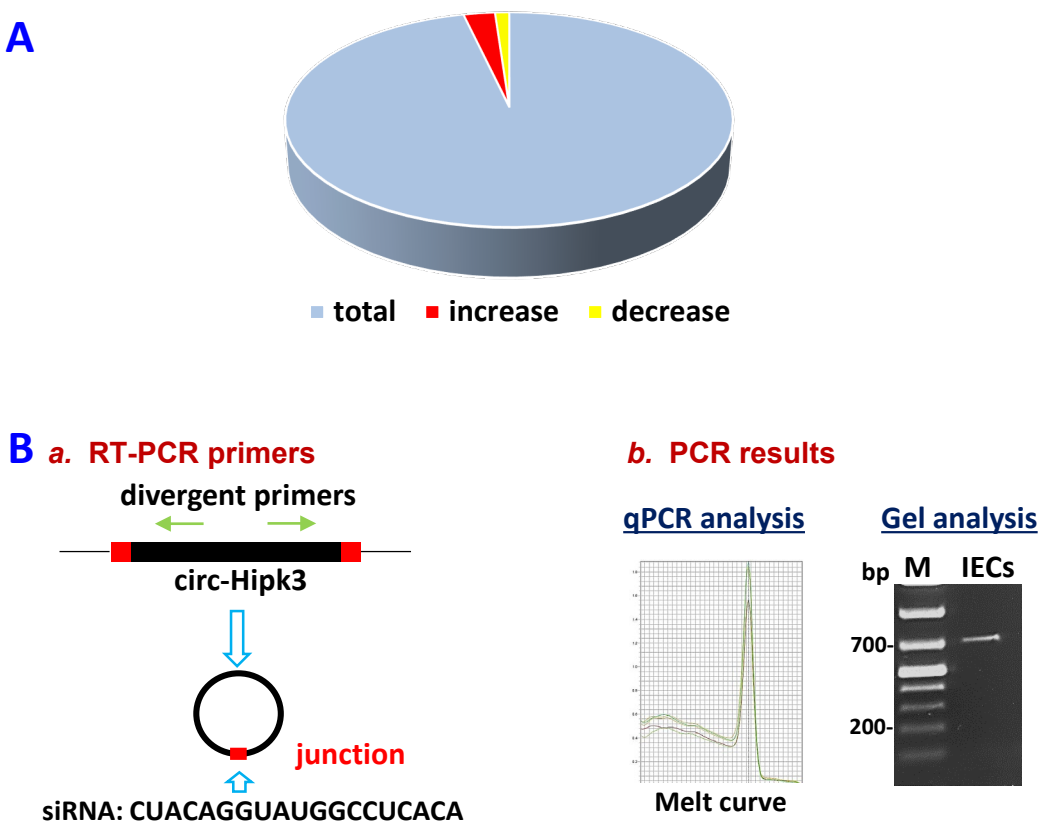
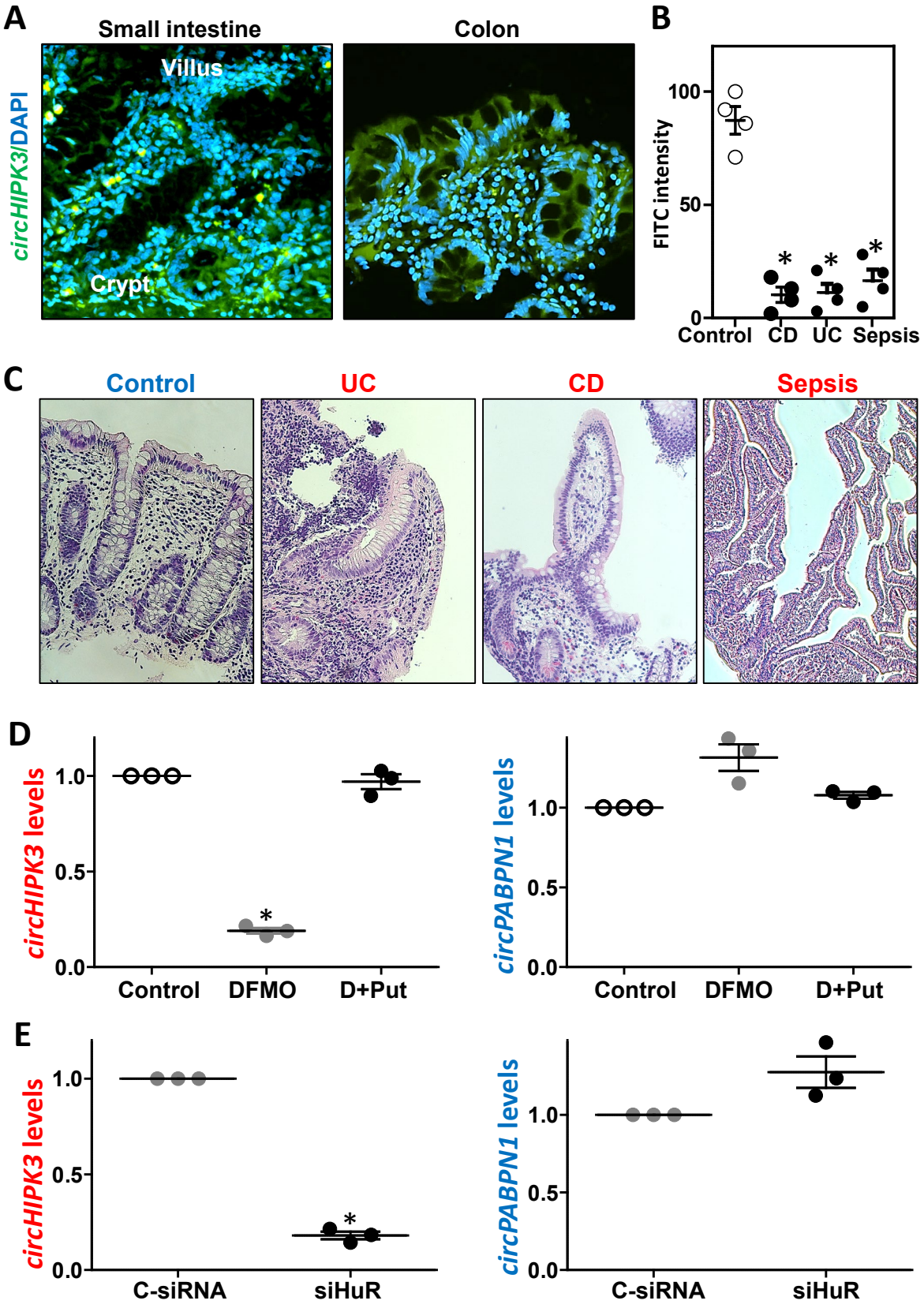
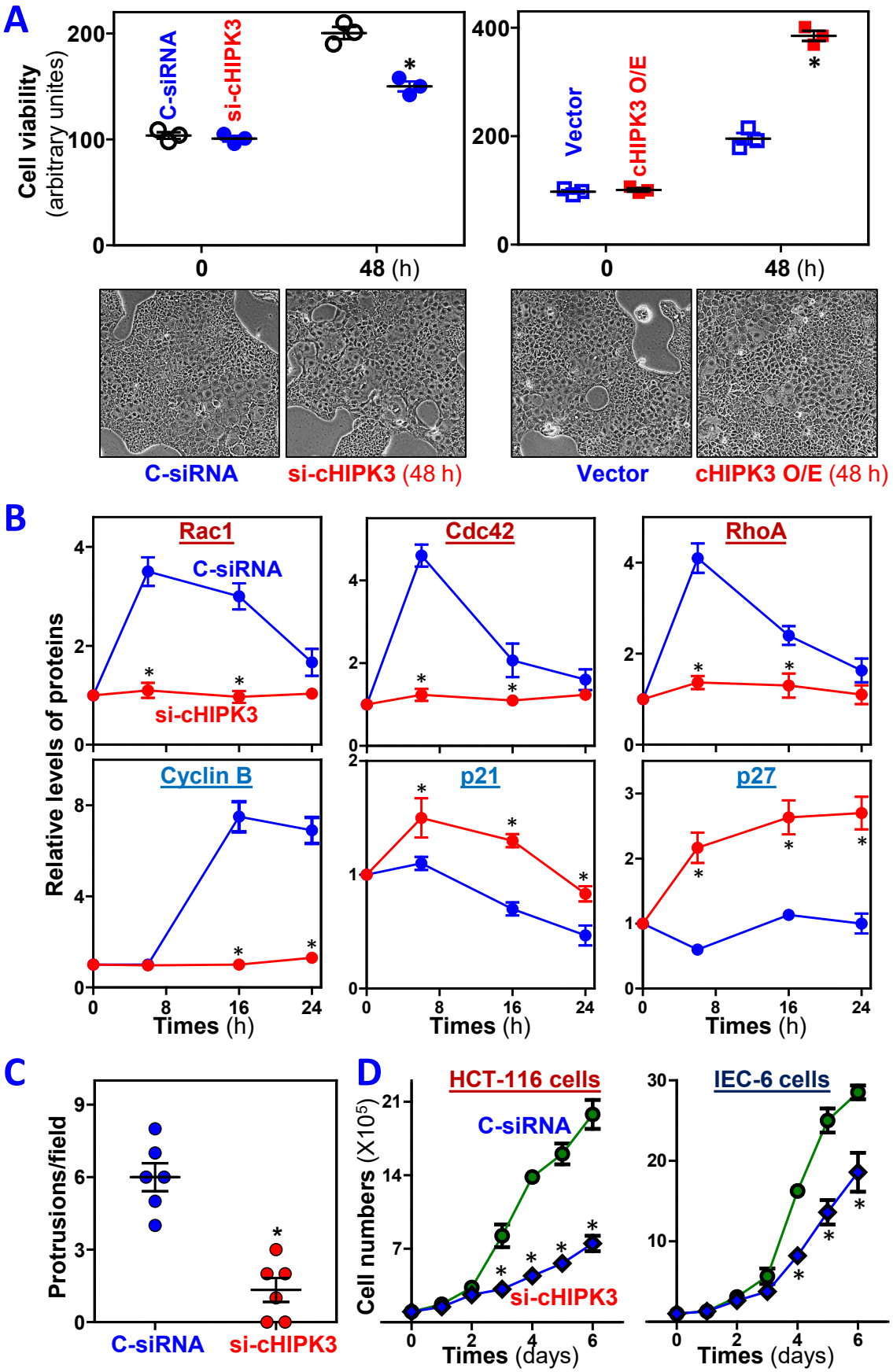


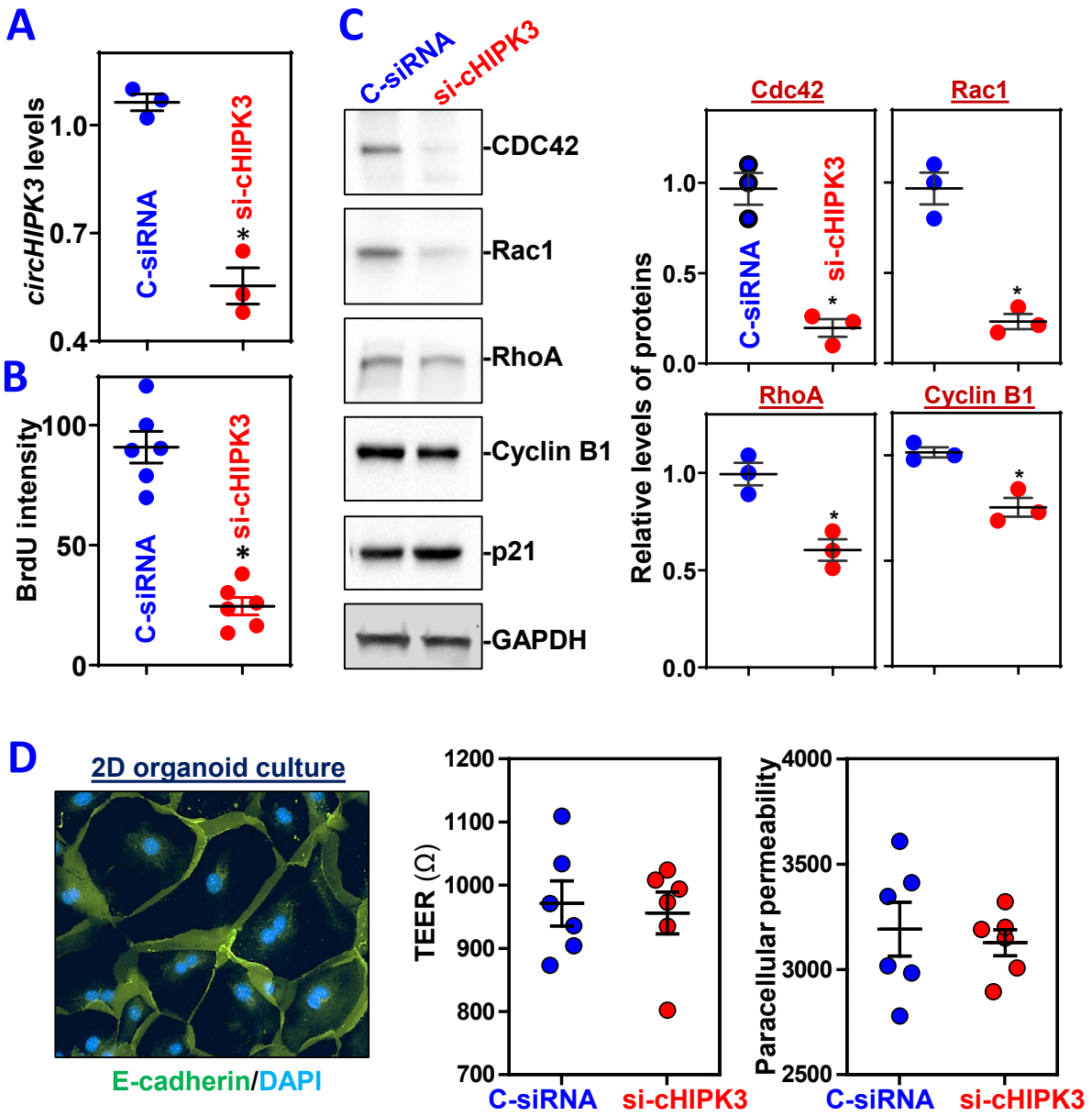
Supplementary Figure 1. Changes in cicrRNA expression profiles in the small intestinal mucosa of CLP-mice. (***A***) Summarized data showing changes in circRNA expression profiles in mice exposed to CLP for 48 as measured by circRNA microarray. (***B***) Methods used to confirm results obtained from microarray assays: ***a***) RT-PCR primers; and ***b***) PCR results. Green arrows indicates the location and direction of the divergent primers used for PCR analysis. The PCR product was analyzed in 1% agarose gel.



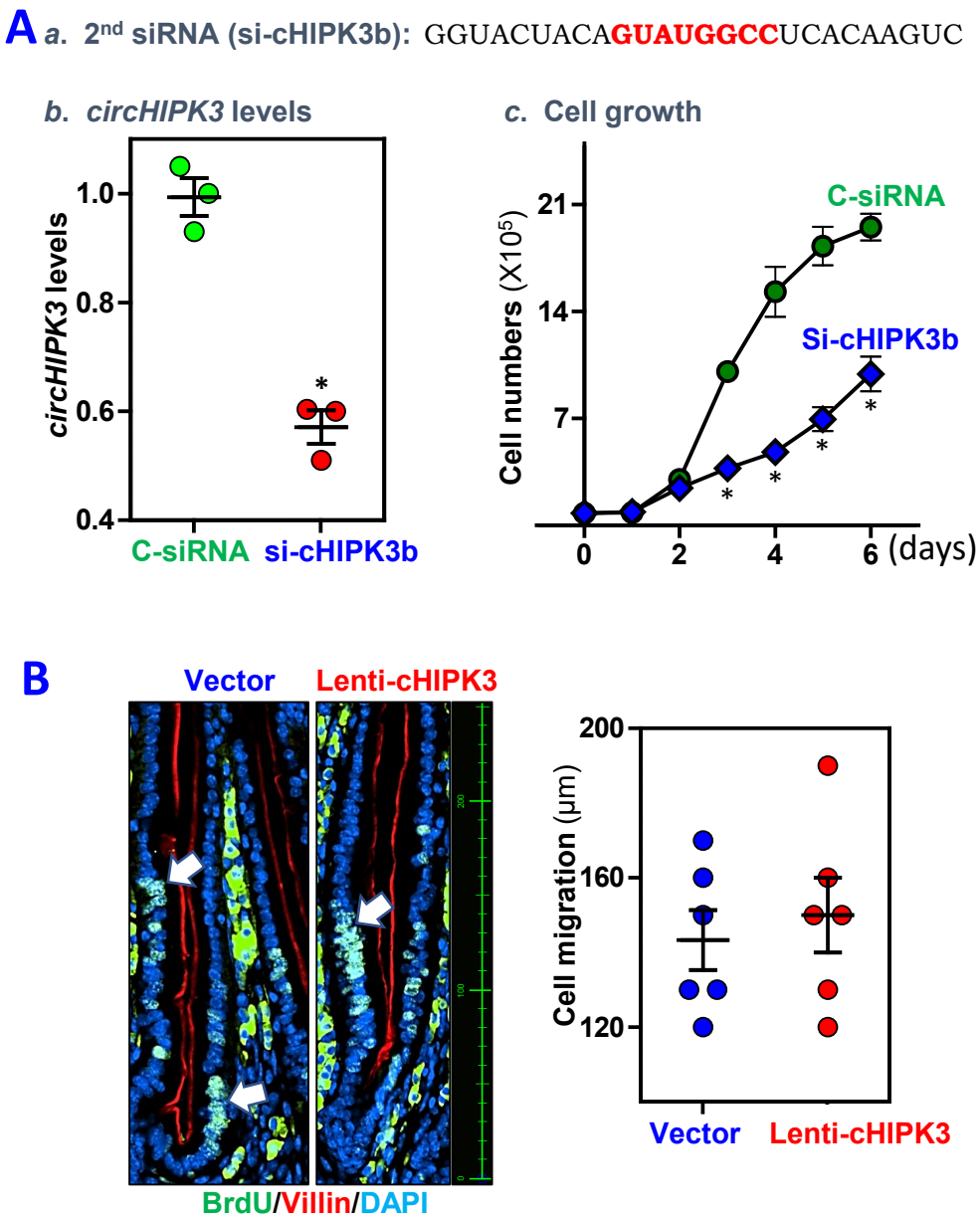
Supplementary Figure 2. (***A***) Distribution of *circHIPK3* in the mucosa of small intestine and colon as measured by RNA-FISH assay. (***B***) Quantification of circHIPK3-FITC intensity in the mucosa from patients with CD, UC, or sepsis as described in **Fig. 1E**. * P < 0.05 compared with controls (n = 4). (***C***) H&E staining of intestinal mucosa from control individuals and patients with UC, CD or sepsis. (***D***) Levels of *circHipk3* (*left*) and *circPabpn1* (*right*) in Caco-2 cells treated with DFMO (5 mmol/L) with or without exogenous putrescine (Put, 10 μmol/L) for 6 days. Values are the means ± SEM (n = 3). * P < 0.05 compared with control or DFMO plus Put. (***E***) Levels of *circHipk3* (*left*) and *circPabpn1* (*right*) in cells transfected with siRNA targeting HuR (siHuR) or control siRNA (C-siRNA) for 48 h. * P < 0.05 compared with C-siRNA (n = 3).



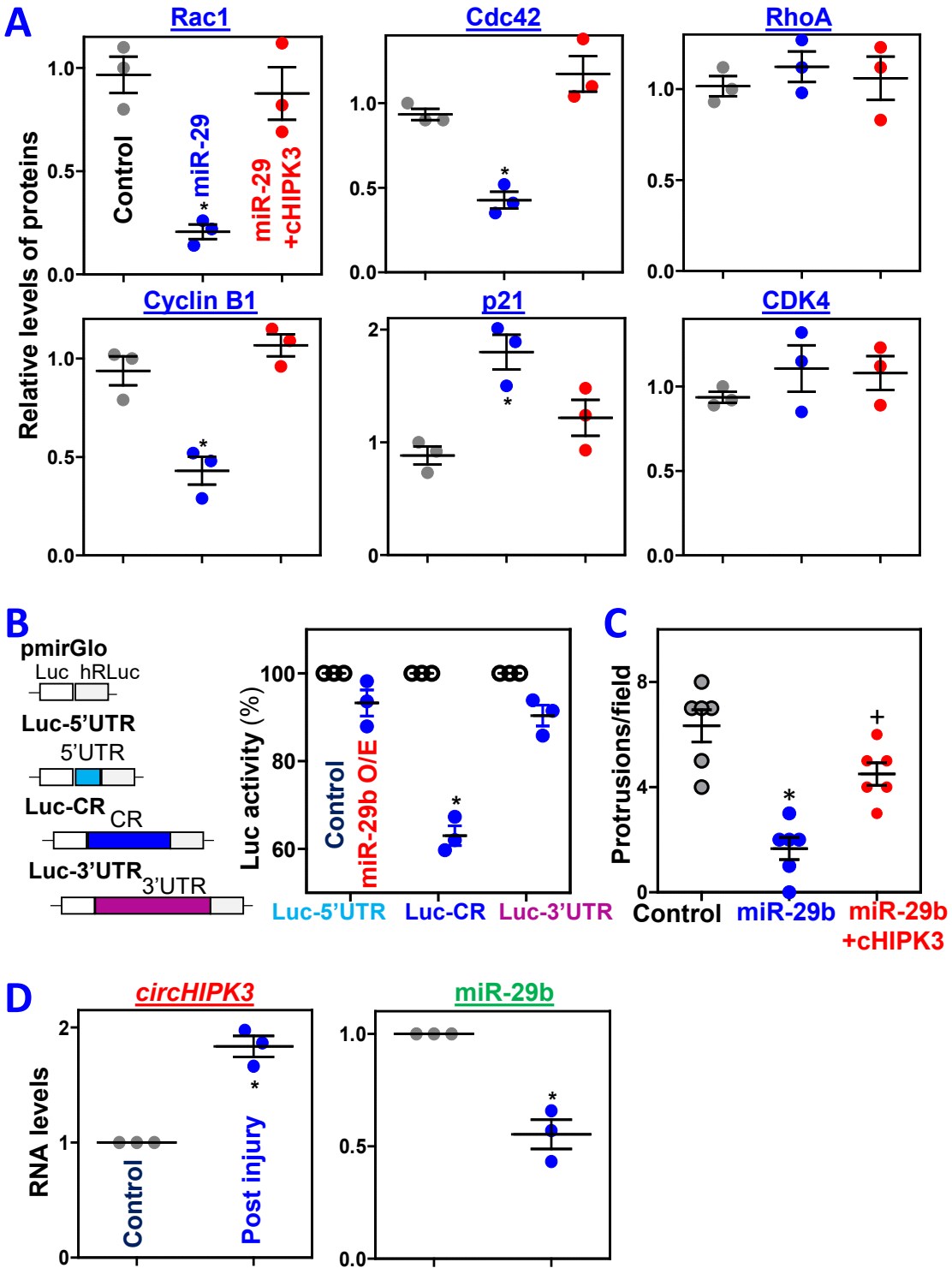
Supplementary Figure 3. (***A***) Cell viability 48h after transfection with si-cHIPK3 or circHIPK3 expression vector, as measured by MTT assay. * $P < 0.05$ compared with C-siRNA or control vector (n = 3). (***B***) Semi-quantitative analysis of immunoblots of various proteins after wounding as described in **Fig. 3A**. * $P < 0.05$ compared with C-siRNA. (***C***) Quantification of cell plasma protrusions 6 h after wounding in cells treated as described in **Fig. 3B**. * $P < 0.05$ compared with C-siRNA. (**D**) circHIPK3 silencing by transfection with si-cHIPK3 inhibits growth of HCT-116 and IEC-6 cells. * $P < 0.05$ compared with C-siRNA ($n = 3$).



Supplementary Figure 4. (***A***) Levels of *circHIPK3* in primarily cultured intestinal organoids on day 3 after transfection with si-cHIPK3 or C-siRNA. Values are the means ± SEM (n = 3). * $P < 0.05$ compared with C-siRNA. (***B***) BrdU intensity of the intestinal organoids treated as described in ***A***. * $P < 0.05$ compared with C-siRNA (n = 6). (***C***) Levels of various proteins in intestinal organoids treated as described in ***A***. *Left*, representative immunoblots; *right*, semi-quantitative analysis of immunoblots. * $P < 0.05$ compared with C-siRNA (n = 3). (***D***) Epithelial barrier function in 2D organoid culture model (*left*) as indicated by transepithelial electrical resistance (TEER) (*middle*) and FITC-dextran paracellular permeability (*right*) after circHIPK3 silencing as described in ***A*** (n = 6).



Supplementary Figure 5. (***A***) Effect of transfection with second siRNA targeting *circHIPK3,* si-cHIPK3b (***a***), on levels of *circHIPK3* (***b***) and cell growth (***c***). Levels of cellular *circHIPK3* were examined 48 h after the transfection. * $P < 0.05$ compared with C-siRNA ($n = 3$). (***B***) Intestinal epithelial cell migration in the small intestinal mucosa after *circHIPK3* overexpression. Mice were intraperitoneally injected with the recombined *circHIPK3* lentiviral vector (Lenti-cHIPK3) or control lentiviral vector (Vector), and BrdU was given on day 5 after the injection. Cell migration was examined 24 h after administration of BrdU ($n = 6$).



Supplementary Figure 6. (***A***) Quantitative results of immunoblots from densitometry analysis in cells transfected with miR-29b alone or co-transfected with miR-29b and cHIPK3 as described in **Fig. 6C.** **P* < 0.05 compared with control or miR-29b+cHIPK3 (*n* = 3). (***B***) Ectopically expressed miR-29b inhibits activity of the Rac1 luciferase reporter in Caco-2 cells. *Left*, schematic of firefly luciferase reporter constructs containing fragments of the Rac1 5'-untranslated region (UTR), coding region (CR), and 3'-UTR. *Right*, levels of Rac1 luciferase reporter activity in cells transfected with the miR-29b expression vector for 48 h. Values are the means ± SEM (*n* = 3). * *P* < 0.05 compared with control. (***C***) Quantification of cell plasma protrusions 6 h after wounding in cells treated as described in **Fig. 6D.** *,+ *P* < 0.05 compared with control and miR-29b alone, respectively (*n* = 6). (***D***) Levels of *circHIPK3* and miR-29 after wounding (6 h) in Caoco-2 cells. * *P* < 0.05 compared with C-siRNA.