

Figure S1: Expression analysis of *CCNY/L1* and *CDK14/16*. **(a)** Cluster annotation of the t-SNE plots shown in Figure 1, Single Cell Portal dataset SCP259. Only the most relevant cell populations are highlighted using the original author annotations. **(b)** RNA-seq gene expression analysis of rectal biopsies from pediatric IBD patients, GEO dataset GSE117993. *CCNY/L1* and *CDK14* expression were modestly increased in ulcerative colitis (UC) and Crohn's disease (CD) samples, but *CDK14* levels were generally low. * p<0.05, ** p<0.01, and *** p<0.001 versus Control (Dunnett's post-hoc test following one-way ANOVA). **(c)** Immunoblot of CDK14. A band of the expected molecular weight was detected in mouse embryonic fibroblasts (MEF), prostate adenocarcinoma cells (PC-3), and, to a lesser extent, human embryonic kidney cells (293T), but not the colorectal cancer (CRC) cell lines HCT116 and Caco-2. Results for SW48 CRC cells were inconclusive due to low protein content. Bulk proteins were detected by Ponceau S staining after transfer. **(d)** RNA-seq gene expression analysis of cancer cell lines, EMBL-EBI dataset E-MTAB-2706. Each dot represents one cell line derived from the indicated tissue of origin.

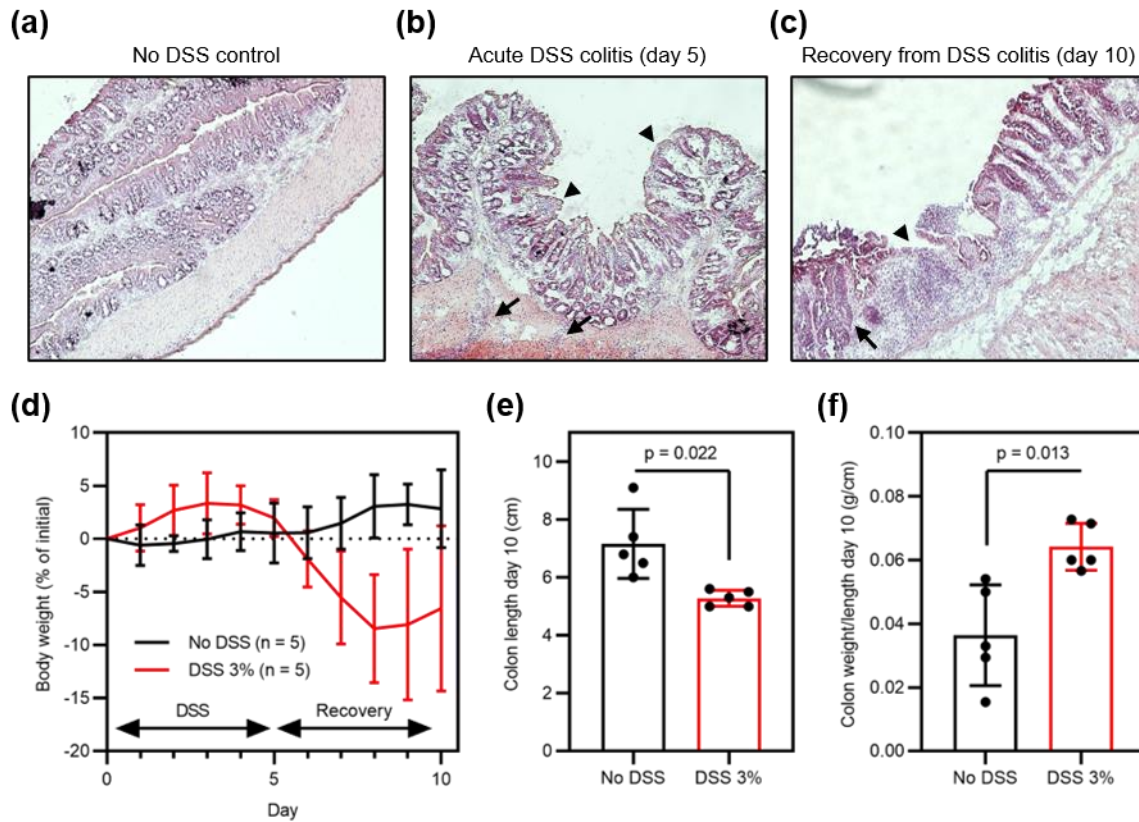


Figure S2: Assessment of DSS colitis disease activity. **(a-c)** Representative H&E images of colon sections from wild-type mice treated, where indicated, with 3% DSS for 5 days. Images were taken at 10x original magnification. In **(b)**, note mucosal leukocyte infiltration (arrows) and epithelial damage (arrowheads) characteristic for acute DSS colitis. In **(c)**, note crypt fission (arrow) and re-epithelization (arrowhead) indicative of tissue regeneration. **(d)** Body weight change in wild-type mice treated with 3% DSS as indicated. **(e, f)** Colon length and colon weight/length ratio of the animals from panel **(d)**. Data were analyzed using Welch's unpaired t-test.

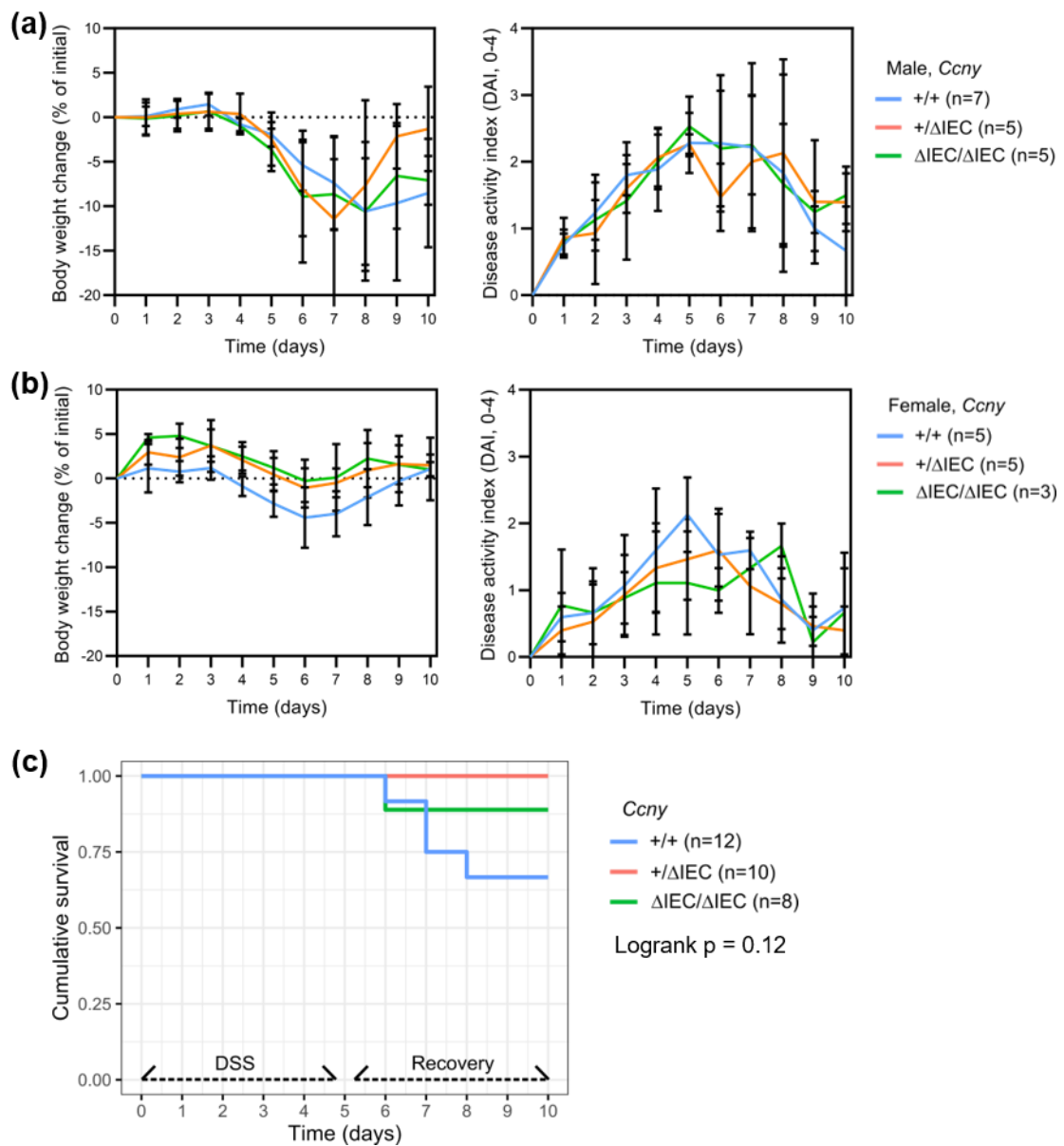


Figure S3: Loss of intestinal epithelial *Ccny* does not affect the susceptibility to DSS colitis. (a, b) Body weight change and disease activity of male (a) and female (b) *Ccny* ^{Δ IEC} mice during the recovery from dextran sulfate sodium (DSS)-induced colitis. No difference was observed compared to littermate controls. (c) Kaplan-Meier survival plot of mice that were removed from the experiment at an ethical endpoint.

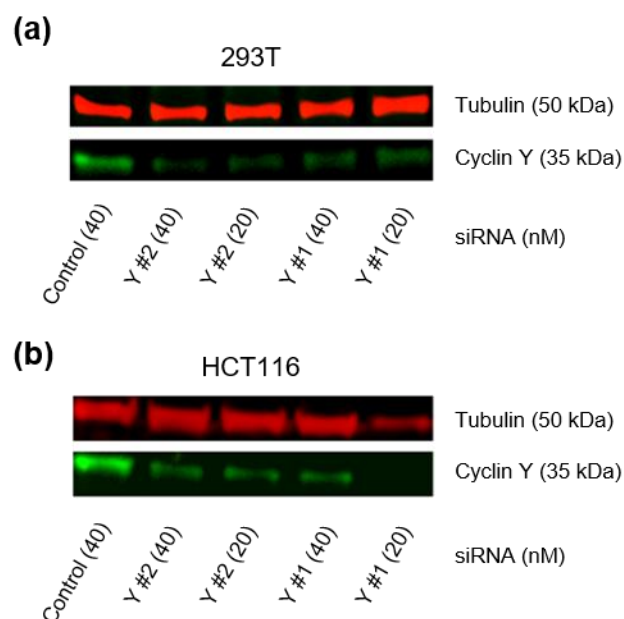


Figure S4: *CCNY* siRNA and antibody validation. **(a, b)** Cyclin Y loss-of-function was assessed by RNA interference, using two independent *CCNY* (Y #1/2) or scrambled control siRNAs at the indicated concentrations. Knockdown efficiency across all experiments, as determined by cyclin Y immunoblot, was approximately 50-70% for 293T cells **(a)** and 60-70% for HCT116 cells **(b)**. Tubulin was used as loading control.