# Figure S1

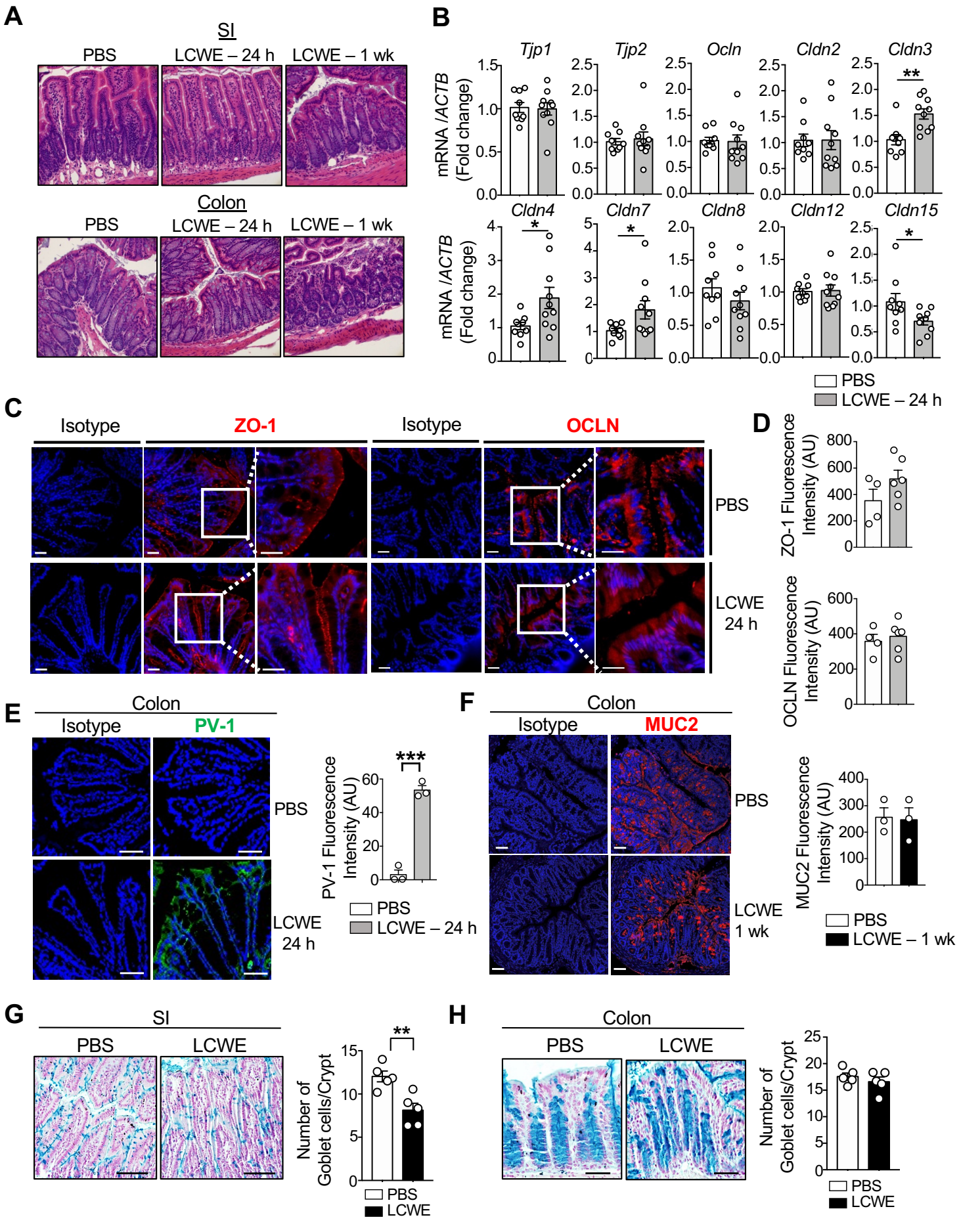
A
SI
PBS
LCWE – 24 h
LCWE – 1 wk
Colon
PBS
LCWE – 24 h
LCWE – 1 wk
B
Tjp1
Tjp2
Ocln
Cldn2
Cldn3
Cldn4
Cldn7
Cldn8
Cldn12
Cldn15
mRNA /ACTB (Fold change)
PBS
LCWE – 24 h
C
Isotype
ZO-1
Isotype
OCLN
PBS
LCWE 24 h
D
ZO-1 Fluorescence Intensity (AU)
OCLN Fluorescence Intensity (AU)
E
Colon
Isotype
PV-1
PBS
LCWE 24 h
PV-1 Fluorescence Intensity (AU)
PBS
LCWE – 24 h
F
Colon
Isotype
MUC2
PBS
LCWE 1 wk
MUC2 Fluorescence Intensity (AU)
PBS
LCWE – 1 wk
G
SI
PBS
LCWE
Number of Goblet cells/Crypt
PBS
LCWE
H
Colon
PBS
LCWE
Number of Goblet cells/Crypt
PBS
LCWE

**Figure S1. LCWE-injected mice display no anatomical changes in the colon and no changes in colonic TJ expression, Related to Figure 1.** (**A**) H&E stained sections of the SI and colon of PBS or LCWE-injected mice 24 h and 1wk post-LCWE injection (n=5 per group). (**B**) Colon expression of TJ genes relative to β-actin 24 h after PBS (n=9) or LCWE injection (n=10). (**C**) Immunofluorescent staining of ZO-1 (red, left panel) and OCLN (red, right panel) in the colon of PBS or LCWE-injected mice 24 h after injection. Scale bars: 25μm. (**D**) Quantification of ZO-1 and OCLN by immunofluorescence intensity in the colon of PBS or LCWE-injected mice 24 h post-injection. (**E**) Immunofluorescent staining and PV-1 fluorescence intensity in colon sections of PBS or LCWE-injected mice 24 h post-injection. PV-1 (green) and DAPI (Blue). Scale bars: 25μm. (**F**) Immunofluorescent staining and quantification of MUC2 by fluorescence intensity in the colon of PBS or LCWE-injected mice 1 wk post injection. Representative images of n=3 per group. MUC2 (red) and DAPI (Blue). Scale bars: 50μm. (**G, H**) Alcian blue staining and count of Alcian blue positive goblet cells in the SI (G) and colon (H) of PBS or LCWE-injected mice 1 wk post-injection (n=5 per group). Scale bars: 250μm. Immunofluorescence images are representative of n= 4-6 per group. Data are presented as mean ± s.e.m., *$p<0.05$, **$p<0.01$, ***$p<0.001$ by two-tailed unpaired t test. AU, arbitrary units.

# Figure S2

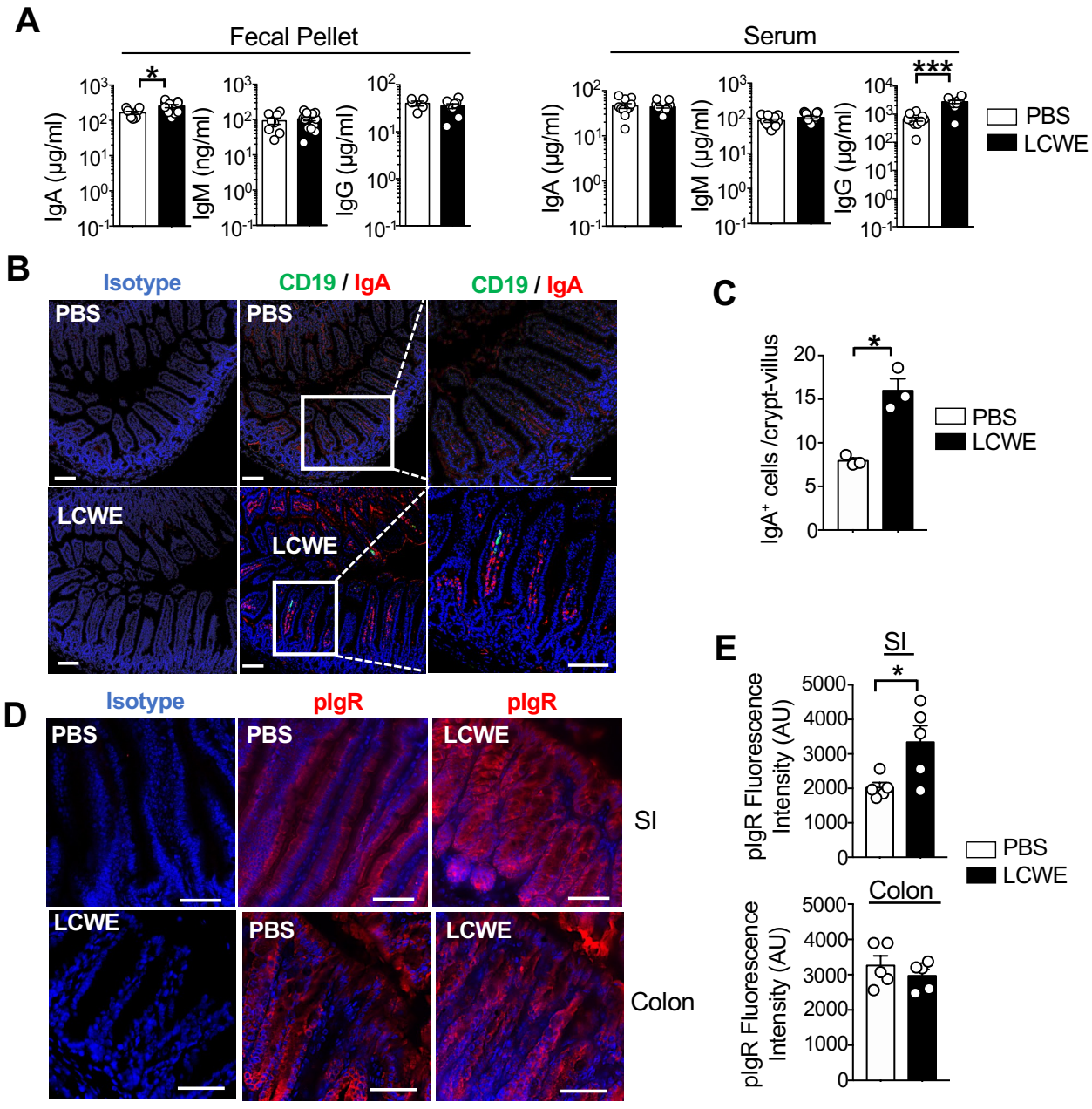


**Figure S2. Increased IgA production in the SI of LCWE-injected KD mice, Related to Figure 3.** (**A**) IgA (n=11 for PBS and n=15 for LCWE), IgM (n=10 for PBS and n=14 for LCWE) and IgG (n=5 PBS and n=9 LCWE) concentrations measured in the fecal pellets and serum of PBS or LCWE-injected mice. (**B, C**) Immunofluorescent staining of CD19 (green) and IgA (red) (B) and numbers of $IgA^+$ cells per crypt-villus (C) in the SI of PBS or LCWE-injected mice. Scale bars: 100µm. (**D, E**) Immunofluorescent staining of pIgR (D) and pIgR fluorescence intensity (E) in the SI and colon of PBS or LCWE-injected mice. Scale bars: 250µm. Data in **A, C and E** are mean ± s.e.m., *p<0.05, ***p<0.001 by two-tailed unpaired t test with Welch's correction when required. Data pooled from 2 independent experiments. Immunofluorescence images are representative of n=3-5 per group and nuclei were stained with DAPI (blue). AU, Arbitrary units.

# Figure S3

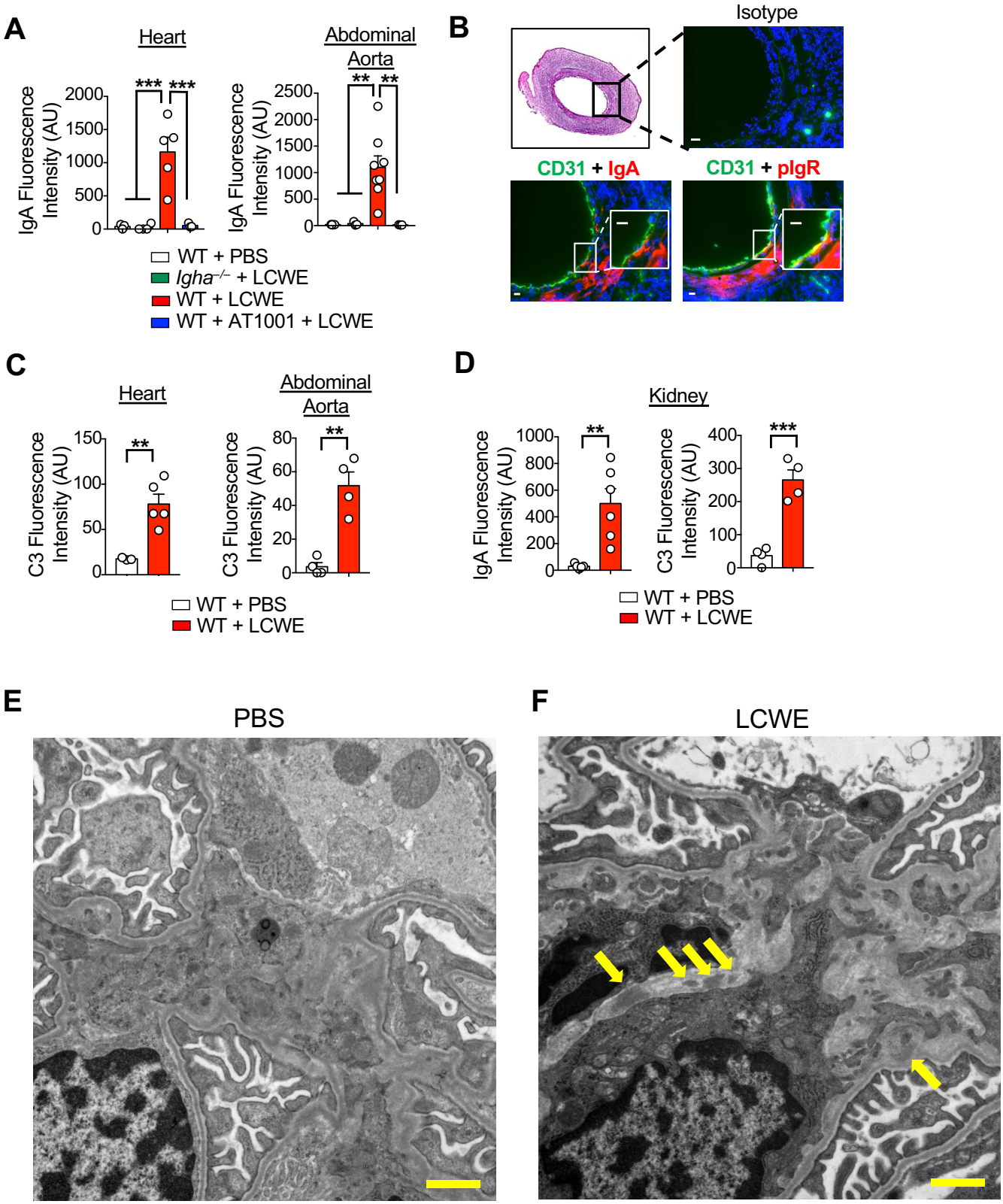
A
Heart
Abdominal Aorta
IgA Fluorescence Intensity (AU)
2000
1500
1000
500
0
2500
***
**
WT + PBS
Igha−/− + LCWE
WT + LCWE
WT + AT1001 + LCWE
B
Isotype
CD31 + IgA
CD31 + pIgR
C
Heart
Abdominal Aorta
C3 Fluorescence Intensity (AU)
150
100
50
80
60
40
20
WT + PBS
WT + LCWE
D
Kidney
IgA Fluorescence Intensity (AU)
1000
800
600
400
200
C3 Fluorescence Intensity (AU)
400
300
200
100
E
PBS
F
LCWE

**Figure S3. IgA and C3 deposition in heart, abdominal aorta and glomerular mesangial areas of LCWE-injected KD mice kidneys, Related to Figure 4.** (**A**) IgA fluorescence intensity in heart and abdominal aorta tissues of PBS-injected WT mice and LCWE-injected WT, *Igha*$^{-/-}$ and WT mice treated with AT1001. (**B**) Immunofluorescent staining of CD31 (green) plus IgA (red) and CD31 (green) plus pIgR (red) on abdominal aorta serial sections of LCWE-injected WT mice. Nuclei were stained with DAPI (blue). Scale bars: 10μm (**C**) C3 fluorescence intensity in heart and abdominal aorta tissues of PBS or LCWE-injected WT mice. (**D**) IgA (left panel) and C3 (right panel) fluorescence intensity in kidney tissues of PBS or LCWE-injected WT mice. (**E**) Electron microscope image of kidney tissues from PBS-injected mice showing mesangial areas with normal cellularity and a normal amount of matrix without electron dense deposits. (**F**) LCWE-injected mice showed frequent electron dense deposits (yellow arrows) corresponding to IgA deposition in mesangial areas with mesangial hypercellularity and an increased matrix. Direct magnification: x14,000, Scale bars,1 μm. AU; arbitrary units.

## Figure S4

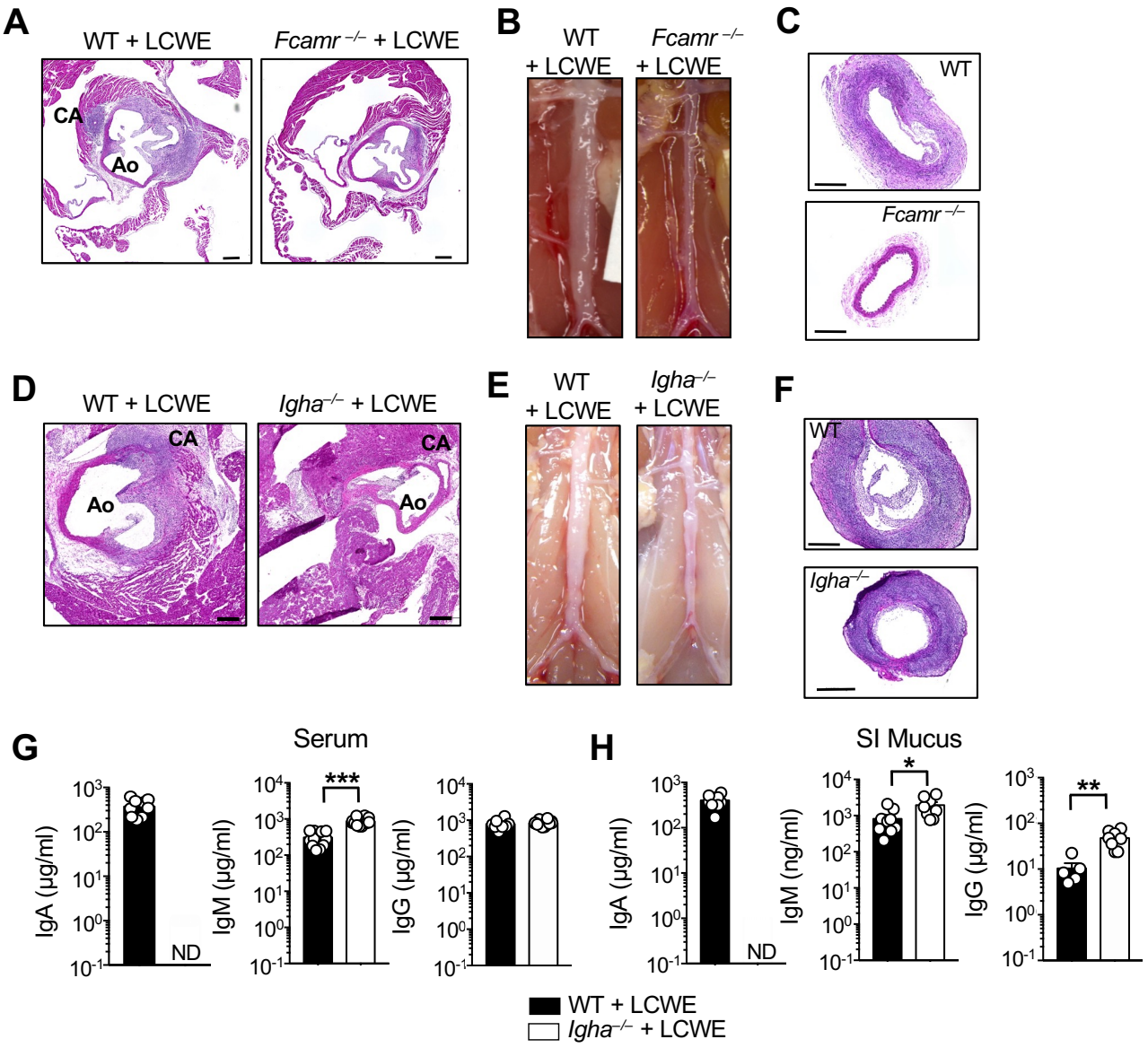


**Figure S4. Blocking IgA signaling and production decreases LCWE-induced KD vasculitis, Related to Figure 5.** (**A**) Representative H&E staining of heart sections of LCWE-injected WT (n=10) and *Fcamr* $^{-/-}$ mice (n=10) 1 wk post-LCWE injection. (**B**) Representative pictures of abdominal area of LCWE-injected WT (n=10) and *Fcamr* $^{-/-}$ mice (n=10) 1 wk post-LCWE injection. (**C**) H&E staining of abdominal aorta cross-section from LCWE-injected WT (n=10) and *Fcamr* $^{-/-}$ mice (n=10) 1 wk post-LCWE injection. (**D**) Representative H&E staining of heart sections of LCWE-injected WT (n=11) and *Igha*$^{-/-}$ mice (n=10) 1 wk post-LCWE injection. (**E)** Representative pictures of abdominal area of LCWE-injected WT (n=11) and *Igha*$^{-/-}$ mice (n=10) 1 wk post-LCWE injection. (**F**) H&E staining of abdominal aorta cross-section from LCWE-injected WT (n=11) and *Igha*$^{-/-}$ mice (n=10) 1 wk post-LCWE injection. (**G, H**) Serum (G) and SI mucus (H) concentrations of IgA, IgM and IgG in LCWE-injected WT (n=5-12) and *Igha*$^{-/-}$ (n=8-12) mice 1 wk post-LCWE injection. Data in **G** and **H** are mean ± s.e.m. **p<0.01, ***p<0.001 by two-tailed unpaired t test. Data representative of 2 to 3 independent experiments. Scale bars: 250µm.

## Figure S5

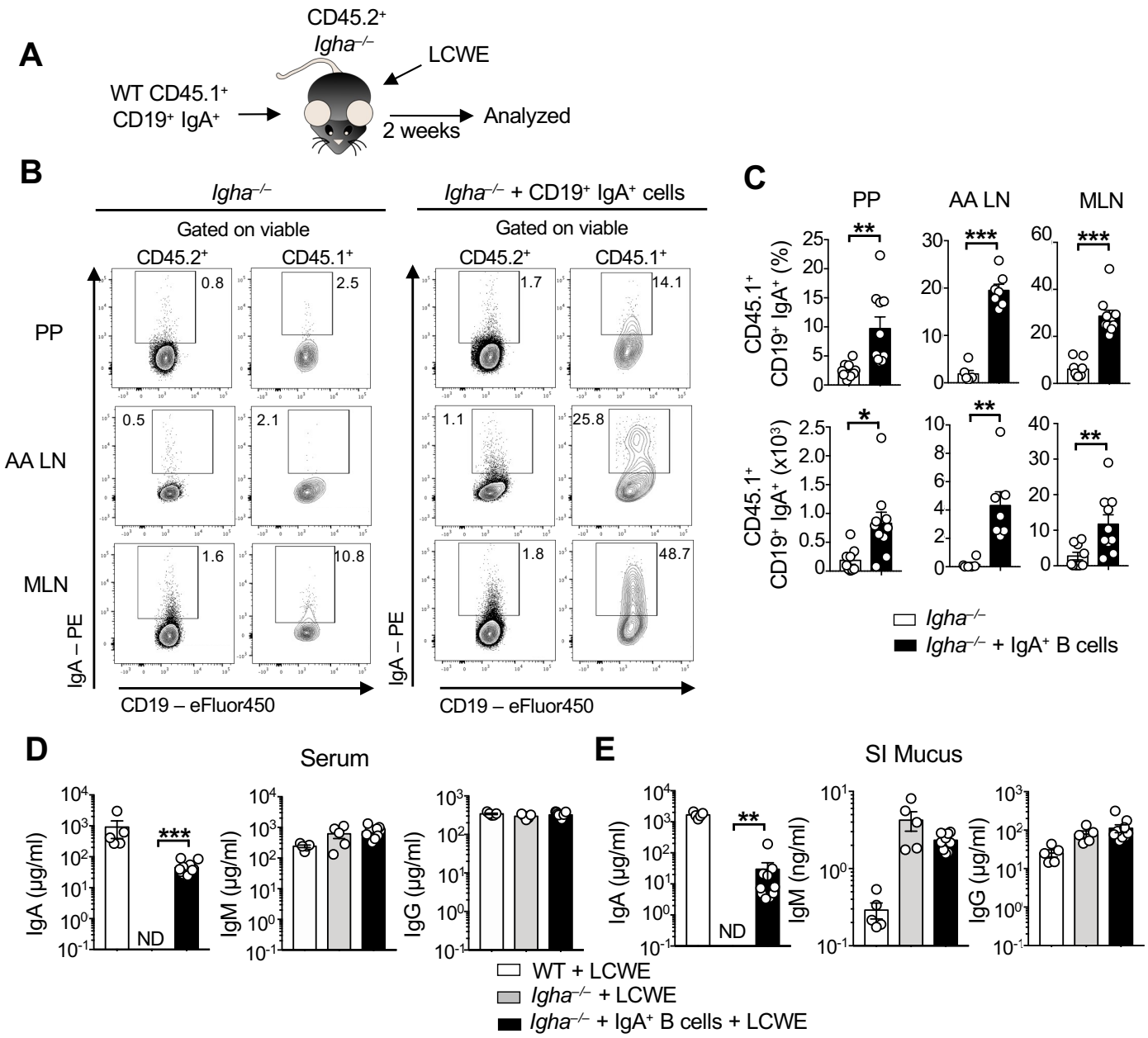


**Figure S5. Adoptive transfer of IgA⁺ PP B cells restores intestinal and serum IgA production, Related to Figure 5.** (**A**) Schematic representation of the experimental design. CD45.2⁺ *Igha*$^{-/-}$ mice received congenic CD45.1⁺ CD19⁺ IgA⁺ B cells isolated by cell-sorting from the PP of CD45.1⁺ WT mice. *Igha*$^{-/-}$ recipients were then injected with LCWE. (**B**) Representative flow cytometric analysis of viable CD45.1⁺ CD19⁺ IgA⁺ B cells found in the PP, AA LN and MLN of LCWE-injected *Igha*$^{-/-}$ (n= 9) and LCWE-injected *Igha*$^{-/-}$ mice that received CD45.1⁺ CD19⁺ IgA⁺ B cells (n=10) 1 wk post LCWE-injection. (**C**) Frequencies (top panel) and absolute numbers (bottom panel) of viable CD45.1⁺ CD19⁺ IgA⁺ B cells found in the PP, AA LN and MLN of LCWE-injected *Igha*$^{-/-}$ (n= 9) and *Igha*$^{-/-}$ mice that received CD45.1⁺ CD19⁺ IgA⁺ B cells (n=7-10) 1 wk post LCWE-injection. (**D, E**) Serum (D) and SI mucus (E) IgA concentrations in WT (n=5), *Igha*$^{-/-}$ (n=5-10) *Igha*$^{-/-}$ that received CD45.1⁺ CD19⁺ IgA⁺ B cells (n=10). Data in **C**–**E** are mean ± s.e.m. Results combined 2 to 3 independent experiments. *p<0.05, **p<0.01, ***p<0.001 by two-tailed unpaired t tests. ND = not detected.

# Figure S6

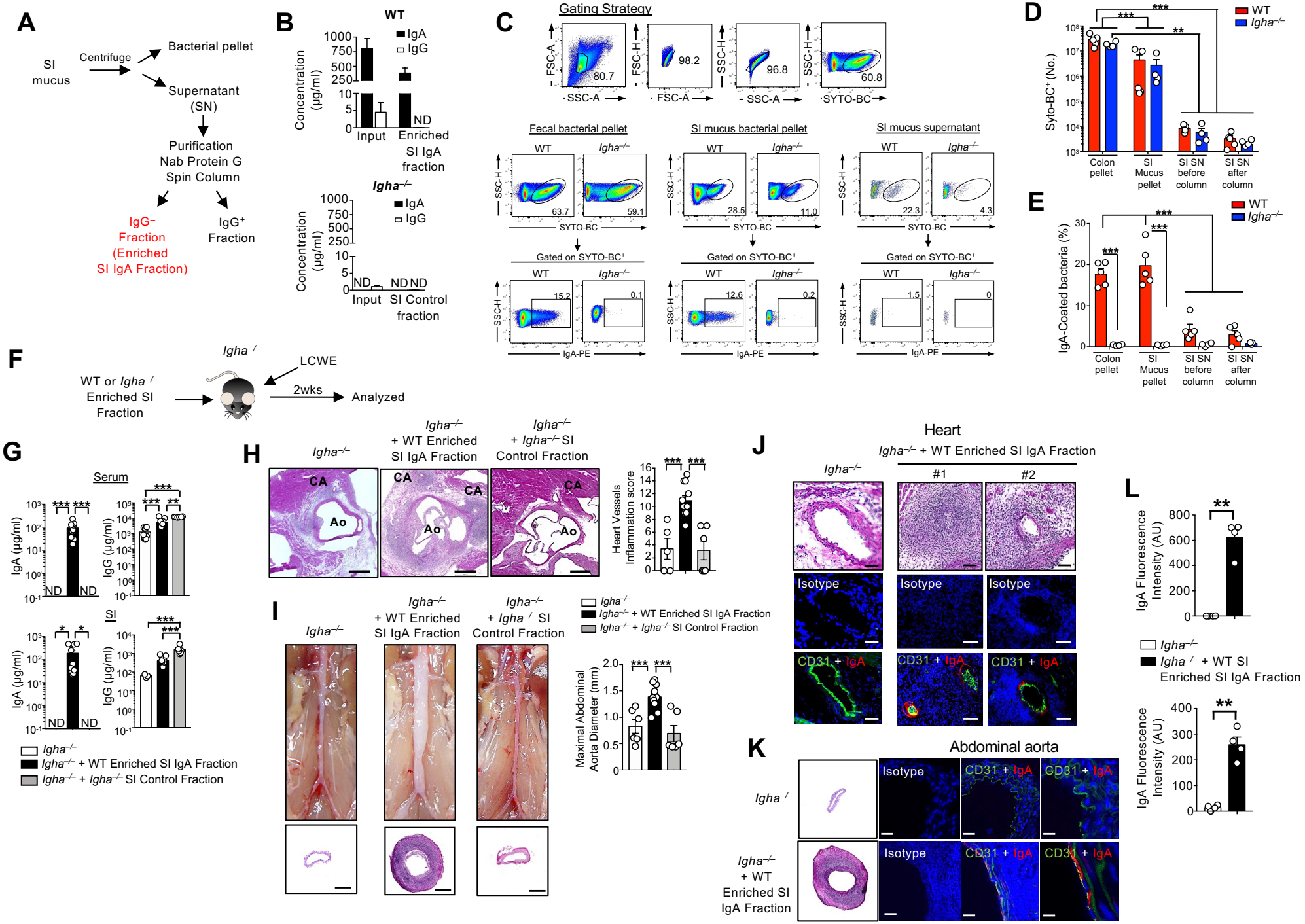
A
SI mucus
Centrifuge
Bacterial pellet
Supernatant (SN)
Purification Nab Protein G Spin Column
IgG⁻ Fraction (Enriched SI IgA Fraction)
IgG⁺ Fraction
B
WT
IgA
IgG
Concentration (µg/ml)
Input
Enriched SI IgA fraction
Igha⁻/⁻
ND
SI Control fraction
C
Gating Strategy
FSC-A
SSC-A
FSC-H
SSC-H
SYTO-BC
80.7
98.2
96.8
60.8
Fecal bacterial pellet
SI mucus bacterial pellet
SI mucus supernatant
Gated on SYTO-BC⁺
IgA-PE
63.7
59.1
28.5
11.0
22.3
4.3
15.2
0.1
12.6
0.2
1.5
0
D
Syto-BC⁺ (No.)
Colon pellet
SI Mucus pellet
SI SN before column
SI SN after column
E
IgA-Coated bacteria (%)
F
Igha⁻/⁻
LCWE
2wks
WT or Igha⁻/⁻ Enriched SI Fraction
Analyzed
G
Serum
SI
IgA (µg/ml)
IgG (µg/ml)
ND
Igha⁻/⁻
Igha⁻/⁻ + WT Enriched SI IgA Fraction
Igha⁻/⁻ + Igha⁻/⁻ SI Control Fraction
H
Igha⁻/⁻
Igha⁻/⁻ + WT Enriched SI IgA Fraction
Igha⁻/⁻ + Igha⁻/⁻ SI Control Fraction
CA
Ao
Heart Vessels Inflammation score
I
Maximal Abdominal Aorta Diameter (mm)
J
Heart
Igha⁻/⁻ + WT Enriched SI IgA Fraction
#1
#2
Isotype
CD31 + IgA
K
Abdominal aorta
Igha⁻/⁻ + WT Enriched SI IgA Fraction
L
IgA Fluorescence Intensity (AU)
Igha⁻/⁻ + WT SI Enriched SI IgA Fraction

**Figure S6. WT Enriched intestinal IgA fraction promotes vasculitis and abdominal aorta dilatation in *Igha*$^{-/-}$ mice, Related to Figure 5.** (**A**) Schematic representation of the experimental design. IgA was enriched from the SI scraped mucus of WT mice by discarding the bacterial pellet and depleting IgG from the remaining supernatant (WT enriched SI IgA fraction). A SI control mucus fraction lacking IgA was prepared similarly from SI mucus of *Igha*$^{-/-}$ mice (SI control fraction). (**B**) IgA and IgG concentrations in the SI mucus input, the WT enriched SI IgA fraction and the *Igha*$^{-/-}$ *S*I control fraction. (**C**) Flow cytometric plots showing the gating strategy used to detect the presence of SYTO-BC$^{+}$ bacteria in the experimental samples (upper panel). IgA-coated bacteria were further identified as SYTO-BC$^{+}$ IgA$^{+}$. Flow cytometric analysis was performed on WT fecal pellets (positive control, bottom right panel), the SI mucus bacterial pellet (bottom, middle panel) and SI mucus supernatant preparation (bottom, left panel). (**D, E**) Absolute numbers of SYTO-BC$^{+}$ bacteria (H) and frequencies of IgA-coated bacteria (E) in WT fecal pellets, SI mucus bacterial pellet and SI mucus supernatant before and after IgG depletion. (**F**) Schematic representation of the experimental design. WT Enriched SI IgA fraction and *Igha*$^{-/-}$ SI control fraction were given by oral gavage to *Igha*$^{-/-}$ mice at days -1 and 3 post-LCWE injection. (**G)** Serum and intestinal IgA and IgG concentrations in *Igha*$^{-/-}$ *mice* and *Igha*$^{-/-}$ mice that received either the WT enriched SI IgA fraction or the *Igha*$^{-/-}$ SI control fraction (n=6-11 per group). (**H**) Representative H&E staining of heart section and heart vessel inflammation score of LCWE-injected *Igha*$^{-/-}$ (n=5) and *Igha*$^{-/-}$ that received either the enriched WT SI IgA fraction (n=11) or the *Igha*$^{-/-}$ SI control fraction (n=6) at 1 wk post-LCWE injection. Scale bars: 500µm. (**I**) Representative pictures of abdominal area, H&E staining of abdominal aorta cross-section and maximal abdominal aorta diameter of LCWE-injected *Igha*$^{-/-}$ (n=6) and *Igha*$^{-/-}$ that received either the WT enriched SI IgA fraction (n=11) or the *Igha*$^{-/-}$ SI control fraction (n=6) at 1 wk post-LCWE injection. Scale bars: 250µm. (**J, K**) H&E staining and immunostaining of CD31 (green) and IgA (red) on the coronary artery (J) and abdominal aorta cross-sections (K) of LCWE-injected *Igha*$^{-/-}$ and *Igha*$^{-/-}$ that received the enriched WT SI IgA fraction 1 wk post-LCWE injection. Scale bars: 50µm. (**L**) Fluorescence intensity showing quantification of IgA in heart (top panel) and abdominal aorta (bottom panel) tissues of LCWE-injected *Igha*$^{-/-}$ and *Igha*$^{-/-}$ that received the enriched WT SI IgA fraction 1 wk post-LCWE injection. Data are presented as mean ± s.e.m., *p<0.05, **p<0.01 and ***p<0.001 by either two-tailed unpaired t test, 1-way or 2-way ANOVA. Data compiled from 2 to 3 independent experiments and immunofluorescence images are representative of n=4 mice per group. AU, arbitrary units.

**Table S1.**
Demographics of febrile controls and KD subjects

| | **Febrile Controls (*n*=25)** | **KD patients (*n*=34)** |
|---|---|---|
| **Age at onset, months** (average ± SD) | 35.24 ± 26.31 | 39.67 ± 37.06 |
| **Sex, n (%)** | | |
| Female | 16 (64) | 11 (32.4) |
| Male | 9 (36) | 23 (67.6) |
| **Disease, n (%)** | | |
| Enteritis | 4 (16) | N/A |
| Joint Infection | 3 (12) | N/A |
| Lower Respiratory Tract Infection | 8 (32) | N/A |
| Polynephritis | 1 (4) | N/A |
| Pyomyositis | 1 (4) | N/A |
| Upper Respiratory Tract Infection | 7 (28) | N/A |
| Viral Illness | 1 (4) | N/A |
| **Treatment, n (%)** | | |
| IVIG + ASA | N/A | 28 (82.4) |
| IVIG + ASA + PDN | N/A | 6 (17.6) |
| **IVIG resistance** | N/A | 4 (11.8) |
| **Coronary artery lesions (CAL)** | N/A | 8 (23.5) |

***Abbreviations***: KD; Kawasaki Disease, PDN; Prednisone, ASA; Aspirin, IVIG; Intravenous Immunoglobulin, CAL; coronary artery lesion, N/A; Not applicable

**Table S1. Demographic characteristics of Febrile Controls and KD patients used to quantify serum concentrations of sIgA, Calprotectin and Zonulin, Related to Figures 2 and 3.**
The study population was composed of 2 groups. Group (1) contains 25 febrile controls and group (2) 34 acute phase KD patients. The febrile control subjects included 9 boys and 16 girls, ranging in age from 1 month to 9 years. The KD patient group is composed of 23 boys and 11 girls, ranging from 4 months to 15 years.