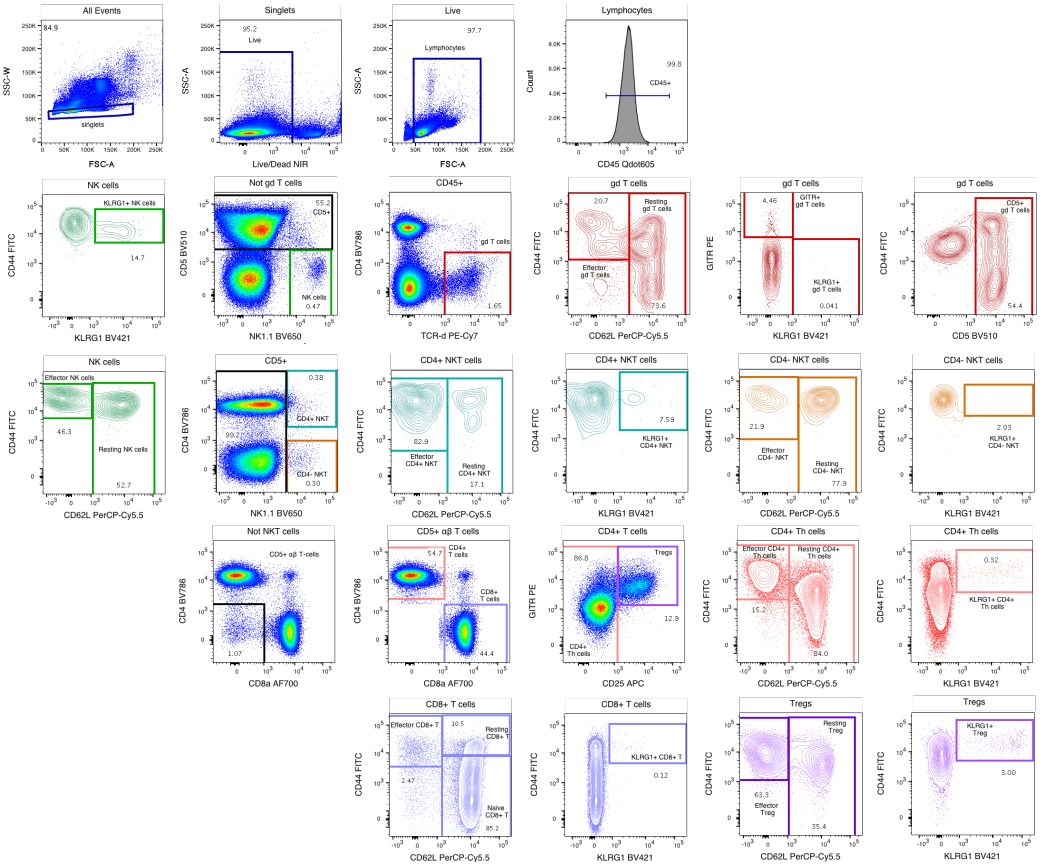
Supplementary Figure 1

a

Tests performed at WTSI	
Viability / Fertility	Viability Fertility Recessive lethality
Anatomy	X-ray imaging Dysmorphology Hair dysmorphology Hair Follicle Cycling Heart weight
Metabolism	Body Composition (DEXA) Indirect Calorimetry Glucose Tolerance Insulin
Immune System	Blood cytometric analysis Salmonella challenge Citrobacter challenge
Other	Modified Shirpa Grip Strength Erythrocyte Micronuclei Auditory Brainstem Response Plasma Chemistry Haematology

b



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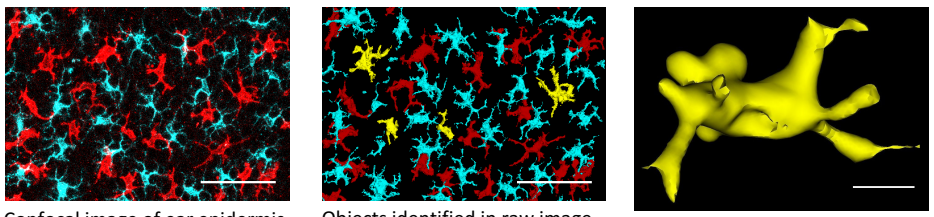

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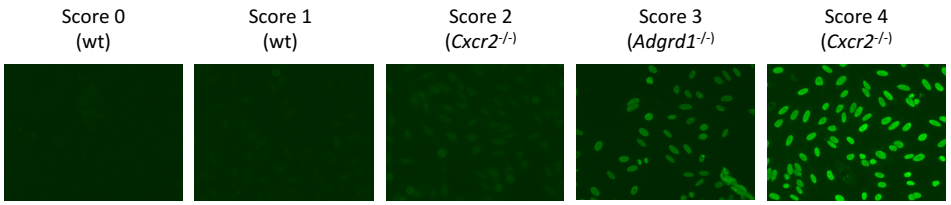

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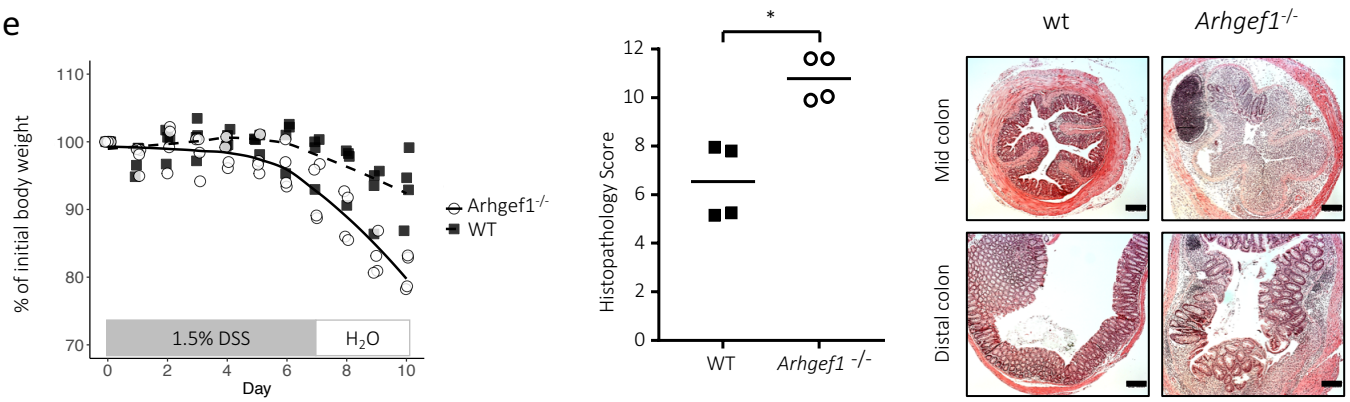

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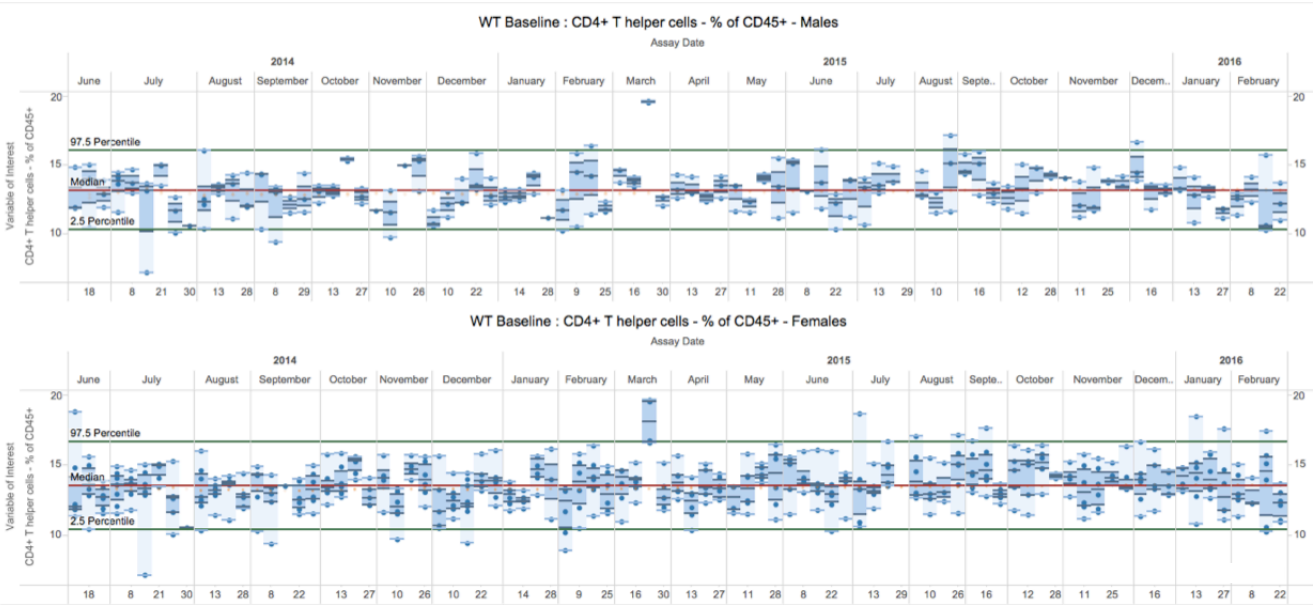
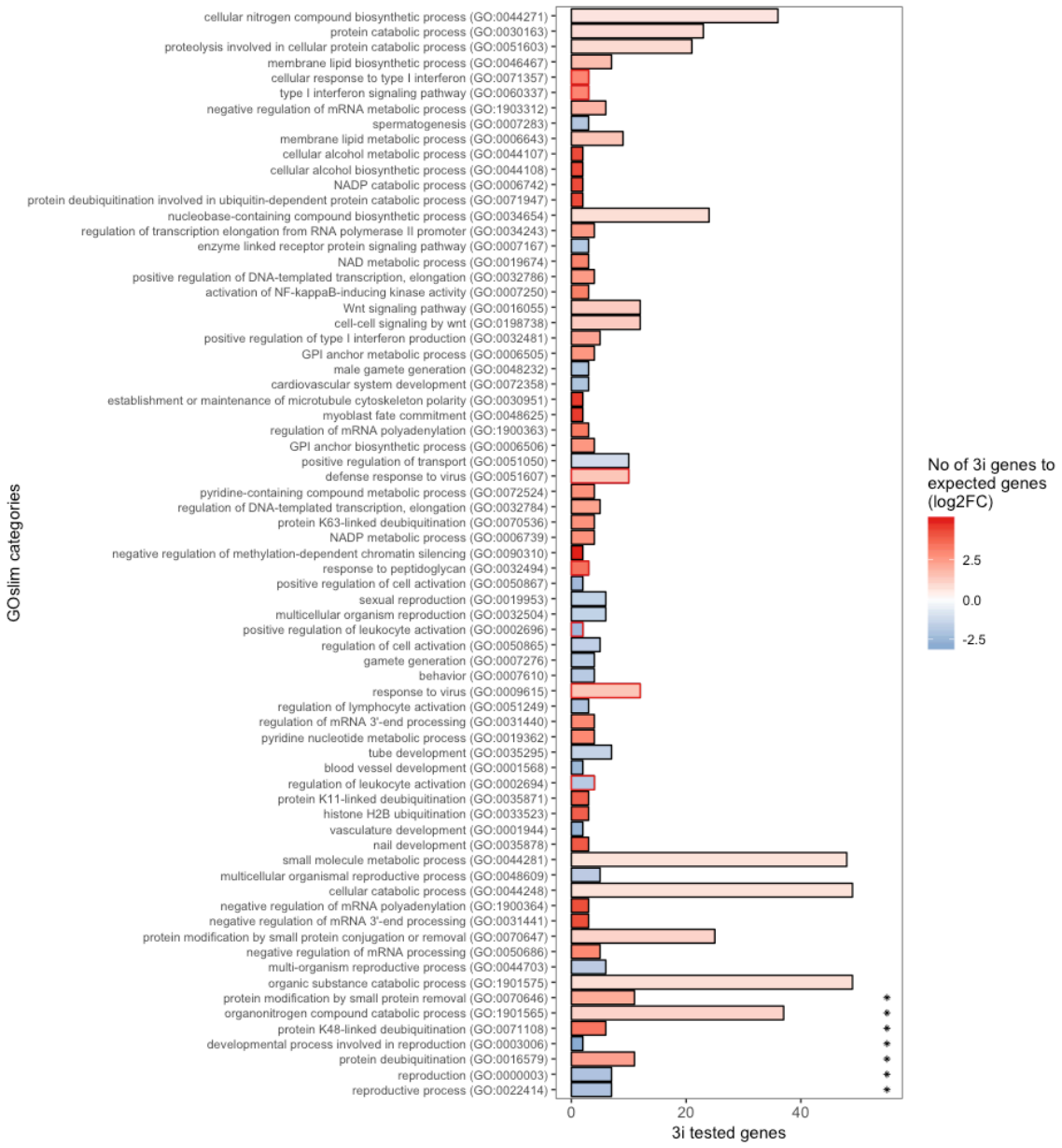
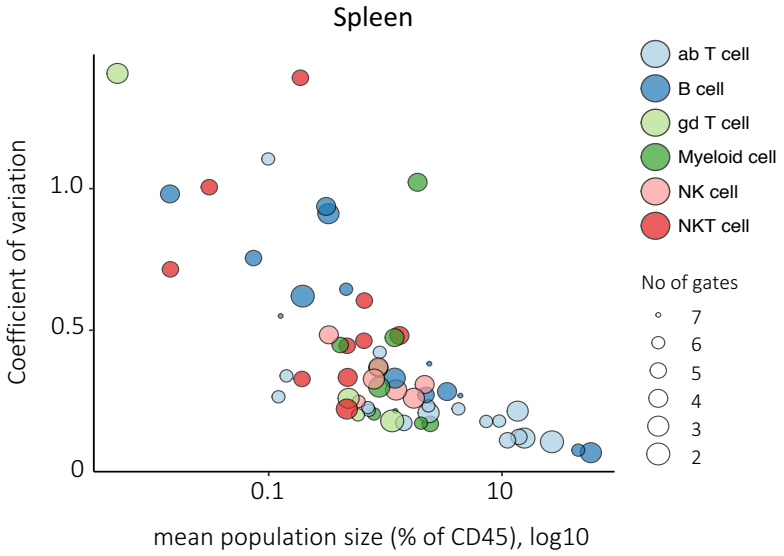

WT Baseline : CD4+ T helper cells - % of CD45+ - Males
Assay Date
2014
2015
2016
June
July
August
September
October
November
December
January
February
March
April
May
June
July
August
Septe..
October
November
Decem..
January
February
97.5 Percentile
Median
2.5 Percentile
Variable of Interest
CD4+ T helper cells - % of CD45+
WT Baseline : CD4+ T helper cells - % of CD45+ - Females
Assay Date
97.5 Percentile
Median
2.5 Percentile
Variable of Interest
CD4+ T helper cells - % of CD45+

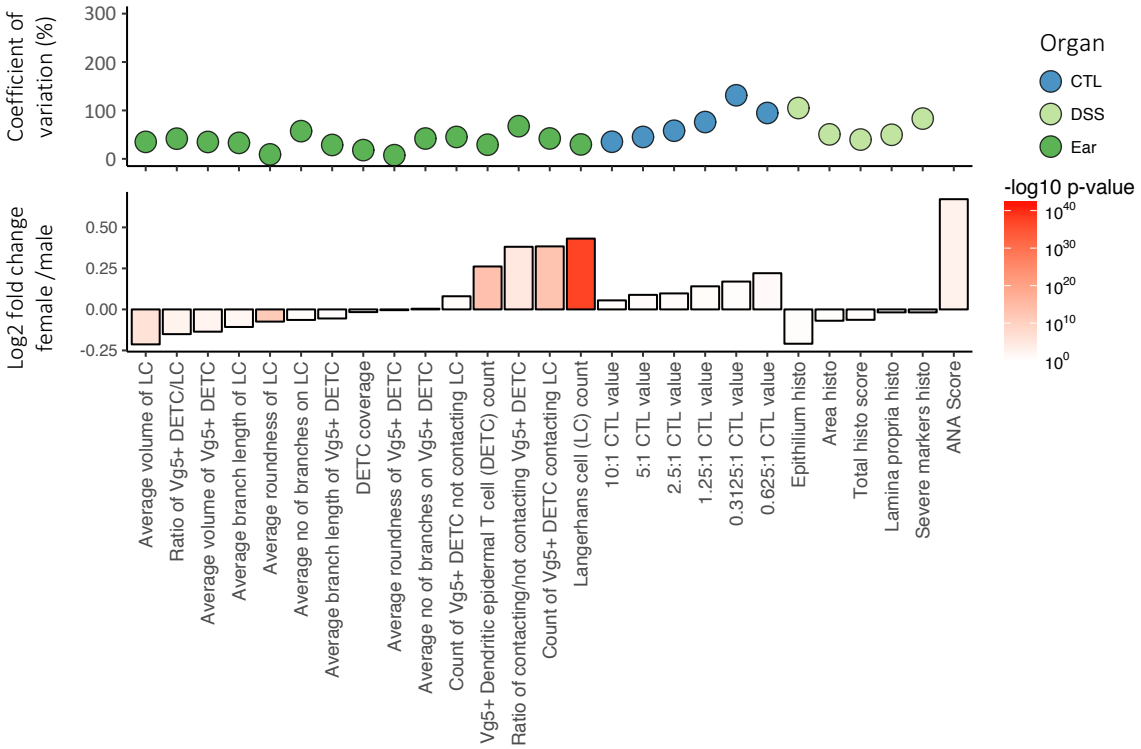
g


cellular nitrogen compound biosynthetic process (GO:0044271)
protein catabolic process (GO:0030163)
proteolysis involved in cellular protein catabolic process (GO:0051603)
membrane lipid biosynthetic process (GO:0046467)
cellular response to type I interferon (GO:0071357)
type I interferon signaling pathway (GO:0060337)
negative regulation of mRNA metabolic process (GO:1903312)
spermatogenesis (GO:0007283)
membrane lipid metabolic process (GO:0006643)
cellular alcohol metabolic process (GO:0044107)
cellular alcohol biosynthetic process (GO:0044108)
NADP catabolic process (GO:0006742)
protein deubiquitination involved in ubiquitin-dependent protein catabolic process (GO:0071947)
nucleobase-containing compound biosynthetic process (GO:0034654)
regulation of transcription elongation from RNA polymerase II promoter (GO:0034243)
enzyme linked receptor protein signaling pathway (GO:0007167)
NAD metabolic process (GO:0019674)
positive regulation of DNA-templated transcription, elongation (GO:0032786)
activation of NF-kappaB-inducing kinase activity (GO:0007250)
Wnt signaling pathway (GO:0016055)
cell-cell signaling by wnt (GO:0198738)
positive regulation of type I interferon production (GO:0032481)
GPI anchor metabolic process (GO:0006505)
male gamete generation (GO:0048232)
cardiovascular system development (GO:0072358)
establishment or maintenance of microtubule cytoskeleton polarity (GO:0030951)
myoblast fate commitment (GO:0048625)
regulation of mRNA polyadenylation (GO:1900363)
GPI anchor biosynthetic process (GO:0006506)
positive regulation of transport (GO:0051050)
defense response to virus (GO:0051607)
pyridine-containing compound metabolic process (GO:0072524)
regulation of DNA-templated transcription, elongation (GO:0032784)
protein K63-linked deubiquitination (GO:0070536)
NADP metabolic process (GO:0006739)
negative regulation of methylation-dependent chromatin silencing (GO:0090310)
response to peptidoglycan (GO:0032494)
positive regulation of cell activation (GO:0050867)
sexual reproduction (GO:0019953)
multicellular organism reproduction (GO:0032504)
positive regulation of leukocyte activation (GO:0002696)
regulation of cell activation (GO:0050865)
gamete generation (GO:0007276)
behavior (GO:0007610)
response to virus (GO:0009615)
regulation of lymphocyte activation (GO:0051249)
regulation of mRNA 3'-end processing (GO:0031440)
pyridine nucleotide metabolic process (GO:0019362)
tube development (GO:0035295)
blood vessel development (GO:0001568)
regulation of leukocyte activation (GO:0002694)
protein K11-linked deubiquitination (GO:0035871)
histone H2B ubiquitination (GO:0033523)
vasculature development (GO:0001944)
nail development (GO:0035878)
small molecule metabolic process (GO:0044281)
multicellular organismal reproductive process (GO:0048609)
cellular catabolic process (GO:0044248)
negative regulation of mRNA polyadenylation (GO:1900364)
negative regulation of mRNA 3'-end processing (GO:0031441)
protein modification by small protein conjugation or removal (GO:0070647)
negative regulation of mRNA processing (GO:0050686)
multi-organism reproductive process (GO:0044703)
organic substance catabolic process (GO:1901575)
protein modification by small protein removal (GO:0070646)
organonitrogen compound catabolic process (GO:1901565)
protein K48-linked deubiquitination (GO:0071108)
developmental process involved in reproduction (GO:0003006)
protein deubiquitination (GO:0016579)
reproduction (GO:0000003)
reproductive process (GO:0022414)
GOslim categories
0
20
40
3i tested genes
No of 3i genes to expected genes (log2FC)
2.5
0.0
-2.5

h

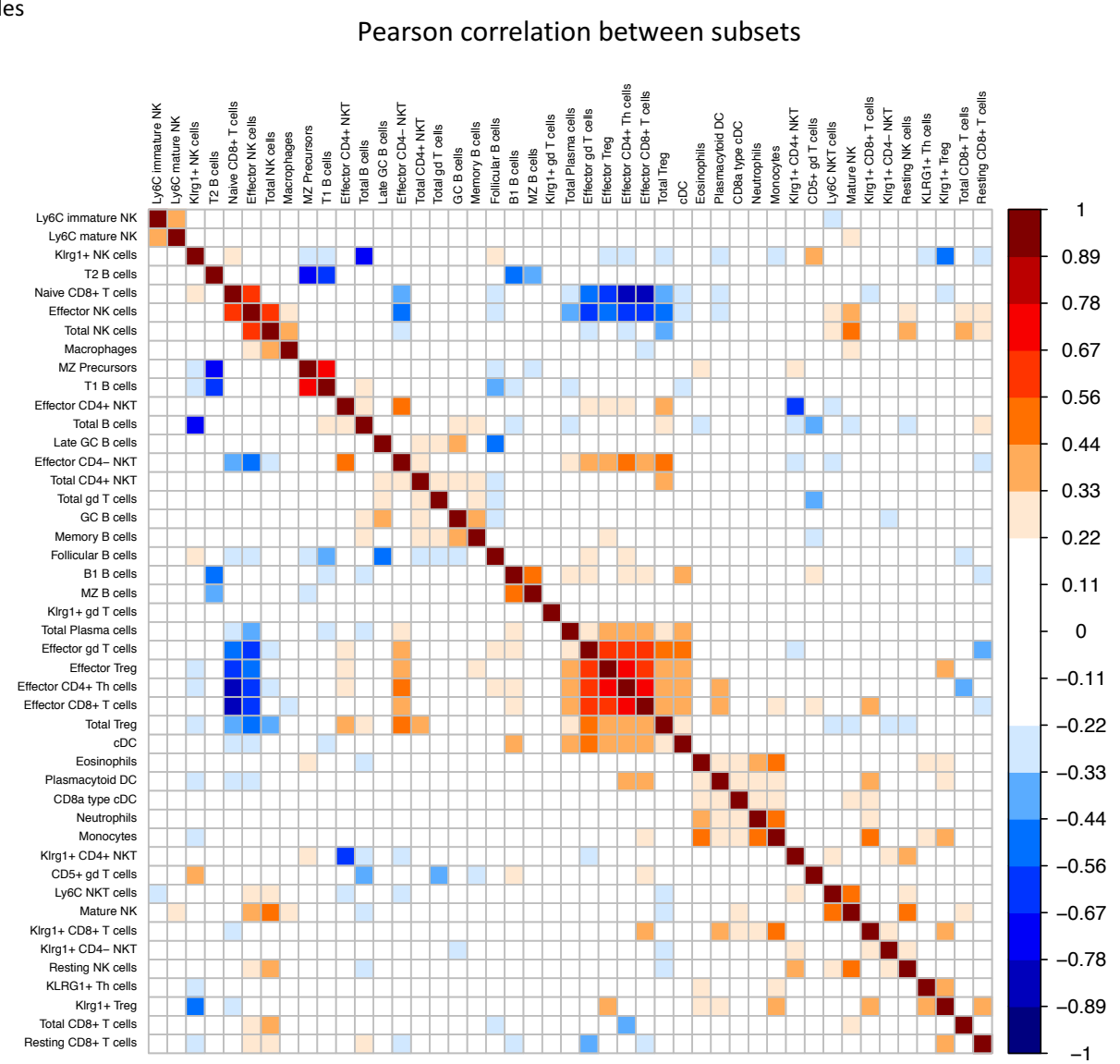

Spleen
Coefficient of variation
1.0
0.5
0
0.1
10
mean population size (% of CD45), log10
ab T cell
B cell
gd T cell
Myeloid cell
NK cell
NKT cell
No of gates
7
6
5
4
3
2

i


Coefficient of variation (%)
300
200
100
0
Log2 fold change female /male
0.50
0.25
0.00
-0.25
Organ
CTL
DSS
Ear
-log10 p-value
10^{40}
10^{30}
10^{20}
10^{10}
10^{0}
Average volume of LC
Ratio of Vg5+ DETC/LC
Average volume of Vg5+ DETC
Average branch length of LC
Average roundness of LC
Average no of branches on LC
Average branch length of Vg5+ DETC
DETC coverage
Average roundness of Vg5+ DETC
Average no of branches on Vg5+ DETC
Count of Vg5+ DETC not contacting LC
Vg5+ Dendritic epidermal T cell (DETC) count
Ratio of contacting/not contacting Vg5+ DETC
Count of Vg5+ DETC contacting LC
Langerhans cell (LC) count
10:1 CTL value
5:1 CTL value
2.5:1 CTL value
1.25:1 CTL value
0.3125:1 CTL value
0.625:1 CTL value
Epithilium histo
Area histo
Total histo score
Lamina propria histo
Severe markers histo
ANA Score

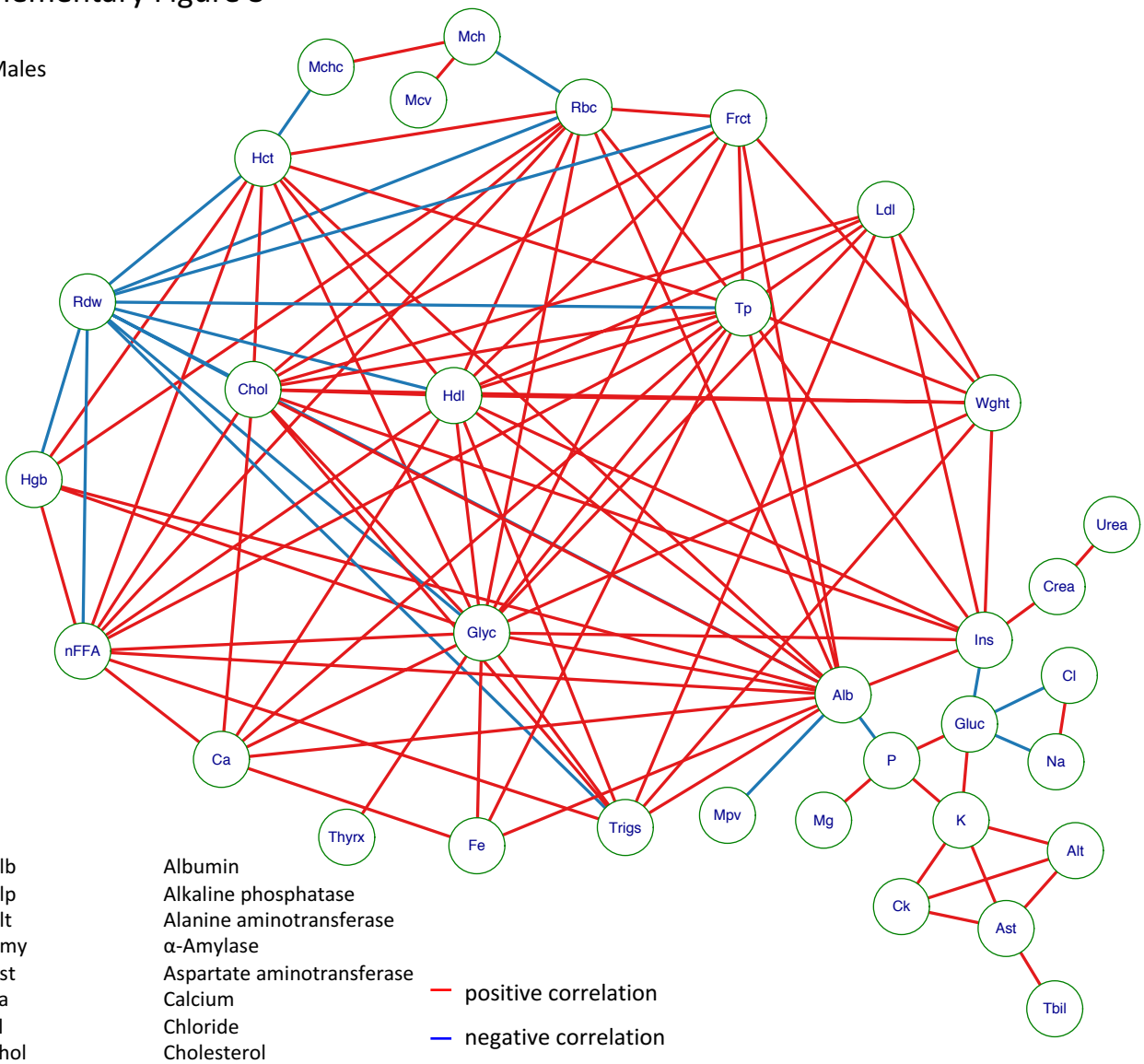
Supplementary Figure 2

Females



Supplementary Figure 3

a Males

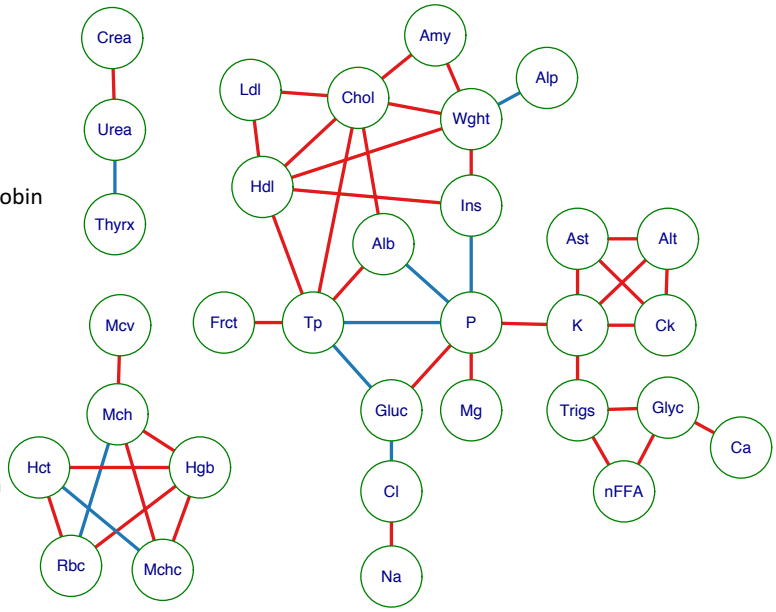


positive correlation

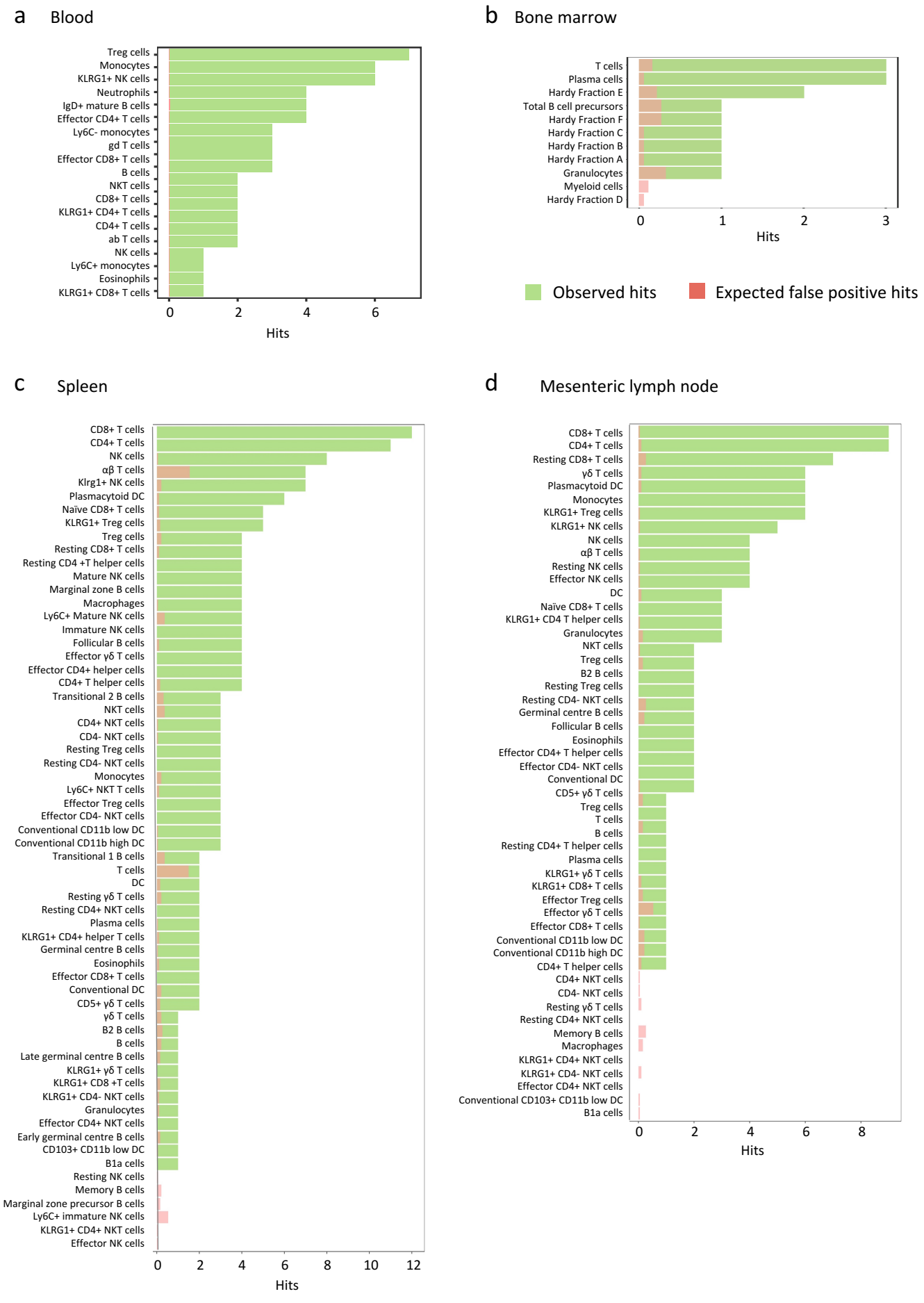
negative correlation

Alb	Albumin
Alp	Alkaline phosphatase
Alt	Alanine aminotransferase
Amy	α-Amylase
Ast	Aspartate aminotransferase
Ca	Calcium
Cl	Chloride
Chol	Cholesterol
Ck	Creatinine kinase
Crea	Creatinine
Fe	Iron
Fruct	Fructosamine
Gluc	Glucose
Glyc	Glycerol
Hct	Hematocrit
Hdl	HDL cholesterol
Hgb	Hemoglobulin
Ins	Insulin
K	Potassium
Ldl	LDL cholesterol
Mch	Mean corpuscular hemoglobin
Mchc	Mean cell hemoglobin concentration
Mcv	Mean corpuscular volume
Mg	Magnesium
Mpv	Mean platelet volume
Na	Sodium
nFFA	Free fatty acids
P	Phosphorus
Rbc	Red blood cell count
Rdw	Red blood cell distribution width
Tbil	Total bilirubin
Thyrx	Thyroxine
Tp	Total protein
Trigs	Triglycerides
Urea	Urea

b Females

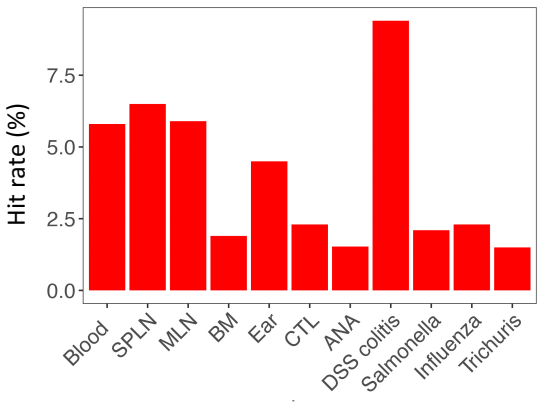


Supplementary Figure 4



Supplementary Figure 5

a



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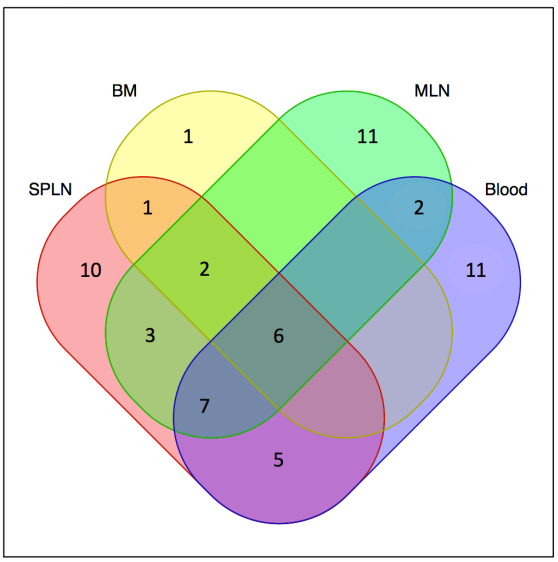
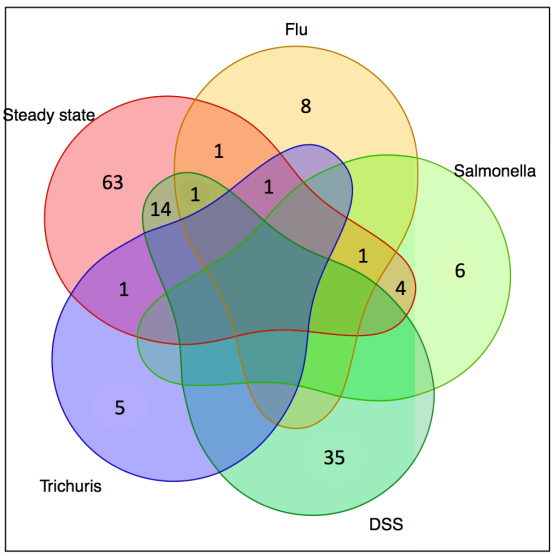
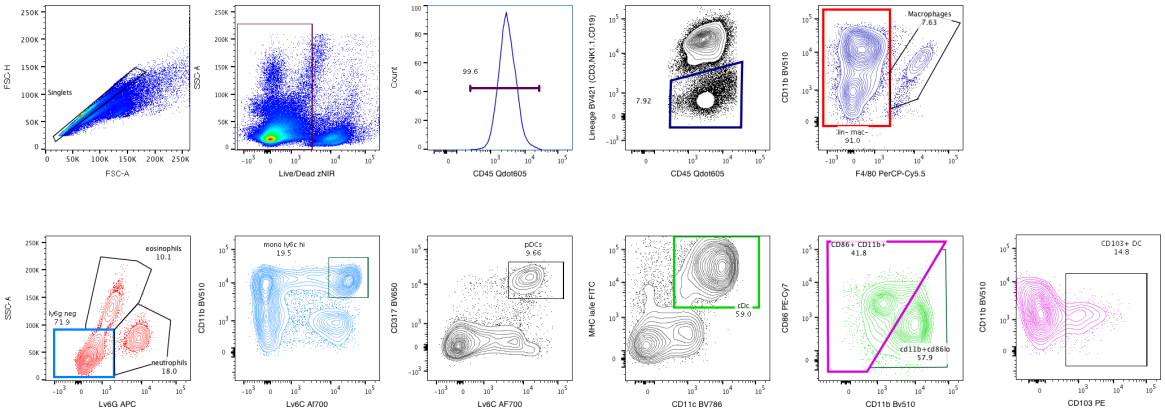




Supplementary Figure 6

a



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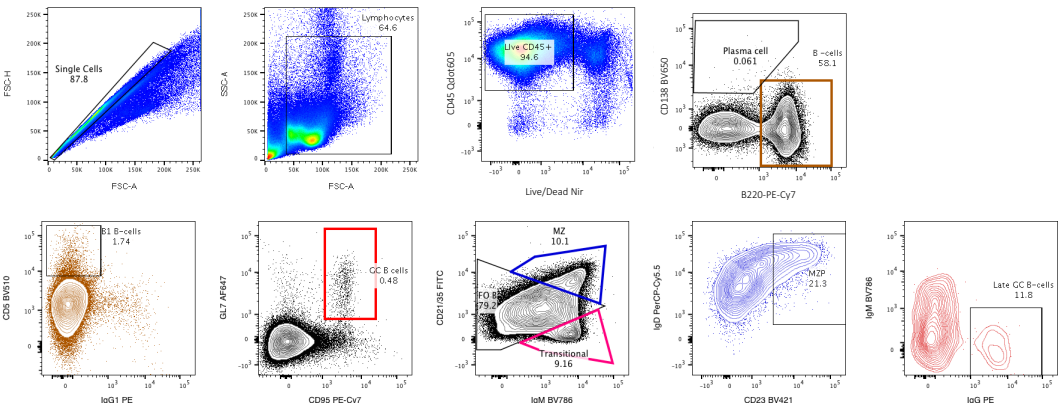
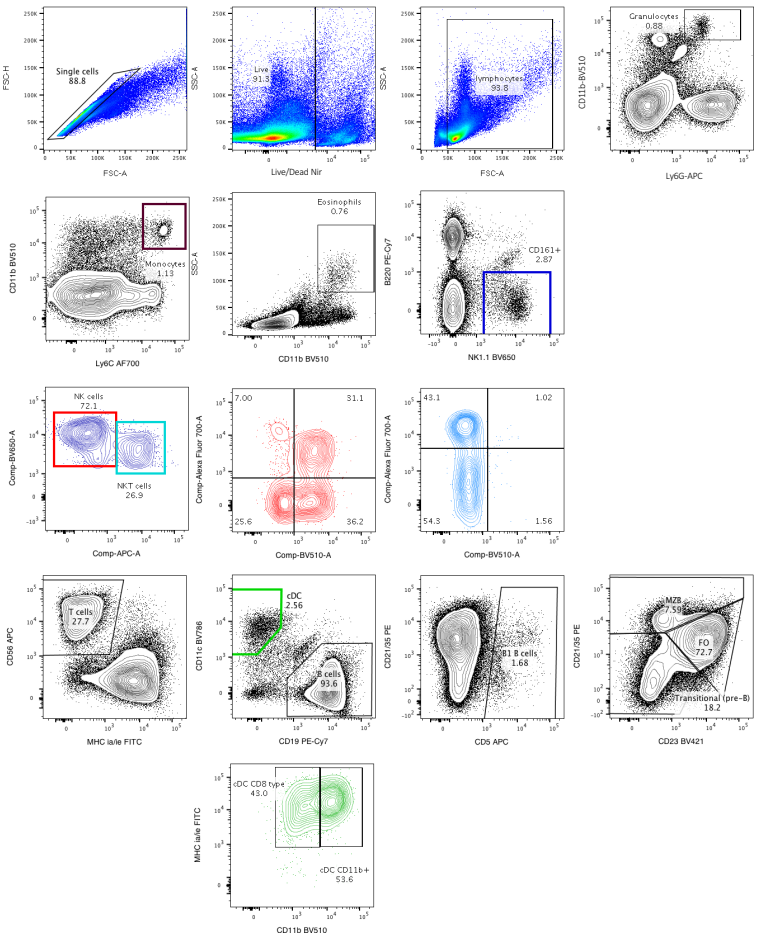


c



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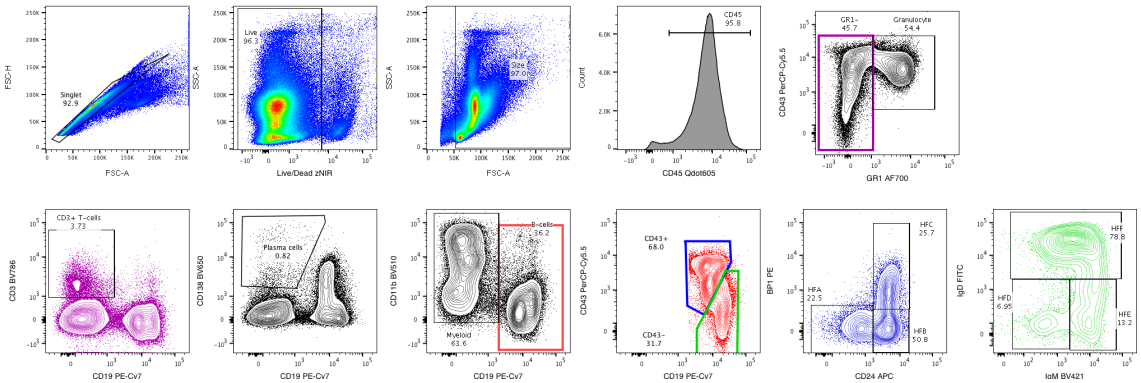
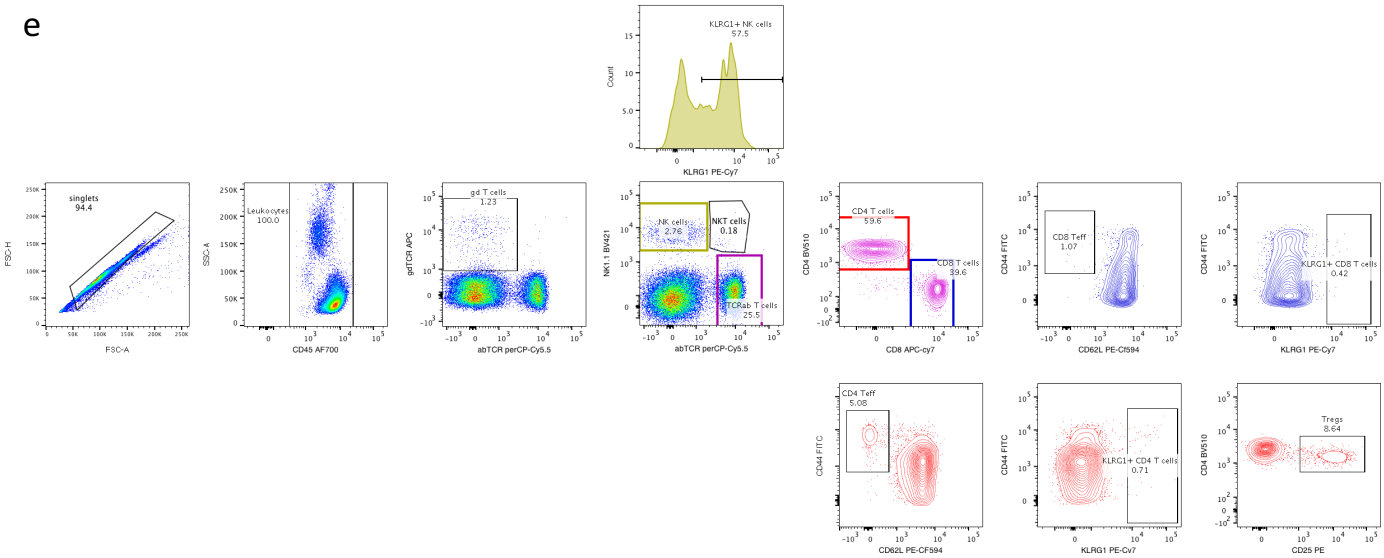
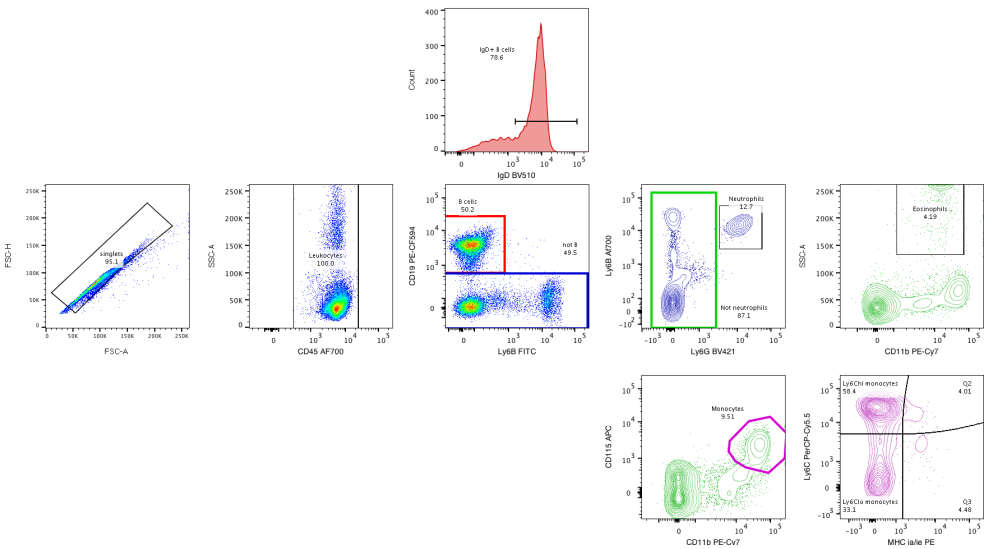

Singlet
92.9
Live
96.3
Live
97.0
CD45
95.8
GR1-
45.7
Granulocyte
54.4
CD3+ T-cells
3.73
Plasma cells
0.82
B-cells
36.2
Myeloid
63.6
CD43+
68.0
CD43-
31.7
HFC
25.7
HFA
22.5
HFB
50.8
HFF
78.8
HFD
6.95
HFE
13.2

e


KLRG1+ NK cells
57.5
singlets
94.4
Leukocytes
100.0
gd T cells
1.23
NK cells
2.76
NKT cells
0.18
TCRab T cells
25.5
CD4 T cells
59.6
CD8 T cells
39.6
CD8 Teff
1.07
KLRG1+ CD8 T cells
0.42
CD4 Teff
5.08
KLRG1+ CD4 T cells
0.71
Tregs
8.64

f


IgD+ B cells
78.6
singlets
95.1
Leukocytes
100.0
B cells
50.2
not B
49.5
Neutrophils
12.7
Not neutrophils
87.1
Eosinophils
4.19
Monocytes
9.51
Ly6Chi monocytes
58.4
Q2
4.01
Ly6Clo monocytes
33.1
Q3
4.48

Supplementary Figure 1: Assay overview.

a. Overview of the IMPC tests performed at Wellcome Trust Sanger Institute (WTSI) prior to the substantial expansion by 3i.

b. Flow cytometry screen. Representative MLN data illustrate gating strategy for T cells, NKT cells and NK cells. Subsets of key populations are shown in gates of the same colour. Percentages denote percentages of parent population. Panels can be found in Supplementary Table 1, populations are quantitated in Supplementary Table 2.

c. Epidermis screen. Left panel: Maximal intensity projection of a z-stack 2-channel overlay. Pseudocolouring scheme was applied to represent Dendritic Epidermal Vγ5$^+$ γδ T Cells (DETC) in red and MHC-II+ Langerhans cells (LC) in cyan, scale bar 50 µm. Middle panel: 3D quantitative object-based image analysis (Definiens Developer XD) of DETC that contact LC (red) versus not contacting LC (yellow), and LC (cyan); scale bar: 50 µm. Right panel: 3D representation of a DETC rendering in Definiens Developer from which parameters such as dendricity and roundness were quantitated; scale bar: 10 µm. Measurements were performed on three vision fields from the same slide per animal.

d. ANA screen. Antinuclear antibody staining in Hep2 cells using serum from wt mice and different ko lines. Sera were scored on a scale of 0 to 4. The images illustrate that sera from wt or specific mutant strains do not all score equally. Scores of $\leq$1 were regarded as negative; scores of $\geq$2 as positive. Test performed once per animal.

e. DSS histology screen. Left: Body weight curves of wt and *Arhgef1*$^{-/-}$ mice in the same experiment (n=4[2M2F] for wt; n=4[2M2f] for *Arhgef1*$^{-/-}$). Middle: histopathology scores of wt and *Arhgef1*$^{-/-}$ mice. Symbols denote the average histopathology score for mid- and distal-colon in each mouse, and horizontal bars represent the median across mice for this group. Right: representative photomicrographs of H&E-stained colonic sections of wt and *Arhgef1*$^{-/-}$ mice; scale bar 0.2 mm. One mid-colon and one distal colon section scored per animal.

f. Longitudinal monitoring of manually analysed flow cytometry data for quality controls (QC), illustrated by CD4$^+$ T helper cells. Daily inner quantiles are shaded dark blue, outer quantiles light blue, middle line is daily median. All individual data points

are shown. Temporal QC are further considered in Materials and Methods.

g. Top GO-slim categories (all categories with raw p-value < 0.01 shown, two-sided Fisher's exact test) among 466 of genes with GO annotation in 3i gene set. X axis: number of genes from given category in the 3i set. Coloured by ratio of observed to expected number of genes. Red frame: immune-system related categories. Categories significantly different from whole mouse genome at FDR 5% marked with asterisk.

h. Variation in immune cell subsets (colours denote cell lineages) detected by flow cytometry (denoted by size of circles). Data from 16-week old wt C57BL/6N SPL (n>500 for all parameters).

i. Variation and sexual dimorphism in analyses of ear epidermal microscopy; CD8 cytotoxicity; DSS colitis; and ANA. Lower panel: sexual dimorphism of mean values as log2 fold change (middle panel, female/male); colour indicates p value (two tailed unpaired t test) Upper panel: coefficient of variation; colour indicates assay. Number of wt samples for each of the assays are listed in Supplementary Table 3.

Supplementary Figure 2: Immunological correlations across parameters

Heat map represents Pearson correlations of 46 splenic immune cell subsets with each other in wt females (n>230 for all parameters) as determined by flow cytometry. Dark red fields denote strong positive, dark blue fields strong negative correlations.

Supplementary Figure 3: Non-immunological correlations across parameters

Correlations of nonimmune parameters (haematological, clinical blood chemistry, and additional data) in males (a) and females (b). Depicted are correlations with an R-value >0.33 and p<0.001; red lines denote positive correlations; blue lines, negative correlations (n>780 per sex for all parameters).

Supplementary Figure 4: False positive rates are far below hit rates.

Expected number of false positives estimated by simulation (re-sampling of wt controls, performed 10000 times and adjusted to the actual number of performed tests per parameter) compared to the number of significant phenotypes detected in: (a) PBL

(n>450 per sex for all parameters), (b) BM (n>350 per sex for all parameters), (c) SPL (n>250 per sex for all parameters), and (d) MLN (n>250 per sex for all parameters). Observed hits depicted in green; expected false positives in red. Significance established by windowed 70 wt mice reference range, details in Materials and Methods.

Supplementary Figure 5: 140 out of 530 genes perturb the immunophenotype

a. Hit rate per assay.
b. Venn diagrams showing the overlap of significantly different phenotypes between assays.

Supplementary Figure 6: Flow cytometry gating strategies**.** Subsets of key populations are shown in gates of the same colour. Percentages denote percentages of parent population. Panels can be found in Supplementary Table 1, populations are quantitated in Supplementary Table 2. T cells from spleen can be found in Supplementary Fig 1b. Representative data for:

a. Myeloid cells (data from spleen)
b. B cells (data from spleen)
c. Additional NK subsets (data from spleen)
d. Bone marrow
e. T/NK cells (data from blood)
f. B cells/monocytes (data from blood)

Supplementary Tables 1-5

Supplementary Table 1

Markers and fluorochromes used to identify immune cell populations by flow cytometry

Laser	LP Filter	BP filter	Fluoro-chrome	SPL/MLN T/NK cells	SPL/MLN B cells	SPL/MLN Myeloid cells	SPL Myeloid / B cells	Bone marrow
405	-	450/50	BV421	Klrg1	CD23	CD5/19/161	CD23	IgM
405	505	525/50	BV510	CD5	CD5	CD11b	CD11b	CD11b
405	595	610/20	Qdot-605	CD45	CD45	CD45		CD45
405	630	670/30	BV650	CD161	CD138	CD317	CD161	CD138
405	750	780/60	BV786	CD4	IgM	CD11c	CD11c	CD3
488	505	530/30	FITC	CD44	CD21/35	MHC II	MHC II	IgD
488	685	710/50	PerCP-Cy5.5	CD62L	IgD	F4/80		CD43
561	570	585/15	PE	GITR	IgG1	CD103	CD21/35	BP-1
561	750	780/60	PE-Cy7	TCRδ	CD95	CD86	CD19	B220
640	-	670/14	APC	CD25		Ly6G	CD5	CD24
			AF647		GL7			
640	690	730/45	AF700	CD8α	B220	Ly6C	Ly6C	Gr1
640	750	780/60	NIR	Live/Dead	Live/Dead	Live/Dead	Live/Dead	Live/Dead

Laser	LP Filter	BP filter	Fluoro-chrome	PBL T/NK cells	PBL Myeloid/ B cells
405	-	450/50	BV421	CD161	
			V450		Ly6G
405	505	525/50	BV510	CD4	IgD
488	505	530/30	FITC	CD44	Ly6B
488	550	575/26	PE	CD25	MHC II
488	600	610/20	PE-CF594	CD62L	CD19
488	685	695/40	PerCP-Cy5.5	TCRβ	Ly6C
488	755	780/60	PE-Cy7	Klrg1	CD11b
633	-	660/20	APC	TCRδ	CD115
633	710	730/45	AF700	CD45	CD45
633	755	780/60	APC-H7	CD8α	

Supplementary Table 2: Parameters of flow cytometry and ear epidermis assays

Parameter	Cell markers
Spleen and mesenteric lymph node	
Total γδ T cells	TCRδ+
CD5+ γδ T cells	TCRδ+ CD5+
Effector γδ T cells	TCRδ+ CD62L- CD44+
Resting γδ T cells	TCRδ+ CD62L+
KLRG1+ γδ T cells	TCRδ+ KLRG1+
Total αβ T cells	TCRδ- CD5+ CD4+ or CD8+
Total CD4+ T cells	TCRδ- CD5+ CD4+
CD4+ T helper cells	TCRδ- CD5+ CD4+ CD25- GITR-
Effector CD4+ T helper cells	TCRδ- CD5+ CD4+ CD25- GITR- CD62L- CD44+
Resting CD4+ T helper cells	TCRδ- CD5+ CD4+ CD25- GITR- CD62L+
KLRG1+ CD4+ T helper cells	TCRδ- CD5+ CD4+ CD25- GITR- KLRG1+
Total T_{reg} cells	TCRδ- CD5+ CD4+ CD25+ GITR+
Effector T_{reg} cells	TCRδ- CD5+ CD4+ CD25+ GITR+ CD62L- CD44+
Resting T_{reg} cells	TCRδ- CD5+ CD4+ CD25+ GITR+ CD62L+
KLRG1+ T_{reg} cells	TCRδ- CD5+ CD4+ CD25+ GITR+ KLRG1+
Total CD8+ T cells	TCRδ- CD5+ CD8+
Effector CD8+ T cells	TCRδ- CD5+ CD8+ CD62L- CD44+
Resting CD8+ T cells	TCRδ- CD5+ CD8+ CD62L+ CD44+
Naive CD8+ T cells	TCRδ- CD5+ CD8+ CD62L+ CD44-
KLRG1+ CD8+ T cells	TCRδ- CD5+ CD8+ KLRG1+
Total NKT cells	TCRδ- CD5+ CD161+
Total CD4- NKT cells	TCRδ- CD5+ CD161+ CD4-
Effector CD4- NKT cells	TCRδ- CD5+ CD161+ CD4- CD62L-
Resting CD4- NKT cells	TCRδ- CD5+ CD161+ CD4- CD62L+
KLRG1+ CD4- NKT cells	TCRδ- CD5+ CD161+ CD4- KLRG1+
Total CD4+ NKT cells	TCRδ- CD5+ CD161+ CD4+
Effector CD4+ NKT cells	TCRδ- CD5+ CD161+ CD4+ CD62L-
Resting CD4+ NKT cells	TCRδ- CD5+ CD161+ CD4+ CD62L+
KLRG1+ CD4+ NKT cells	TCRδ- CD5+ CD161+ CD4+ KLRG1+
Total NK cells	TCRδ- CD5- CD161+
Effector NK cells	TCRδ- CD5- CD161+ CD62L-
Resting NK cells	TCRδ- CD5- CD161+ CD62L+
KLRG1+ NK cells	TCRδ- CD5- CD161+ KLRG1+
Plasma cells	CD138+
B1a cells	CD138- B220+ CD5+
B2 cells	CD138- B220+ CD5-
Follicular B cells	CD138- B220+ CD5- GL7- CD95- CD21/35^{int} IgM^{int}
Memory B cells	CD138- B220+ CD5- GL7- CD95- IgG+
Macrophages	F4/80+ CD11b^{int}
Granulocytes	F4/80- Ly6G^{high} CD11b+
Eosinophils	F4/80- Ly6G^{int} CD11b+ SSC^{high}

Monocytes	F4/80- Ly6G- Ly6C^{high} CD11b+
Plasmacytoid DC	F4/80- Ly6G- Ly6C$^{low/int}$ CD317+
Conventional DC	F4/80- Ly6G- Ly6C$^{low/int}$ CD317- CD11c+ MHCII+
Conventional CD11b^{high} DC	F4/80- Ly6G- Ly6C$^{low/int}$ CD317- CD11c+ MHCII+ CD11b^{high} CD86^{low}
Conventional CD11b^{low} DC	F4/80- Ly6G- Ly6C$^{low/int}$ CD317- CD11c+ MHCII+ CD11b^{low} CD86^{high}
CD103+ conventional CD11b^{low} DC	F4/80- Ly6G- Ly6C$^{low/int}$ CD317- CD11c+ MHCII+ CD11b^{low} CD86^{high} CD103+
Spleen only	
Immature NK cells	Ly6G- CD161+ CD5- CD11b- Ly6C-
Ly6C+ immature NK cells	Ly6G- CD161+ CD5- CD11b- Ly6C+
Mature NK cells	Ly6G- CD161+ CD5- CD11b+ Ly6C-
Ly6C+ mature NK cells	Ly6G- CD161+ CD5- CD11b+ Ly6C+
Germinal centre B cells	CD138- B220+ CD5- GL7+ CD95+
Early germinal centre B cells	CD138- B220+ CD5- GL7+ CD95+ IgM+ IgG-
Late germinal centre B cells	CD138- B220+ CD5- GL7+ CD95+ IgM- IgG+
Marginal zone precursor B cells	CD138- B220+ CD5- GL7- CD95- CD21/35+ CD23-
Marginal zone B cells	CD138- B220+ CD5- GL7- CD95- CD21/35+ CD23+
Transitional 1 B cells	CD138- B220+ CD5- GL7- CD95- CD21/35- CD23-
Transitional 2 B cells	CD138- B220+ CD5- GL7- CD95- CD21/35- CD23+
Blood	
Total T cells	TCRβ+ or TCRδ+
Total αβ T cells	TCRβ+
Total CD4+ T cells	TCRβ+ CD4+
Effector CD4+ T cells	TCRβ+ CD4+ CD62L- CD44+
KLRG1+ CD4+ T cells	TCRβ+ CD4+ KLRG1+
Total T_{reg} cells	TCRβ+ CD4+ CD25+
Total CD8+ T cells	TCRβ+ CD8+
Effector CD8+ T cells	TCRβ+ CD8+ CD62L- CD44+
KLRG1+ CD8+ T cells	TCRβ+ CD8+ KLRG1+
Total γδ T cells	TCRδ+
Total NKT cells	TCRβ+ CD161+
Total NK cells	TCRβ- CD161+
KLRG1+ NK cells	TCRβ- CD161+ KLRG1+
Total B cells	CD19+
IgD+ mature B cells	CD19+ IgD+
Monocytes	CD19- Ly6G- CD11b+
Ly6C+ monocytes	CD19- Ly6G- CD11b+ Ly6C+
Ly6C- monocytes	CD19- Ly6G- CD11b+ Ly6C-

Neutrophils	CD19- Ly6G+ Ly6B+
Eosinophils	CD19- Ly6B- Ly6G- SSC^{high} CD11b+
Bone marrow	
Granulocytes	GR+ CD43+
T cells	GR- CD3+
Plasma cells	GR- CD3- CD138+
Myeloid cells	GR- CD3- CD138- CD11b+
Total B cell precursors	GR- CD3- CD138- B220+
Pre-pro B cells (Hardy fraction A)	GR- CD3- CD138- B220+ CD43+ BP1- CD24-
Pro-B cells (Hardy fraction B)	GR- CD3- CD138- B220+ CD43+ BP1- CD24+
Pro-B cells (Hardy fraction C)	GR- CD3- CD138- B220+ CD43+ BP1+ CD24+
Pre-B cells (Hardy fraction D)	GR- CD3- CD138- B220+ CD43- IgD- IgM-
Immature B cells (Hardy fraction E)	GR- CD3- CD138- B220+ CD43- IgD- IgM+
Mature B cells (Hardy fraction F)	GR- CD3- CD138- B220+ CD43- IgD+ IgM+
Ear epidermis	
DETC coverage	
Count of DETC Vγ5+	
Count of atypical CD45+ cells	
Count of DETC Vγ5+ contacting LC	
Count of DETC Vγ5+ not contacting LC	
Count of LC	
Average volume of DETC Vγ5+	
Average volume of atypical CD45+ cells	
Average volume of DETC Vγ5+ contacting LC	
Average volume of DETC Vγ5+ not contacting LC	
Average volume of LC	
Average roundness of DETC Vγ5+	
Average roundness of atypical CD45+ cells	
Average roundness of DETC Vγ5+ contacting LC	
Average roundness of DETC Vγ5+ not contacting LC	
Average roundness of LC	
Average number of branches on DETC Vγ5+	
Average number of branches on DETC Vγ5+ contacting LC	
Average number of branches on DETC Vγ5+ not contacting LC	
Average number of branches on LC	
Average branch length of on DETC Vγ5+	
Average branch length of on DETC Vγ5+ contacting LC	
Average branch length of on DETC Vγ5+ not contacting LC	

Supplementary Table 3: Summary of statistical procedures per assay and readout

Assay	Readouts	Statistical test	Choice of controls	Successfully phenotyped strains/mice
Ear epidermis (2F, 2M)	Number of cells and morphological parameters recorded by 3D confocal analysis and analysed by an automated script using Definiens developer software	Mutant samples were considered phenodeviant when falling into the lower or upper 2.5 percentiles of the wild type distribution of their respective sex. A mutant line was considered phenodeviant when ≥60% of samples across sexes (3/4 or 3/3) fell outside their respective reference range.	all wt data, sex-matched	496 genes 499 strains 2066 ko mice 728 wt mice
Cytotoxic T cell lysis (2F, 2M)	Percentage of target cell lysis recorded relative to a positive control (detergent)	As for ear epidermis. A sample was considered outside the reference range if three consecutive points in the target:effector ratio fell outside the reference range for this ratio.	all wt data, sex-matched	263 genes 265 strains 1130 ko mice 566 wt mice
Blood (7F, 7M)	Frequencies/cell numbers of cell populations recorded by flow cytometry. Frequencies are reported as a percentage of parental population, absolute numbers are calculated using white blood cell counts from haematology data.	As for ear epidermis, but owing to the larger sample size, phenodeviants were also identified within each sex separately.*	all wt data, sex-matched	530 genes 533 strains 7010 ko mice 2652 wt mice
Spleen/ MLN/BM (3F, 3M)	Frequencies of cell populations recorded by flow cytometry.	As for ear epidermis. A mutant line was considered phenodeviant when ≥60% of samples	70 sex matched wt samples that were	Spleen: 517 genes 520 strains 3169 ko mi.

	Frequencies are reported as a percentage of parental population or as percentage of $CD45^+$, live, single cells.	across sexes (6/6, 5/6, 4/6, 3/5, 3/4 or 3/3) fell outside their respective reference range.	closest in time to the mutant sample assessed.	947 wt mice MLN: 508 genes 511 strains 2986 ko mi. 858 wt mice Bone marrow: 479 genes 482 strains 2622 ko mi. 795 wt mice
DSS histology and weight data (2F, 2M or 4F)	A) Histological scoring of gut sections B) Percentage of reduction in body weight compared to the start of the experiment.	As for ear epidermis	sex-matched wt data, 70 individuals closest in starting weight (A) or age (B)	489 genes 492 strains 2001 ko mice 868 wt mice
Salmonella bacterial burden and serum antibodies (4F, 4M)	A) Colony forming units (CFU) of bacteria cultured on LB agar isolated from spleen and liver homogenates B) Titers of antigen-specific antibodies in serum measured by ELISA	Hits were identified by a Mann-Whitney-U test with a p-value cut-off of 0.05 in comparison to concurrent wt controls, combining data from male and female mice. Significant lines were retested with a second cohort. A final call was made on the combined data from both experiments.	concurrent wt controls	516 genes 518 strains 4133 ko mice 1723 wt mice
Influenza weight data: (3F, 3M)	Percentage of reduction in body weight compared to the start of the experiment.	Hits were identified by fitting a robust mixed model (corresponding to two-way Anova) with a p-value cut-off of 0.0001, in comparison to concurrent wt controls, taking into account sex and genotype, using the R package Phenstat[61]. Residuals were assumed	concurrent wt controls	489 genes 490 strains 3033 ko mice 1054 wt mice

		to be normally distributed.		
ANA (3F, 3M)	Scores for ANA positivity assessed by microscopy and analysed using a Python script. Scores from 0 to 1.5 were considered negative; scores of 2- 4 positive.	Hits were identified by Fisher's exact test with a p-value cut-off of 0.01, comparing the frequency of positive samples in mutant and wt	wt animals from the contempor-aneous 3 months' period	518 genes 520 strains 3286 ko mice 1123 wt mice
Trichuris (6F)	Presence or absence of worms in the cecum on day 33 as categorical measure.	Hits were identified by Fisher's exact test with a p-value cut-off of 0.01, comparing the frequency of positive samples in mutant and wt.	all wt animals	287 genes 289 strains 1704 ko mice 431 wt mice
DSS and influenza survival data	Number of mice having to be culled because of excessive weight loss before the end of the experiment	Hits were identified by Fisher's exact test with a p-value cut-off of 0.01, comparing the frequency of mice with above threshold weight loss in a mutant strain with wt population, combining data from both sexes.	all wt animals	as for DSS and influenza above

*Please note that Blood hits are analysed with a mixed model on the IMPC website as the IMPC statistical pipeline was not offering the option of a reference range approach at the time of writing. The number of hits for blood is therefore higher on the IMPC website.

Supplementary Table 4: Alleles of knockout lines included in the study

1700001C02Rik$^{tm1a(EUCOMM)Wtsi}$	*Dpy30*$^{tm1a(KOMP)Wtsi}$	*Pclaf*$^{tm1a\ (EUCOMM)Wtsi}$
1700007K13Rik$^{tm2b(EUCOMM)Wtsi}$	*Duoxa2*$^{tm1b(KOMP)Wtsi}$	*Pdcd2*$^{tm1b(EUCOMM)Wtsi}$
1700011A15Rik$^{tm1a(KOMP)Wtsi}$	*Dusp5*$^{tm1a(KOMP)Wtsi}$	*Pdia4*$^{tm1b\ (EUCOMM)Wtsi}$
1700024P04Rik$^{tm1b(EUCOMM)Wtsi}$	*Dynlrb2*$^{tm1a(KOMP)Wtsi}$	*Pdk3*$^{tm2a(KOMP)Wtsi}$
1700029H14Rik$^{tm2b(KOMP)Wtsi}$	*Eci3*$^{tm1b(EUCOMM)Wtsi}$	*Pdzk1*$^{tm2b(EUCOMM)Wtsi}$
1700034J05Rik$^{tm1a(KOMP)Wtsi}$	*Eif3h*$^{tm1a(EUCOMM)Hmgu}$	*Pepd*$^{tm1a(KOMP)Wtsi}$
1700067K01Rik$^{tm2a(KOMP)Wtsi}$	*Elac2*$^{tm1b(EUCOMM)Wtsi}$	*Pgap2*$^{tm1b(EUCOMM)Wtsi}$
1700112E06Rik$^{tm1e(EUCOMM)Wtsi}$	*Ell2*$^{tm1b(EUCOMM)Wtsi}$	*Pigf*$^{tm1a(KOMP)Wtsi}$
1700123O20Rik$^{tm1a(EUCOMM)Wtsi}$	*Enc1*$^{tm1a(EUCOMM)Wtsi}$	*Pigl*$^{tm1b(KOMP)Wtsi}$
2010300C02Rik$^{tm1b(KOMP)Wtsi}$	*Enthd2*$^{tm1b(KOMP)Wtsi}$	*Pitrm1*$^{tm1a(KOMP)Wtsi}$
2610034B18Rik$^{tm1b(EUCOMM)Wtsi}$	*Erlin2*$^{tm1a(EUCOMM)Wtsi}$	*Pitx1*$^{em1(IMPC)Wtsi}$
3300002A11Rik$^{tm1a(KOMP)Wtsi}$	*Evi5*$^{tm1a(KOMP)Wtsi}$	*Pla2g6*$^{tm1a(EUCOMM)Wtsi}$
3830406C13Rik$^{tm1b(KOMP)Wtsi}$	*Exoc3l2*$^{tm1b(KOMP)Wtsi}$	*Pld3*$^{tm1e(EUCOMM)Wtsi}$
4930404H24Rik$^{tm1a(KOMP)Wtsi}$	*Exosc9*$^{tm1b(EUCOMM)Wtsi}$	*Plet1*$^{em1(IMPC)Wtsi}$
4930590J08Rik$^{tm1a(EUCOMM)Wtsi}$	*Fads3*$^{tm1b(EUCOMM)Wtsi}$	*Plscr2*$^{tm1b(KOMP)Wtsi}$
4931429L15Rik$^{tm1a(EUCOMM)Wtsi}$	*Fam122c*$^{tm1b(EUCOMM)Wtsi}$	*Plxnb3*$^{tm1a(KOMP)Wtsi}$
4932431P20Rik$^{em1(IMPC)Wtsi}$	*Fam160a1*$^{tm1b(EUCOMM)Wtsi}$	*Polb*$^{tm1a(KOMP)Wtsi}$
4933402N03Rik$^{tm2a(KOMP)Wtsi}$	*Fam163a*$^{tm2b(KOMP)Wtsi}$	*Pold3*$^{tm1b(EUCOMM)Wtsi}$
4933434E20Rik$^{tm1a(EUCOMM)Wtsi}$	*Fam212b*$^{tm1a(KOMP)Wtsi}$	*Polr3f*$^{tm1a(EUCOMM)Wtsi}$
5730559C18Rik$^{tm2a(EUCOMM)Wtsi}$	*Fam47e*$^{tm1a(EUCOMM)Wtsi}$	*Polr3g*$^{tm1a(EUCOMM)Wtsi}$
9330182L06Rik$^{tm1a(KOMP)Wtsi}$	*Fam69a*$^{tm1a(EUCOMM)Wtsi}$	*Ppil3*$^{tm1b(EUCOMM)Wtsi}$
A430005L14Rik$^{tm1a(KOMP)Wtsi}$	*Fam71b*$^{tm1a(KOMP)Wtsi}$	*Prame*$^{tm1a(KOMP)Wtsi}$
A430078G23Rik$^{tm1a(KOMP)Wtsi}$	*Fam92a*$^{tm1b(KOMP)Wtsi}$	*Prkab1*$^{tm1b(KOMP)Wtsi}$
A730017C20Rik$^{tm1b(KOMP)Wtsi}$	*Fbf1*$^{tm1a(EUCOMM)Wtsi}$	*Prrc2b*$^{tm1a(EUCOMM)Wtsi}$
Abhd14a$^{tm2a(EUCOMM)Wtsi}$	*Fbxo33*$^{tm1b(EUCOMM)Wtsi}$	*Prrg2*$^{tm1b(EUCOMM)Wtsi}$
Abhd17a$^{tm1a(KOMP)Wtsi}$	*Fbxw26*$^{tm1b(KOMP)Wtsi}$	*Prrt2*$^{tm1a(KOMP)Wtsi}$
Acbd5$^{tm1b(EUCOMM)Wtsi}$	*Fdft1*$^{tm1a(KOMP)Wtsi}$	*Prss52*$^{tm2a(KOMP)Wtsi}$
Acer1$^{tm1a(EUCOMM)Wtsi}$	*Fkbp3*$^{tm2a(EUCOMM)Wtsi}$	*Psph*$^{tm1a(EUCOMM)Hmgu}$
Actl10$^{tm1a(EUCOMM)Wtsi}$	*Fnip2*$^{tm1a(KOMP)Wtsi}$	*Pth1r*$^{tm1a(EUCOMM)Hmgu}$
Adal$^{tm1a(EUCOMM)Wtsi}$	*Fryl*$^{tm1b(KOMP)Wtsi}$	*Pth*$^{tm1a(EUCOMM)Wtsi}$
Adamts19$^{tm4a(EUCOMM)Wtsi}$	*Fxyd3*$^{tm1a(KOMP)Wtsi}$	*Ptprd*$^{tm2a(KOMP)Wtsi}$

Adamts3$^{tm1b(KOMP)Wtsi}$	*Fzd6*$^{tm2a(EUCOMM)Wtsi}$	*Pwp1*$^{tm1a(EUCOMM)Wtsi}$
Adap1$^{tm1a(EUCOMM)Wtsi}$	*Galnt18*$^{tm1b(KOMP)Wtsi}$	*Pycr2*$^{tm1a(EUCOMM)Wtsi}$
Adcy2$^{tm1a(KOMP)Wtsi}$	*Galntl5*$^{tm1b(KOMP)Wtsi}$	*Rab17*$^{tm1a(KOMP)Wtsi}$
Adcy9$^{tm1b(EUCOMM)Wtsi}$	*Gbp5*$^{em1(IMPC)Wtsi}$	*Rab21*$^{tm1b(KOMP)Wtsi}$
Adgrd1$^{tm1b(EUCOMM)Wtsi}$	*Gda*$^{tm1a(KOMP)Wtsi}$	*Raph1*$^{tm1b(EUCOMM)Wtsi}$
Adpgk$^{tm2a(EUCOMM)Wtsi}$	*Gdpd2*$^{tm1a(KOMP)Wtsi}$	*Rbak*$^{tm1b(KOMP)Wtsi}$
Agap1$^{tm1a(EUCOMM)Wtsi}$	*Gimap6*$^{tm1a(KOMP)Wtsi}$	*Rbm14*$^{tm1a(KOMP)Wtsi}$
Aicda$^{tm1b(EUCOMM)Hmgu}$	*Glo1*$^{tm1a(KOMP)Wtsi}$	*Rbm33*$^{tm1b(EUCOMM)Wtsi}$
Aldh1b1$^{tm2a(EUCOMM)Wtsi}$	*Glyatl3*$^{em1(IMPC)Wtsi}$	*Rbm47*$^{tm1a(EUCOMM)Wtsi}$
Aldh3b1$^{tm1b(EUCOMM)Wtsi}$	*Gm12253*$^{tm1a(KOMP)Wtsi}$	*Rbmx*$^{tm2b(KOMP)Wtsi}$
Alox12e$^{tm1b(EUCOMM)Wtsi}$	*Gm13119*$^{tm2b(KOMP)Wtsi}$	*Reg3d*$^{tm1b(EUCOMM)Wtsi}$
Alpk1$^{em1(IMPC)Wtsi}$	*Gm13125*$^{tm1b(KOMP)Wtsi}$	*Repin1*$^{tm1a(EUCOMM)Wtsi}$
Amz2$^{tm1e(KOMP)Wtsi}$	*Gm16432*$^{tm1b(KOMP)Wtsi}$	*Rida*$^{tm1a(KOMP)Wtsi}$
Ankrd13d$^{tm1a(KOMP)Wtsi}$	*Gm16515*$^{tm1b(EUCOMM)Wtsi}$	*Rimbp2*$^{em1(IMPC)Wtsi}$
Ankrd6$^{tm1b(KOMP)Wtsi}$	*Gm5544*$^{tm1a(KOMP)Wtsi}$	*Rnasek*$^{tm1b(EUCOMM)Wtsi}$
Ankrd9$^{tm1(KOMP)Wtsi}$	*Gmds*$^{tm1a(KOMP)Wtsi}$	*Rnf10*$^{tm1b(KOMP)Wtsi}$
Anks6$^{tm1b(KOMP)Wtsi}$	*Gmnc*$^{tm1b(KOMP)Wtsi}$	*Rnf125*$^{tm1a\ (EUCOMM)Wtsi}$
Ano10$^{tm1a(EUCOMM)Wtsi}$	*Gnb3*$^{tm1b(EUCOMM)Wtsi}$	*Rnf138*$^{tm1b(EUCOMM)Hmgu}$
Anxa9$^{tm1b(EUCOMM)Wtsi}$	*Gpbp1l1*$^{tm1a(EUCOMM)Wtsi}$	*Rnf157*$^{tm1b(EUCOMM)Wtsi}$
Ap2a2$^{em1(IMPC)Wtsi}$	*Gpr152*$^{tm1b(EUCOMM)Wtsi}$	*Rpia*$^{tm1a(KOMP)Wtsi}$
Ap4e1$^{tm1b(KOMP)Wtsi}$	*Gpr35*$^{tm1b(EUCOMM)Hmgu}$	*Rspo4*$^{tm1a(KOMP)Wtsi}$
Ap4m1$^{tm1b(EUCOMM)Wtsi}$	*Grb7*$^{tm1b(EUCOMM)Wtsi}$	*Rundc1*$^{tm1b(EUCOMM)Wtsi}$
Apip$^{tm1b(EUCOMM)Wtsi}$	*Grsf1*$^{tm1b(EUCOMM)Wtsi}$	*Rwdd1*$^{tm1b(KOMP)Wtsi}$
Apol9b$^{tm2a(KOMP)Wtsi}$	*Gsdme*$^{tm1b(KOMP)Wtsi}$	*Sap130*$^{tm1a(KOMP)Mbp}$
Apoo$^{tm1b(KOMP)Wtsi}$	*Gsto2*$^{tm2a(KOMP)Wtsi}$	*Scaf11*$^{em1(IMPC)Wtsi}$
Arap2$^{tm2b(EUCOMM)Wtsi}$	*Gt(ROSA)26Sor*$^{ROSA26\_Dre\_C03}$	*Selenow*$^{tm1b(EUCOMM)Wtsi}$
Arhgap17$^{tm1b(EUCOMM)Wtsi}$	*Gtf2a1*$^{tm1a(KOMP)Wtsi}$	*Sept10*$^{tm1a(KOMP)Wtsi}$
Arhgap22$^{tm1a(KOMP)Wtsi}$	*Gtf2h2*$^{tm1a(EUCOMM)Wtsi}$	*Serinc3*$^{tm1a(KOMP)Wtsi}$
Arhgef1$^{tm1a(EUCOMM)Wtsi}$	*H13*$^{tm1b(KOMP)Wtsi}$	*Setd5*$^{tm1a(EUCOMM)Wtsi}$
Arid1b$^{tm1b(EUCOMM)Hmgu}$	*Hao2*$^{em1(IMPC)Wtsi}$	*Sfxn3*$^{tm1b(KOMP)Wtsi}$
Armc7$^{tm1.1(KOMP)Wtsi}$	*Hbs1l*$^{tm1a(KOMP)Wtsi}$	*Sgms1*$^{tm1a(EUCOMM)Wtsi}$
Armh3$^{tm1a(EUCOMM)Wtsi}$	*Hecw2*$^{tm1a(EUCOMM)Wtsi}$	*Sgsm1*$^{tm1b(EUCOMM)Wtsi}$
Arpc1b$^{tm1a(EUCOMM)Wtsi}$	*Herc1*$^{em1\text{-}3(IMPC)Wtsi}$**	*Sh3bgrl3*$^{tm2b(EUCOMM)Wtsi}$

Arrdc5$^{tm1b(EUCOMM)Wtsi}$	*Hibadh*$^{tm1b(EUCOMM)Wtsi}$	*Sh3bp4*$^{tm1a(EUCOMM)Wtsi}$
Art4$^{tm1a(KOMP)Wtsi}$	*Hmgxb3*$^{tm1a(EUCOMM)Wtsi}$	*Sh3pxd2a*$^{tm1b(EUCOMM)Wtsi}$
Atad3a$^{tm1a(KOMP)Wtsi}$	*Homez*$^{tm1e(KOMP)Wtsi}$	*Sik3*$^{tm1a(EUCOMM)Hmgu}$
Atg16l2$^{tm1a(EUCOMM)Wtsi}$	*Hpf1*$^{em1(IMPC)Wtsi}$	*Slamf9*$^{tm1b(EUCOMM)Wtsi}$
Atp11a$^{tm1a(KOMP)Wtsi}$	*Hrnr*$^{em1(IMPC)Wtsi}$	*Slc16a4*$^{tm2e(EUCOMM)Wtsi}$
Atp5e$^{tm1b(EUCOMM)Wtsi}$	*Ifi27*$^{tm1b(EUCOMM)Wtsi}$	*Slc25a20*$^{tm1a(EUCOMM)Wtsi}$
Atp5f1$^{tm1b(EUCOMM)Wtsi}$	*Ifitm6*$^{tm1b(EUCOMM)Wtsi}$	*Slc25a28*$^{tm1b(EUCOMM)Wtsi}$
Atp8b2$^{tm1a(KOMP)Wtsi}$	*Ifnar1*$^{tm2a(EUCOMM)Wtsi}$	*Slc38a2*$^{tm1a(KOMP)Wtsi}$
Atxn10$^{tm1b(KOMP)Wtsi}$	*Ifnlr1*$^{tm1a(EUCOMM)Wtsi}$	*Slc5a7*$^{tm1a(KOMP)Wtsi}$
Atxn3$^{tm1a(KOMP)Wtsi}$	*Ift140*$^{tm1a(KOMP)Wtsi}$	*Slc9a3r2*$^{tm2a(EUCOMM)Hmgu}$
Bach2$^{tm1a(EUCOMM)Wtsi}$	*Il1r2*$^{tm1a(EUCOMM)Wtsi}$	*Slitrk4*$^{tm1b(KOMP)Wtsi}$
Bai1$^{tm2a(EUCOMM)Wtsi}$	*Il23r*$^{tm2a(EUCOMM)Wtsi}$	*Slu7*$^{tm1a(KOMP)Wtsi}$
Bap1$^{tm1a(EUCOMM)Hmgu}$	*Il27*$^{tm1b(EUCOMM)Wtsi}$	*Slx4ip*$^{tm1a(EUCOMM)Wtsi}$
Barhl1$^{tm1(EGFP\_CreERT2)Wtsi}$	*Irak1*$^{tm1b(EUCOMM)Hmgu}$	*Smg9*$^{tm1b(EUCOMM)Wtsi}$
Bivm$^{tm1b(KOMP)Wtsi}$	*Irf5*$^{tm1e(EUCOMM)Wtsi}$	*Smpd4*$^{tm2b(KOMP)Wtsi}$
Bnip2$^{tm1b(EUCOMM)Wtsi}$	*Izumo1r*$^{tm2a(KOMP)Wtsi}$	*Snx31*$^{tm1a(KOMP)Wtsi}$
Bpgm$^{tm1a(KOMP)Wtsi}$	*Josd1*$^{em1(IMPC)Wtsi}$	*Snx8*$^{tm2a(EUCOMM)Hmgu}$
Bpifb1$^{tm1e(KOMP)Wtsi}$	*Kat2b*$^{em1(IMPC)Wtsi}$	*Spata25*$^{tm1(KOMP)Wtsi}$
Bpifb5$^{tm2a(KOMP)Wtsi}$	*Kcnh4*$^{tm1b(KOMP)Wtsi}$	*Spink14*$^{tm1e(KOMP)Wtsi}$
Brd2$^{em1(IMPC)Wtsi}$	*Kera*$^{em1(IMPC)Wtsi}$	*Sqle*$^{tm1a(EUCOMM)Wtsi}$
Camkmt$^{tm1b(EUCOMM)Wtsi}$	*Kif13b*$^{tm1b(EUCOMM)Wtsi}$	*Srsf7*$^{tm1a(EUCOMM)Wtsi}$
Camsap3$^{tm1a(EUCOMM)Wtsi}$	*Kif18b*$^{tm1a(EUCOMM)Wtsi}$	*Ssr2*$^{tm1b(EUCOMM)Wtsi}$
Capn11$^{tm1b(EUCOMM)Wtsi}$	*Kif1bp*$^{tm1a(KOMP)Wtsi}$	*Stard8*$^{tm1b(EUCOMM)Wtsi}$
Capza2$^{tm1b(KOMP)Wtsi}$	*Kif24*$^{tm1b(KOMP)Wtsi}$	*Stau2*$^{tm1a(EUCOMM)Wtsi}$
Card9$^{tm1a(EUCOMM)Hmgu}$	*Kif3b*$^{tm1b(EUCOMM)Wtsi}$	*Stxbp4*$^{tm1a(EUCOMM)Wtsi}$
Casc4$^{tm2b(EUCOMM)Wtsi}$	*Klc2*$^{tm1e(EUCOMM)Wtsi}$	*Sult1c1*$^{tm1b(KOMP)Wtsi}$
Catip$^{tm1b(KOMP)Wtsi}$	*Klf17*$^{tm1b(KOMP)Wtsi}$	*Supt3*$^{tm1a(EUCOMM)Hmgu}$
Cbr2$^{tm1b(EUCOMM)Hmgu}$	*Klhl18*$^{tm1a(KOMP)Wtsi}$	*Supt5*$^{tm2a(KOMP)Wtsi}$
Ccdc127$^{tm1b(EUCOMM)Wtsi}$	*Klhl30*$^{tm1a(KOMP)Wtsi}$	*Tbc1d22a*$^{tm1b(KOMP)Wtsi}$
Ccdc159$^{tm1a(KOMP)Wtsi}$	*Klk5*$^{tm2a(KOMP)Wtsi}$	*Tceal5*$^{tm1b(KOMP)Wtsi}$
Ccdc18$^{tm1a(EUCOMM)Wtsi}$	*Klk6*$^{em1(IMPC)Wtsi}$	*Tcf7l2*$^{tm1a(EUCOMM)Wtsi}$
Ccdc69$^{tm1b(KOMP)Wtsi}$	*Klrb1a*$^{tm1a(KOMP)Wtsi}$	*Tchp*$^{tm1a(EUCOMM)Wtsi}$
Ccdc6$^{em1(IMPC)Wtsi}$	*Krt31*$^{tm1e(KOMP)Wtsi}$	*Tcp11*$^{tm1a(EUCOMM)Wtsi}$

Cdkn2aipnl$^{tm1b(KOMP)Wtsi}$	*Krt7*$^{tm1b(KOMP)Wtsi}$	*Tctex1d2*$^{tm1e(EUCOMM)Wtsi}$
Celf4$^{tm1a(EUCOMM)Wtsi}$	*Krt83*$^{tm1b(KOMP)Wtsi}$	*Tead3*$^{tm1a(EUCOMM)Wtsi}$
Cenpl$^{tm1b(EUCOMM)Wtsi}$	*L3mbtl2*$^{tm2a(EUCOMM)Wtsi}$	*Tent5c*$^{tm1b(KOMP)Wtsi}$
Cep250$^{tm1a(EUCOMM)Wtsi}$	*Lars*$^{tm1b(KOMP)Wtsi}$	*Tet1*$^{tm1a(KOMP)Wtsi}$
Cfap53$^{em1(IMPC)Wtsi}$	*Lce1m*$^{tm1b(EUCOMM)Wtsi}$	*Tex38*$^{tm1a(KOMP)Wtsi}$
Cfap61$^{tm2a(EUCOMM)Wtsi}$	*Lce3c*$^{tm2a(EUCOMM)Wtsi}$	*Tgfb1i1*$^{tm1b(KOMP)Wtsi}$
Cgrrf1$^{tm1b(KOMP)Wtsi}$****	*Ldhb*$^{tm1b(KOMP)Wtsi}$	*Tgm6*$^{tm1a(KOMP)Wtsi}$
Chd9$^{tm1a(EUCOMM)Wtsi}$	*Ldlrad4*$^{tm1b(EUCOMM)Wtsi}$	*Timeless*$^{tm1b(EUCOMM)Hmgu}$
Chil4$^{tm1b(EUCOMM)Hmgu}$	*Leo1*$^{tm1a(EUCOMM)Wtsi}$	*Timmdc1*$^{tm1b(EUCOMM)Wtsi}$
Chmp6$^{tm1b(KOMP)Wtsi}$	*Leprot*$^{tm2b(KOMP)Wtsi}$	*Tmc3*$^{tm2b(KOMP)Wtsi}$
Chst11$^{tm1a(KOMP)Wtsi}$	*Lmna*^{G609G}***	*Tmem110*$^{tm2b(KOMP)Wtsi}$
Chtop$^{tm1a(EUCOMM)Wtsi}$	*Lonrf3*$^{tm1b(KOMP)Wtsi}$	*Tmem126a*$^{tm1a(EUCOMM)Wtsi}$
Cir1$^{tm3a(KOMP)Wtsi}$	*Lpxn*$^{tm1b(EUCOMM)Hmgu}$	*Tmem127*$^{tm1(KOMP)Wtsi}$
Clpp$^{tm1a(EUCOMM)Wtsi}$	*Lrmp*$^{tm1b(EUCOMM)Wtsi}$	*Tmem18*$^{tm1b(EUCOMM)Wtsi}$
(Cluster5N1$^{)(tm1)Brd}$*	*Lrrc23*$^{tm1a(EUCOMM)Wtsi}$	*Tmem241*$^{tm1b(EUCOMM)Wtsi}$
(ClusterXN1)$^{tm1(Brd)}$*	*Lrrc71*$^{tm1a(KOMP)Wtsi}$	*Tmem254b*$^{tm1a(KOMP)Wtsi}$
Cmbl$^{tm1b(KOMP)Wtsi}$	*Lrrc8d*$^{tm1a(EUCOMM)Wtsi}$	*Tmem30a*$^{tm1a(KOMP)Wtsi}$
Cmtm5$^{tm1a(KOMP)Wtsi}$	*Lyplal1*$^{tm1a(KOMP)Wtsi}$	*Tmem37*$^{tm1a(EUCOMM)Wtsi}$
Cnbd1$^{tm1b(EUCOMM)Wtsi}$	*Lyrm9*$^{tm1a(KOMP)Mbp}$	*Tmem42*$^{tm1b(KOMP)Wtsi}$
Cnot4$^{tm1b(EUCOMM)Wtsi}$	*Macrod1*$^{em1(IMPC)Wtsi}$	*Tomm20l*$^{tm1b(EUCOMM)Wtsi}$
Cog6$^{tm1a(EUCOMM)Wtsi}$	*Mamstr*$^{tm1b(EUCOMM)Wtsi}$	*Traf2*$^{tm1a(EUCOMM)Wtsi}$
Col24a1$^{tm1b(EUCOMM)Wtsi}$	*Mast2*$^{tm1a(KOMP)Wtsi}$	*Traf6*$^{tm2a(EUCOMM)Wtsi}$
Col4a3bp$^{tm1a(KOMP)Wtsi}$	*Mau2*$^{tm1b(KOMP)Wtsi}$	*Trappc10*$^{tm1b(KOMP)Wtsi}$
Coro6$^{tm1e(EUCOMM)Wtsi}$	*Mbd1*$^{em1(IMPC)Wtsi}$	*Trappc9*$^{tm1a(EUCOMM)Wtsi}$
Cpgi81$^{tm1.1(NCC)WCS}$*	*Mbl2*$^{em1(IMPC)Wtsi}$	*Trem1*$^{tm1(KOMP)Vlcg}$
Cpsf3$^{tm1b(EUCOMM)Wtsi}$	*Mcf2l*$^{tm1a(EUCOMM)Hmgu}$	*Trim21*$^{em1(IMPC)Wtsi}$
Cpt2$^{tm1b(KOMP)Wtsi}$	*Med22*$^{tm1a(EUCOMM)Wtsi}$	*Trim25*$^{tm2b(EUCOMM)Hmgu}$
Crim1$^{em1(IMPC)Wtsi}$	*Med23*$^{em1(IMPC)Wtsi}$	*Trim56*$^{tm1a(EUCOMM)Wtsi}$
Crlf3$^{em1(IMPC)Wtsi}$	*Medag*$^{tm2b(KOMP)Wtsi}$	*Trim65*$^{tm1b(KOMP)Wtsi}$
Crls1$^{tm1a(EUCOMM)Wtsi}$	*Metrnl*$^{tm1b(KOMP)Wtsi}$	*Trmt2a*$^{tm2b(EUCOMM)Wtsi}$
Csmd1$^{em1(IMPC)Wtsi}$	*Mettl24*$^{tm1a(KOMP)Wtsi}$	*Trp53rkb*$^{tm1a(EUCOMM)Wtsi}$
Csnk1g3$^{tm1a(EUCOMM)Wtsi}$	*Mgat4c*$^{tm1a(EUCOMM)Wtsi}$	*Trub2*$^{tm2a(EUCOMM)Wtsi}$
Ctr9$^{tm1b(EUCOMM)Wtsi}$	*Mir32*$^{(tm1)Brd}$	*Tuba3a*$^{tm1b(KOMP)Wtsi}$

Cttnbp2$^{tm1b(KOMP)Wtsi}$	*Mir96*$^{tm2.2(IMPC)Wtsi}$	*Tuft1*$^{tm1a(KOMP)Wtsi}$
Cutal$^{tm1a(EUCOMM)Wtsi}$	*Mir122*$^{(tm1)Brd}$	*Ube2d1*$^{tm3e(EUCOMM)Wtsi}$
Cxcr1$^{tm1a\ (EUCOMM)Wtsi}$	*Mir210*$^{(tm1)Brd}$	*Ubxn10*$^{tm1b(EUCOMM)Wtsi}$
Cxcr2$^{tm1a(EUCOMM)Wtsi}$	*Mir211*$^{(tm1)Brd}$	*Uevld*$^{tm1a(EUCOMM)Wtsi}$
Cyp2b13$^{tm1b(KOMP)Wtsi}$	*Mir342*$^{(tm1)Brd}$	*Umodl1*$^{tm1a(KOMP)Wtsi}$
Cyp2r1$^{tm1b(EUCOMM)Wtsi}$	*Mkrn2*$^{tm1b(KOMP)Wtsi/em1(IMPC)Wtsi}$**	*Uri1*$^{tm1a(EUCOMM)Wtsi}$
D630023F18Rik$^{tm1b(KOMP)Wtsi}$	*Mospd1*$^{tm1a(KOMP)Wtsi}$	*Usp11*$^{tm1(KOMP)Wtsi}$
D6Wsu163e$^{tm1b(EUCOMM)Wtsi}$	*Mpg*$^{tm1a(EUCOMM)Wtsi}$	*Usp20*$^{tm1a(EUCOMM)Hmgu}$
D7Ertd443e$^{tm2a(KOMP)Wtsi}$	*Mrm1*$^{tm2a(EUCOMM)Wtsi}$	*Usp30*$^{tm2b(EUCOMM)Hmgu}$
D930028M14Rik$^{tm1a(EUCOMM)Wtsi}$	*Mroh4*$^{tm1b(KOMP)Wtsi}$	*Usp37*$^{em1(IMPC)Wtsi}$
Dact3$^{tm1b(KOMP)Wtsi}$	*Mroh9*$^{tm1a(EUCOMM)Wtsi}$	*Usp5*$^{tm1a(EUCOMM)Hmgu}$
Daf2$^{tm1a(KOMP)Wtsi}$	*Mrps21*$^{tm1e(EUCOMM)Wtsi}$	*Vamp3*$^{tm2b(EUCOMM)Wtsi}$
Dap$^{tm1a(KOMP)Mbp}$	*Mrps5*$^{tm1b(EUCOMM)Wtsi}$	*Vps13a*$^{tm1b(EUCOMM)Wtsi}$
Dapk2$^{tm1b(EUCOMM)Wtsi}$	*Mybphl*$^{tm1b(KOMP)Wtsi}$	*Vps33b*$^{tm1a(EUCOMM)Wtsi}$
Dbn1$^{tm1b(KOMP)Wtsi}$	*Myh7b*$^{tm1a(KOMP)Wtsi}$	*Vps51*$^{tm1a(KOMP)Wtsi}$
Dcaf11$^{tm1a(KOMP)Wtsi}$	*Myo10*$^{tm2(KOMP)Wtsi}$	*Vps72*$^{tm1a(EUCOMM)Wtsi}$
Dcbld2$^{tm1a(KOMP)Wtsi}$	*Myo9a*$^{tm1b(EUCOMM)Wtsi}$	*Vwa3a*$^{tm1b(KOMP)Wtsi}$
Dcdc2b$^{tm1b(KOMP)Wtsi}$	*N6amt2*$^{tm1a(EUCOMM)Wtsi}$	*Wac*$^{tm1b(EUCOMM)Wtsi}$
Dclk1$^{tm1a(EUCOMM)Wtsi}$	*Nacc2*$^{tm2b(EUCOMM)Wtsi}$	*Washc2*$^{tm2b(KOMP)Wtsi}$
Dcn$^{em1(IMPC)Wtsi}$	*Nadk2*$^{tm1b(EUCOMM)Wtsi}$	*Wdr89*$^{tm1a(KOMP)Wtsi}$
Dctn4$^{em1(IMPC)Wtsi}$	*Nat10*$^{tm1a(KOMP)Wtsi}$	*Wdtc1*$^{tm1a(KOMP)Wtsi}$
Ddah1$^{tm2a(EUCOMM)Wtsi}$	*Ncf2*$^{tm1a(EUCOMM)Wtsi}$	*Wnt16*$^{tm2b(EUCOMM)Wtsi}$
Ddx42$^{tm1b(EUCOMM)Wtsi}$	*Ndufb8*$^{tm1a(EUCOMM)Wtsi}$	*Wrap53*$^{tm1b(EUCOMM)Wtsi}$
Ddx51$^{tm1a(KOMP)Wtsi}$	*Nebl*$^{tm1b(EUCOMM)Wtsi}$	*Xkrx*$^{tm1b(EUCOMM)Wtsi}$
Defb14$^{tm1b(KOMP)Wtsi}$	*Nek3*$^{tm1b(EUCOMM)Wtsi}$	*Xpnpep1*$^{tm1a(KOMP)Wtsi}$
Defb22$^{tm1a(KOMP)Wtsi}$	*Nek9*$^{tm1a(EUCOMM)Wtsi}$	*Xxylt1*$^{tm1a(EUCOMM)Hmgu}$
Defb30$^{tm2b(KOMP)Wtsi}$	*Nelfe*$^{tm1a(EUCOMM)Wtsi}$	*Ydjc*$^{tm1(KOMP)Wtsi}$
Dennd1b$^{tm1a(EUCOMM)Hmgu}$	*Nfkbil1*$^{tm1a(KOMP)Wtsi}$	*Yipf7*$^{tm1e(KOMP)Wtsi}$
Dennd1c$^{tm1b(EUCOMM)Wtsi}$	*Nhlrc2*$^{tm1a(KOMP)Wtsi}$	*Ypel4*$^{tm1a(EUCOMM)Wtsi}$
Dennd4c$^{tm1b(EUCOMM)Wtsi}$	*Nipsnap3a*$^{tm1b(KOMP)Wtsi}$	*Zbed5*$^{tm1b(EUCOMM)Wtsi}$
Denr$^{tm1b(KOMP)Wtsi}$	*Nme4*$^{tm1a(EUCOMM)Wtsi}$	*Zfp182*$^{tm1b(KOMP)Wtsi}$
Dffb$^{em1(IMPC)Wtsi}$	*Nmrk1*$^{tm1a(KOMP)Wtsi}$	*Zfp239*$^{tm1b(KOMP)Wtsi}$
Dhodh$^{tm1b(EUCOMM)Wtsi}$	*Npat*$^{tm1b(EUCOMM)Wtsi}$	*Zfp266*$^{tm1b(EUCOMM)Wtsi}$

Dhps$^{tm2a(EUCOMM)Wtsi}$	*Nrbp1*$^{tm3b(EUCOMM)Wtsi}$	*Zfp287*$^{tm1b(EUCOMM)Wtsi}$
Dhx33$^{tm1b(KOMP)Wtsi}$	*Nrde2*$^{tm2a(KOMP)Wtsi}$	*Zfp341*$^{tm1a(KOMP)Wtsi}$
Dhx35$^{tm1b(EUCOMM)Wtsi}$	*Nudt12*$^{tm1a(KOMP)Wtsi}$	*Zfp365*$^{tm1a(KOMP)Wtsi}$
Dip2a$^{tm2b(KOMP)Wtsi}$	*Nup85*$^{tm1a(KOMP)Wtsi}$	*Zfp408*$^{tm1b(EUCOMM)Wtsi}$
Dlg3$^{tm1a(EUCOMM)Wtsi}$	*Nutm2*$^{tm2b(EUCOMM)Wtsi}$	*Zfp616*$^{tm1b(KOMP)Wtsi}$
Dlg4$^{tm1e(EUCOMM)Wtsi}$	*Nxn*$^{tm1b(EUCOMM)Wtsi}$	*Zfp658*$^{tm1b(EUCOMM)Wtsi}$
Dlk1$^{em1(IMPC)Wtsi}$	*Oaf*$^{tm1a(EUCOMM)Wtsi}$	*Zfp719*$^{tm1a(EUCOMM)Wtsi}$
Dmgdh$^{tm1a(KOMP)Wtsi}$	*Oog2*$^{tm1a(EUCOMM)Wtsi}$	*Zfp719*$^{tm1b(EUCOMM)Wtsi}$
Dnah17$^{tm1e(KOMP)Wtsi}$	*Orc1*$^{tm1a(KOMP)Wtsi}$	*Zfp763*$^{em1(IMPC)Wtsi}$
Dnajc8$^{tm1b(KOMP)Wtsi}$	*Os9*$^{tm1a(EUCOMM)Wtsi}$	*Zfp791*$^{tm1a(KOMP)Wtsi}$
Dnase1l2$^{tm1.1(KOMP)Wtsi}$	*Osbpl3*$^{tm1a(EUCOMM)Wtsi}$	*Zfp84*$^{tm1b(KOMP)Wtsi}$
Dnmt3a$^{tm1a(KOMP)Wtsi}$	*Otud7b*$^{tm1b(EUCOMM)Wtsi}$	*Zfp879*$^{tm2b(KOMP)Wtsi}$
Dnpep$^{tm1e(EUCOMM)Wtsi}$	*Pam16*$^{tm1b(EUCOMM)Wtsi}$	*Zfyve28*$^{tm1b(EUCOMM)Wtsi}$
Dph6$^{tm1a(KOMP)Wtsi}$	*Pced1a*$^{tm1b(EUCOMM)Wtsi}$	*Zranb1*$^{tm1a(EUCOMM)Hmgu}$
Dpm1$^{tm1b(KOMP)Wtsi}$		

* Knockouts of multi-gene or regulatory regions:

Cluster 5N1: mmu-mir-25 (ENSMUSG00000065394), mmu-mir-93 (ENSMUSG00000065527), mmu-mir-106b (ENSMUSG00000065514)

ClusterXN1: ENSMUSG00000070106, ENSMUSG00000065613 ENSMUSG00000065473, ENSMUSG00000076041 ENSMUSG00000077111, ENSMUSG00000065456

Cpgi81: CpG island 81, Chr1:23255875-23257106 bp

** More than one mouse line has been phenotyped for these genes.

*** The Lmna allele is not an IMPC allele and has been described previously[62].

**** The Cgrrf1 ko strain has a mixed C57BL/6N; C57BL/6NTac background.

Supplementary Table 5: Key resources

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies		
CD3ε Functional grade purified, clone eBio500A2	eBioscience	16-0033-86; RRID: AB_842782
CD3ε BV421, clone 145-2C11	BD Biosciences	562600
CD3ε BV785, clone 145-2C11	BioLegend UK Ltd	100232
CD4 PE, clone RM4-5	BioLegend UK Ltd	00511; RRID: AB_312714
CD4 BV510, clone RM4-5	BioLegend UK Ltd	100553 RRID:AB_2561388
CD4 BV786, clone RM4-5	BD Biosciences	563331
CD5 APC, clone 53-7.3	BD Biosciences	550035
CD5 BV510, clone 53-7.3	BD Biosciences	563069
CD8a APC, clone 53-6.7	BioLegend UK Ltd	100712; RRID: AB_312750
CD8α AF700, clone 53-6.7	BD Biosciences	557959
CD8α APC-H7, clone 53-6.7	BD Biosciences	560182 RRID:AB_1645237
CD11b BV510, clone M1/70	BioLegend UK Ltd	101245
CD11b PE-Cy7, clone M1/70	BioLegend UK Ltd	101216 RRID:AB_312799
CD11c BV786, clone HL3	BD Biosciences	563735
CD19 BV421, clone ID3	BD Biosciences	562701
CD19 PE-CF594, clone ID3	BD Biosciences	562291 RRID:AB_11154223
CD19 PECY7, clone ID3	BD Biosciences	552854
CD21/35 FITC, clone 7G6	BD Biosciences	553818
CD21/35 PE, clone 7G6	BD Biosciences	552957
CD23 BV421, clone B3B4	BD Biosciences	562929
CD24 APC, clone M1/69	BD Biosciences	562349
CD25 APC, clone PC61	BD Biosciences	557192
CD25 PE, clone PC61	BioLegend UK Ltd	102008 RRID:AB_312857
CD28 Functional grade purified, clone 37.51	eBioscience	16-0281-86;RRID: AB_468923
CD43 PerCP-Cy5.5	BioLegend UK Ltd	121224
CD44 FITC, clone 1B11	BD Biosciences	553133
CD44 FITC, clone IM7	BD Biosciences	561859 RRID:AB_10894581
CD45 Alexa 700, clone 30-F11	BioLegend UK Ltd	103128 RRID:AB_493715
CD45 e450, clone 30-F11	eBioscience	48-0451-82
CD45 eVolve™ 605 (Qdot), clone 30-F11	eBioscience	83-0451-42
CD45 eFluor450, clone 30-F11	eBioscience	48-0451-82
CD45R (B220) PeCY7, clone RA3-6B2	BioLegend UK Ltd	103222

CD45R (B220) AF700, clone RA3-6B2	BD Biosciences	557957
CD62L PE-CF594, clone MEL-14	BD Biosciences	562404 RRID:AB_11154046
CD62L PerCP Cy5.5, clone MEL-14	BD Biosciences	560513
CD86 PECY7, clone GL1	BD Biosciences	560582
CD95 PECY7, clone Jo2	BD Biosciences	557653
CD103 PE, M290	BD Biosciences	557495
CD115 APC, clone AF598	BioLegend UK Ltd	135510 RRID:AB_2085221
CD138 BV650, clone 281-2	BioLegend UK Ltd	142517
CD161 (NK1.1) BV421, clone PK136	BioLegend UK Ltd	108732 RRID:AB_2562218
CD161 (NK1.1) BV650, clone PK136	BioLegend UK Ltd	108736
CD317 BV650, clone 927	BioLegend UK Ltd	127019
F4/80 PerCP-Cy5.5, clone BM8	BioLegend UK Ltd	123128
Fc block	BD Biosciences	553142
GITR PE, clone DTA-1	BD Biosciences	558119
GL-7 AF647, clone GL7	BD Biosciences	561529
Gr-1 AF700, clone RB6-8C5	BioLegend UK Ltd	108422
Ig HRP, polyclonal	Dako	P0447
IgG (H+L) FITC, polyclonal	Invitrogen	626511
IgG1 HRP, clone X56	BD Biosciences	559626
IgG2a HRP, clone R19-15	BD Biosciences	553391
IgD BV510, clone 11-26c.2a	BD Biosciences	563110
IgD PerCP-Cy5.5, clone 11-26c.2a	BioLegend UK Ltd	405710
IgD AF488, clone 11-26c.2a	BioLegend UK Ltd	405718
IgG1 PE, clone A85-1	BD Biosciences	550083
IgM BV42, clone RMM-1	BioLegend UK Ltd	406518
IgM BV786, clone R6-60.2	BD Biosciences	564028
KLRG1 BV421, clone 2F1	BD Biosciences	562897
KLRG1 PE-Cy7, clone 2F1	BioLegend UK Ltd	138416 RRID:AB_2561736
Ly-51 PE, clone BP-1	BD Biosciences	553735
Ly6B FITC, clone 7/4	AbD Serotec	MCA771FB RRID:AB_324596
Ly6C AF700, clone AL-21	BD Biosciences	561237
Ly6C PerCP-Cy5.5, clone HK1.4	BioLegend UK Ltd	128012 RRID:AB_1659241
Ly6G APC, clone 1A8	BD Biosciences	560599
Ly6G V450, clone 1A8	BD Biosciences	560603 RRID:AB_1727564
MHC II I-A/I-E PE, clone M5/114.15.2	BioLegend UK Ltd	107608 RRID:AB_313323
MHC II I-A/I-E AF647, clone M5/114.15.2	BioLegend UK Ltd	107618
MHC II I-A/I-E FITC, 2G9	BD Biosciences	553623
MHC II I-A/I-E AF647, clone M5/114.15.2	BioLegend UK Ltd	107618

Vγ5 (aka Vγ3) FITC, clone 536	BD Biosciences	553229
TCRβ PerCP-Cy5.5, clone H57-597	BioLegend UK Ltd	109228 RRID:AB_1575173
TCRδ PE CY7, clone GL3	BioLegend UK Ltd	118124
TCRδ APC, clone GL3	BioLegend UK Ltd	118116 RRID:AB_1731813
Chemicals, Peptides, and Recombinant Proteins		
10mM HEPES	Life Signalling Technologies	15630056
Collagenase	Sigma Aldrich - Roche	11088858001
DNAase	Sigma	DN25
RBC lysis buffer	eBioscience	00-4300-54
EDTA (0.5 M), pH 8.0	Life Technologies	AM9261
Prolong Gold Mounting Medium	New England Biolabs	9071S
Zombie NIR Fixable Viability Kit	Biolegend	423106
BD FACSDiva CS&T Research Beads	BD Biosciences	655051
Ammonium thiocyanate	Sigma	A7149-100G
Nair™ moisturizing hair removal cream	Church & Dwight Co.	N/A
Acetone	VWR	20067-320
Fetal Bovine Serum	Gibco	FBS
Fetal Bovine Serum	Hyclone laboratories - Biosera	FB-1001/500
RPMI 1640	GIBCO - life technologies	21875034
RPMI 1640 (no phenol red)	GIBCO - life technologies	32404014
PBS 10x (neg for CA2+ and Mg2+)	Gibco	14200-067
PBS 10x (with calcium & Magnesium)	Gibco	14080-048
PBS, D'Beccos	GIBCO - life technologies	14190094
D-MEM (HG)	GIBCO - life technologies	41966029
DPBS	Sigma-Aldrich	D8662
Water	Sigma-Aldrich	W3500
Mounting Medium Dropper Vial 5mL	A. Menarini Diagnostics Ltd.	38015
2-mercaptoethanol	GIBCO Invitrogen	31350010
L-Glutamine	GIBCO Invitrogen	25030024

Recombinant murine IL-2	Peprotech	212-12-100
Penicillin/Streptomycin	Sigma-Aldrich	P4333
Sodium Pyruvate MEM	Sigma-Aldrich	11360039
Dextran sulfate, sodium salt	Affymetrix, Inc.	14489; CAS# 9011-18-1
Formaldehyde 4% solution	VWR international ltd	9713.5000
BSA	Sigma-Aldrich	A9056
Sigmafast	Sigma-Aldrich	P9187
LB	Oxoid	CM1018
Ampicillin	Roche	10 835 242 001
Tween 20	Sigma-Aldrich	P1379
Critical Commercial Assays		
Zenit ANA HEp-2 Cells (12 wells)	A. Menarini Diagnostics Ltd.	37806
FITC – QC Slide	A. Menarini Diagnostics Ltd.	38015
Cytotox 96 non-radioactive assay	Promega UK Ltd	G1780
Deposited Data		
3i statistical analysis	This study	www.immunophenotype.org
Raw and analyzed data	This study	www.immunophenotype.org
Experimental Models: Cell Lines		
P815 mastocytoma cell line	ATTC	TIB-64
HEp-2 cell lines, coated on slides	A. Menarini Diagnostics Ltd.	37806
Experimental Models: Organisms/Strains		
C57BL/6N wild type control mice	WTSI	
Knockout mouse strains as detailed in **Table S4**	WTSI	
Salmonella typhimurium M525 :: TetC	Gordon Dougan, WTSI	
Trichuris muris	Richard Grencis, University of Manchester	
Equipment		

Scil Vetabc hematology analyser	Horiba	http://www.horiba.com/uk/medical/products/animal-healthcare/haematology/scil-vet-abc-details/scil-vet-abc-12687/
BD LSR II flow cytometer (Blood)	BD Biosciences	RRID:SCR_002159; http://www.rockefeller.edu/fcrc/pdf/BD_LSRII_Brochure_SJ-0142-00.pdf
BD LSR Fortessa X-20 (Spleen, MLN, and bone marrow)	BD Biosciences	http://www.bdbiosciences.com/us/instruments/research/cell-analyzers/bd-lsrfortessa-x-20/m/1519232/overview
Leica SP2 confocal microscopes, 40x 1.25 NA oil immersion lens and 405 nm, 488 nm and 633 nm lasers (Ear epidermis)	Leica	https://www.leica-microsystems.com/products/confocal-microscopes/details/product/leica-tcs-sp2/
Leica SP5 confocal microscopes, 40x 1.25 NA oil immersion lens and 405 nm, 488 nm and 633 nm lasers (ear epidermis)	Leica	https://www.leica-microsystems.com/products/confocal-microscopes/details/product/leica-tcs-sp5/
Nikon wide-field TE2000U Microscope (ANA)	Nikon	TE2000U
Deltavision Elite widefield system based on an Olympus microscope, LED light source and CoolSNAP HQ2 camera (ANA)	GE Healthcare Life Sciences, Olympus	https://www.gelifesciences.com/en/us/shop/deltavision-elite-high-resolution-microscope-p-04420
Zeiss AxioPlan Microscope with a Plan Neofluar 5x/0.15 Ph1 objective and Moti Cam 10 camera (DSS)	Zeiss	https://www.zeiss.com/microscopy/int/home.html?gclid=EAIaIQobChMIj7KRv-mH4QIVybHtCh0C3w_OEAAYASAAEgJ2afD_BwE
Software and Algorithms		
R version 3.3.1 -3.5.2 and general data analysis packages (data.table, ggplot2, dplyr, igraph, MASS)	The R project for statistical computing	www.r-project.org

PhenStat_2.8 org.Hs.eg.db org.Mm.eg.db	BioConductor	www.bioconductor.org
RStudio 1.0.136	RStudio	https://www.rstudio.com
R code for reference range analysis, assessment of false positive rate	Anna Lorenc	https://github.com/AnnaLorenc/3i_heatmapping available on request
Flow Jo v1.10	Treestar	RRID:SCR_008520; http://www.flowjo.com
Cytoscape 3.6.1	Cytoscape	www.cytoscape.org
BD DIVA 7.0	BD Biosciences	RRID:SCR_001456; http://www.bdbiosciences.com/instruments/software/facsdiva/index.jsp
flowClean	Ryan Brinkman	Fletez-Brant et al 2016
UFO	Ryan Brinkman	available on request
flowDensity	Ryan Brinkman	Malek et al 2015
PRISM 6	Graphpad software	http://www.graphpad.com/scientific-software/prism/
Definiens developer	Definiens	www.definiens.com
ANA assay Fiji/ImageJ macro	Katherine Bull	www.immunophenotype.org
ANA assay Python scoring script	Katherine Bull	www.immunophenotype.org
Microsoft Excel 2010	Microsoft	https://www.microsoftstore.com/store/msuk/en_GB/home
Deposited Data		
3i statistical analysis	This study	www.immunophenotype.org
Raw and analyzed data	This study	www.immunophenotype.org
Other		
30 µm CellTrics filters	Partec Cell Trics	04-0042-2316
96 Well Clear V-Bottom Not Treated Polypropylene Microplate, Nonsterile	SLS	353263
Microtube MaxyClear PP clear 1.7 mL (Axygen)	Fisher	12756799
C-Tubes	Miltenyi Biotec	130-096-334
Superfrost R Plus #72, 26x76x1 mm (75 pieces)	VWR	631-0108
Cover Glass 22 x 40 Mm No. 1,5	VWR	631-1370