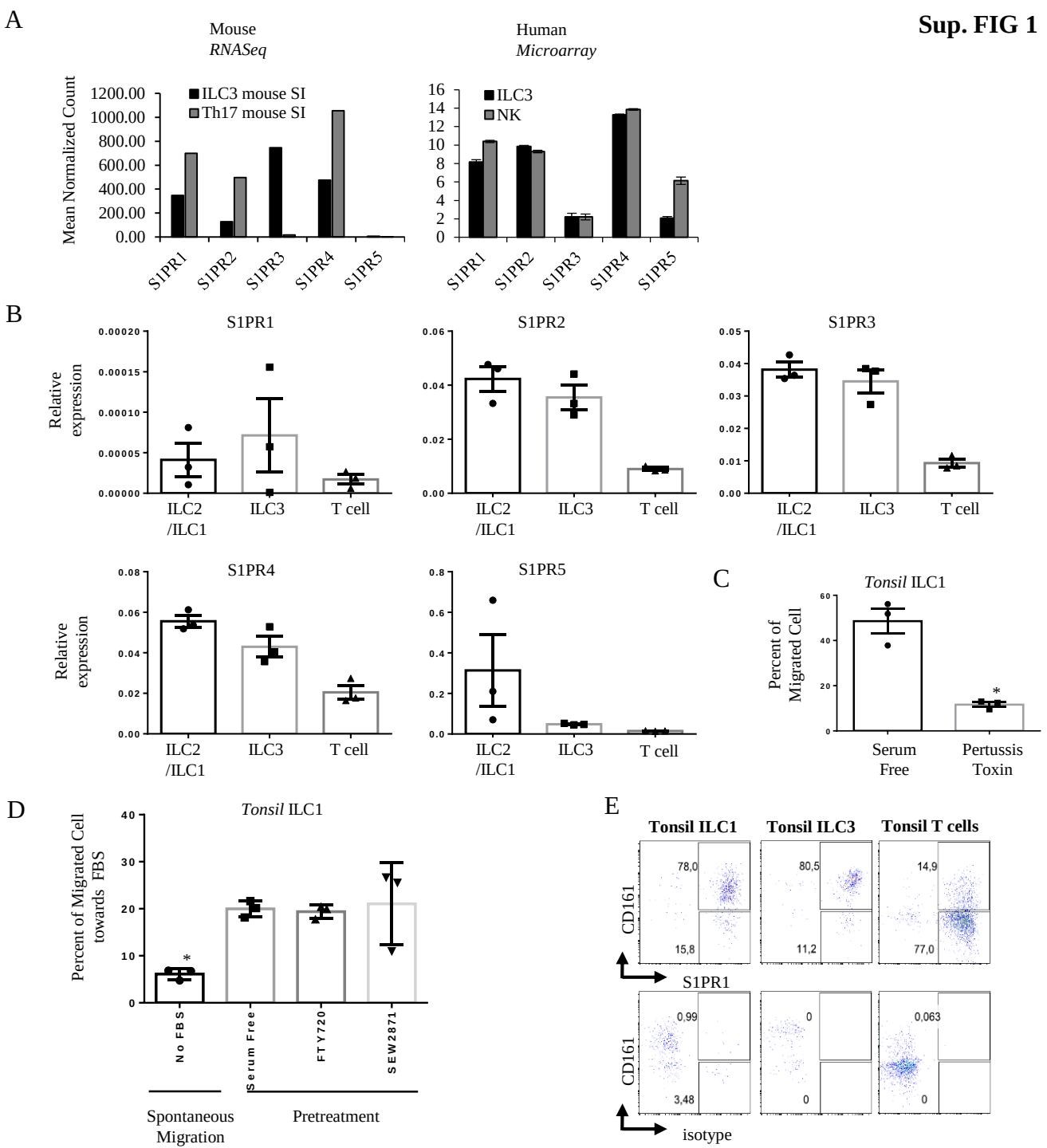
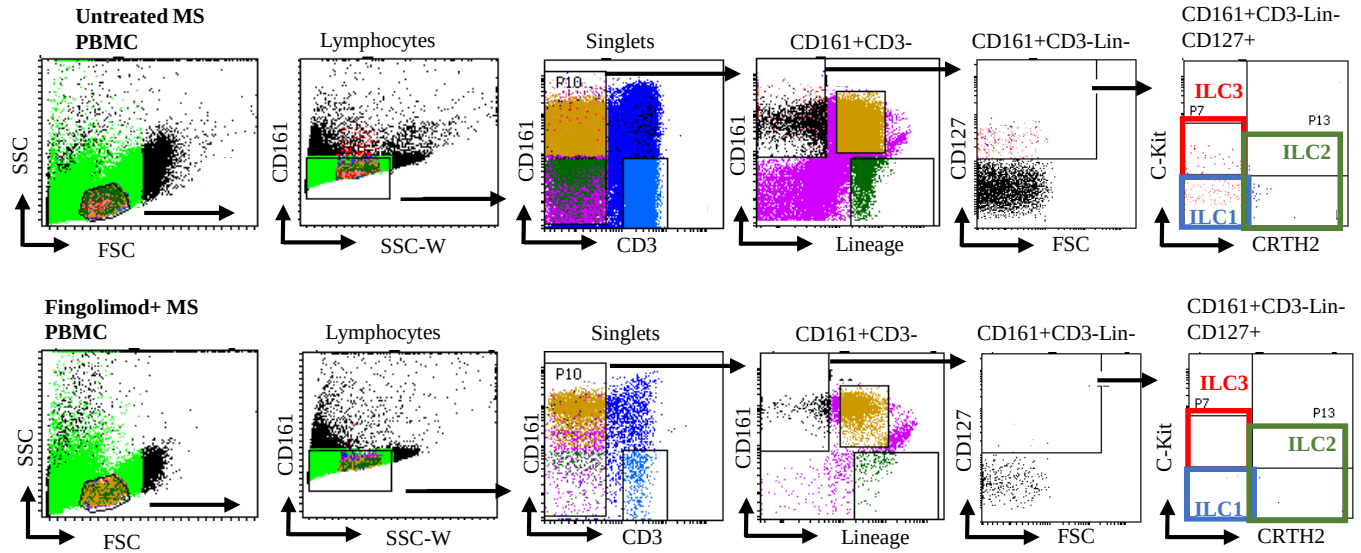
Sup. FIG 1

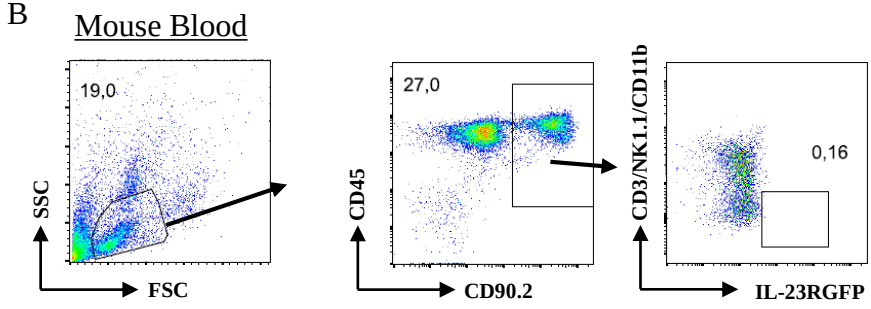

A
Mouse
RNASeq
Human
Microarray
Mean Normalized Count
ILC3 mouse SI
Th17 mouse SI
ILC3
NK
S1PR1
S1PR2
S1PR3
S1PR4
S1PR5
B
S1PR1
S1PR2
S1PR3
S1PR4
S1PR5
Relative expression
ILC2 /ILC1
ILC3
T cell
C
Tonsil ILC1
Percent of Migrated Cell
Serum Free
Pertussis Toxin
D
Tonsil ILC1
Percent of Migrated Cell towards FBS
No FBS
Serum Free
FTY720
SEW2871
Spontaneous Migration
Pretreatment
E
Tonsil ILC1
Tonsil ILC3
Tonsil T cells
CD161
S1PR1
isotype
78,0
15,8
80,5
11,2
14,9
77,0
0,99
3,48
0
0
0,063
0

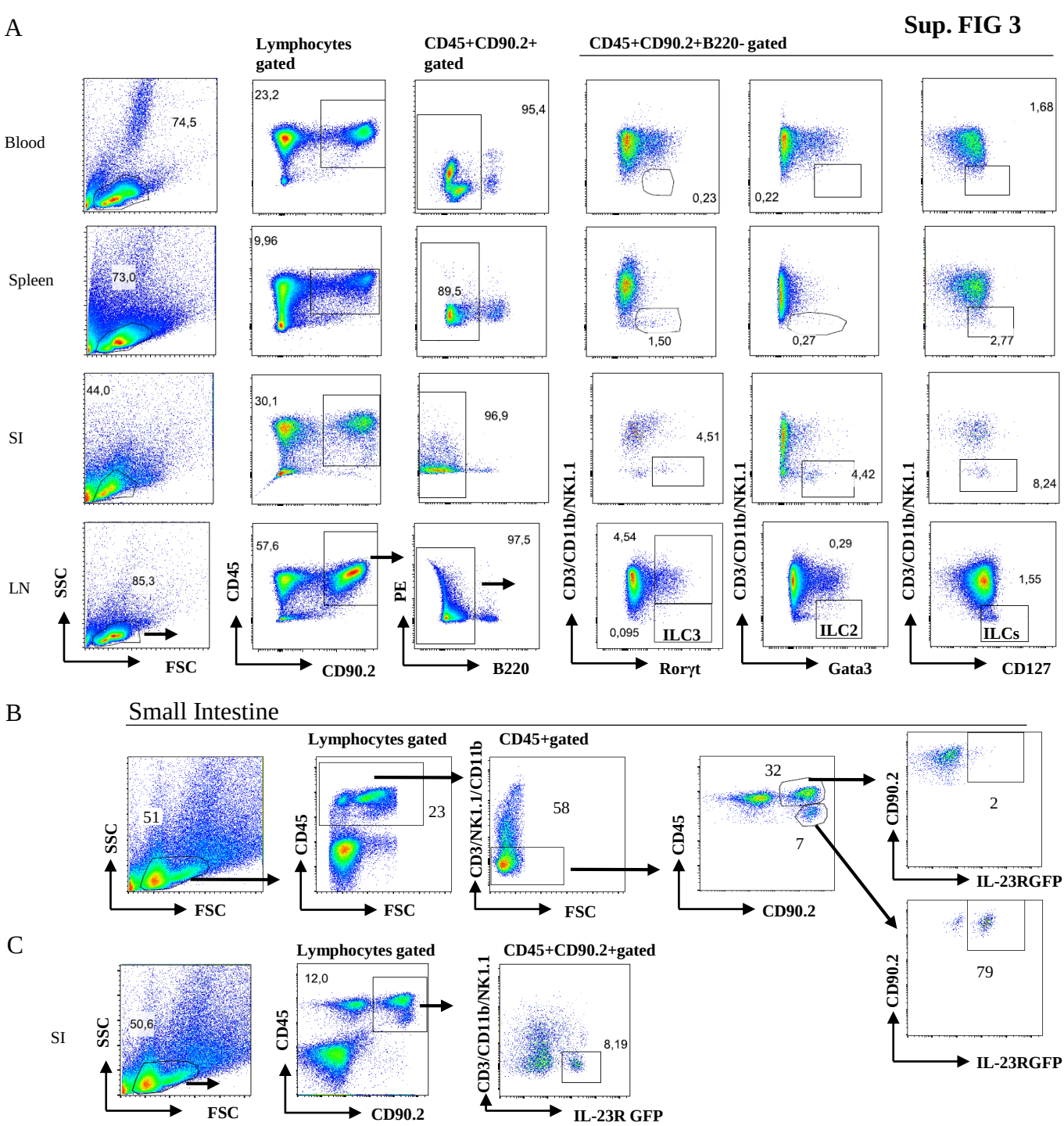
A

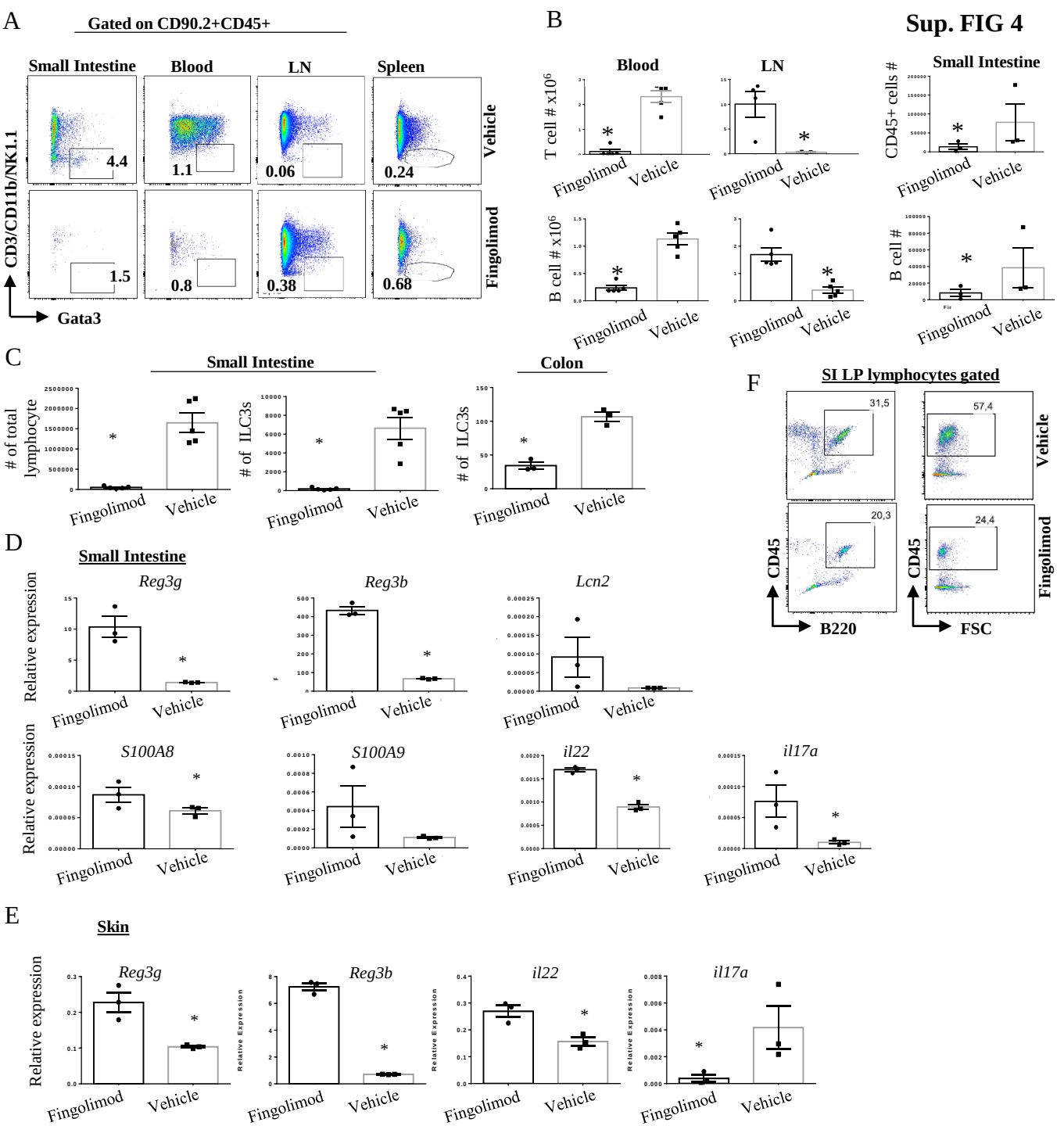
Sup. FIG 2

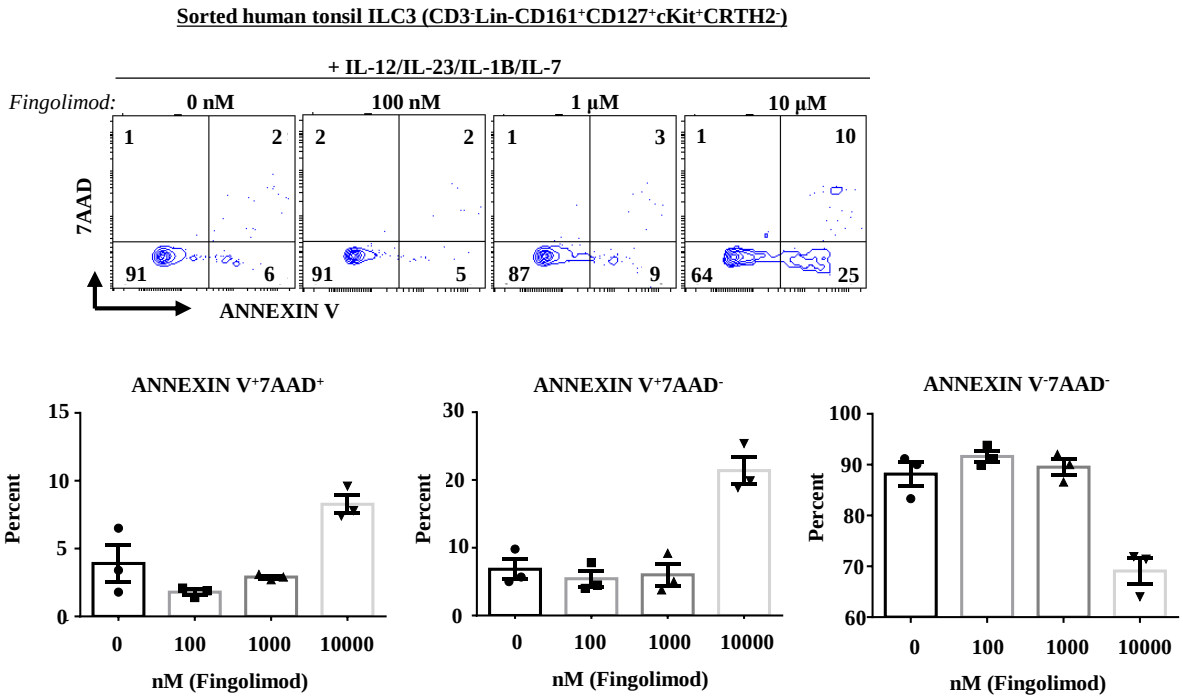

Untreated MS PBMC
Lymphocytes
Singlets
CD161+CD3-
CD161+CD3-Lin-
CD161+CD3-Lin-CD127+
SSC
FSC
CD161
SSC-W
P10
CD3
Lineage
CD127
C-Kit
P7
P13
ILC3
ILC2
ILC1
CRTH2
Fingolimod+ MS PBMC

B


Mouse Blood
19,0
SSC
FSC
27,0
CD45
CD90.2
CD3/NK1.1/CD11b
0,16
IL-23RGFP


A
Lymphocytes gated
CD45+CD90.2+ gated
CD45+CD90.2+B220- gated
Blood
Spleen
SI
LN
74,5
23,2
95,4
0,23
0,22
1,68
73,0
9,96
89,5
1,50
0,27
2,77
44,0
30,1
96,9
4,51
4,42
8,24
85,3
57,6
97,5
4,54
0,095
0,29
1,55
SSC
FSC
CD45
CD90.2
PE
B220
CD3/CD11b/NK1.1
Rorγt
Gata3
CD127
ILC3
ILC2
ILCs
B
Small Intestine
Lymphocytes gated
CD45+gated
51
23
58
32
7
2
79
SSC
FSC
CD45
CD3/NK1.1/CD11b
CD90.2
IL-23RGFP
C
SI
50,6
12,0
8,19
SSC
FSC
CD45
CD90.2
CD45+CD90.2+gated
CD3/CD11b/NK1.1
IL-23R GFP


A
Gated on CD90.2+CD45+
Small Intestine
Blood
LN
Spleen
Vehicle
Fingolimod
CD3/CD11b/NK1.1
Gata3
4.4
1.1
0.06
0.24
1.5
0.8
0.38
0.68
B
Sup. FIG 4
Blood
LN
Small Intestine
T cell # x10^6
CD45+ cells #
B cell # x10^6
B cell #
Fingolimod
Vehicle
C
Small Intestine
Colon
# of total lymphocyte
# of ILC3s
# of ILC3s
F
SI LP lymphocytes gated
31,5
57,4
20,3
24,4
CD45
B220
FSC
D
Small Intestine
Reg3g
Reg3b
Lcn2
S100A8
S100A9
il22
il17a
Relative expression
E
Skin
Reg3g
Reg3b
il22
il17a
Relative expression


Sorted human tonsil ILC3 (CD3-Lin-CD161+CD127+cKit+CRTH2-)
+ IL-12/IL-23/IL-1B/IL-7
Fingolimod:
0 nM
100 nM
1 µM
10 µM
1
2
91
6
2
2
91
5
1
3
87
9
1
10
64
25
7AAD
ANNEXIN V
ANNEXIN V+7AAD+
ANNEXIN V+7AAD-
ANNEXIN V-7AAD-
Percent
nM (Fingolimod)
0
100
1000
10000

Gene Name	Primer Sequence	Reference
hS1PR1_FW	GCTCTCCGAACGCAACTTC	[1]
hS1PR1_RV	GGTGGTTCGATGAGTGATCC	
hS1PR2_FW	CAAGTTCCACTCGGCAATGT	[2]
hS1PR2_RV	CAGGAGGCTGAAGACAGAGG	
hS1PR3_FW	TCAGGGAGGGCAGTATGTTC	[2]
hS1PR3_RV	GAGTAGAGGGGCAGGATGGT	
hS1PR4_FW	GTCTTTGGCTCCAACCTCTG	[3]
hS1PR4_RV	CGGAAGGAGTAGATGATGGG	
hS1PR5_FW	GGCGCGCACCTGTCCTGTAC	
hS1PR5_RV	TCGGGTCTCTGCCGCAGGAG	
mS1PR1_FW	GGAGGTTAAAGCTCTCCGC	
mS1PR1_RV	CGCCCCGATCTTCAAC	
mS1PR2_FW	GCGTGGTCACCATCTTCTCC	[4]
mS1PR2_RV	CGTCTGAGGACCAGCAACATC	
mS1PR3_FW	CATCGCCTTCCTCATCAGTATCTTC	[4]
mS1PR3_RV	CACAATCACTACGGTCCGCA	
mS1PR4_FW	CCACAGCCTCCTCATTGTC	[4]
mS1PR4_RV	TCAGCATCCCTAGCCCTC	
mS1PR5_FW	ACTGCTTAGGACGCCTGGAA	[4]
mS1PR5_RV	CCGCACCTGACAGTAAATCCTT	
mIFNg_FW	TCAAGTGGCATAGATGTGGAAGAA	
mIFNg_RV	TGGCTCTGCAGGATTTTCATG	
mLcn2_FW	GGCCCTGAGTGTCATGTGTC	
mLcn2_RV	TTCTGATCCAGTAGCGACAGC	
mReg3g_FW	CCGTGCCTATGGCTCCTATTG	
mReg3g_RV	GCACAGACACAAGATGTCCTG	
mReg3B_FW	TACTGCCTTAGACCGTGCTTTCTG	
mReg3B_RV	GACATAGGGCAACTTCACCTCACA	
mS100a8_FW	TGCGATGGTGATAAAAGTGG	
mS100a8_RV	GGCCAGAAGCTCTGCTACTC	
mS100a9_FW	CACAGTTGGCAACCTTTATG	
mS100a9_RV	CAGCTGATTGTCCTGGTTTG	

Sup. Table 1

	Fingolimod+ (MS Patient)		***Untreated (MS Patient)***	
	Male	Female	Male	Female
Patients (n)	4	10	4	7
Mean Age	46.5	41.33	30.25	32.83

Supplementary References

1.Sic, H., Kraus, H., Madl, J., Flittner, K.-A., Lilly Von M€ Unchow, A., Pieper, K., … Eibel, H. (2014). Sphingosine-1-phosphate receptors control B-cell migration through signaling components associated with primary immunodeficiencies, chronic lymphocytic leukemia, and multiple sclerosis. *Journal of Allergy and Clinical Immunology*, *134*, 420–428.e15. https://doi.org/10.1016/j.jaci.2014.01.037

2.Gu, Y., Forostyan, T., Sabbadini, R., & Rosenblatt, J. (2011). Epithelial cell extrusion requires the sphingosine-1-phosphate receptor 2 pathway. *Journal of Cell Biology*, *193*(4), 667–676. https://doi.org/10.1083/jcb.201010075

3.He, X., H'ng, S.-C., Leong, D. T., Hutmacher, D. W., & Melendez, A. J. (2010). Sphingosine-1-Phosphate Mediates Proliferation Maintaining the Multipotency of Human Adult Bone Marrow and Adipose Tissue-derived Stem Cells. *Journal of Molecular Cell Biology*, *2*(4), 199–208. https://doi.org/10.1093/jmcb/mjq011

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