Figure 1

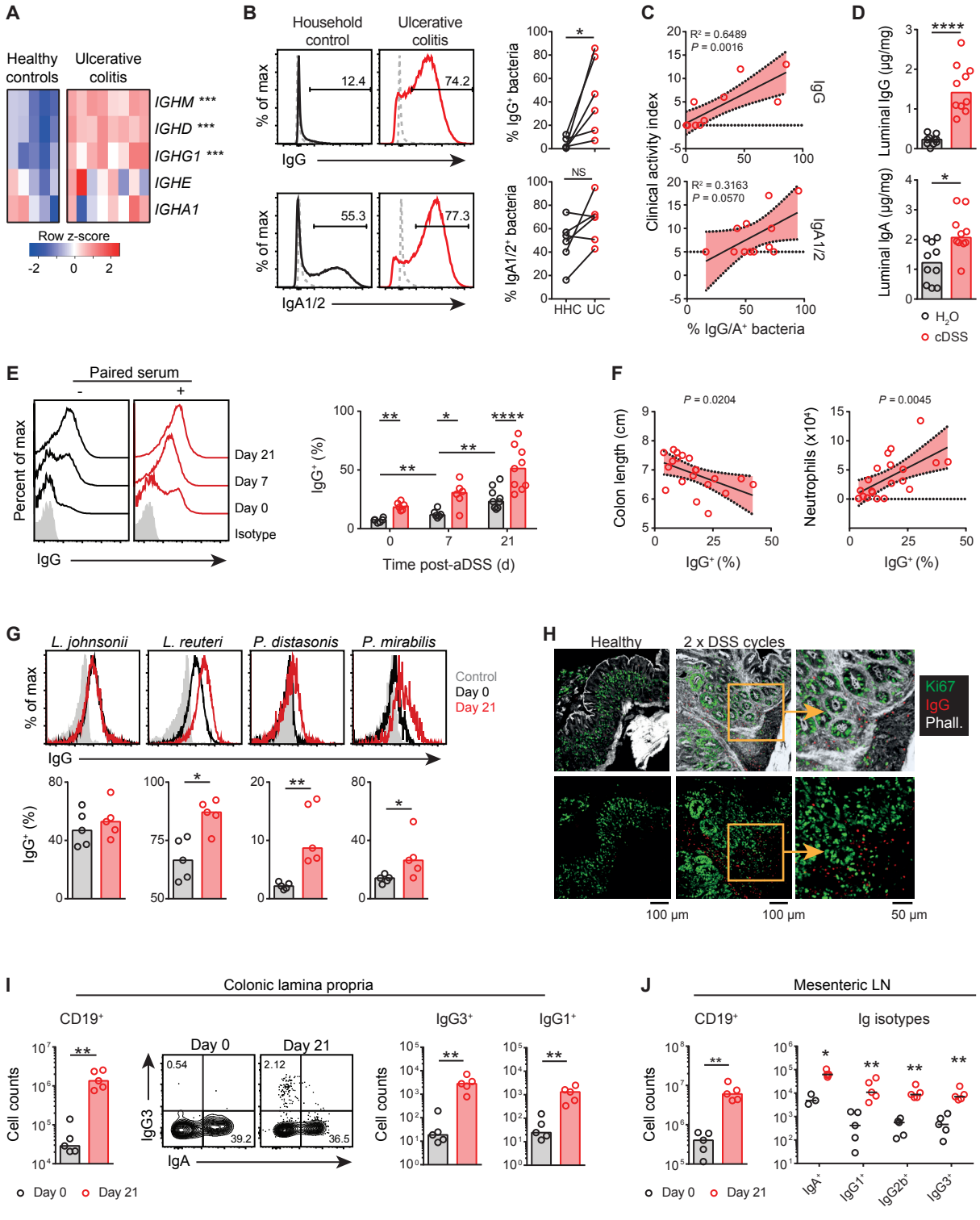

A
Healthy controls
Ulcerative colitis
IGHM ***
IGHD ***
IGHG1 ***
IGHE
IGHA1
Row z-score
-2 0 2
B
Household control
Ulcerative colitis
% of max
12.4
74.2
IgG
55.3
77.3
IgA1/2
% IgG+ bacteria
% IgA1/2+ bacteria
NS
HHC UC
C
R² = 0.6489
P = 0.0016
Clinical activity index
IgG
R² = 0.3163
P = 0.0570
IgA1/2
% IgG/A+ bacteria
D
Luminal IgG (µg/mg)
Luminal IgA (µg/mg)
H2O
cDSS
E
Paired serum
Percent of max
Day 21
Day 7
Day 0
Isotype
IgG
IgG+ (%)
Time post-aDSS (d)
F
P = 0.0204
Colon length (cm)
IgG+ (%)
P = 0.0045
Neutrophils (x10⁴)
IgG+ (%)
G
L. johnsonii
L. reuteri
P. distasonis
P. mirabilis
% of max
IgG
Control
Day 0
Day 21
IgG+ (%)
H
Healthy
2 x DSS cycles
Ki67
IgG
Phall.
100 µm
100 µm
50 µm
I
Colonic lamina propria
CD19+
Cell counts
Day 0
Day 21
0.54
39.2
2.12
36.5
IgG3
IgA
IgG3+
IgG1+
Day 0
Day 21
J
Mesenteric LN
CD19+
Ig isotypes
Cell counts
IgA+
IgG1+
IgG2b+
IgG3+
Day 0
Day 21

Figure 2

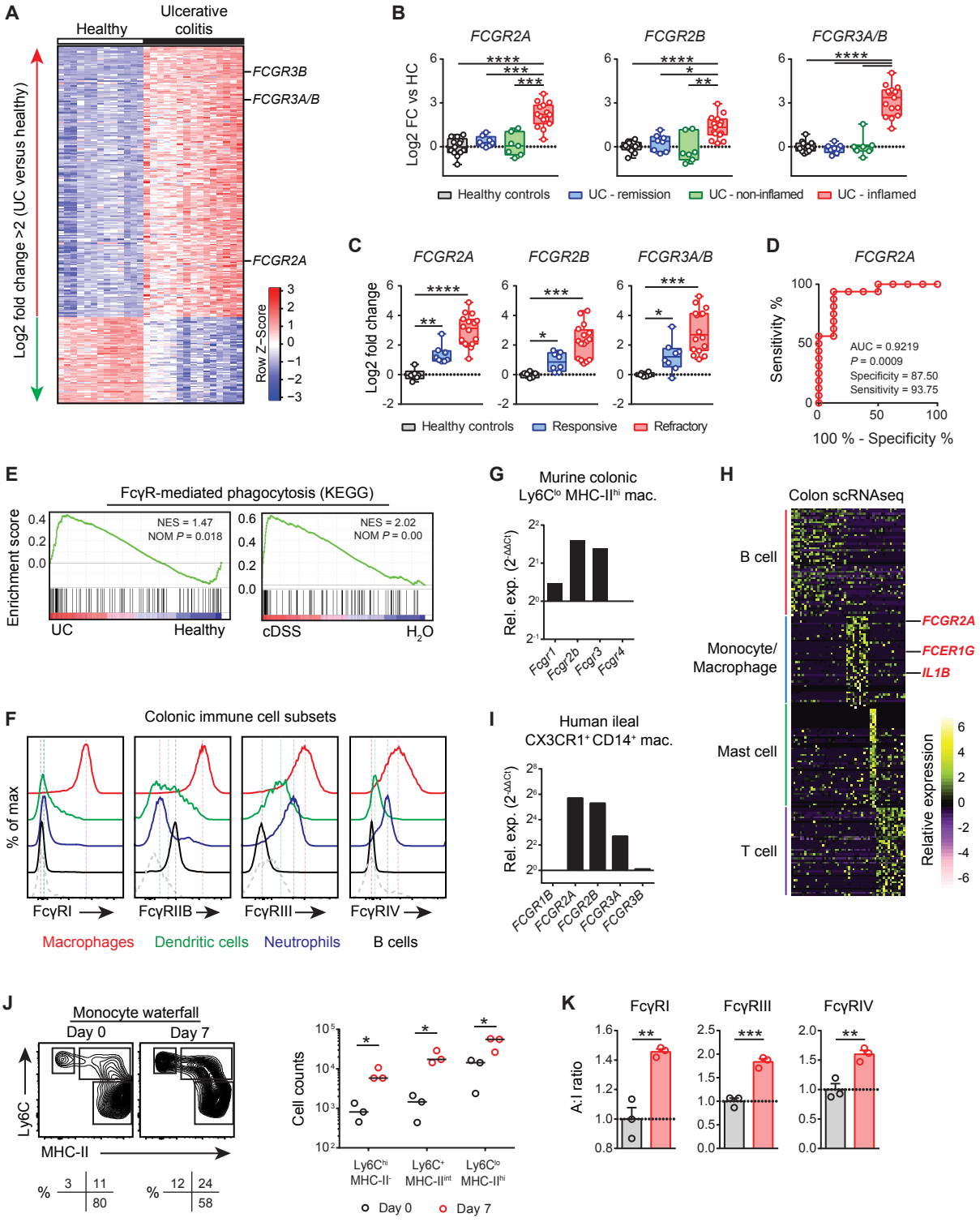

A
Healthy
Ulcerative colitis
Log2 fold change >2 (UC versus healthy)
FCGR3B
FCGR3A/B
FCGR2A
Row Z-Score
B
FCGR2A
FCGR2B
FCGR3A/B
Log2 FC vs HC
Healthy controls
UC - remission
UC - non-inflamed
UC - inflamed
C
FCGR2A
FCGR2B
FCGR3A/B
Log2 fold change
Healthy controls
Responsive
Refractory
D
FCGR2A
Sensitivity %
AUC = 0.9219
P = 0.0009
Specificity = 87.50
Sensitivity = 93.75
100 % - Specificity %
E
FcγR-mediated phagocytosis (KEGG)
Enrichment score
NES = 1.47
NOM P = 0.018
UC
Healthy
NES = 2.02
NOM P = 0.00
cDSS
H2O
F
Colonic immune cell subsets
% of max
FcγRI
FcγRIIB
FcγRIII
FcγRIV
Macrophages
Dendritic cells
Neutrophils
B cells
G
Murine colonic
Ly6Clo MHC-IIhi mac.
Rel. exp. (2-ΔΔCt)
Fcgr1
Fcgr2b
Fcgr3
Fcgr4
H
Colon scRNAseq
B cell
Monocyte/ Macrophage
Mast cell
T cell
FCGR2A
FCER1G
IL1B
Relative expression
I
Human ileal
CX3CR1+ CD14+ mac.
Rel. exp. (2-ΔΔCt)
FCGR1B
FCGR2A
FCGR2B
FCGR3A
FCGR3B
J
Monocyte waterfall
Day 0
Day 7
Ly6C
MHC-II
%
3
11
80
%
12
24
58
Cell counts
Ly6Chi MHC-II-
Ly6C+ MHC-IIint
Ly6Clo MHC-IIhi
Day 0
Day 7
K
FcγRI
FcγRIII
FcγRIV
A:I ratio

Figure 3

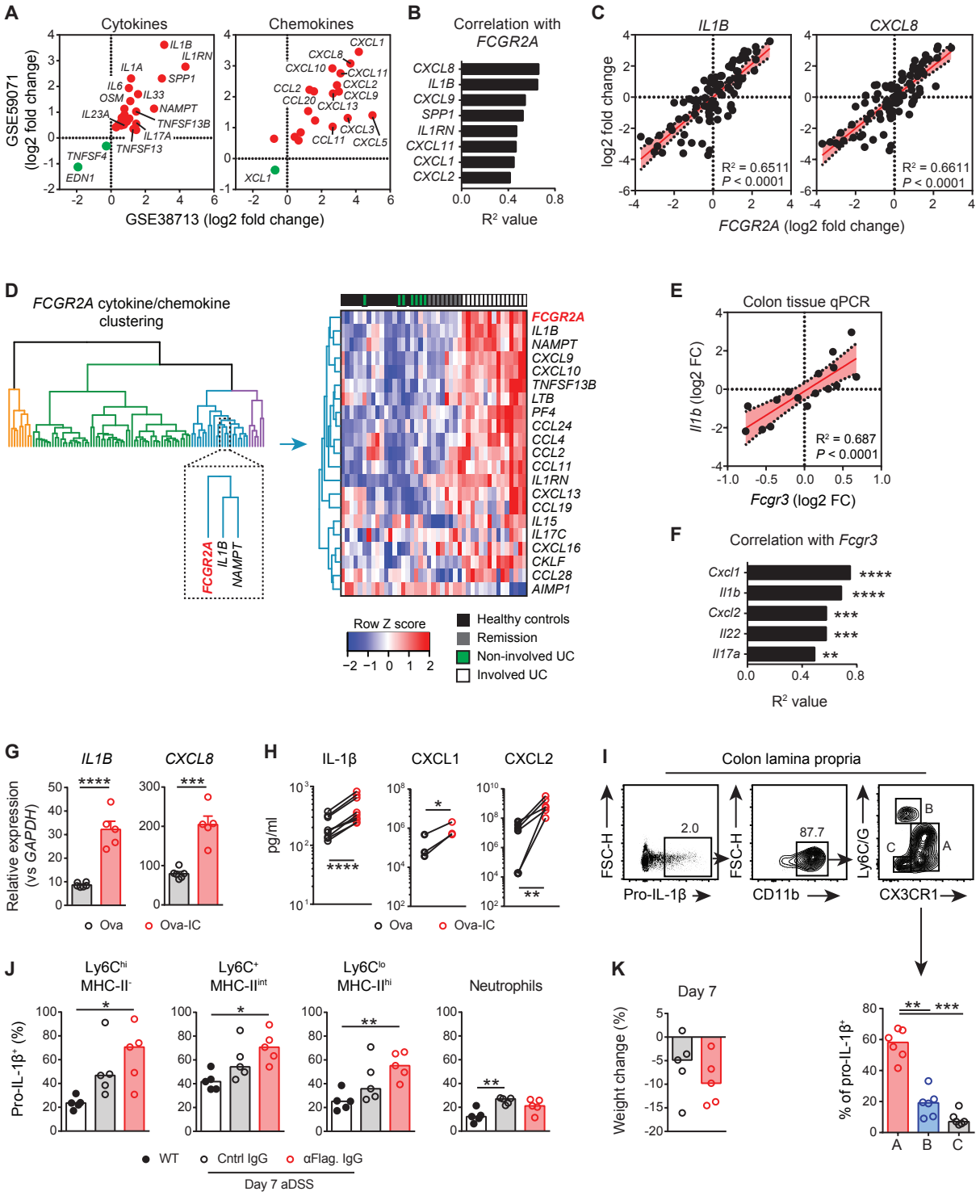

A
Cytokines
Chemokines
GSE59071 (log2 fold change)
GSE38713 (log2 fold change)
IL1B
IL1RN
IL1A
SPP1
IL6
OSM
IL33
NAMPT
IL23A
TNFSF13B
IL17A
TNFSF13
TNFSF4
EDN1
CXCL1
CXCL8
CXCL10
CXCL11
CXCL2
CCL2
CXCL9
CCL20
CXCL13
CXCL3
CCL11
CXCL5
XCL1
B
Correlation with FCGR2A
CXCL8
IL1B
CXCL9
SPP1
IL1RN
CXCL11
CXCL1
CXCL2
R² value
C
IL1B
CXCL8
log2 fold change
R² = 0.6511
P < 0.0001
R² = 0.6611
P < 0.0001
FCGR2A (log2 fold change)
D
FCGR2A cytokine/chemokine clustering
FCGR2A
IL1B
NAMPT
FCGR2A
IL1B
NAMPT
CXCL9
CXCL10
TNFSF13B
LTB
PF4
CCL24
CCL4
CCL2
CCL11
IL1RN
CXCL13
CCL19
IL15
IL17C
CXCL16
CKLF
CCL28
AIMP1
Row Z score
−2 −1 0 1 2
Healthy controls
Remission
Non-involved UC
Involved UC
E
Colon tissue qPCR
Il1b (log2 FC)
R² = 0.687
P < 0.0001
Fcgr3 (log2 FC)
F
Correlation with Fcgr3
Cxcl1
Il1b
Cxcl2
Il22
Il17a
****
****
***
***
**
R² value
G
IL1B
CXCL8
Relative expression (vs GAPDH)
****
***
Ova
Ova-IC
H
IL-1β
CXCL1
CXCL2
pg/ml
****
*
**
Ova
Ova-IC
I
Colon lamina propria
FSC-H
Pro-IL-1β
2.0
FSC-H
CD11b
87.7
Ly6C/G
CX3CR1
A
B
C
J
Ly6C^hi MHC-II^-
Ly6C^+ MHC-II^int
Ly6C^lo MHC-II^hi
Neutrophils
Pro-IL-1β^+ (%)
*
*
**
**
WT
Cntrl IgG
αFlag. IgG
Day 7 aDSS
K
Day 7
Weight change (%)
% of pro-IL-1β^+
**
***
A
B
C

Figure 4

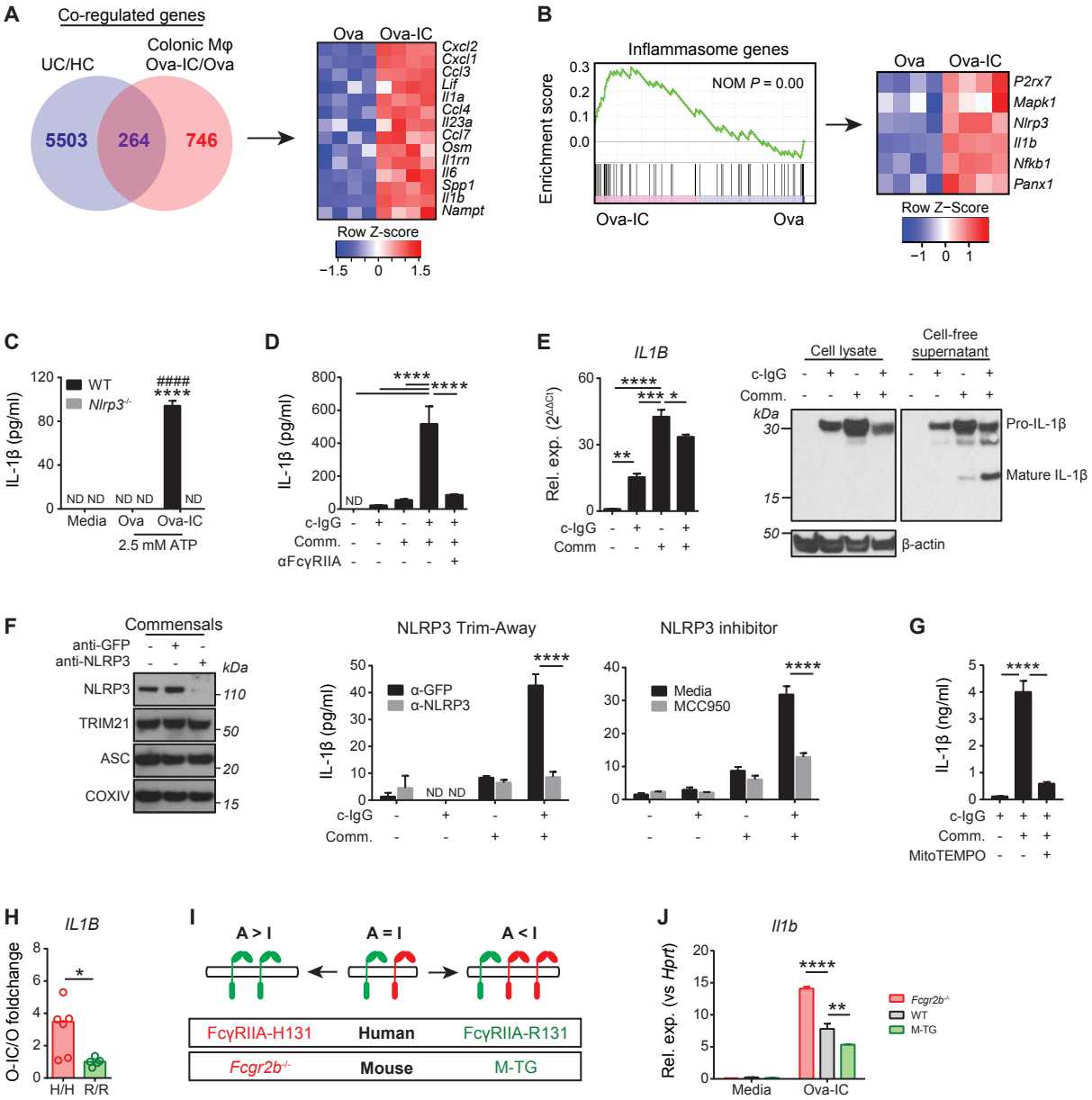

A
Co-regulated genes
UC/HC
Colonic Mφ
Ova-IC/Ova
5503
264
746
Ova
Ova-IC
Cxcl2
Cxcl1
Ccl3
Lif
Il1a
Ccl4
Il23a
Ccl7
Osm
Il1rn
Il6
Spp1
Il1b
Nampt
Row Z-score
−1.5 0 1.5
B
Inflammasome genes
Enrichment score
NOM P = 0.00
Ova-IC
Ova
Ova
Ova-IC
P2rx7
Mapk1
Nlrp3
Il1b
Nfkb1
Panx1
Row Z−Score
−1 0 1
C
IL-1β (pg/ml)
WT
Nlrp3-/-
Media
Ova
Ova-IC
2.5 mM ATP
D
IL-1β (pg/ml)
c-IgG
Comm.
αFcγRIIA
E
IL1B
Rel. exp. (2ΔΔCt)
c-IgG
Comm
Cell lysate
Cell-free supernatant
kDa
Pro-IL-1β
Mature IL-1β
β-actin
F
Commensals
anti-GFP
anti-NLRP3
kDa
NLRP3
TRIM21
ASC
COXIV
NLRP3 Trim-Away
α-GFP
α-NLRP3
IL-1β (pg/ml)
NLRP3 inhibitor
Media
MCC950
G
IL-1β (ng/ml)
c-IgG
Comm.
MitoTEMPO
H
IL1B
O-IC/O foldchange
H/H
R/R
I
A > I
A = I
A < I
FcγRIIA-H131
Human
FcγRIIA-R131
Fcgr2b-/-
Mouse
M-TG
J
Il1b
Rel. exp. (vs Hprt)
Media
Ova-IC
Fcgr2b-/-
WT
M-TG

Figure 5

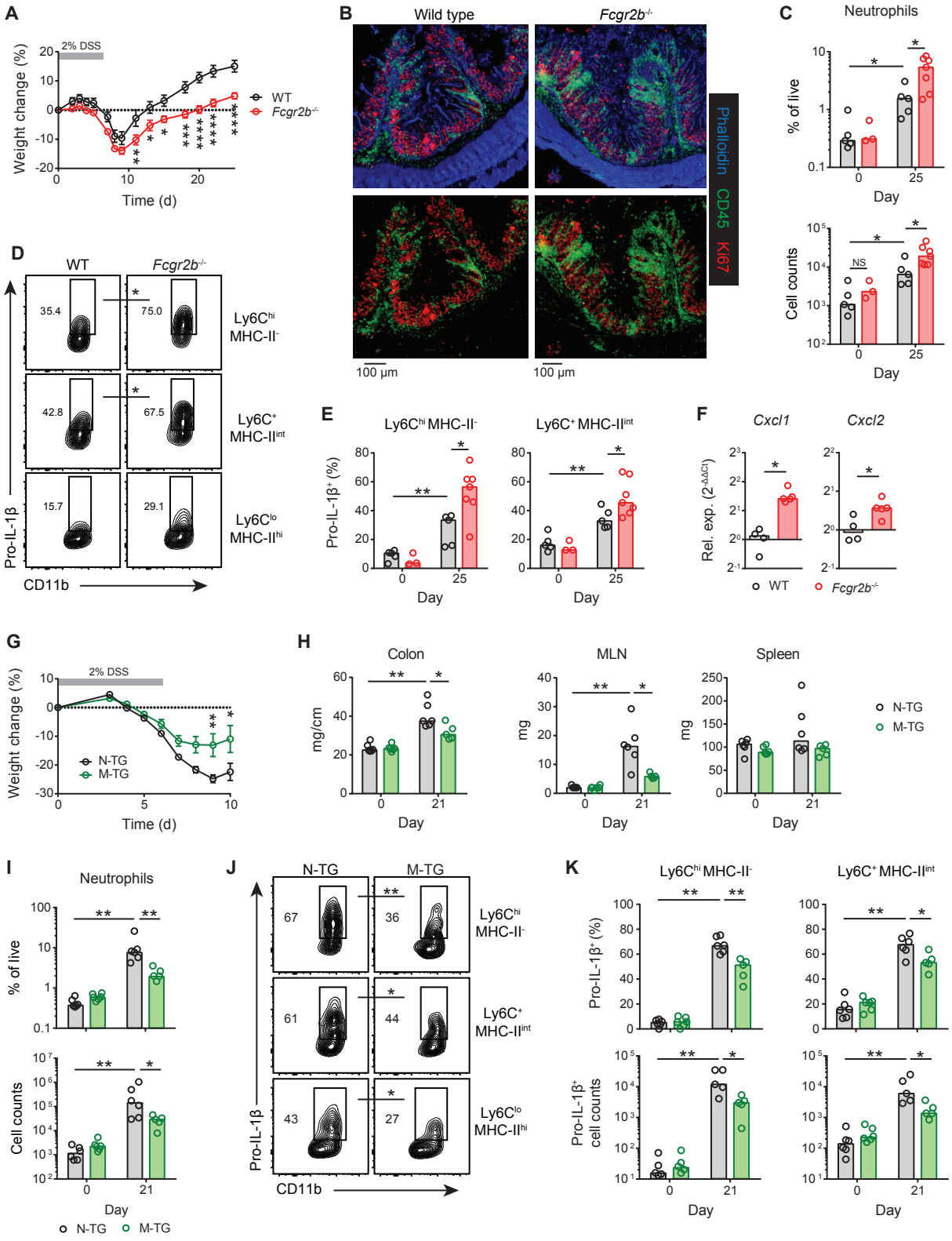
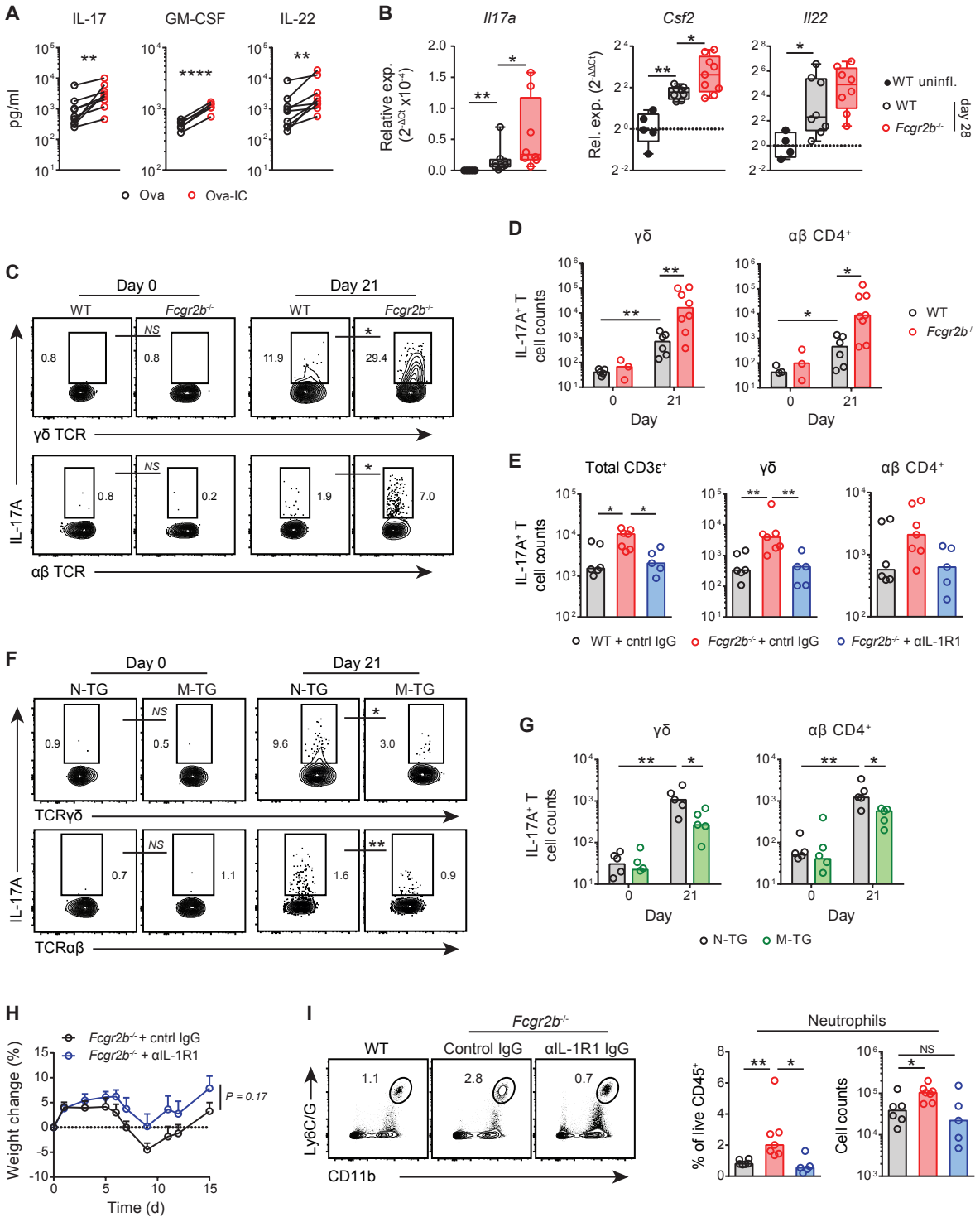

A
2% DSS
Weight change (%)
Time (d)
WT
Fcgr2b-/-
B
Wild type
Fcgr2b-/-
Phalloidin CD45 KI67
100 µm
C
Neutrophils
% of live
Cell counts
Day
NS
D
WT
Fcgr2b-/-
35.4
75.0
42.8
67.5
15.7
29.1
Ly6Chi MHC-II-
Ly6C+ MHC-IIint
Ly6Clo MHC-IIhi
Pro-IL-1β
CD11b
E
Ly6Chi MHC-II-
Ly6C+ MHC-IIint
Pro-IL-1β+ (%)
Day
F
Cxcl1
Cxcl2
Rel. exp. (2-ΔΔCt)
WT
Fcgr2b-/-
G
2% DSS
Weight change (%)
N-TG
M-TG
Time (d)
H
Colon
MLN
Spleen
mg/cm
mg
Day
I
Neutrophils
% of live
Cell counts
Day
J
N-TG
M-TG
67
36
61
44
43
27
Ly6Chi MHC-II-
Ly6C+ MHC-IIint
Ly6Clo MHC-IIhi
Pro-IL-1β
CD11b
K
Ly6Chi MHC-II-
Ly6C+ MHC-IIint
Pro-IL-1β+ (%)
Pro-IL-1β+ cell counts
Day

Figure 6


A
IL-17
GM-CSF
IL-22
pg/ml
Ova
Ova-IC
B
Il17a
Csf2
Il22
Relative exp. (2^-ΔCt x10^-4)
Rel. exp. (2^ΔΔCt)
WT uninfl.
WT
Fcgr2b-/-
day 28
C
Day 0
Day 21
WT
Fcgr2b-/-
NS
0.8
0.8
11.9
29.4
γδ TCR
IL-17A
0.8
0.2
1.9
7.0
αβ TCR
D
γδ
αβ CD4+
IL-17A+ T cell counts
Day
WT
Fcgr2b-/-
E
Total CD3ε+
γδ
αβ CD4+
IL-17A+ T cell counts
WT + cntrl IgG
Fcgr2b-/- + cntrl IgG
Fcgr2b-/- + αIL-1R1
F
Day 0
Day 21
N-TG
M-TG
0.9
0.5
9.6
3.0
TCRγδ
IL-17A
0.7
1.1
1.6
0.9
TCRαβ
G
γδ
αβ CD4+
IL-17A+ T cell counts
Day
N-TG
M-TG
H
Fcgr2b-/- + cntrl IgG
Fcgr2b-/- + αIL-1R1
Weight change (%)
P = 0.17
Time (d)
I
Fcgr2b-/-
WT
Control IgG
αIL-1R1 IgG
1.1
2.8
0.7
Ly6C/G
CD11b
Neutrophils
% of live CD45+
Cell counts
NS