**A** Normal 5% DSS

CCN1

**B**

GFP

**C** 5% DSS

Relative *mRNA* expression

Days

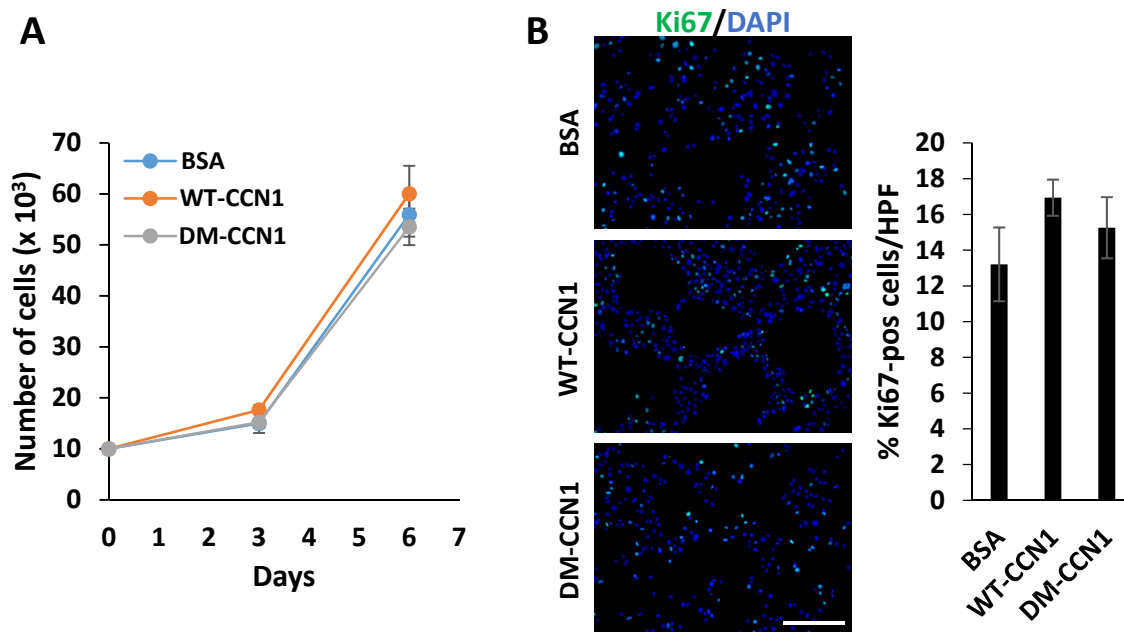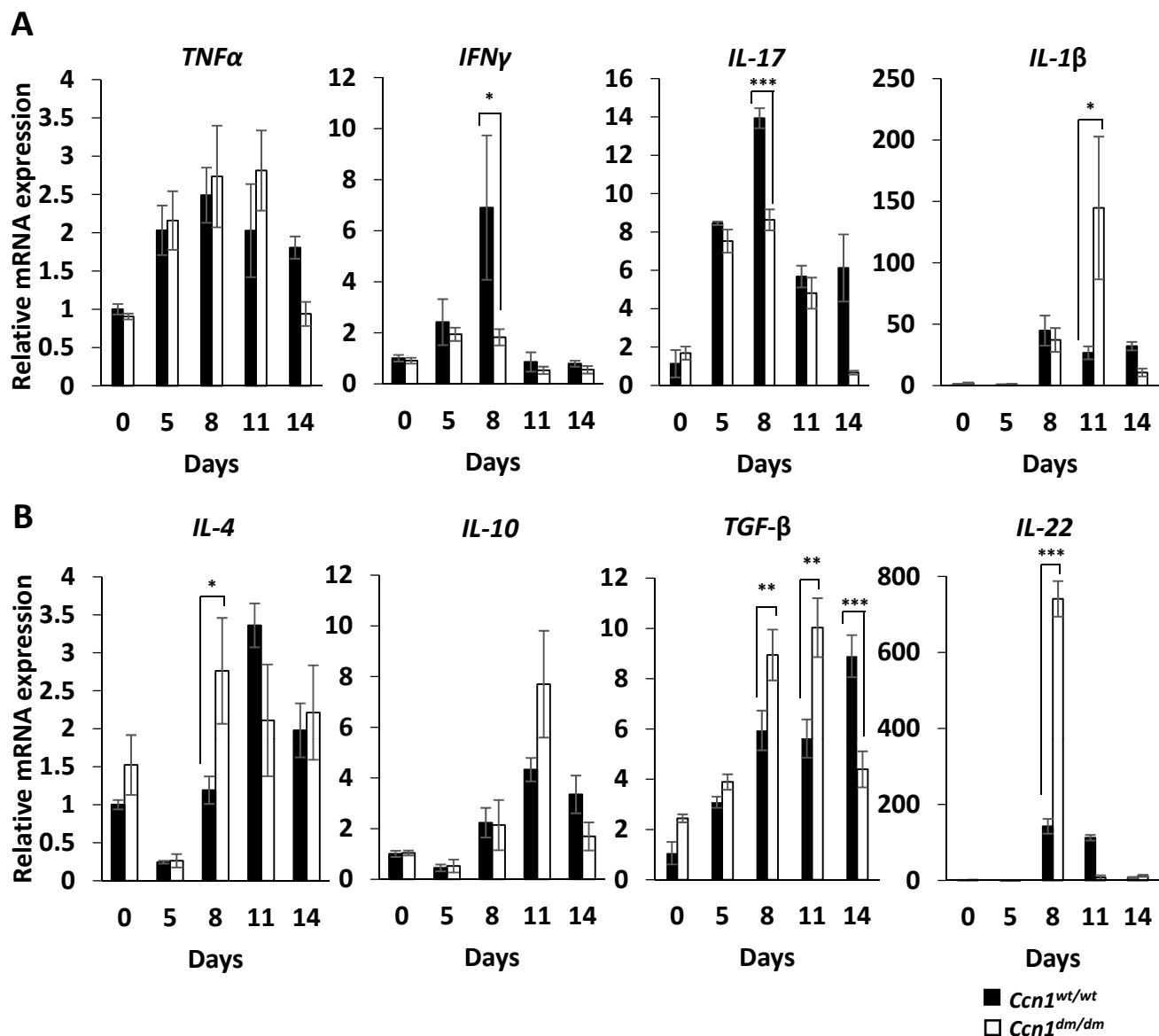**D** 3.5% DSS

Relative mRNA expression

Days

**Supplementary Figure S1. CCN1 expression is increased in murine colitis.**
(A) Distal colon sections of untreated and 5% DSS-challenged wild type mice were stained for CCN1 by immunohistochemistry to evaluate CCN1 expression and localization. Colonic sections were counterstained with hematoxylin. Scale bar=50 µm. (B) GFP immunofluorescence microscopy was performed in normal and DSS-challenged CCN1-EGFP colons and counterstained with DAPI. Scale bar=100 µm. *Ccn1* mRNA in the colon of wild type mice challenged with (C) 5% DSS or (D) 3.5% DSS for 5 days was measured by qRT-PCR at indicated times, and normalized to healthy wild type colon with *cyclophiln E* as internal reference. Sequences of primers used are shown in supplementary table 1. Data shown as mean ± SD; *n*=3; *P <0.01.

**Supplementary Figure S2. CCN1 does not directly induce IEC proliferation.**
YAMC cells were grown in presence of 10 μg/ml of BSA, WT-CCN1, or DM-CCN1 for indicated days in culture. (A) Cells were trypsinized, stained with 1% trypan blue and counted using a hemocytometer. (B) Cells were treated with BSA, WT-CCN1, or DM-CCN1 for 24 hrs and immunostained for Ki67. Number of Ki67-positive cells were counted and normalized to the total number of cells (right). Data shown as mean $\pm$ SD of triplicate experiments.

**Supplementary Figure S3. Cytokine expression in DSS-challenged wild type and *Ccn1dm/dm* mice.** (A) Pro-inflammatory (*TNFα*, *IFNγ*, *IL-17*, *IL-1β*) and (B) anti-inflammatory (*IL-4*, *IL-10*, *TGF-β*) cytokines, and mucosal healing (*IL-22*) gene expression was measured on day 5, 8, 11 and 14 from isolated colon RNA of 3.5% DSS-challenged wild type and *Ccn1dm/dm* mice by qRT-PCR. Sequences of primers used are shown in supplementary table 1. Data are represented as mean ± SD; *n*=3-4; *$p<0.05$, **$p<0.01$, ***$p<0.001$.

| Gene | qPCR Sense Primer (5' to 3') | qPCR Antisense Primer (5' to 3') |
|---|---|---|
| *Tnfα* | CATCTTCTCAAAATTCGAGTGACAA | TGGGAGTAGACAAGGTACAACCC |
| *Ifnγ* | TCAAGTGGCATAGATGTGGAAGAA | TGGCTCTGCAGGATTTTCATG |
| *Il17* | ACCGCAATGAAGACCCTGAT | TCCCTCCGCATTGACACA |
| *Il4* | ACAGGAGAAGGGACGCCAT | GAAGCCCTACAGACGAGCTCA |
| *Il1β* | CAACCAACAAGTGATATTCTCCATG | GATCCACACTCTCCAGCTGCA |
| *Il6* | GAGGATACCACTCCCAACGAGCC | AAGTGCATCATCGTTGTTCATACA |
| *Il10* | GGTTGCCAAGCCTTATCGGA | ACCTGCTCCACTGCCTTGCT |
| *Il22* | AGAACGTCTTCCAGGGTGAA | TCCGAGGAGTCAGTGCTAAA |
| *Tgfβ* | TGACGTCACTGGAGTTGTACGG | GGTTCATGTCATGGATGGTGC |
| *Ccn1* | GGAGGTGGAGTTAACGAGAAAC | GTGGTCTGAACGATGCATTTC |
| *CypE* | TTCACAAACCACAATGGCACAGGG | TGCCGTCCAGCCAATCTGTCTTAT |
| *IL6* | AAATTCGGTACATCCTCGACGGCA | AGTGCCTCTTTGCTGCTTTCACAC |
| *CYPE* | GCAGACAAGGTCCCAAAGACA | CACCCTGACACATAAACCCTG |

**Supplementary Table 1. List of primer sequences used for qRT-PCR.**