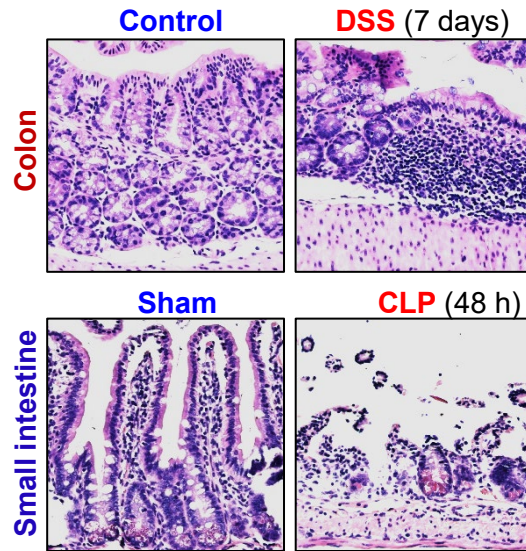
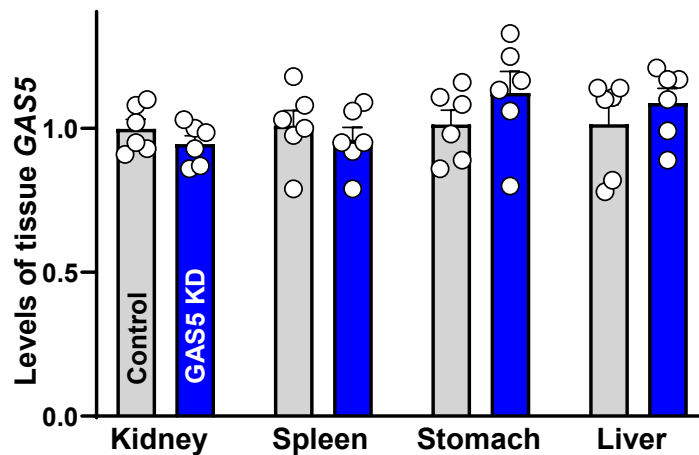
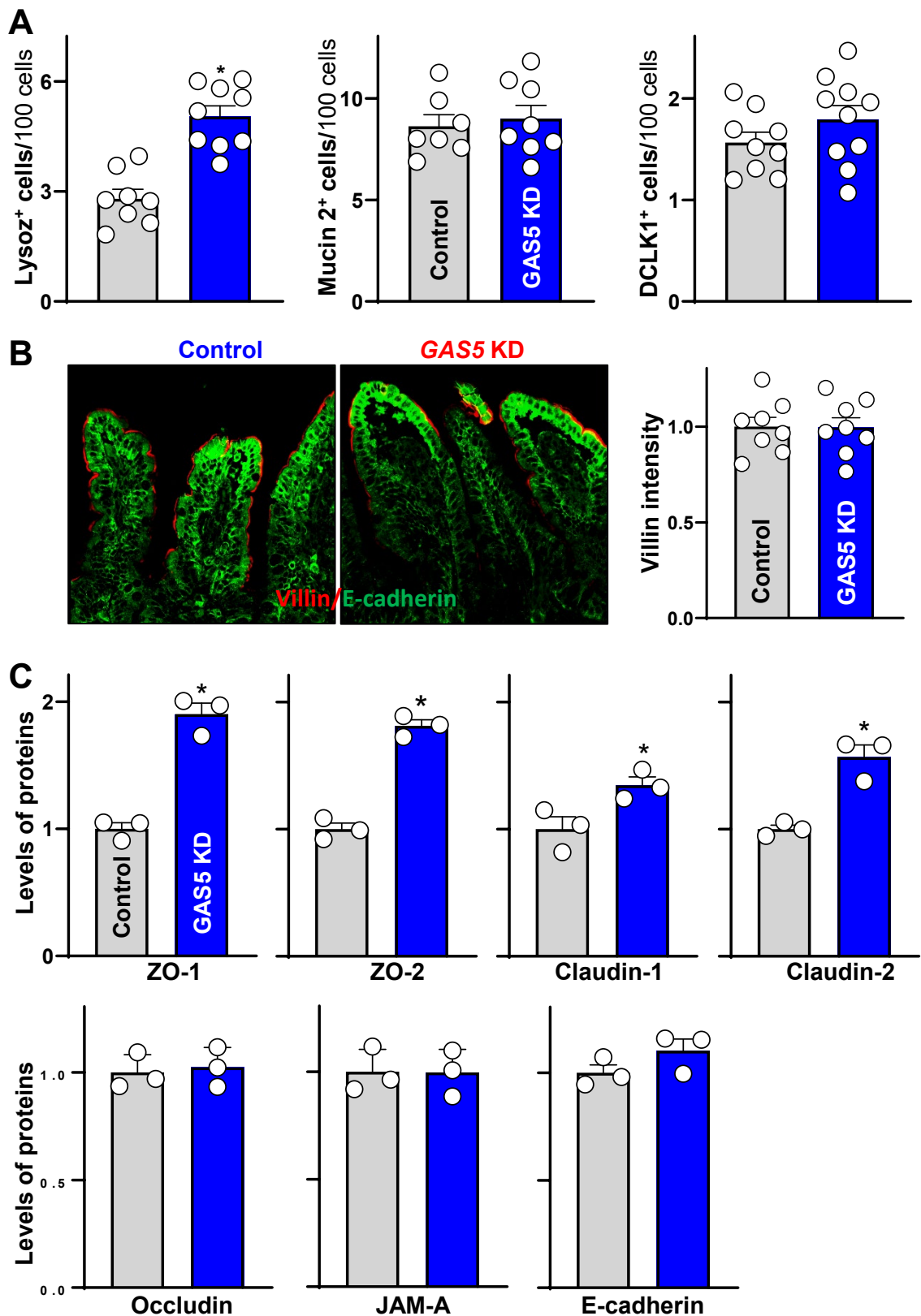


A

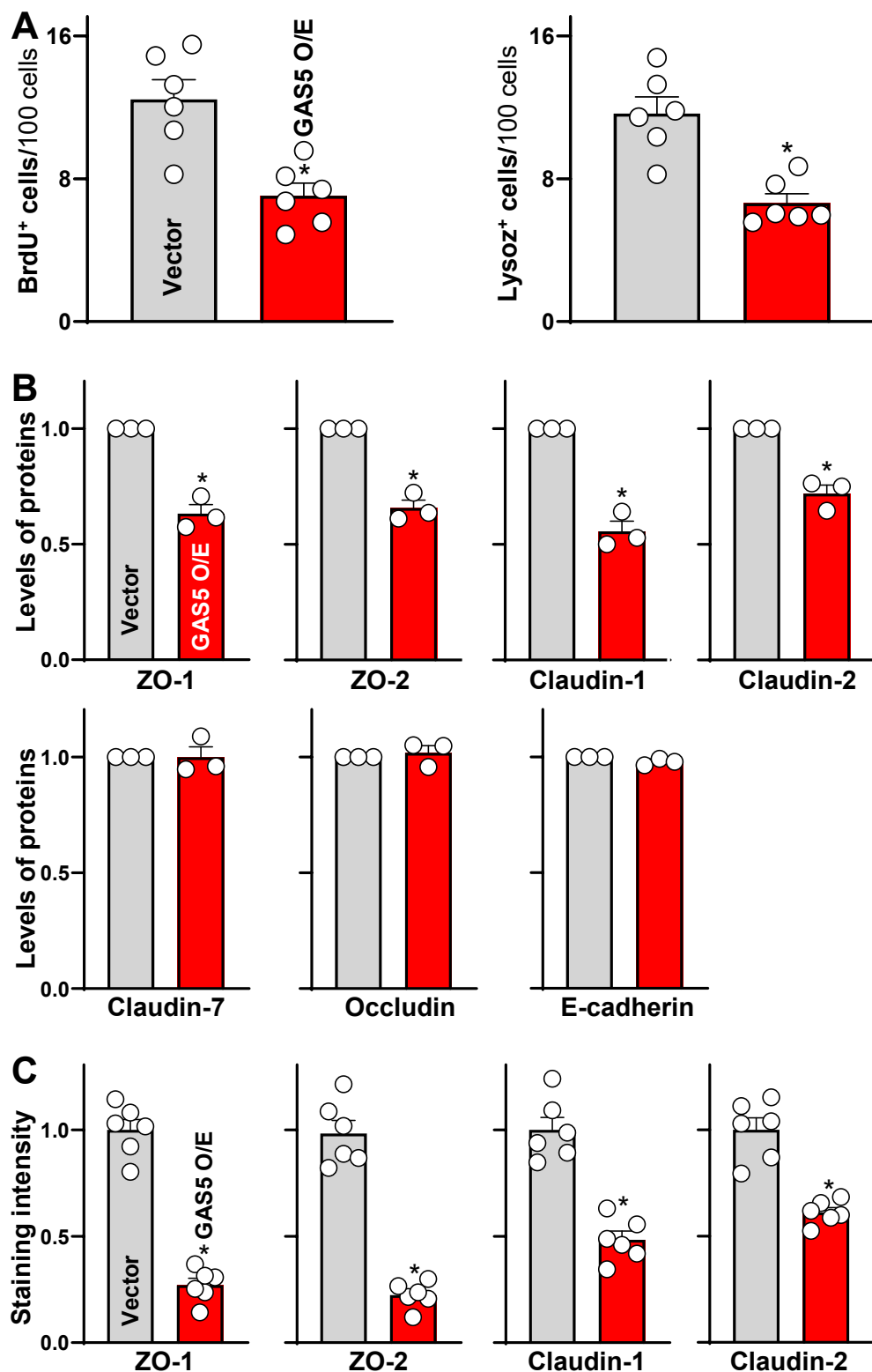
B sgRNA #1: GAGTTGCGGGCGCACAGGTG
Protospacer adjacent motif (PAM) AGG
sgRNA #2: GCCCAGTGACTGGATGGTAT PAM TGG
sgRNA #3: CCCC GCGGCAAGGGAGTTGC PAM GGG
sgRNA #4: ACCAATACCATCCAGTCACT PAM GGG

C

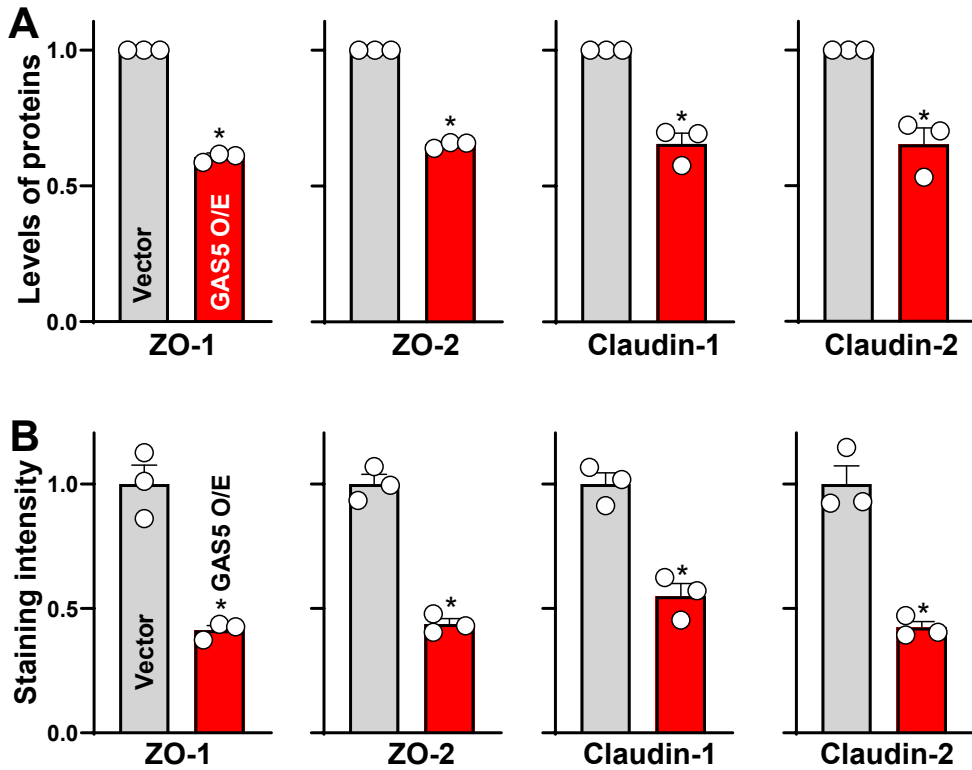
Supplemental Figure 1. (A) Images of H&E staining of mouse DSS-induced colitis (top) and CLP-induced small intestinal mucosal injury (bottom). (B) Sequences of sgRNAs used for deleting GAS5 in IE-Cas9 mice. (C) Changes in the levels of GAS5 in kidney, spleen, stomach, and liver in control and GAS5 KD mice. Values are the means \pm SEM ($n = 6$).



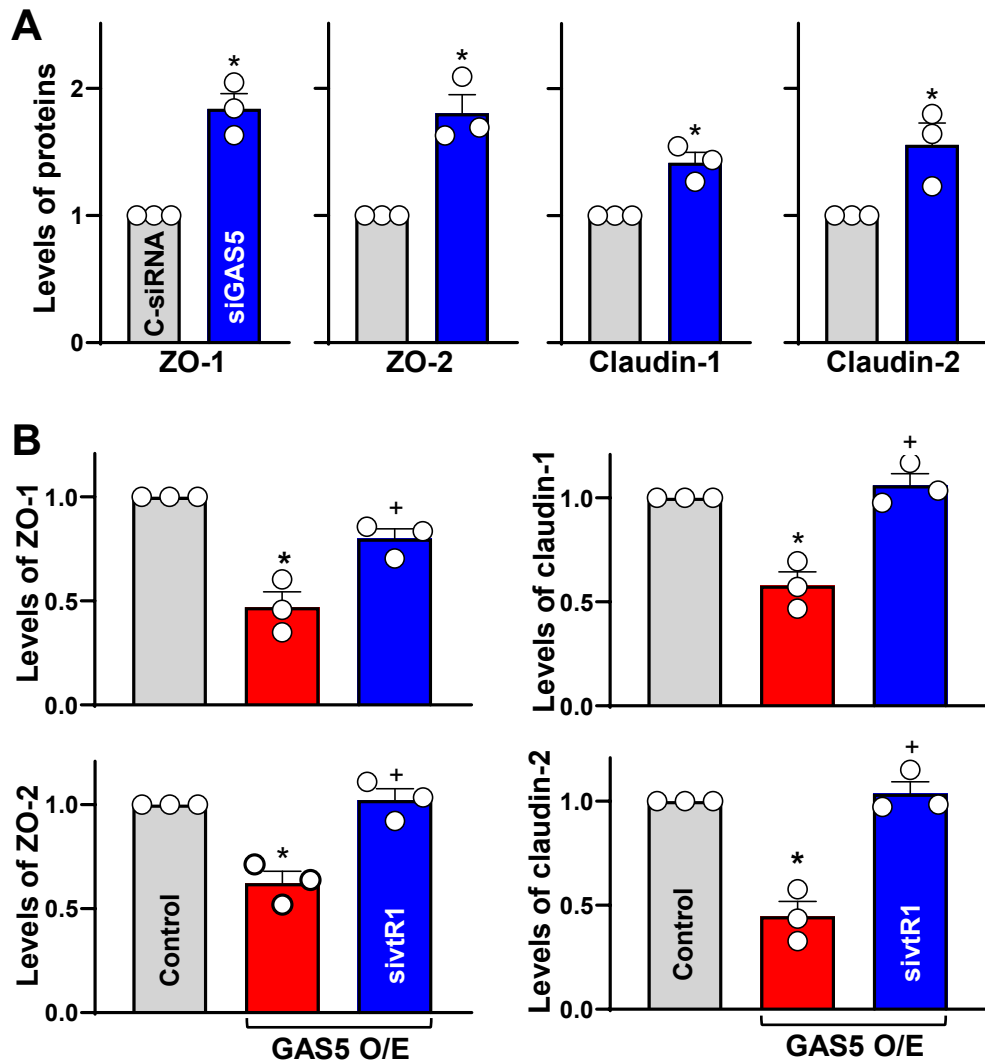
Supplemental Figure 2. (A) Changes in lysozyme (lysoz)-positive, mucin 2-positive, and DCLK1-positive cells in the small intestinal mucosa as described in Figure 3A. Values are the means \pm SEM ($n = 8$ or 10). * $P < 0.05$ compared with controls. (B) Enterocyte differentiation in small intestinal mucosa of control and GAS KD mice as measured by villin immunostaining assay. Values are the means \pm SEM ($n = 8$). (C) Densitometric analysis of immunoblots shown in Figure 3B. Values are the means \pm SEM ($n = 3$). * $P < 0.05$ compared with controls.



Supplemental Figure 3. (A) Changes in the levels of BrdU-positive (*left*) and lysozyme (lysoz)-positive (*right*) cells in intestinal organoids transfected with control vector and GAS5 expression vector (GAS5 O/E) as described in Figure 4C&D. Values are the means \pm SEM ($n = 6$). * $P < 0.05$ compared with control vector. (B) Densitometric analysis of immunoblots shown in Figure 4E. * $P < 0.05$ compared with controls ($n = 3$). (C) Fluorescence staining intensity of various TJ proteins described in in Figure 4F. * $P < 0.05$ compared with controls ($n = 6$).



Supplemental Figure 4. (A) Densitometric analysis of immunoblots of various tight junction proteins in Caco-2 cells after GAS5 overexpression (GAS5 O/E) as shown in Figure 5B. Values are the means \pm SEM ($n = 3$). * $P < 0.05$ compared with control vector. (B) Fluorescence intensity of various tight junction proteins as described in Figure 5C. * $P < 0.05$ compared with controls ($n = 3$).



Supplemental Figure 5. (A) Densitometric analysis of immunoblots of various tight junction protein in Caco-2 cells after GAS5 silencing as shown in Figure 6B. Values are the means \pm SEM ($n = 3$). * $P < 0.05$ compared with C-siRNA. (B) Densitometric analysis of immunoblots of tight junction proteins 48 h after transfection with GAS5 expression vector alone or co-transfection with GAS5 expression vector and siRNA targeting vtRNA1 (sivtR1) as shown in Figure 8B. *+ $P < 0.05$ compared with controls and GAS5 O/E, respectively ($n = 3$).