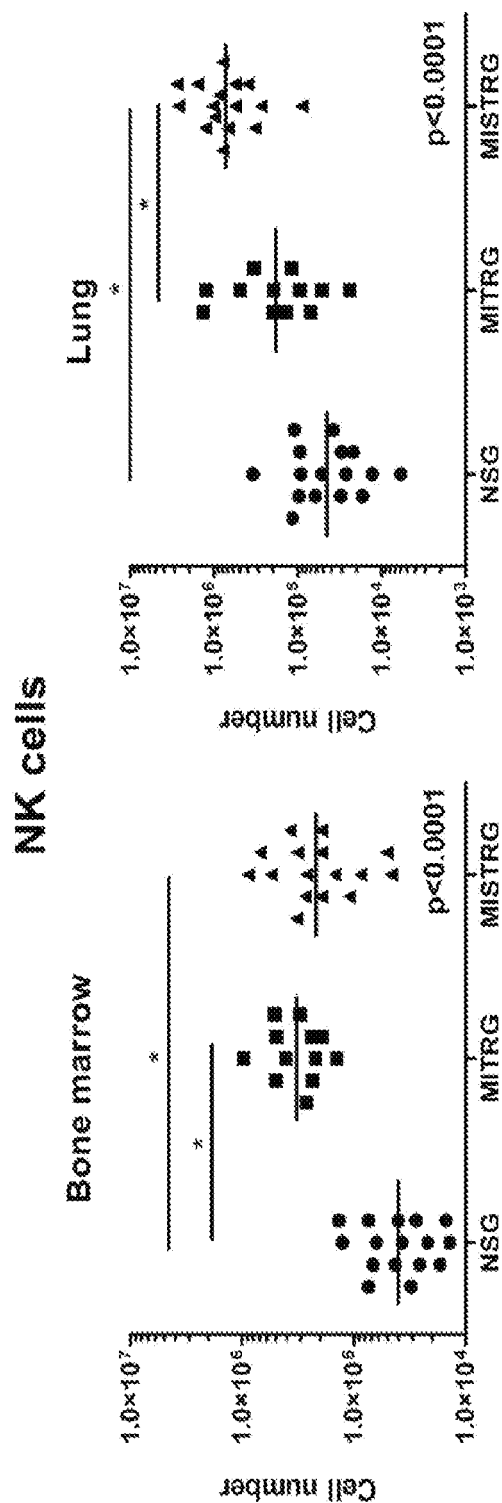


Figure 12B

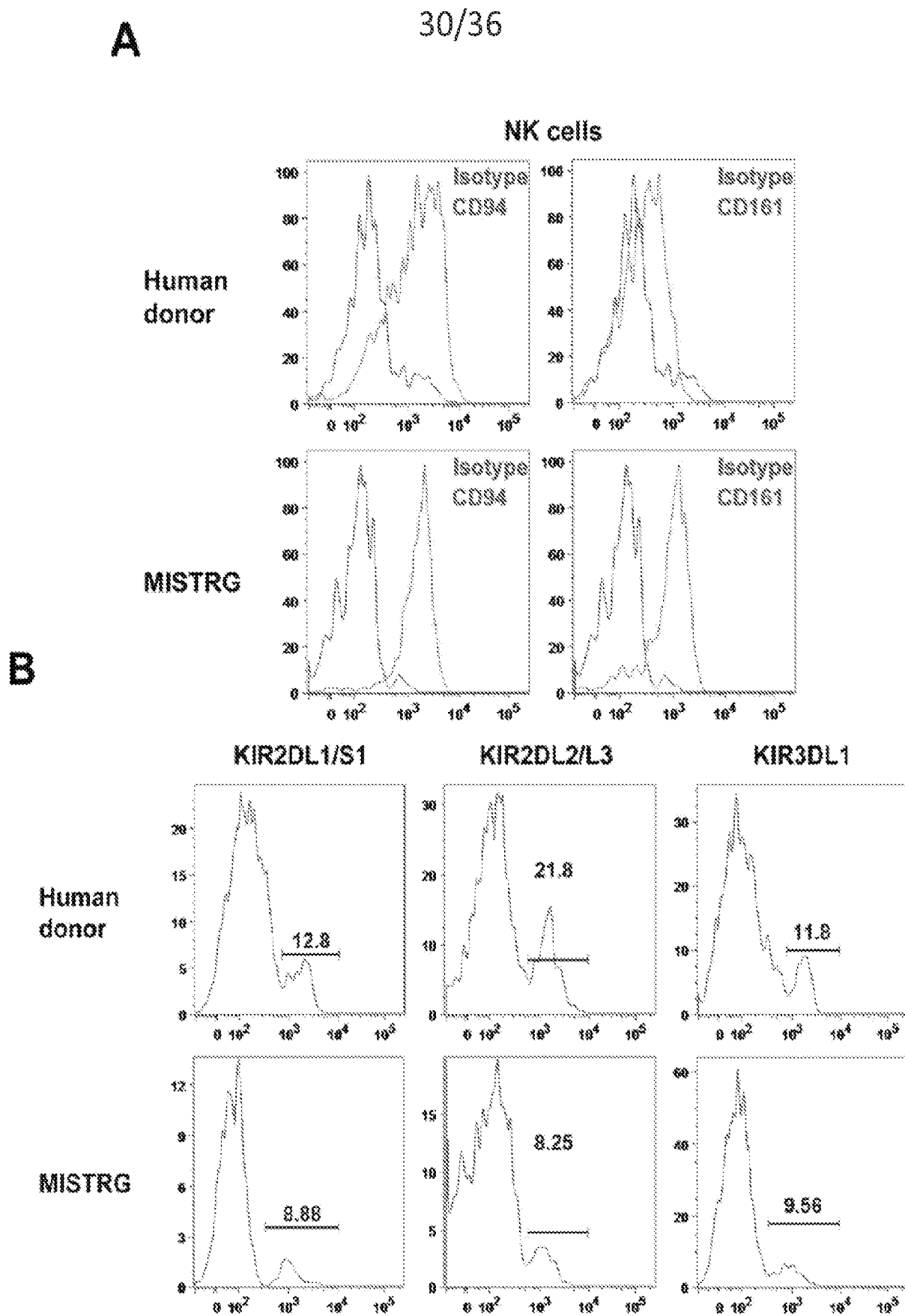


Figure 13A-13B

31/36

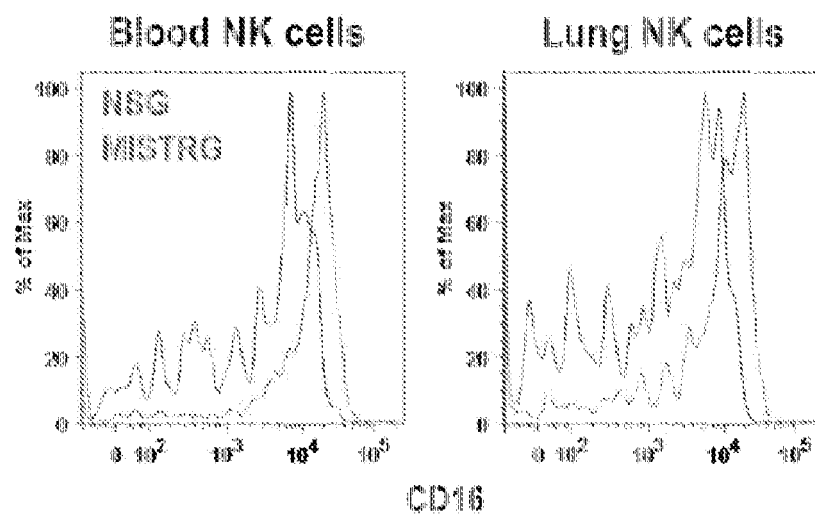
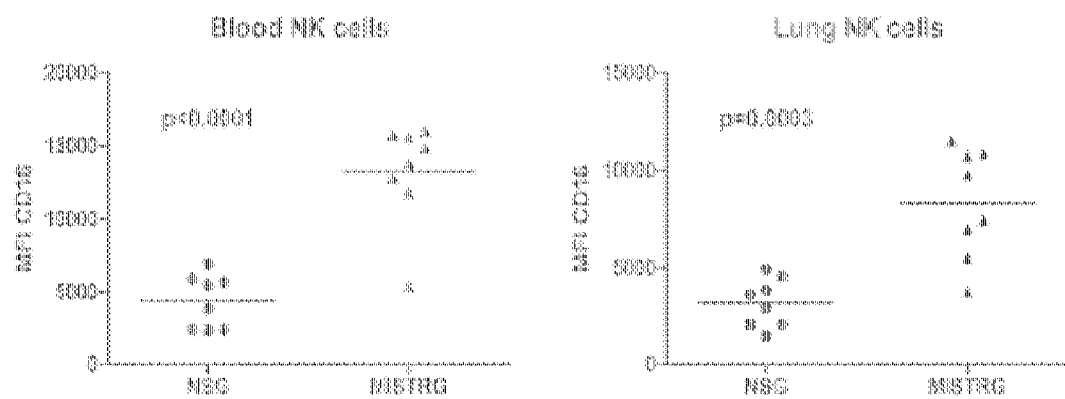
C**D**

Figure 13C-13D

32/36

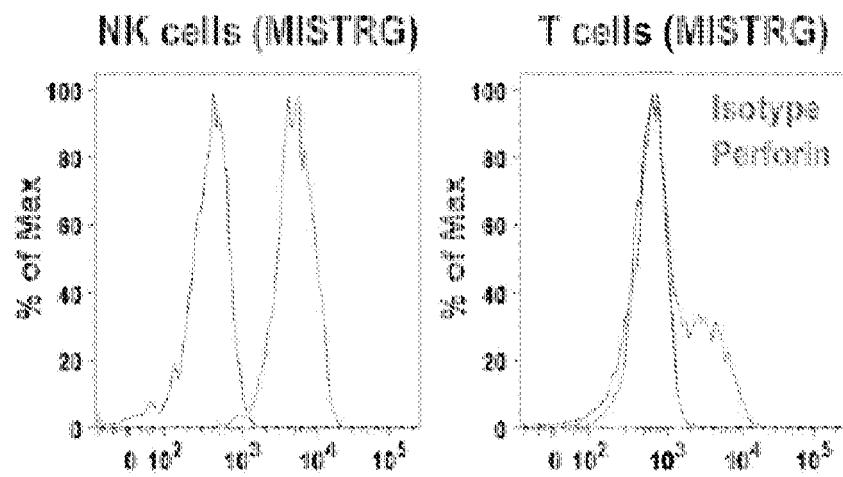
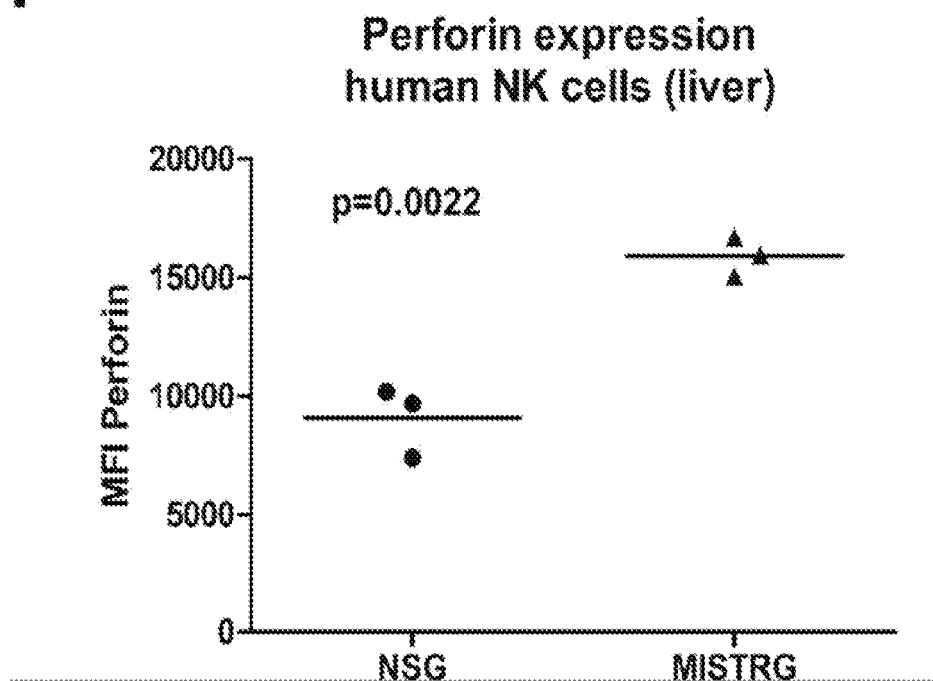
E**F**

Figure 13E-13F

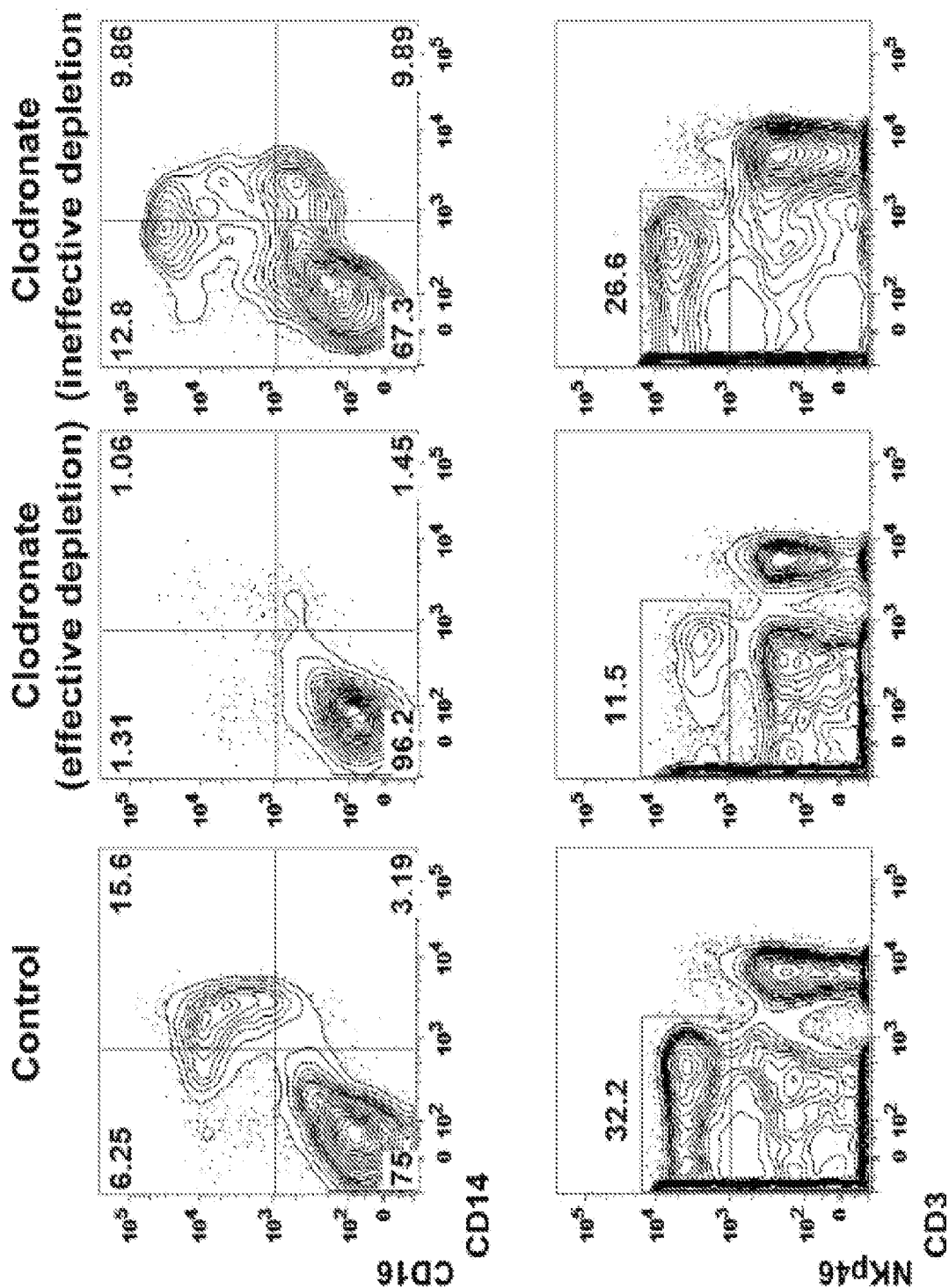


Figure 14

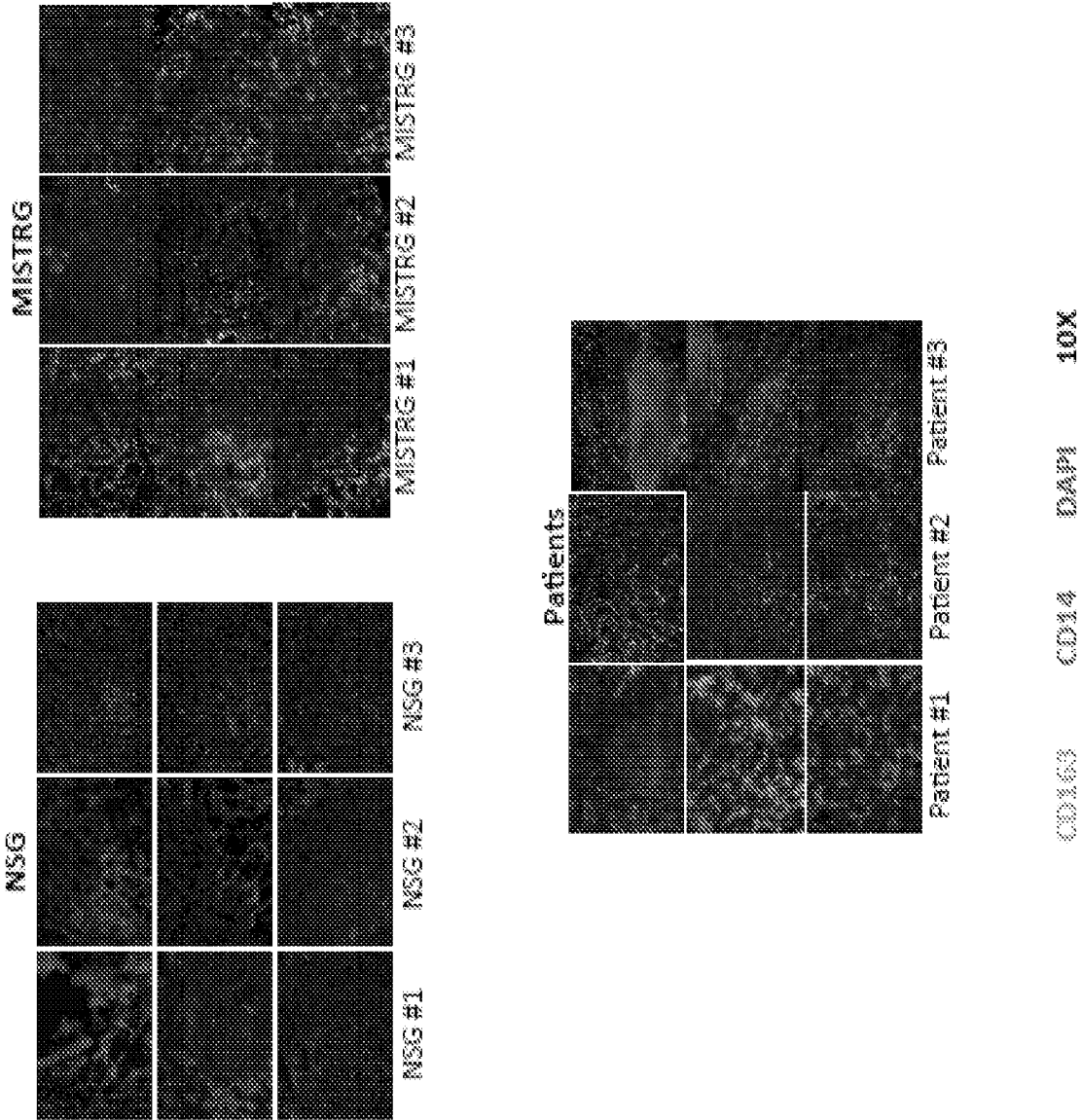


Figure 15

Comparison of engraftment levels and immune cell development and function in recipient mice with single gene replacement, in NSG, MISTRG and in humans

	RAG2 ^{-/-} IL2Rγ ^{-/-} (RG)	RG TPO ^{h/h}	RG IL-3/GM-CSF ^{h/h}	RG M-CSF ^{h/h}	hSIRPα ^{h/h} RG / NSG	MISTRG	Human
Blood hCD45 ⁺ cells (%)	5-20	5-20	5-20	20-40	10-60	10-80	100
BM hCD45 ⁺ (%)	20-80	75-90	20-80	20-80	60-90	85-99	100
Human CD33 ⁺ myeloid cells (% of hCD45)	1-7	10-20	5-10	10-30	5-15	30-50	50-70
Human NK cells (% of hCD45)	0-1	ND	ND	ND	0.5-2	1-7	1-6
Human NK cell function	-	ND	ND	ND	-	+	+
Serum TNFα (ng/ml, 90 min post LPS)	ND	ND	ND	ND	0.3-3	10-200	ND
Lung alveolar macrophages	-	-	+	-	-	+	+

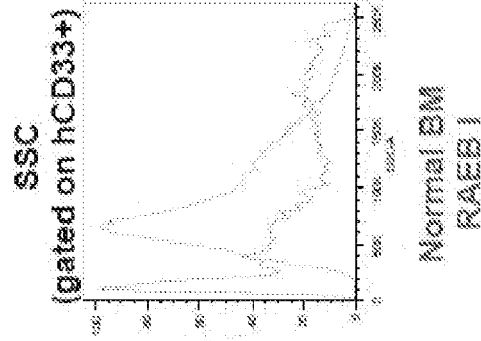
ND: Not determined

Figure 16

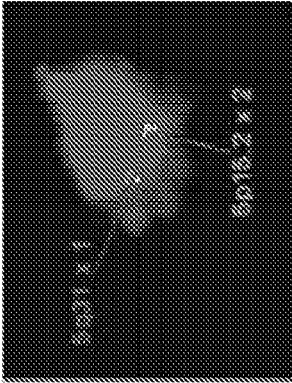
A

Disease	Cell number per mouse	Engrafted	Time after transplant in weeks	Bone Marrow		Genetic abnormality		Comment
				hCD45	hCD33	Patient sample	Engrafted	
RCUD	9x10 ⁴ CD34+ enriched	1/1	11	1.9	89.9	Normal	n.d.	Low granularity of CD33+ cells
RAEB I	1-4x10 ⁵ CD34+ enriched	4/4	10	2.2-38.7	37.3-49.8	Trisomy 8 in 5% of cells	nl FISH x 1	Low granularity of CD33+ cells
RAEB II	7x10 ⁵ CD34+ enriched cells	2/2	15	0.07-0.88	31.9-85.5	5q-	5q- in 24/25 cells	
CMMML	7.5x10 ⁶ T-cell depleted	1/2	15	0.8	48	del(6)(q11.1q22.1)	del(6)(q11.1q22.1)	
2° AML from RAEB II	4.5x10 ⁶ T-cell depleted	2/2	12	73.8-81.5	77.5-84.1	Complex including 5q-	Complex including 5q-	

B



C



D

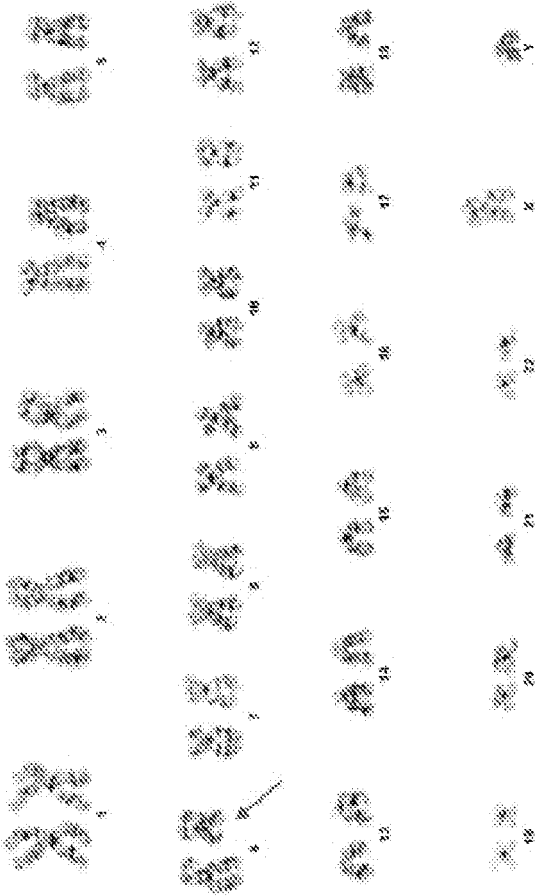


Figure 17