

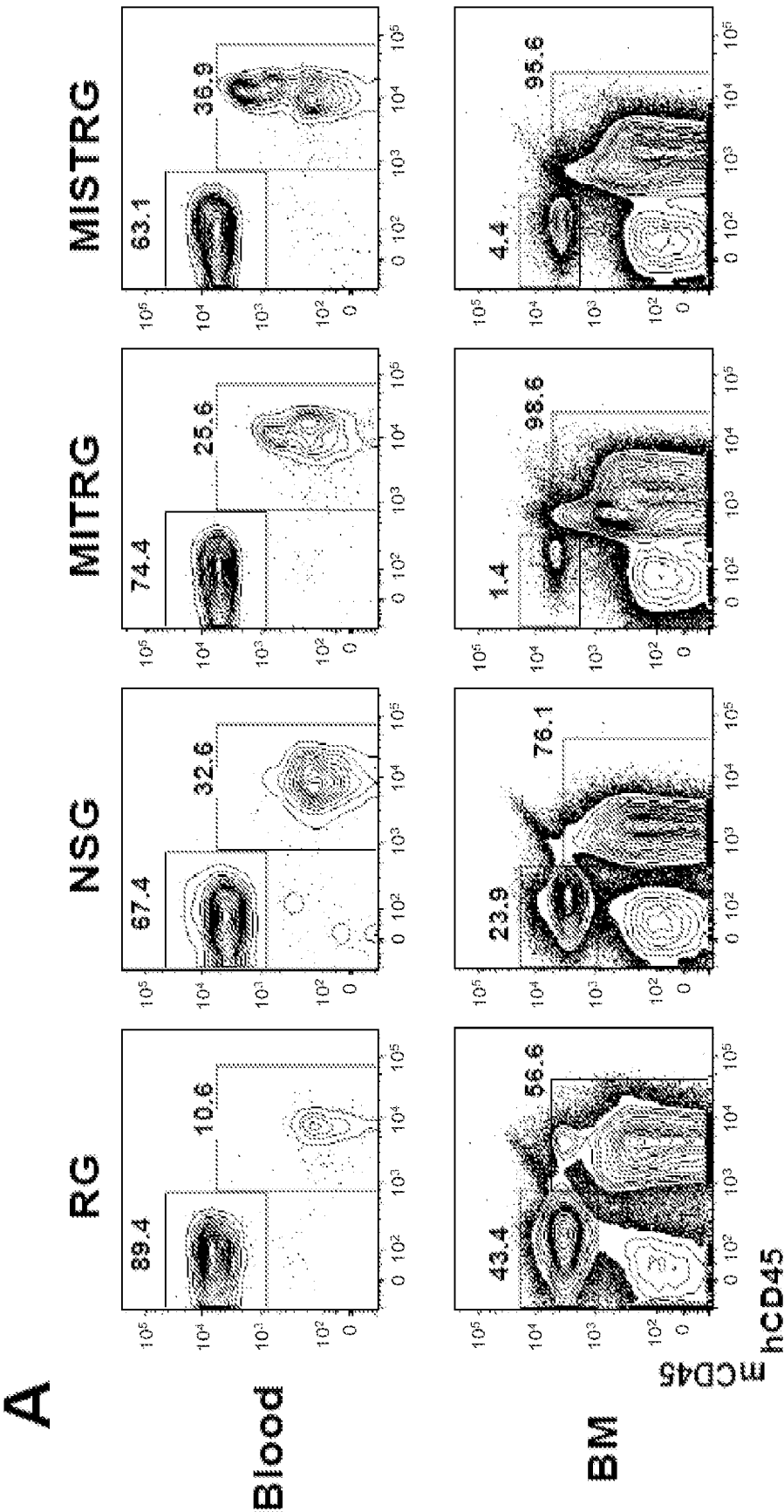


Figure 1A

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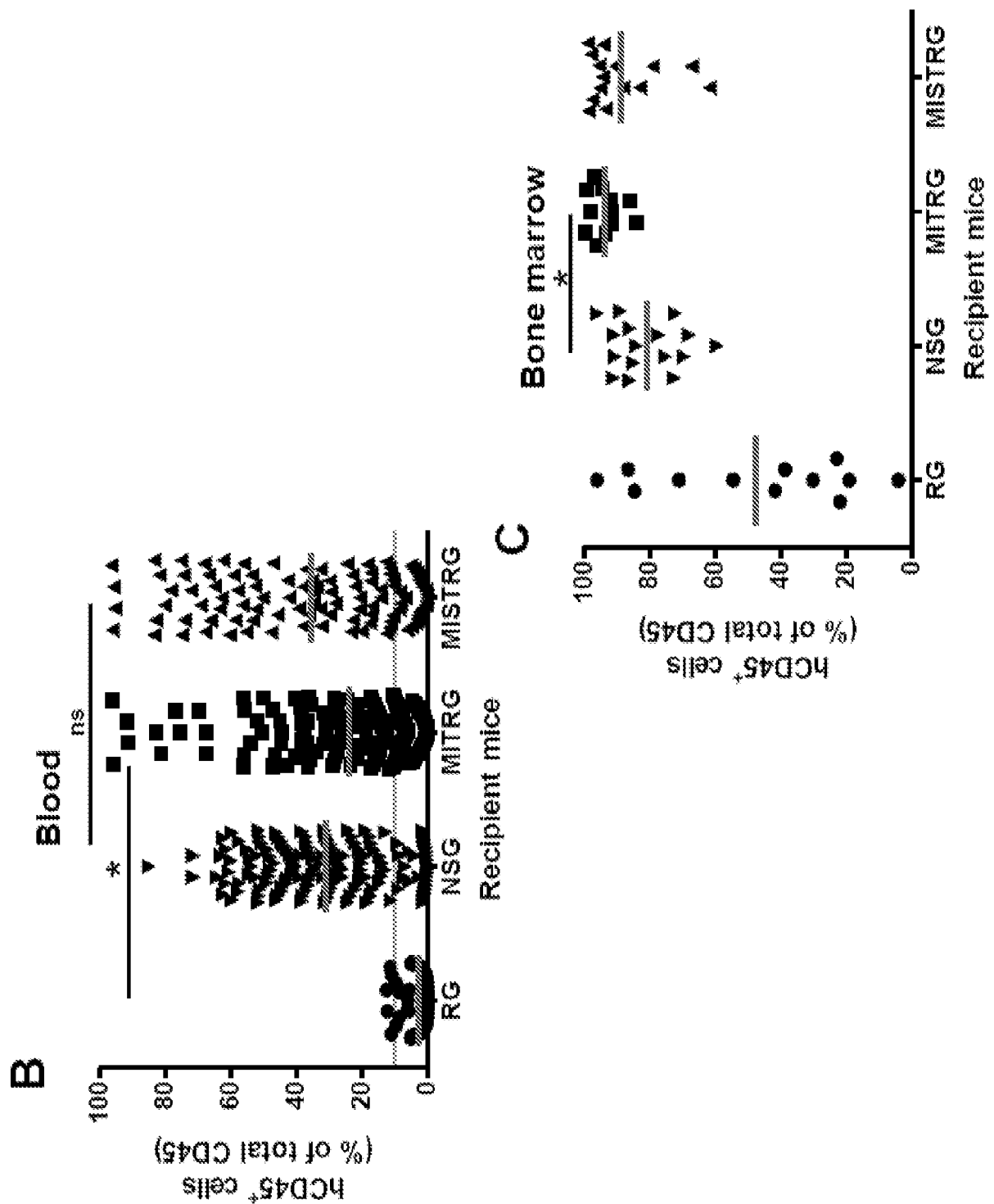


Figure 1B-1C

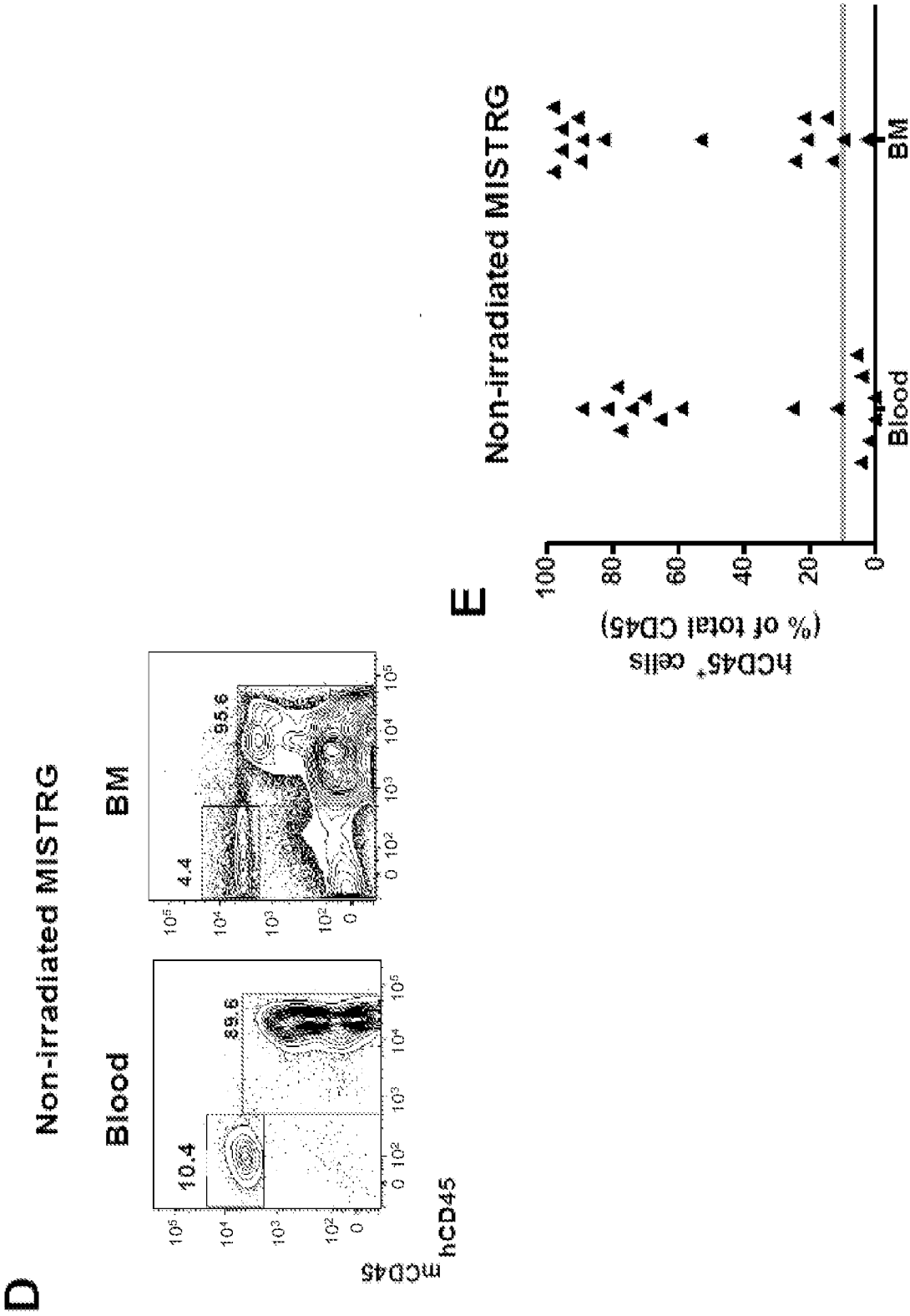


Figure 1D-1E

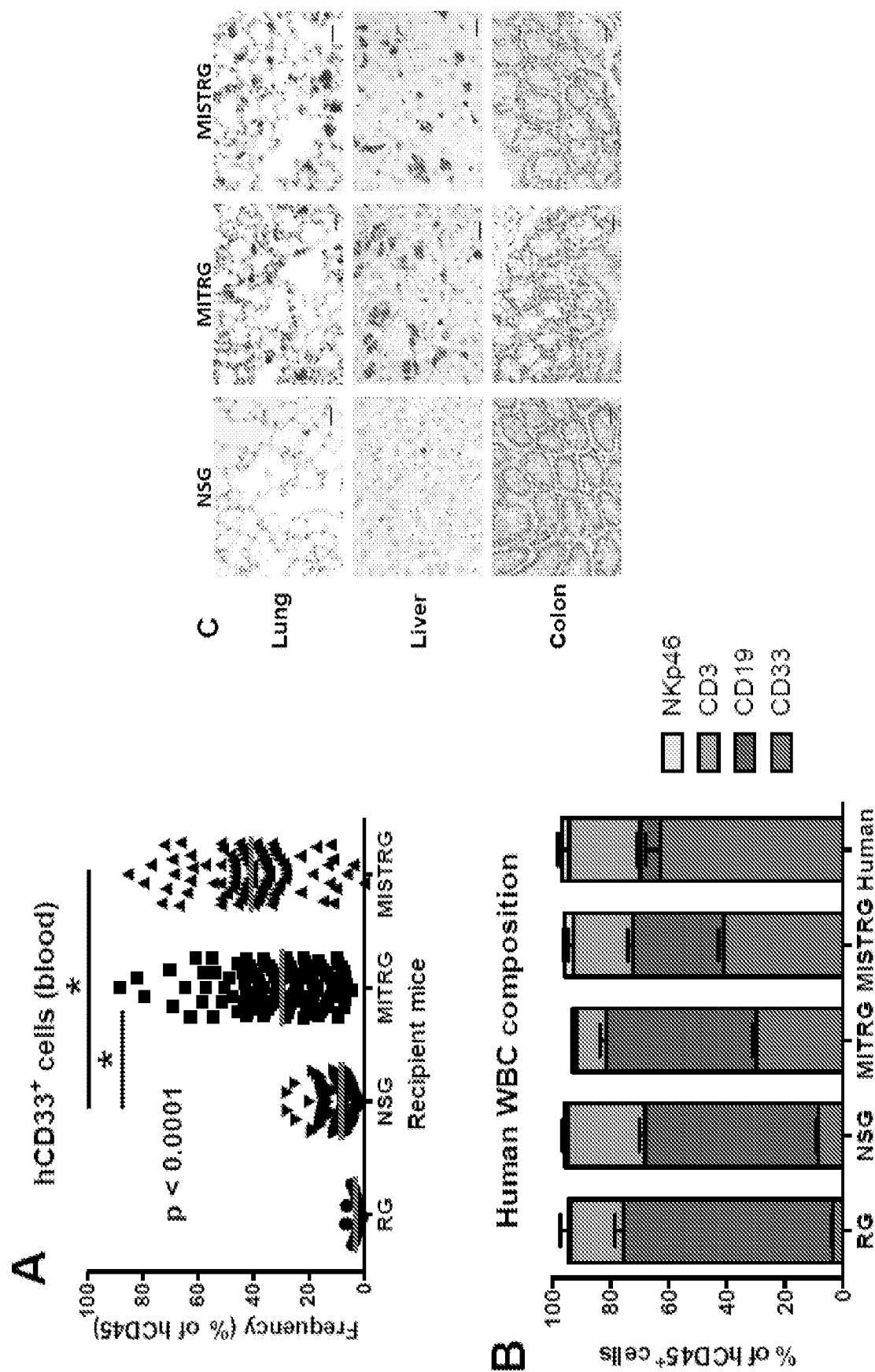


Figure 2A-2C

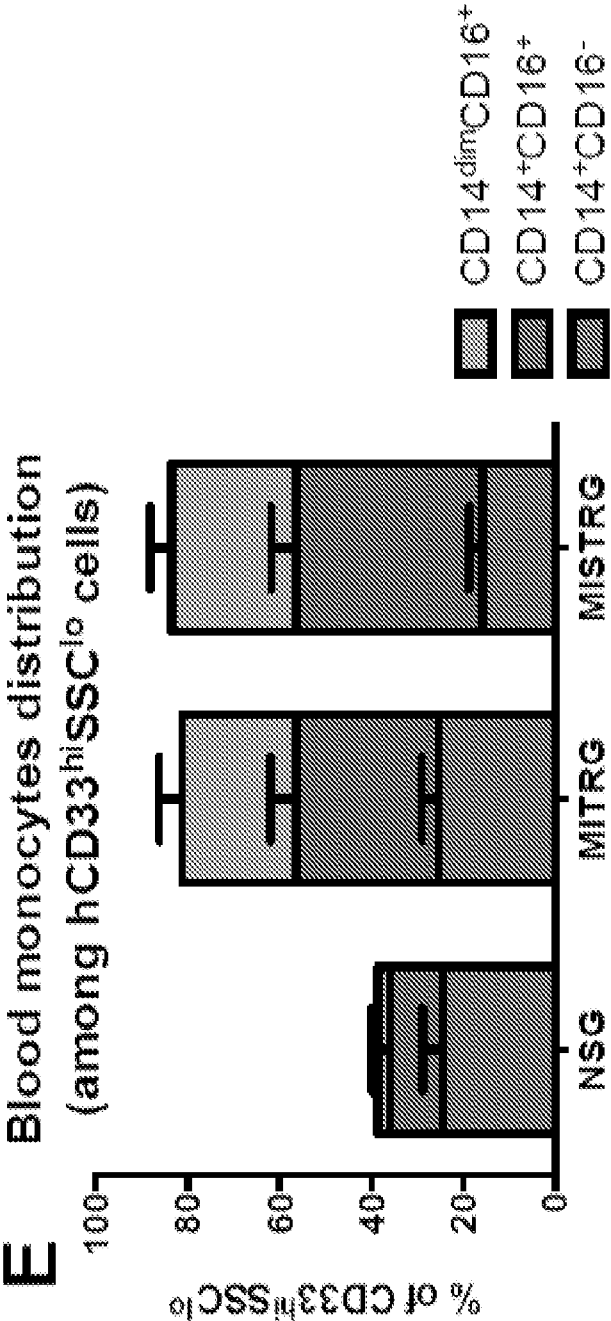
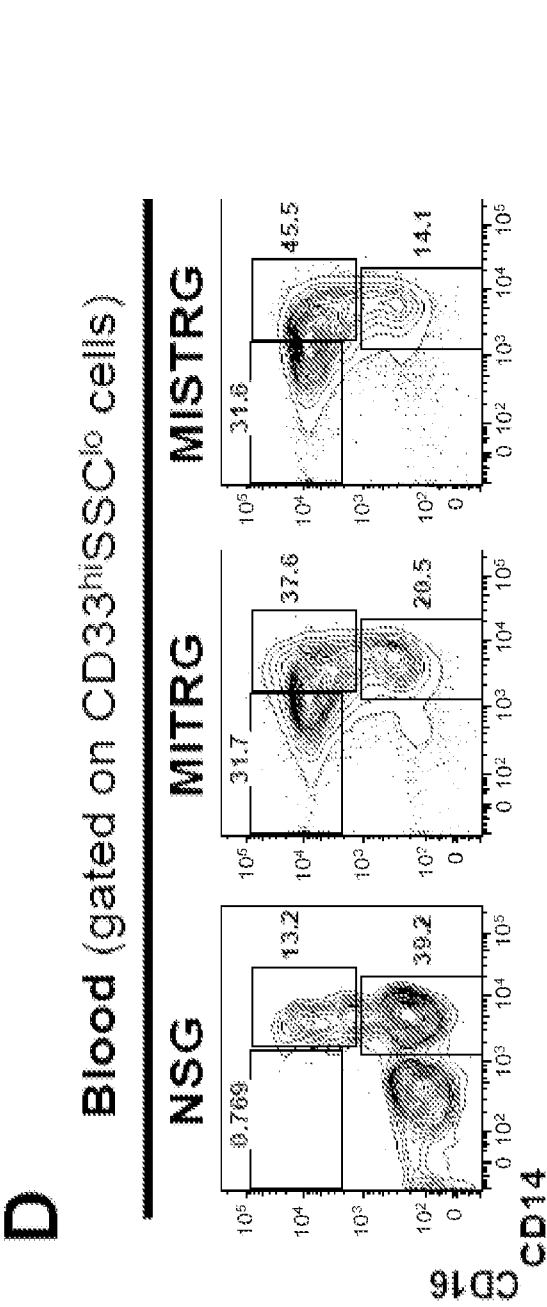
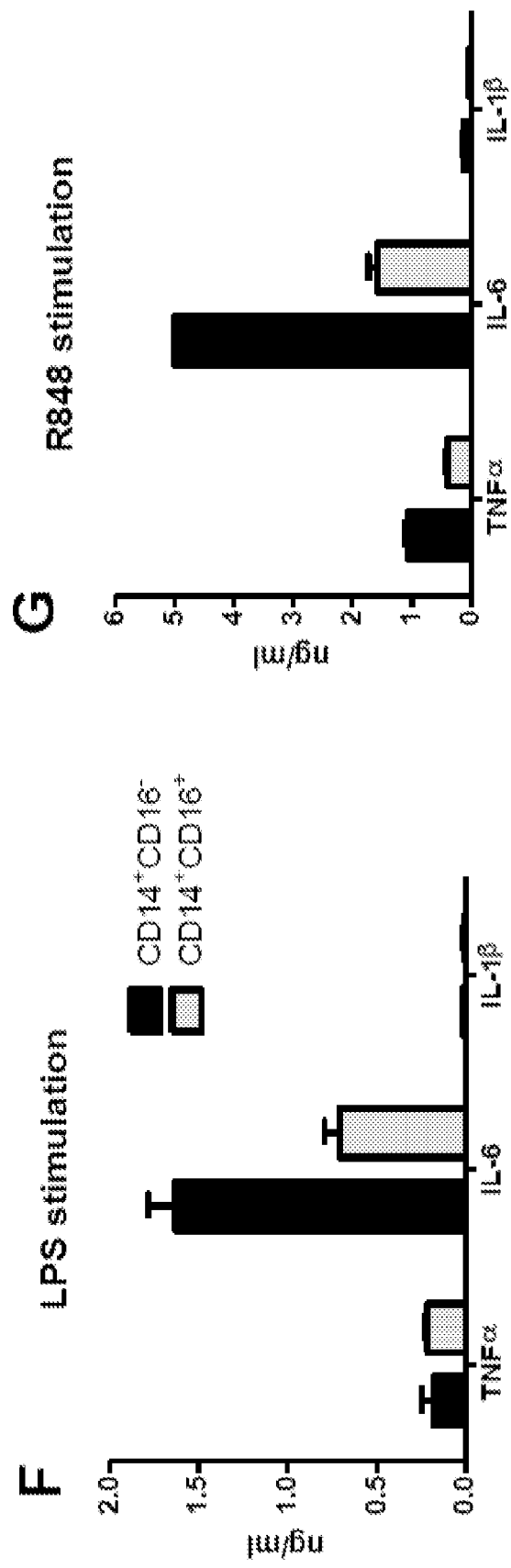


Figure 2D-2E



H *E. coli*-GFP phagocytosis

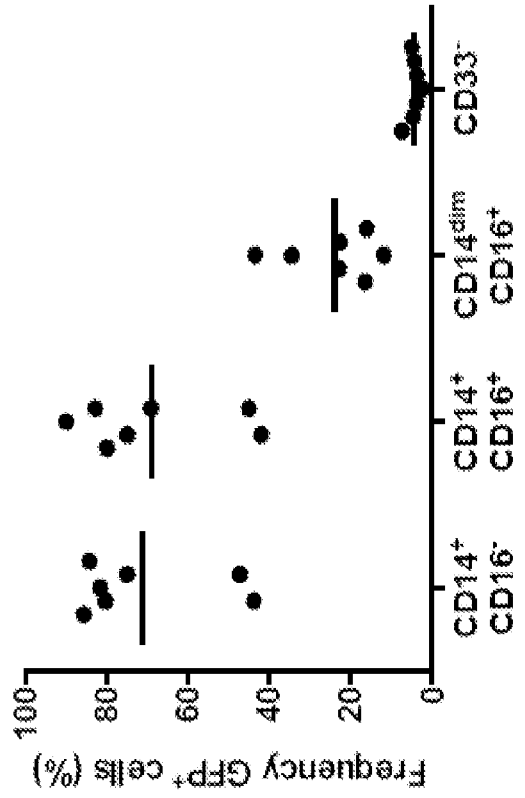


Figure 2F-2H

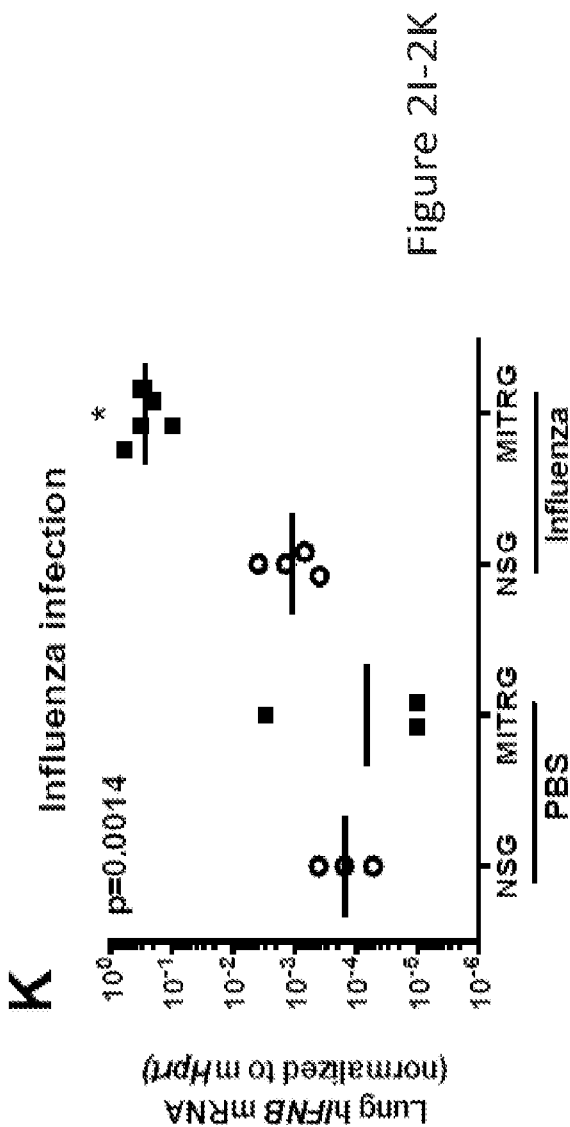
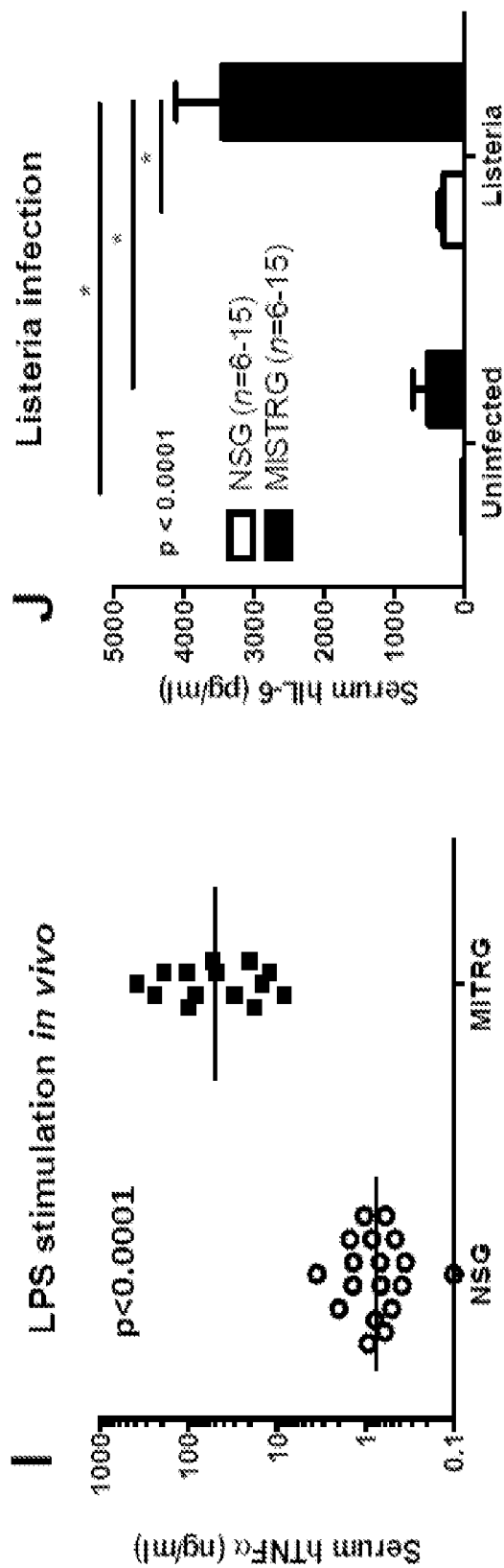


Figure 2I-2K

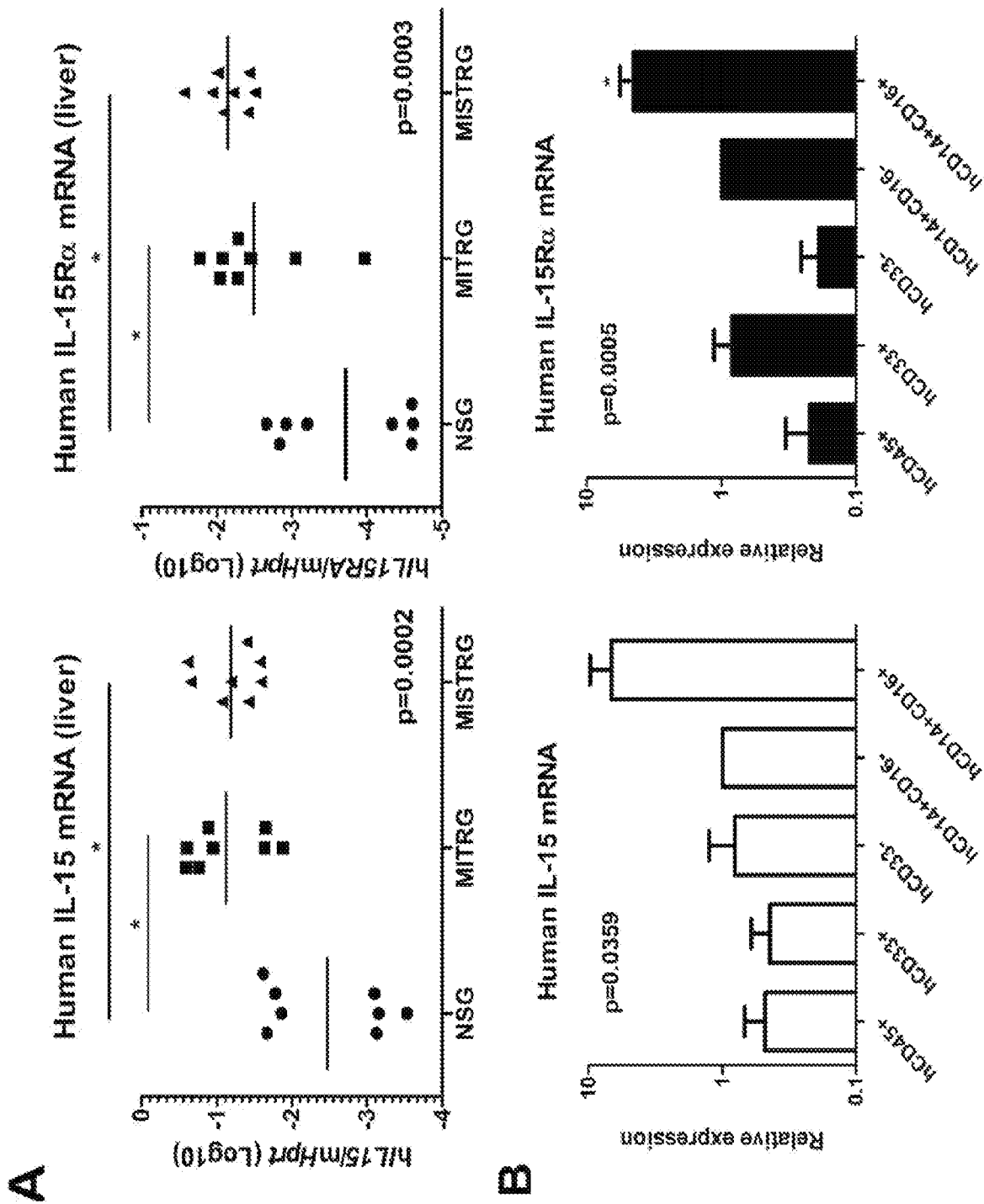


Figure 3A-3B

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C

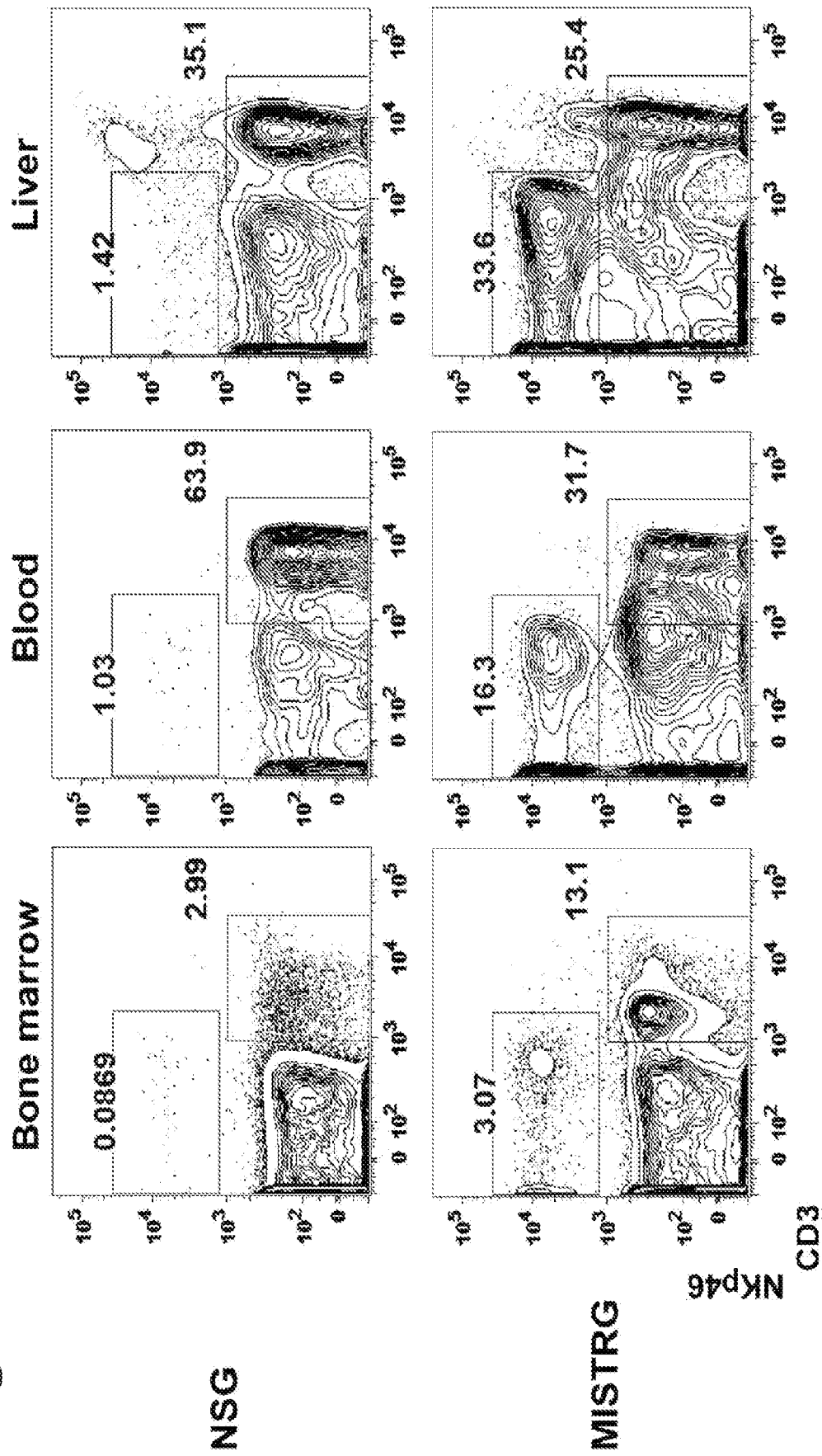


Figure 3C

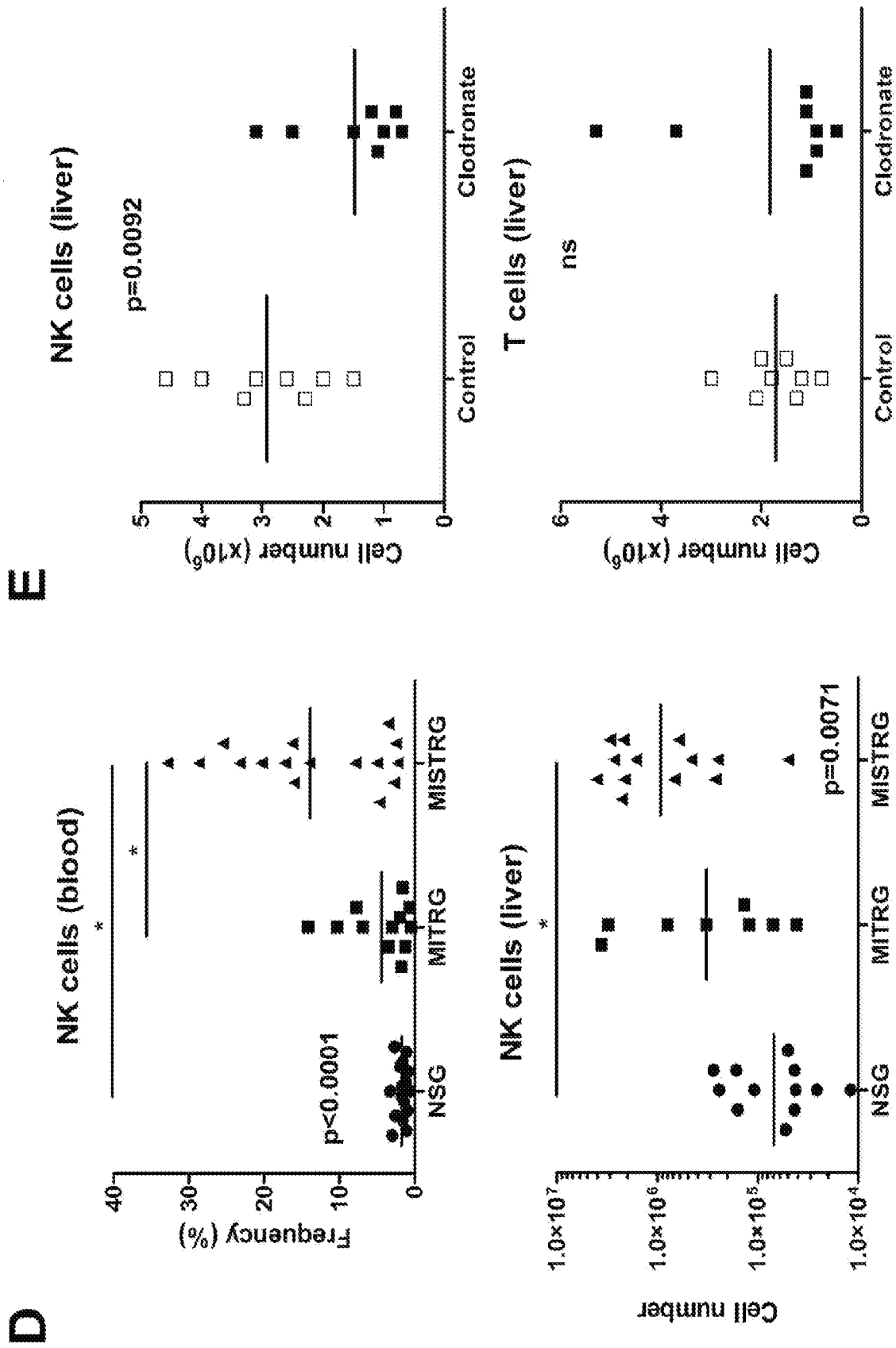


Figure 3D-3E

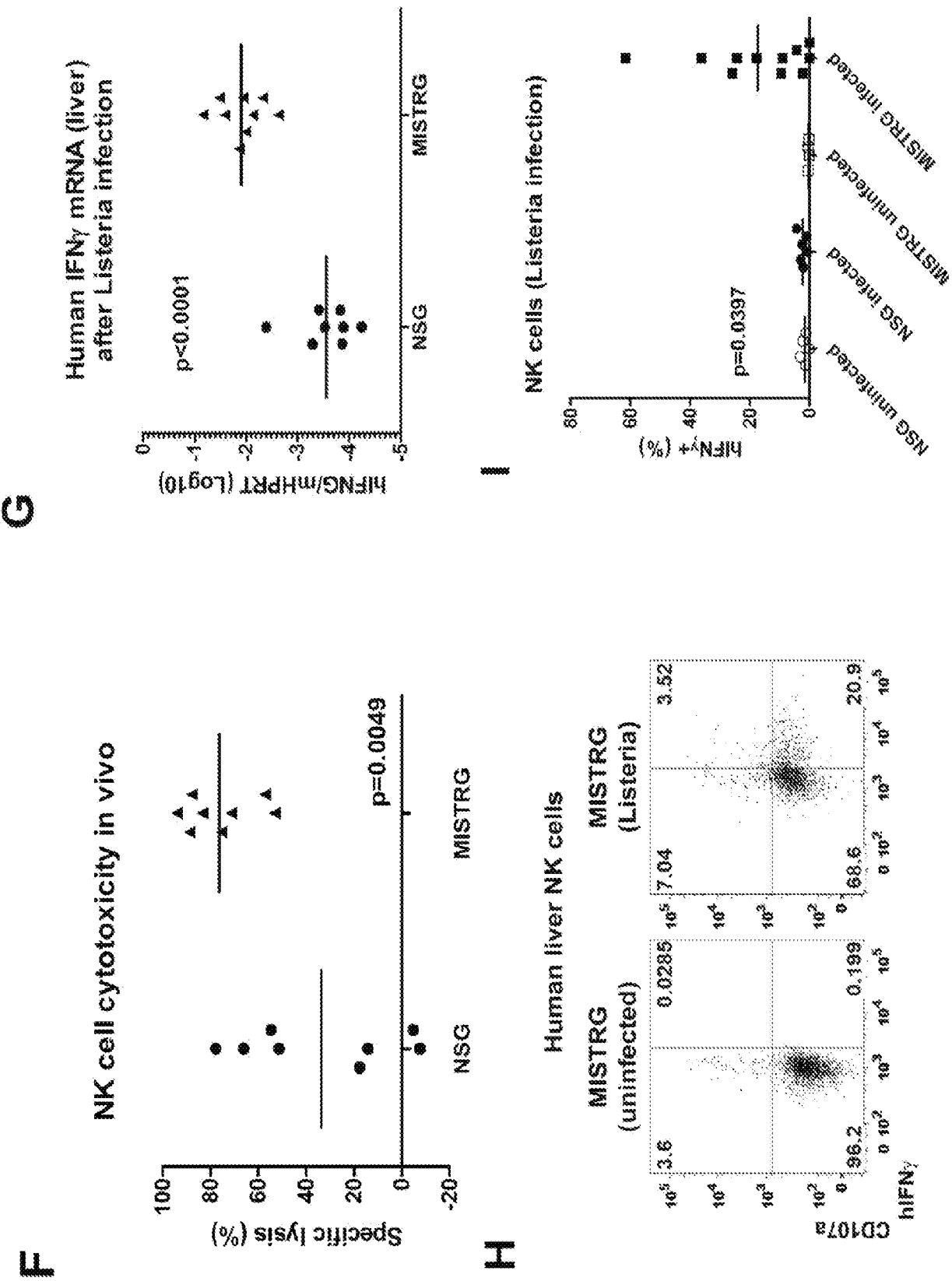


Figure 3F-3I

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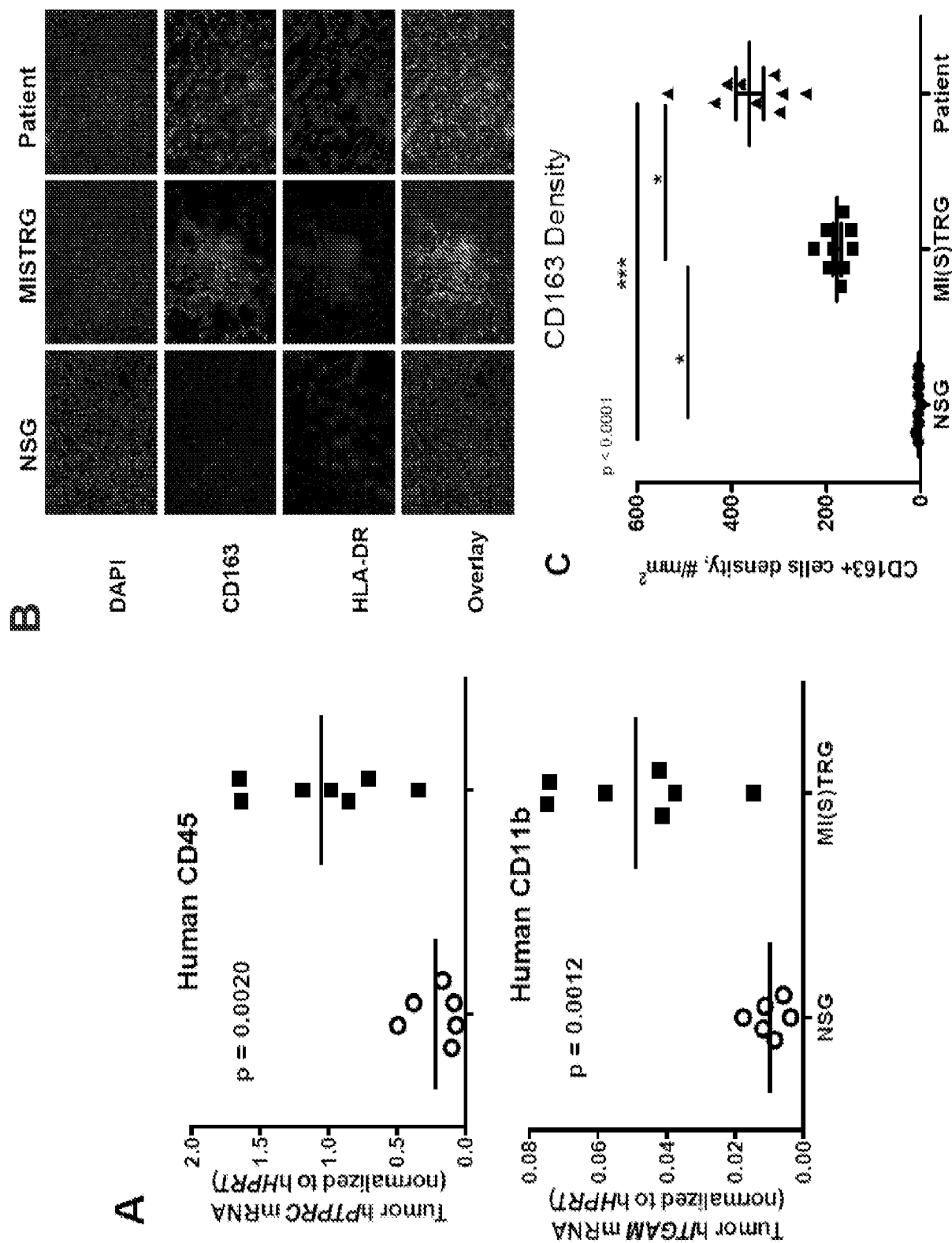


Figure 4A-4C

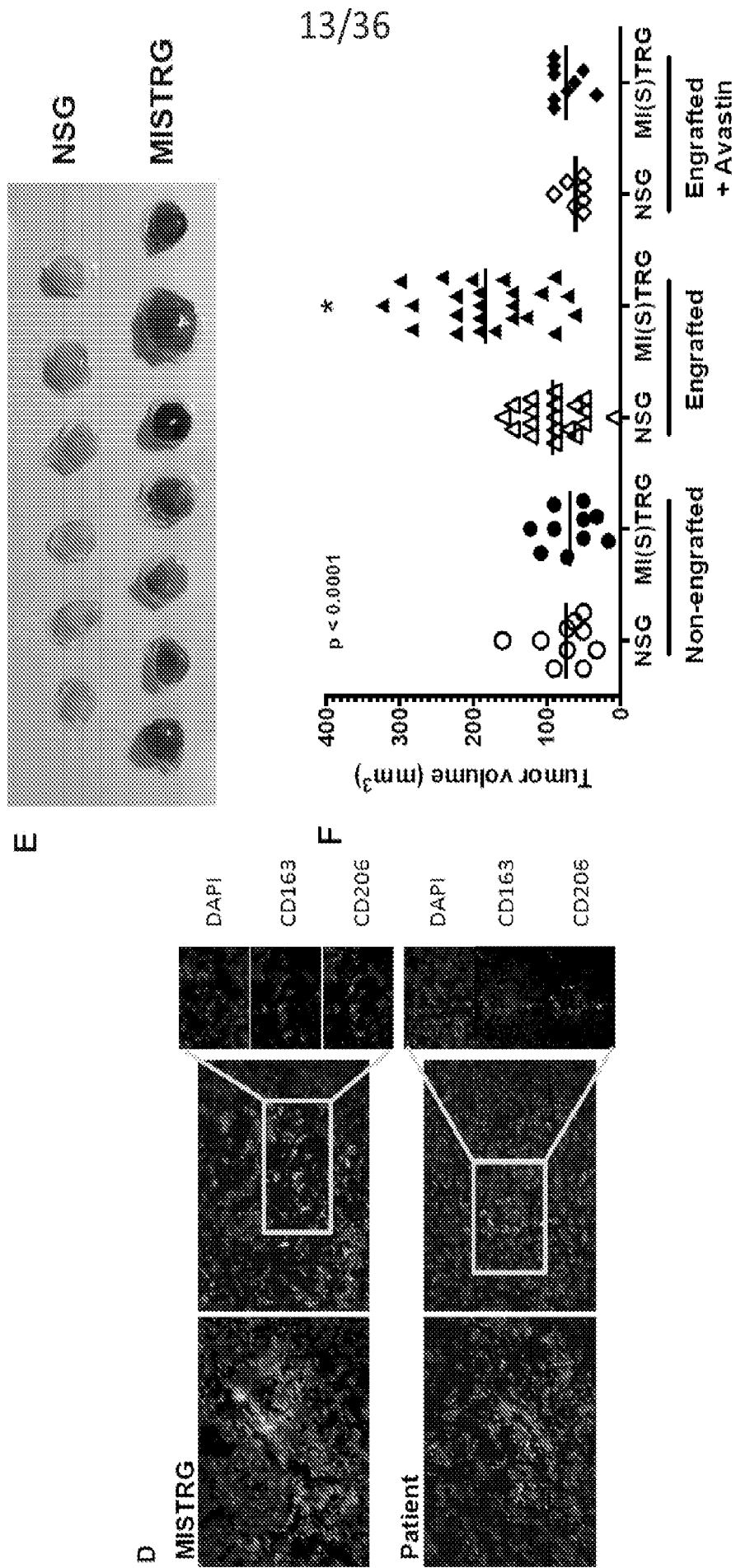


Figure 4D-4F

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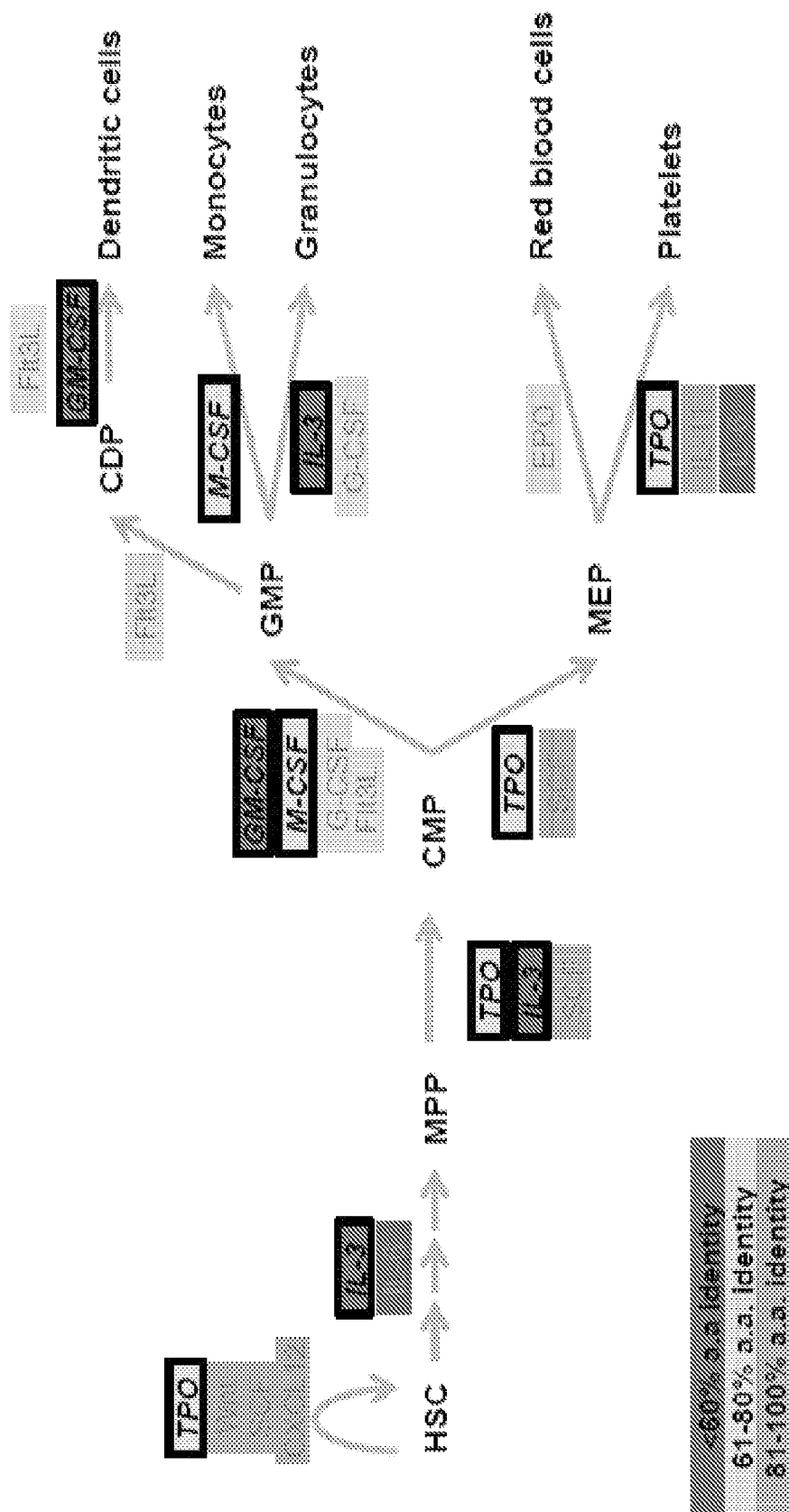


Figure 5

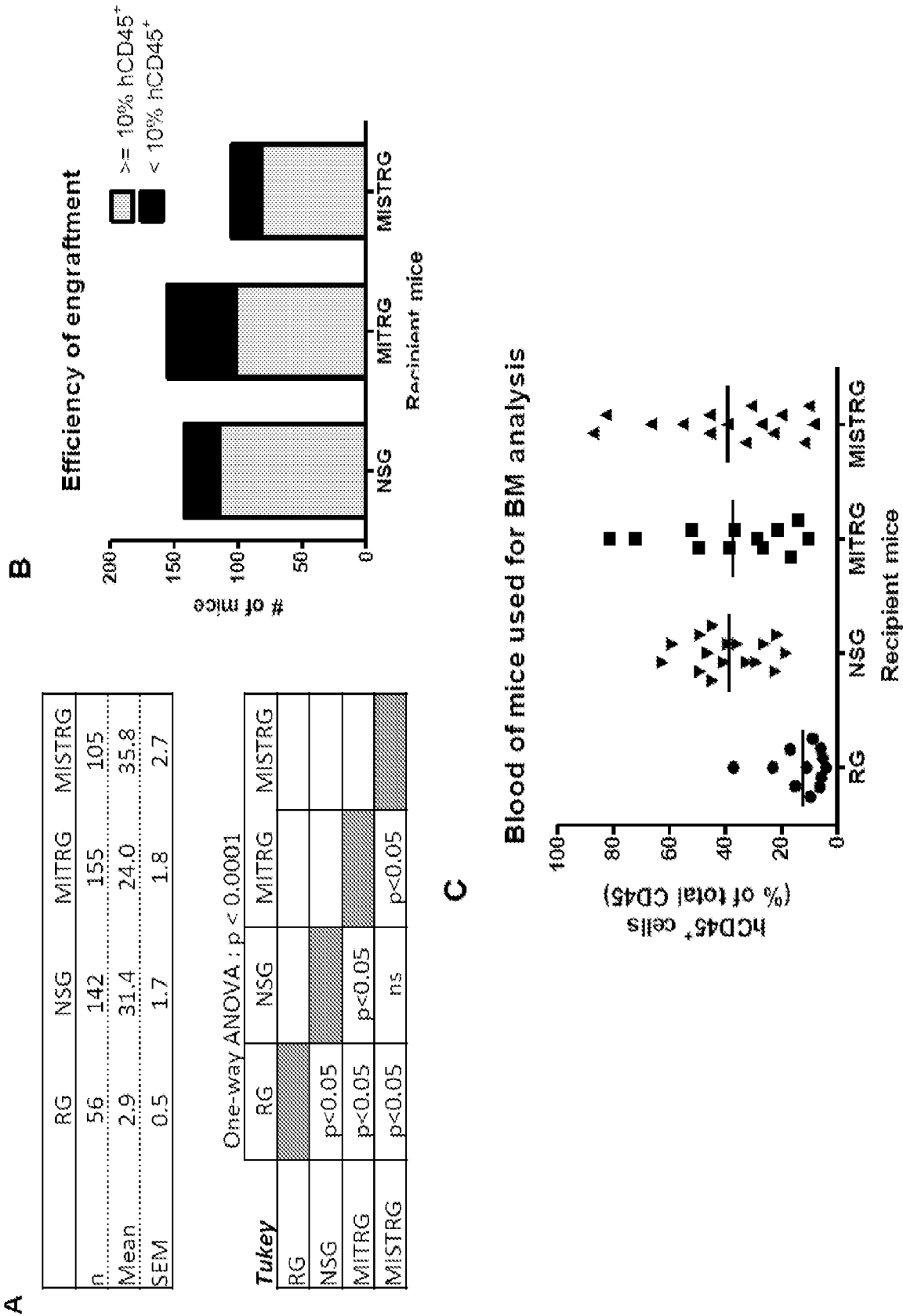


Figure 6A-6C

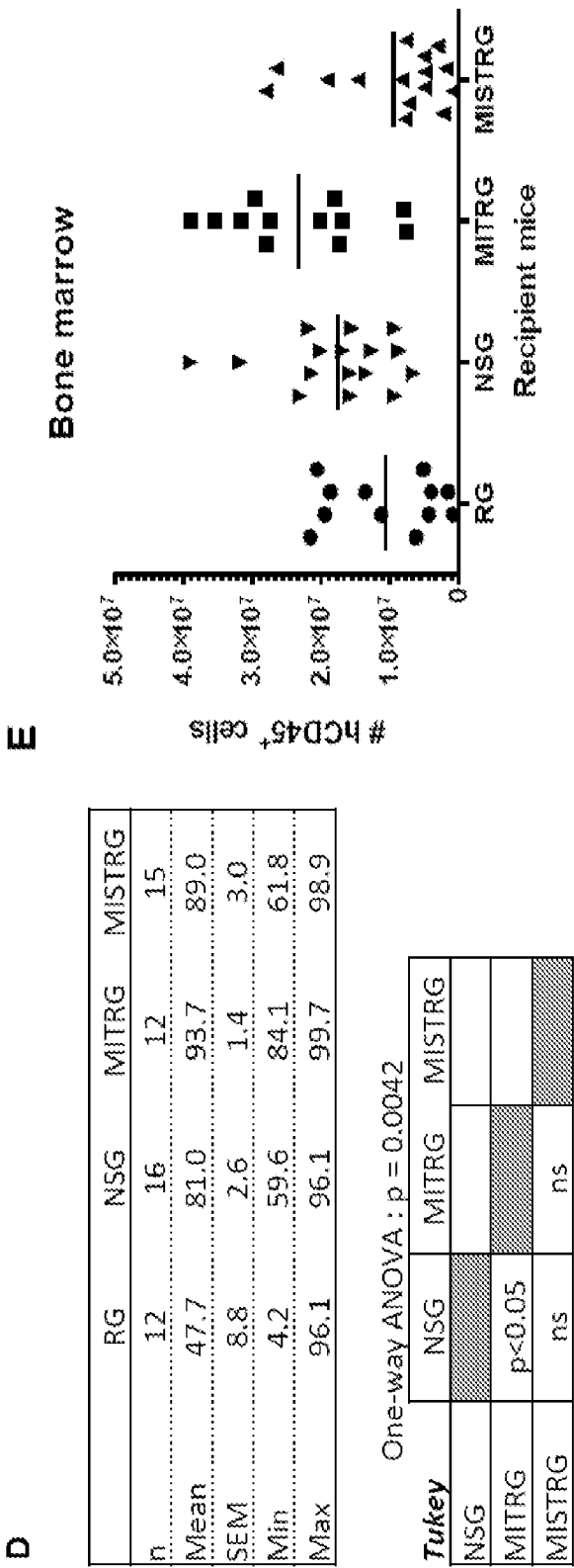


Figure 6D-6E

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	$p < 0.05$	$p < 0.05$	$p < 0.05$	

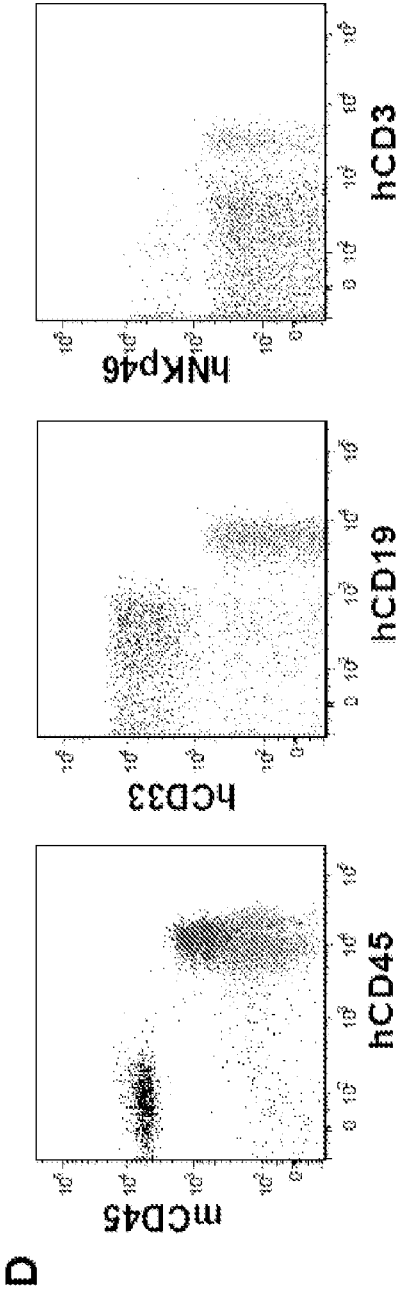
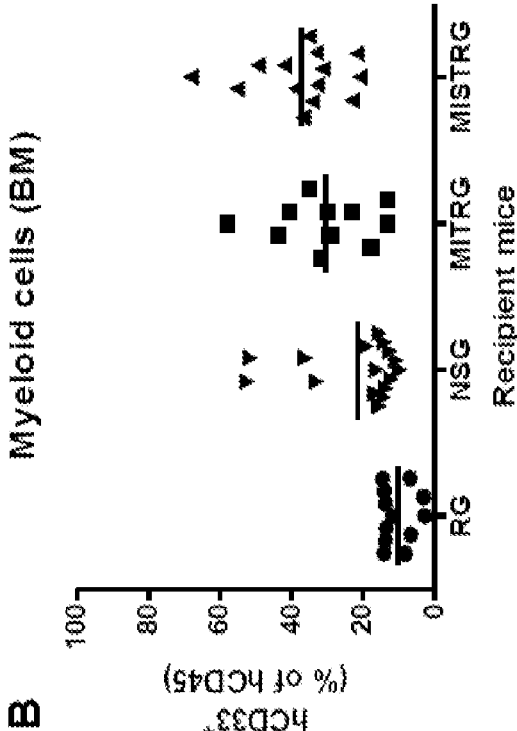


Figure 7A-7D

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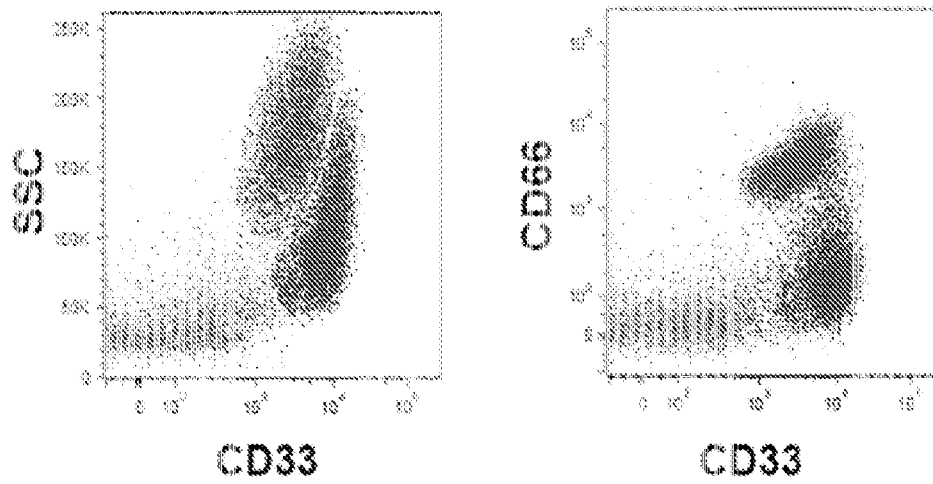
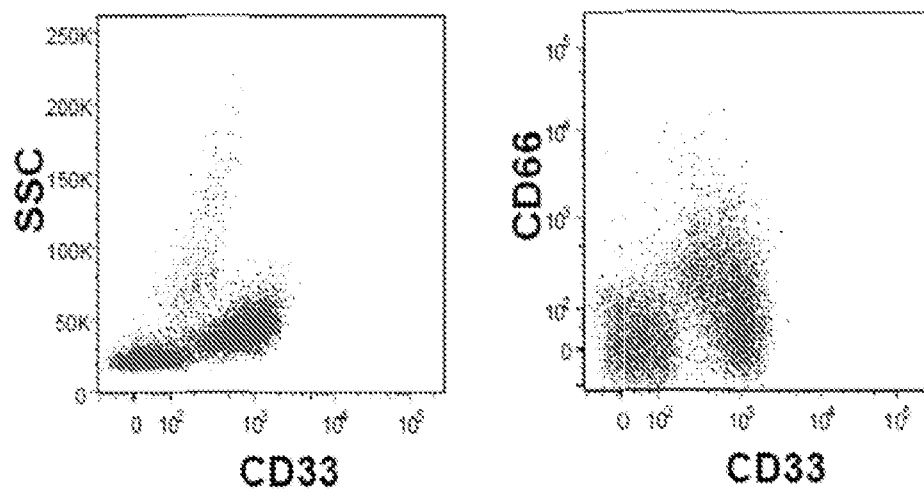
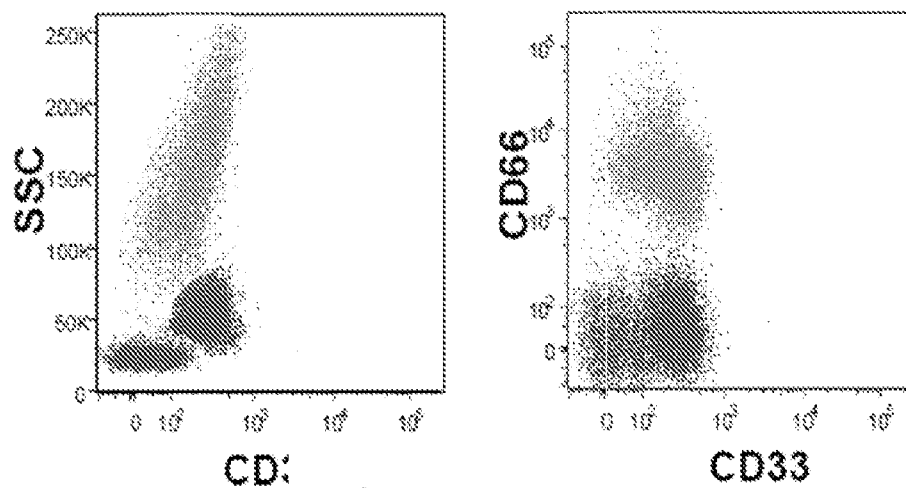
E**MISTRG BM (gated on hCD45⁺)****F****MISTRG blood (gated on hCD45⁺)****Human blood**

Figure 7E-7F

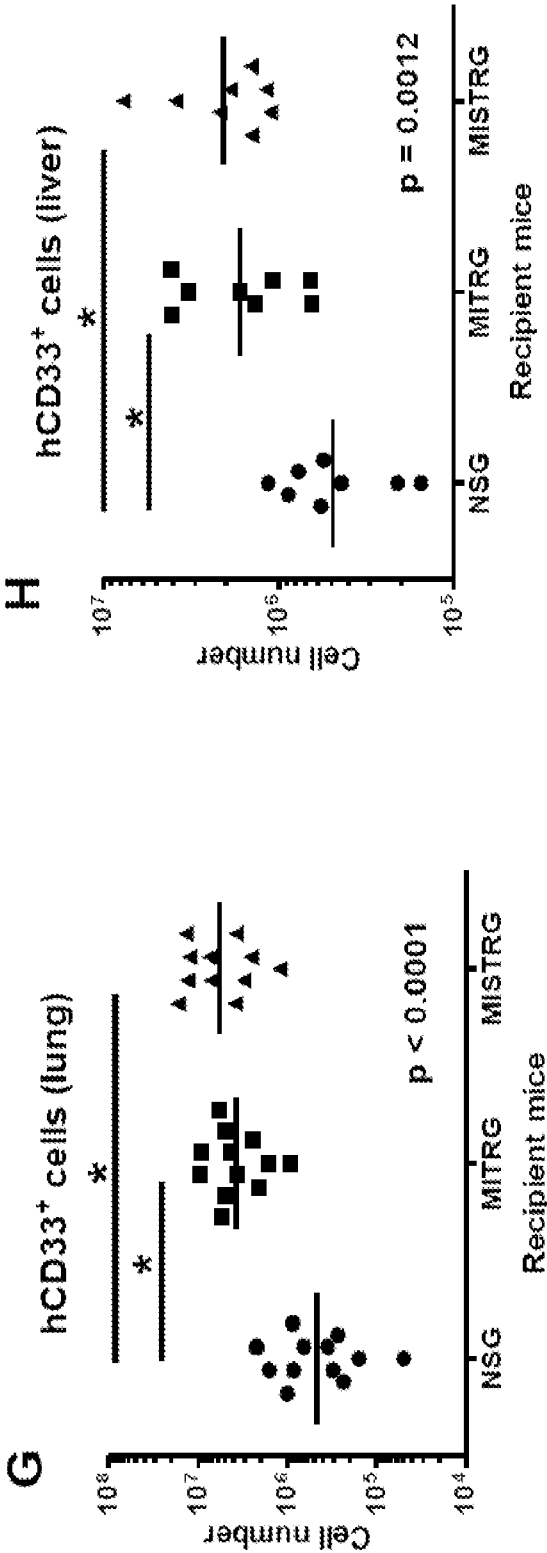


Figure 7G-7H

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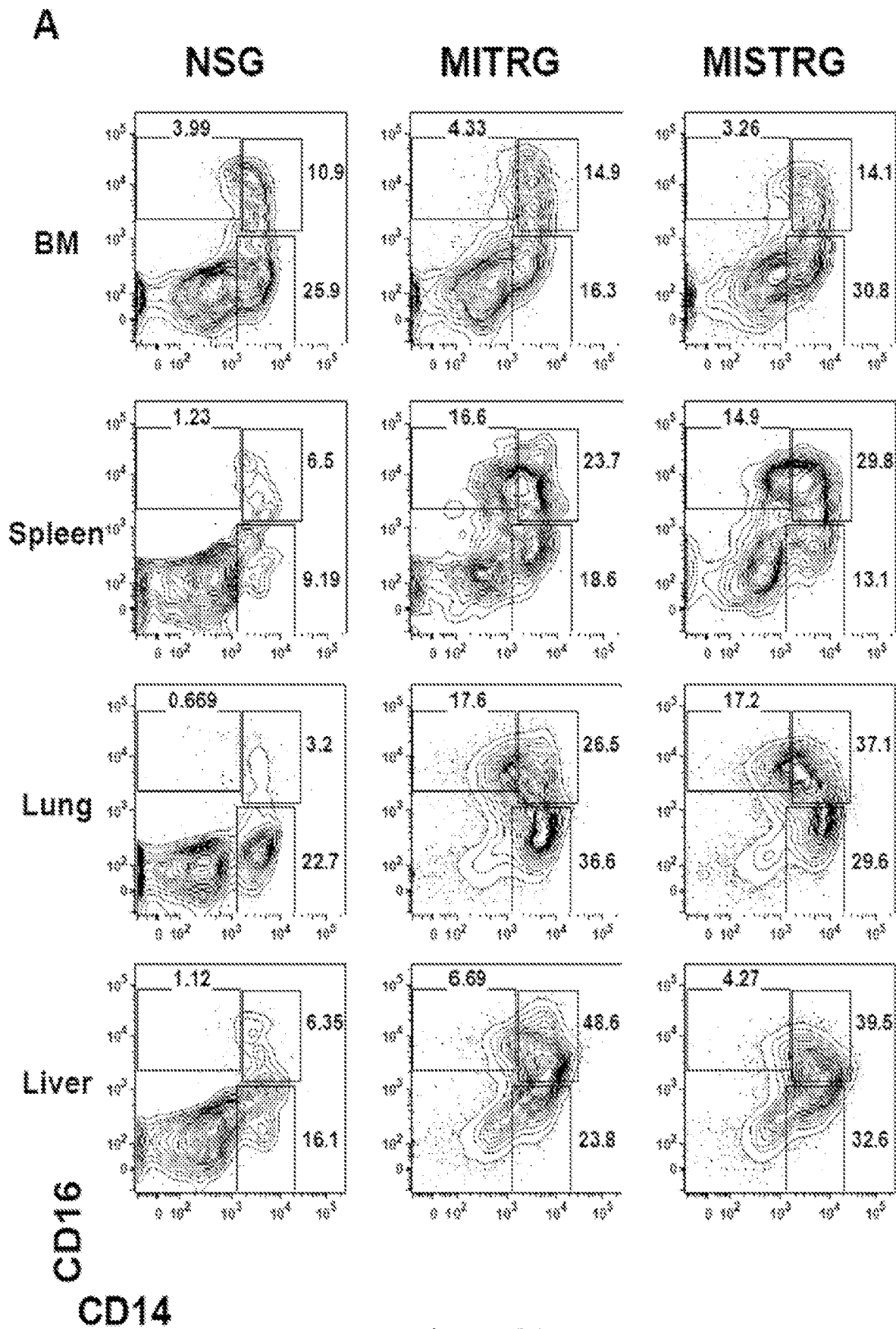


Figure 8A

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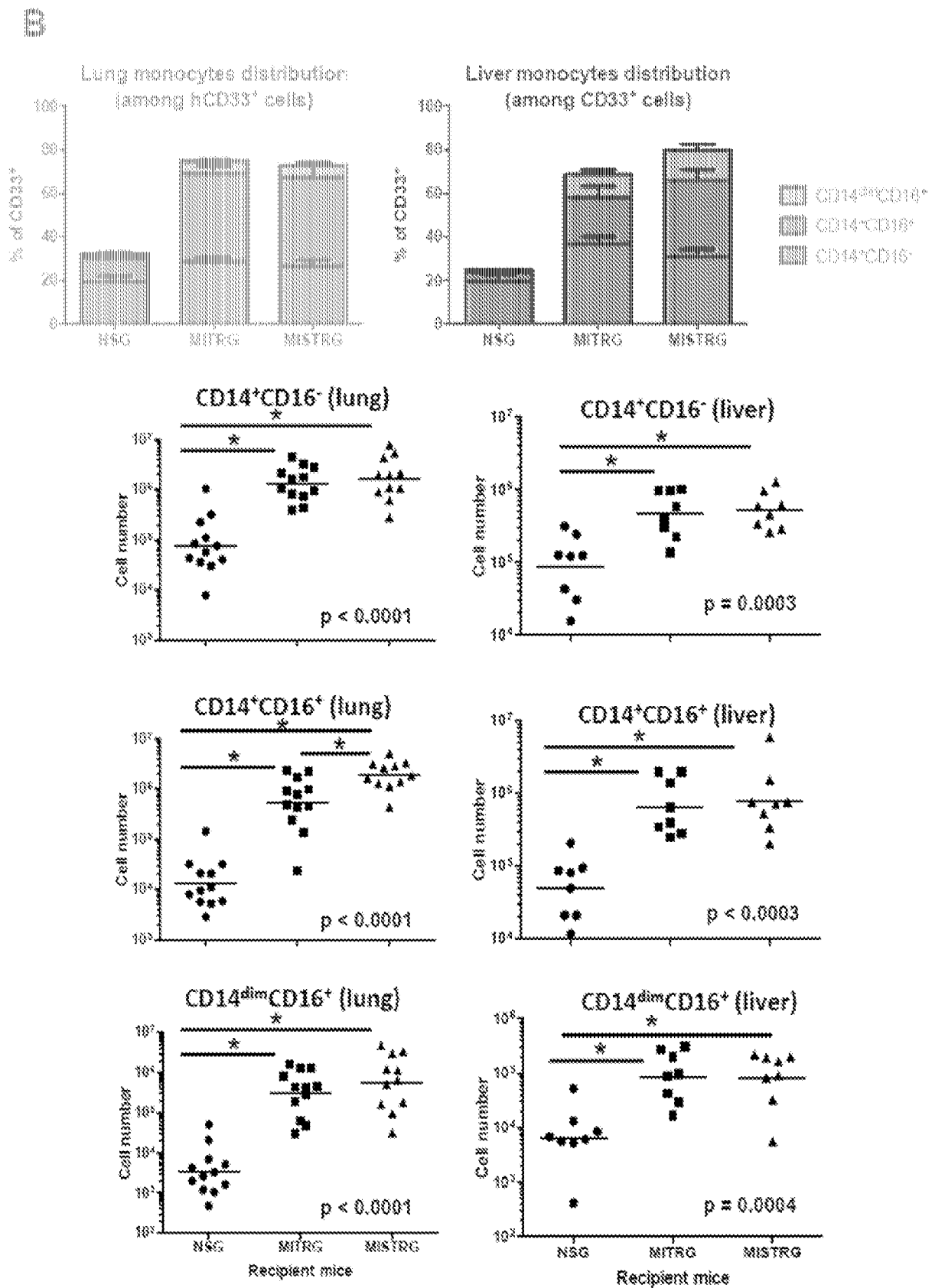


Figure 8B

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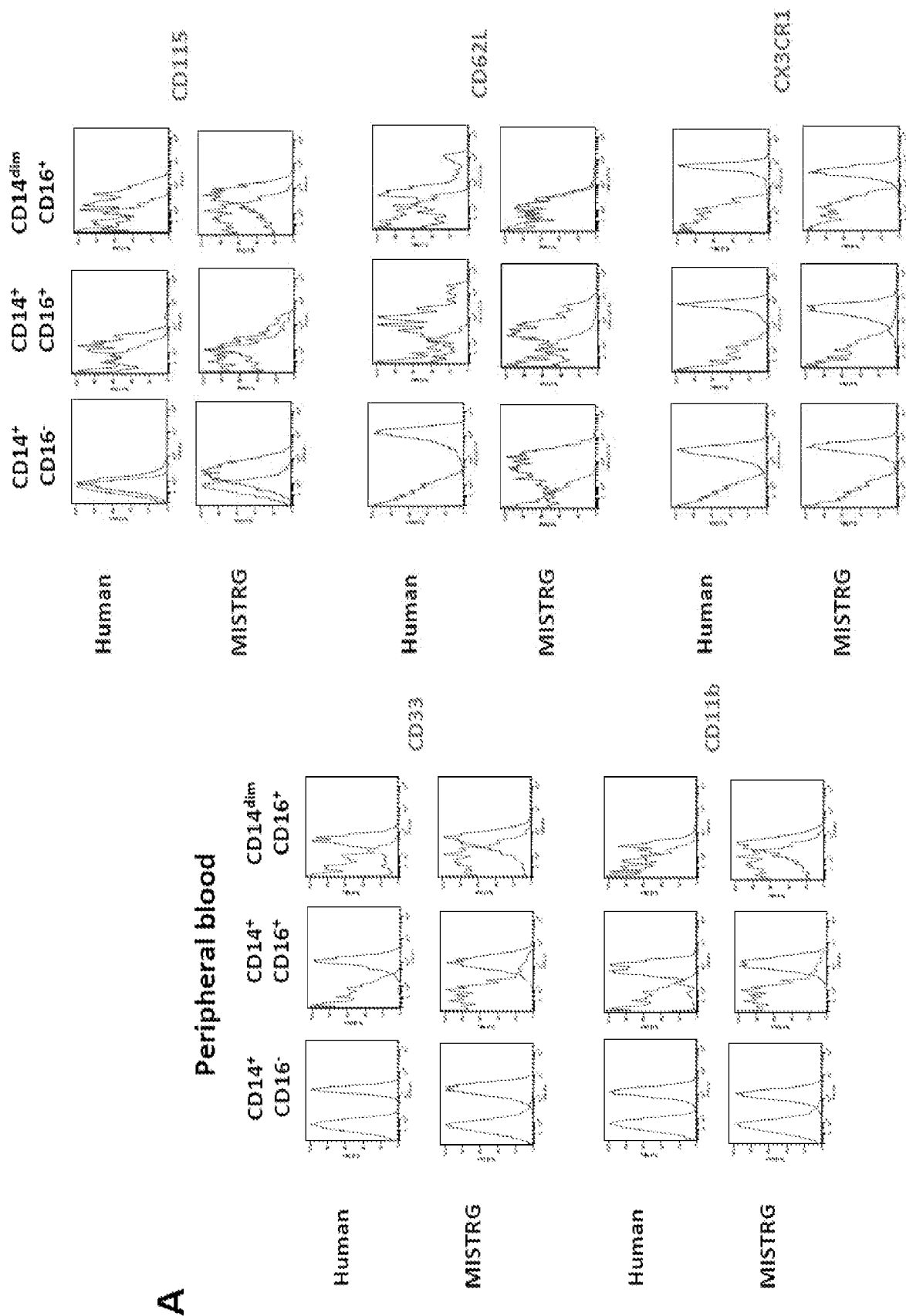


Figure 9A

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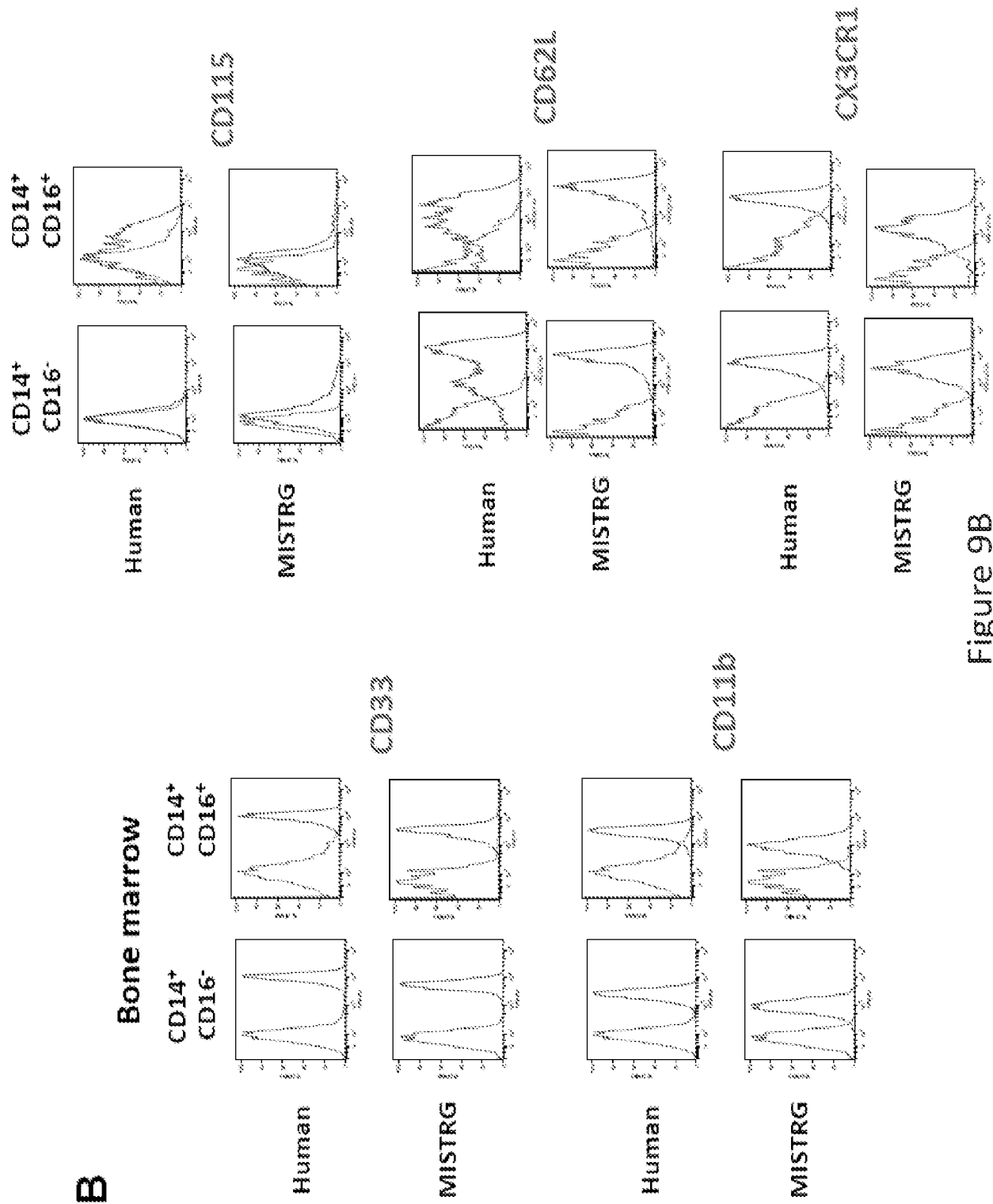


Figure 9B

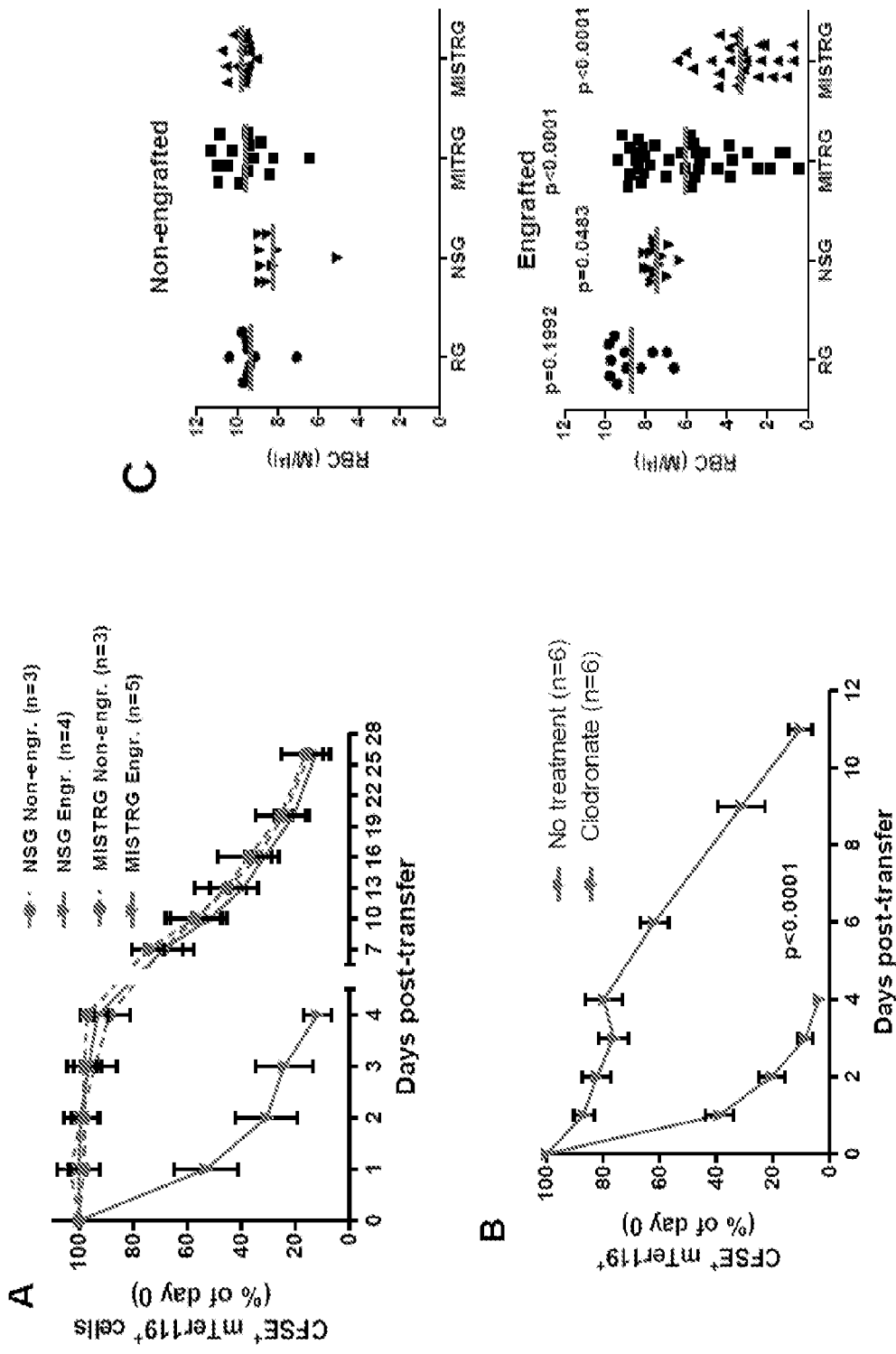


Figure 10A-10C

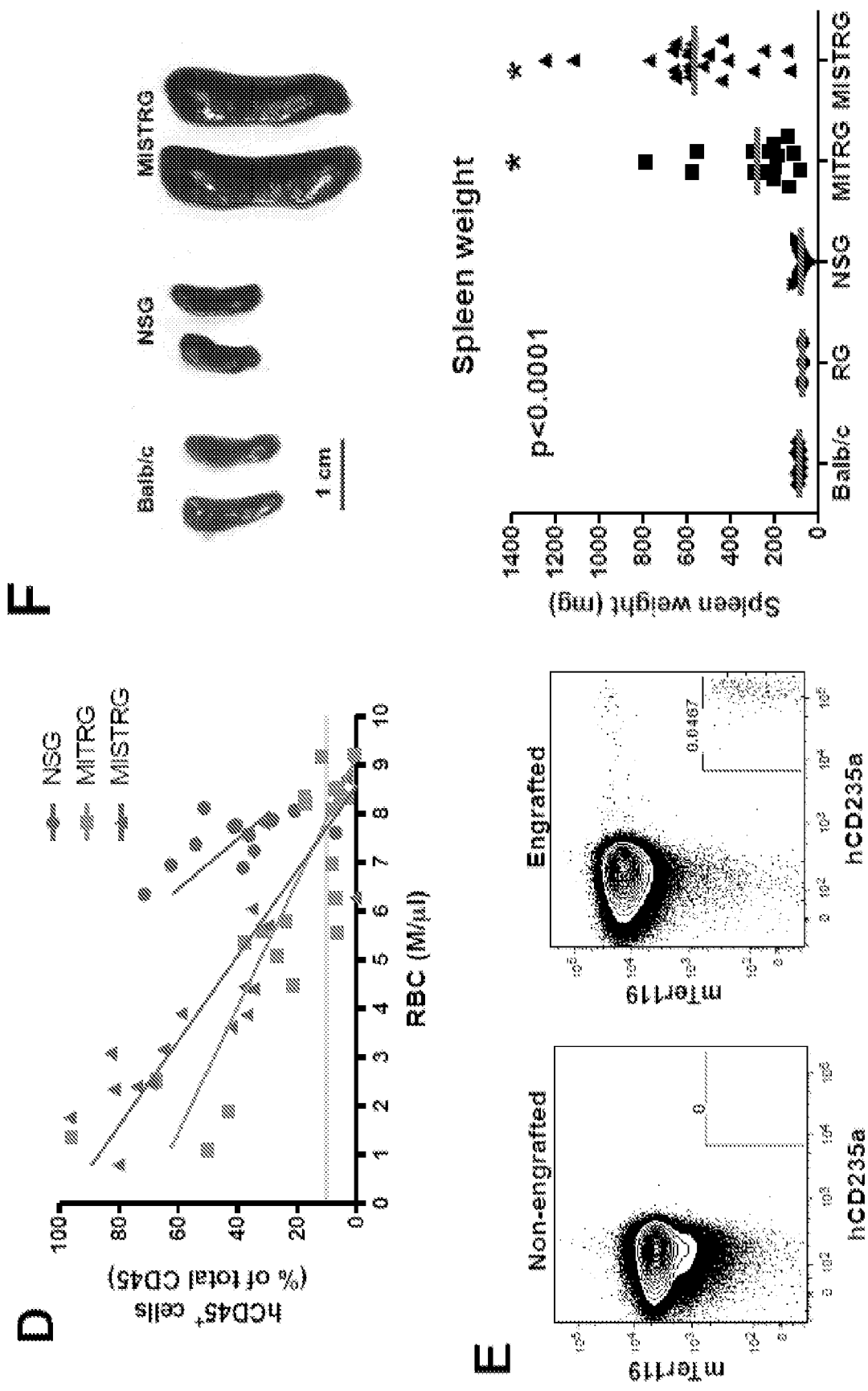


Figure 10D-10F

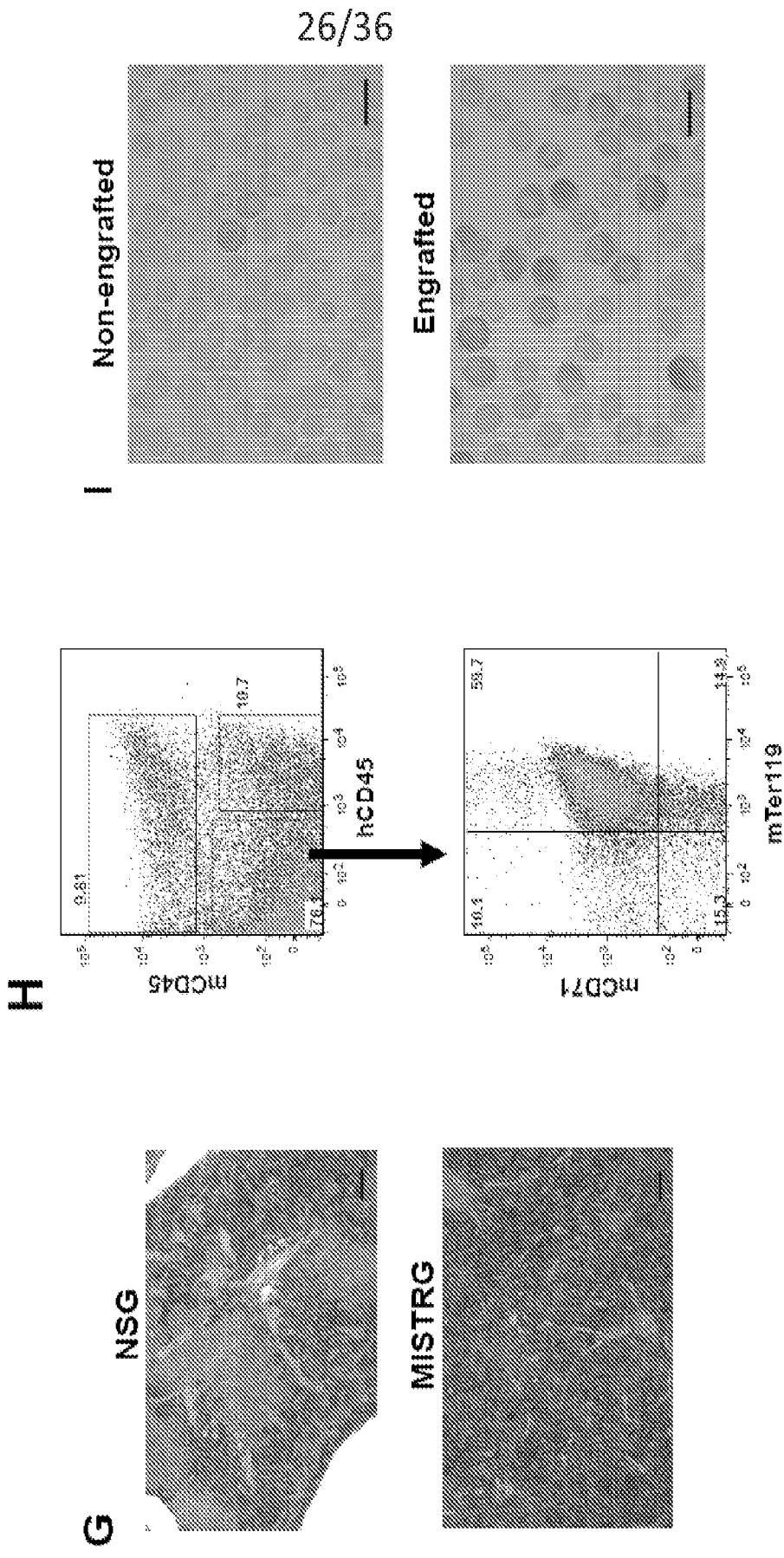


Figure 10G-10I

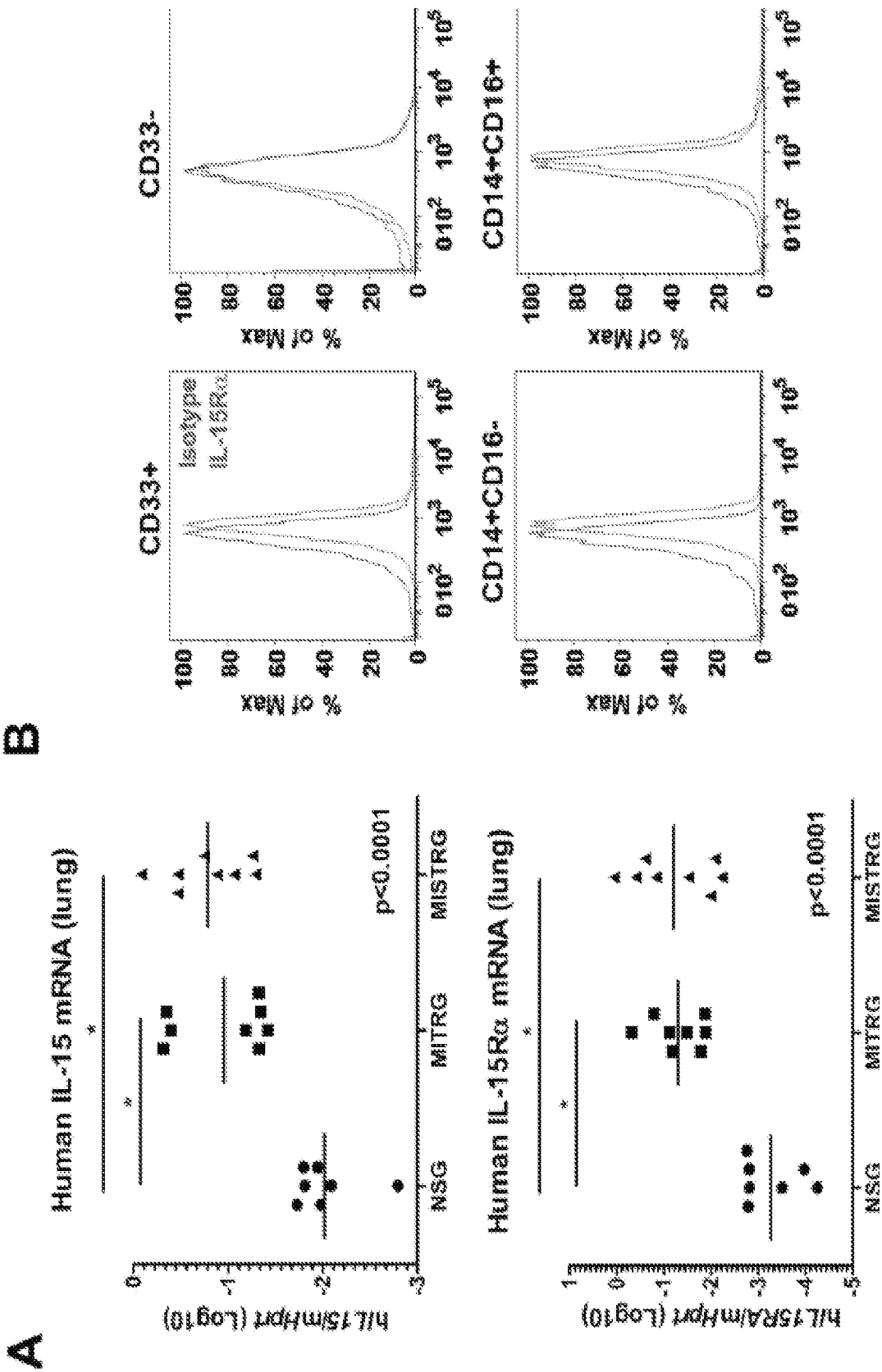


Figure 11

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NK cells

A

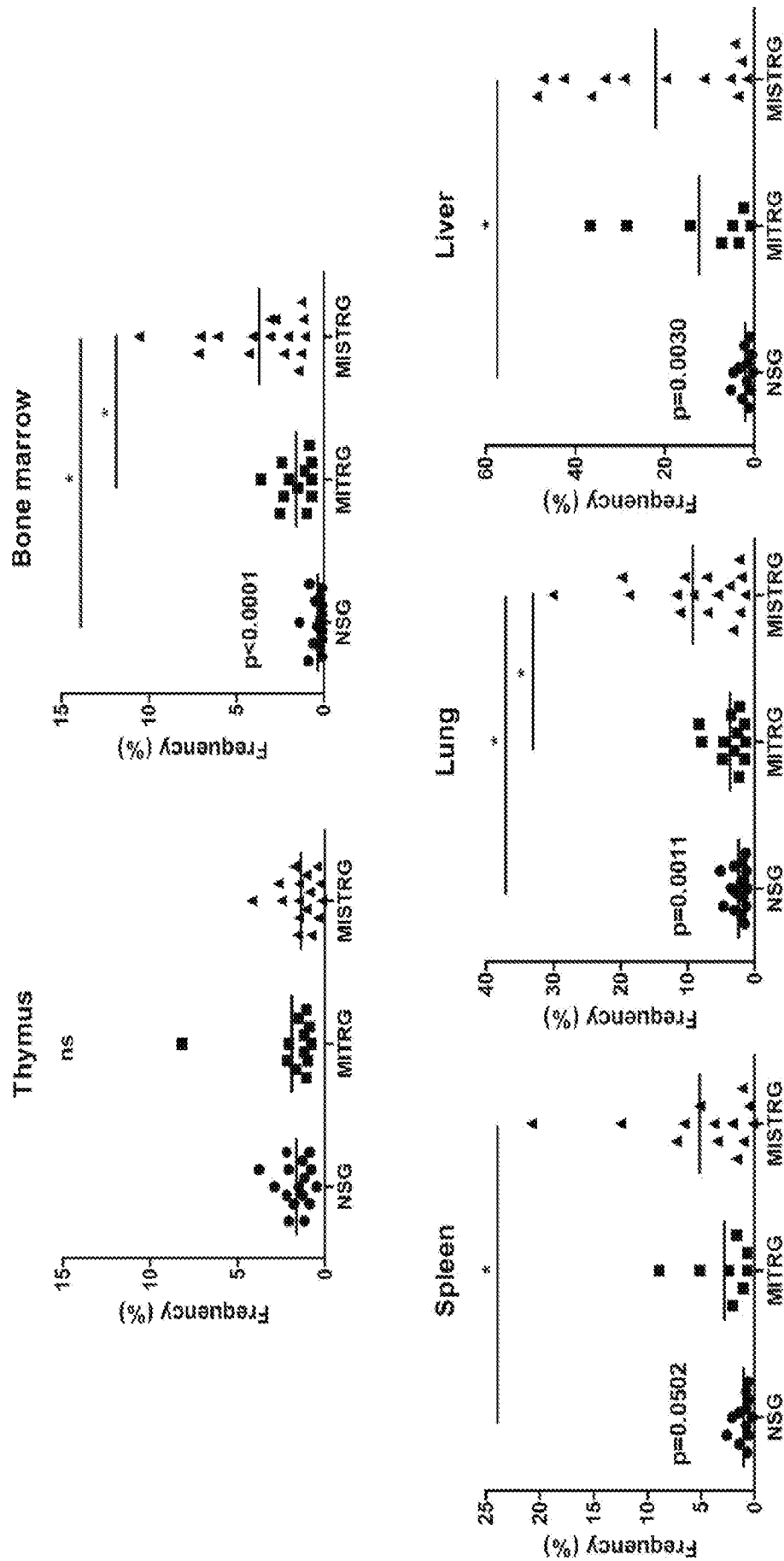


Figure 12A

B

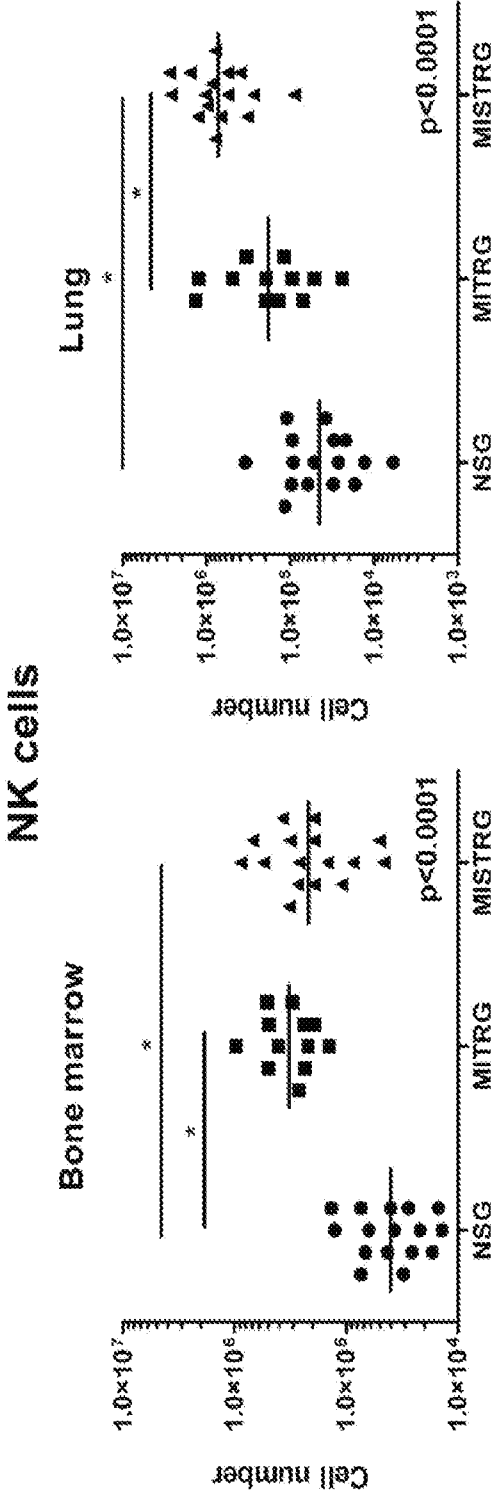


Figure 12B

A

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NK cells

Human donor

MISTRG

B

KIR2DL1/S1

KIR2DL2/L3

KIR3DL1

Human donor

MISTRG

Figure 13A-13B

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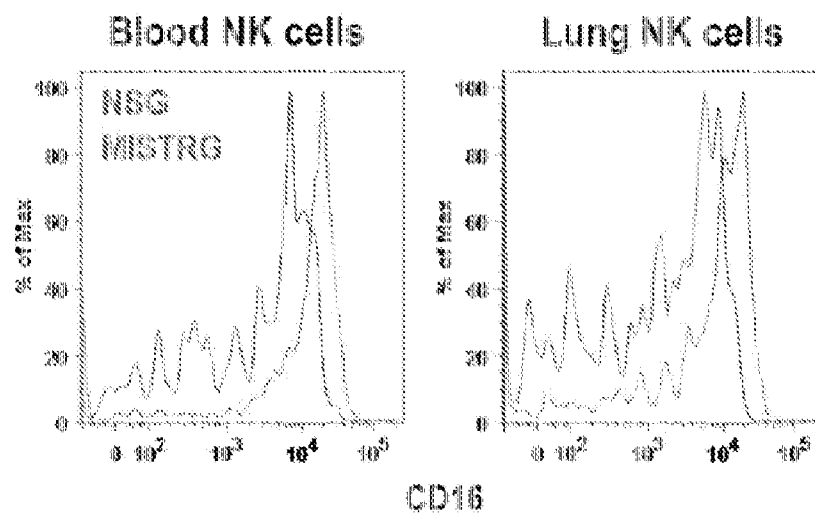
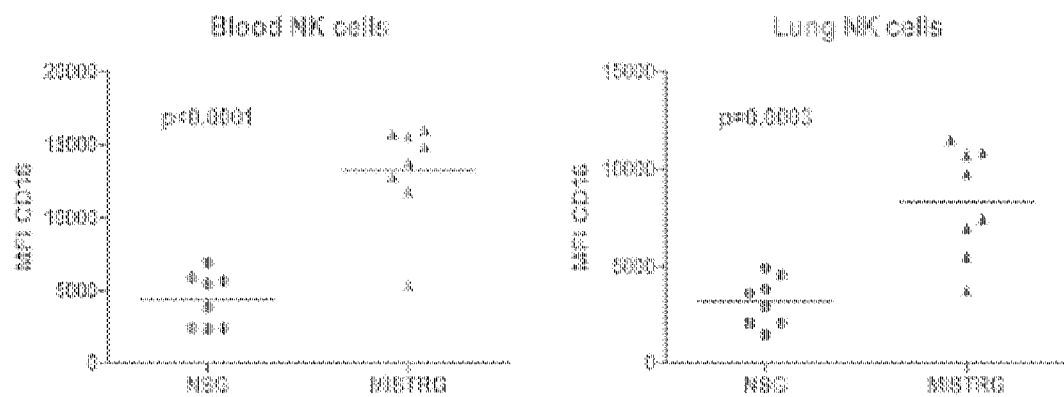
C**D**

Figure 13C-13D

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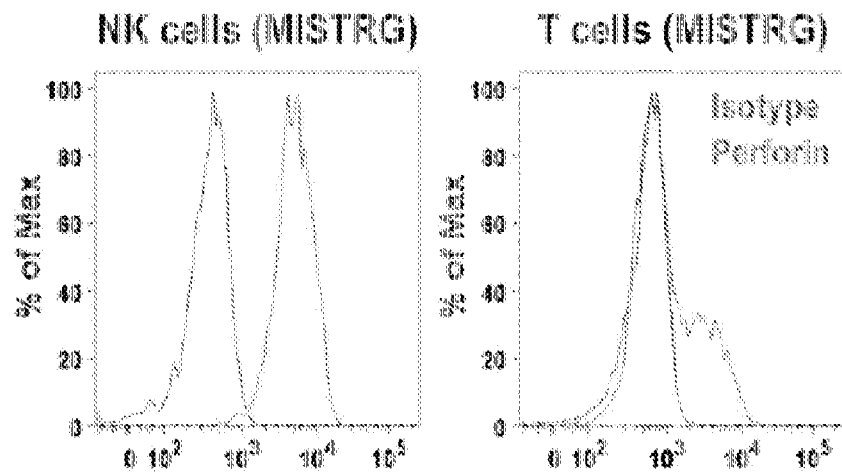
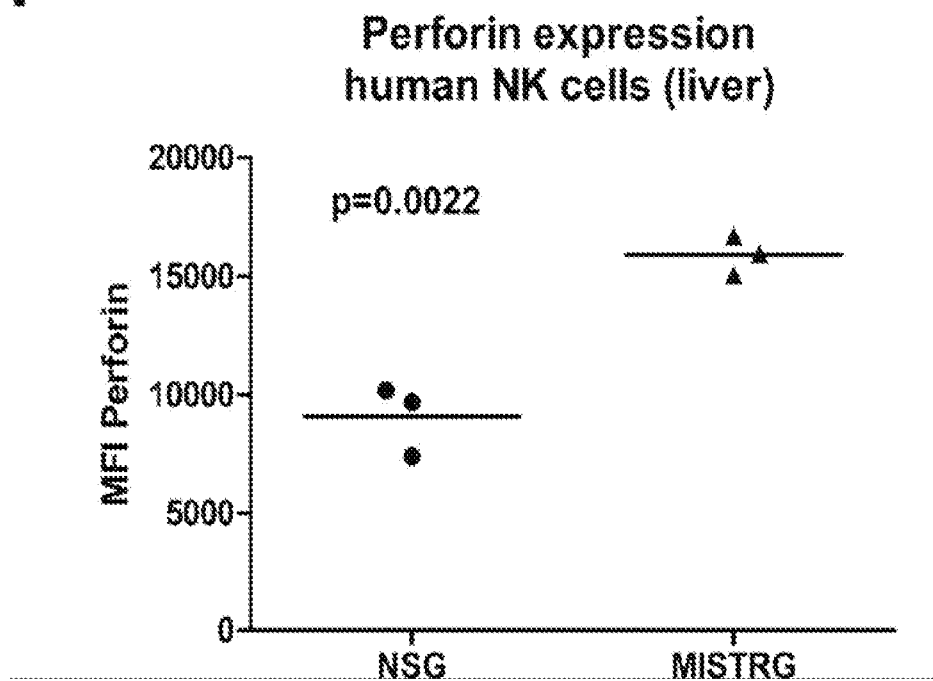
E**F**

Figure 13E-13F

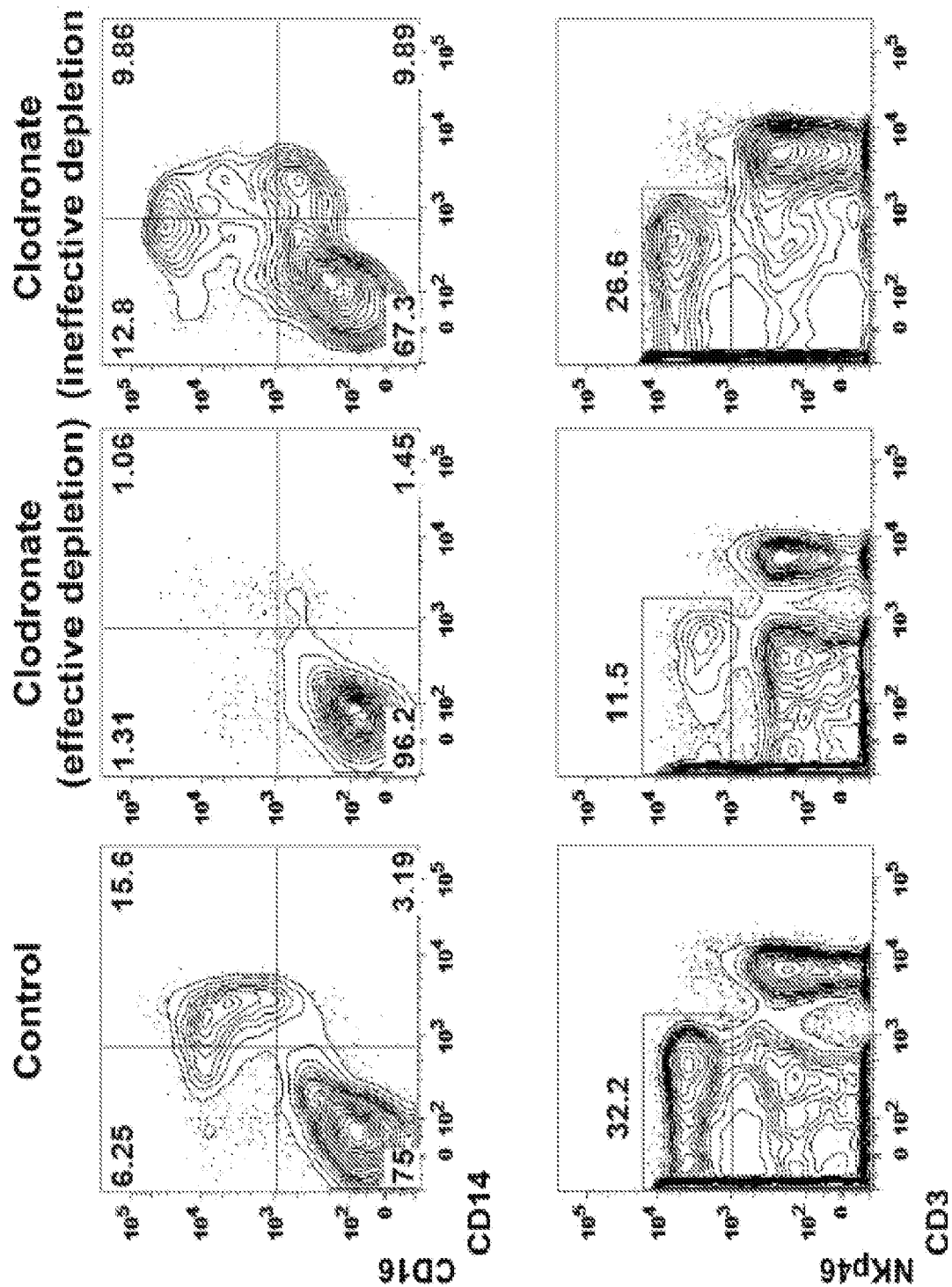


Figure 14

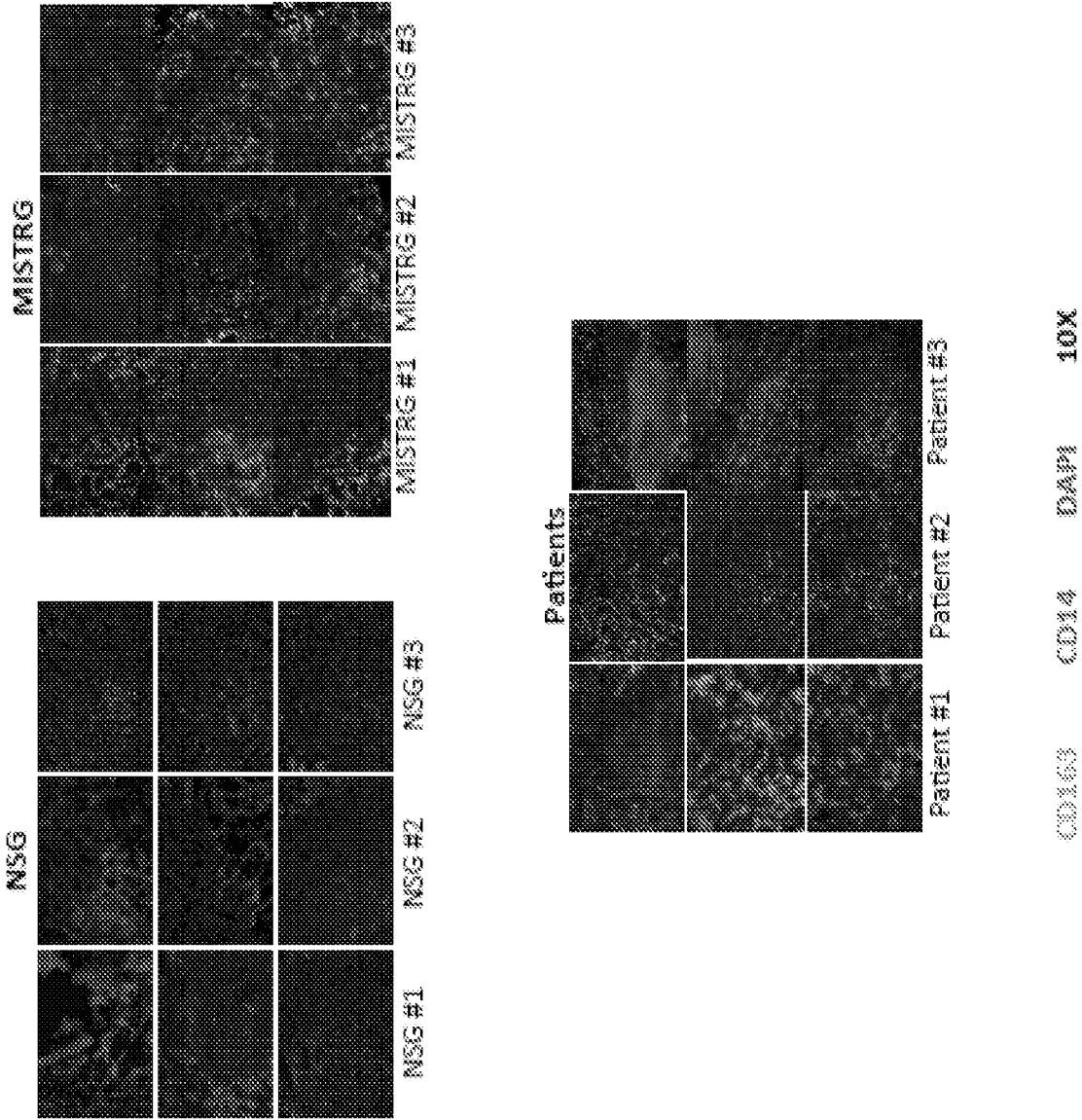


Figure 15

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}	HSRPa ^{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	-	-	+	-	-	+	+

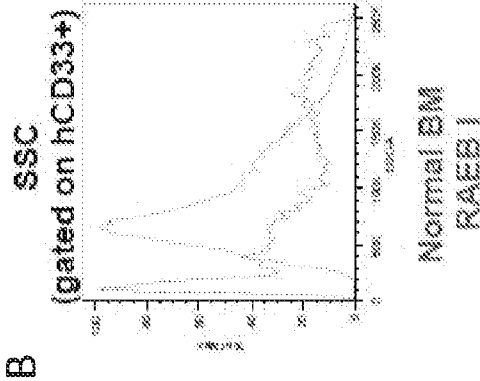
ND: Not determined

Figure 16

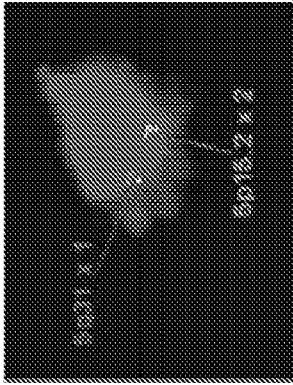
A

Disease	Cell number per mouse	Engrafted	Time after transplant in weeks	Bone Marrow		Genetic abnormality		Comment
				hCD45	hCD33	Patient sample	Engrafted	
RCUD	9x10e4 CD34+ enriched	1/1	11	1.9	89.9	Normal	n.d.	Low granularity of CD33+ cells
RAEB I	1-4x10e5 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	7x10e5 CD34+ enriched cells	2/2	15	0.07-0.88	31.9-85.5	5q-	5q- in 24/25 cells	
CMMML	7.5x10e6 T-cell depleted	1/2	15	0.8	48	del(6)(q11.1q22.1)	del(6)(q11.1q22.1)	
2° AML from RAEB II	4.5x10e6 T-cell depleted	2/2	12	73.8-81.5	77.5-84.1	Complex including 5q-	Complex including 5q-	

B



C



D

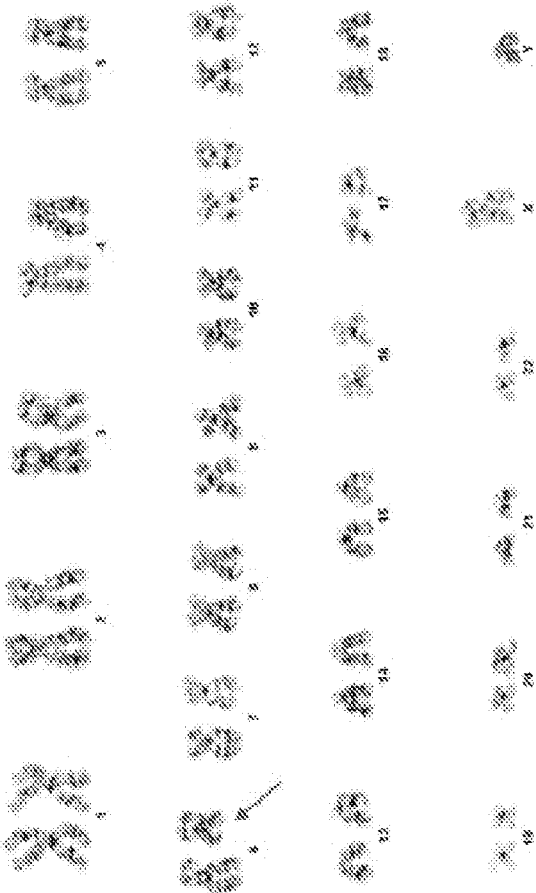


Figure 17