

Supplementary Table 1

| Name                                                                            | Conc.                                                 | Cat#             | Manufacturer                |
|---------------------------------------------------------------------------------|-------------------------------------------------------|------------------|-----------------------------|
| <b>Ligands and reagents for colonoid culturing and stimulation*</b>             |                                                       |                  |                             |
| Nicotinamide                                                                    | 1221.2µg/mL                                           | N3376-100G       | MerckMillipore              |
| SB202190                                                                        | 3.31µg/mL                                             | S7067            | Sigma-Aldrich               |
| DAPT                                                                            | 4.3µg/mL                                              | 2634             | Bio-Techne                  |
| Matrigel® Growth Factor Reduced (GFR) Basement Membrane Matrix, phenol red-free | 100 cells/µL                                          | 734-1101         | Corning®                    |
| Richard-Allan Scientific™ HistoGel™ Specimen Processing Gel                     |                                                       | HG-4000-012      | Thermo Scientific           |
| Recombinant human Tumor necrosis factor- $\alpha$ (TNF)                         | 100 ng/mL                                             | 300-01A          | PeproTech                   |
| Polyinosinic:polycytidylic acid (Poly(I:C))                                     | 20 µg/mL                                              | tlrl-pic         | InvivoGen                   |
| Tofacitinib Citrate (Tofacitinib)                                               | 50 µM                                                 | S5001, CP-690550 | Selleckchem.com             |
| Budesonide                                                                      | 10 µM                                                 | S1286            | Selleckchem.com             |
| Wnt-3A conditioned medium                                                       | 50% for growth media and 5% for differentiation media | CRL-2647         | ATCC                        |
| <b>Western blot reagents</b>                                                    |                                                       |                  |                             |
| 1x Complete® EDTA-free protease inhibitor                                       | 1X                                                    | 11836170001      | Roche Life Science Products |
| Utrapure EDTA (0.5M)                                                            | 5nM                                                   | 15575-038        | Thermo Scientific           |
| NP-40                                                                           | 1 %                                                   | 492018           | Sigma-Aldrich               |
| Phosphatase inhibitor cocktail 2 (PIC2)                                         | 1X                                                    | P5726            | Sigma-Aldrich               |
| Phosphatase inhibitor cocktail 3 (PIC3)                                         | 1X                                                    | P0044            | Sigma-Aldrich               |
| 4-12% Nupage Bis-Tris gel                                                       |                                                       | NP0321BOX        | Thermo Scientific           |
| Trans-Blot Turbo nitrocellulose membrane 0.2 µm                                 |                                                       | 1704158          | Bio-Rad laboratories        |
| NuPage LDS Sample buffer (4X)                                                   | 1X                                                    | NP0007           | Thermo Scientific           |
| Blocking Buffer for fluorescent Western blot                                    |                                                       | MB-070           | Rockland Immunochemicals    |
| <b>Staining Kits and associated reagents</b>                                    |                                                       |                  |                             |
| EnVision FLEX+, Mouse, High pH                                                  |                                                       | K8012            | Dako Agilent                |
| MaxDouble M488&R650 ImmunoFluorescence Double Staining Kit for human tissue     |                                                       | DSMR-H3          | MaxVision Biosciences Inc.  |

|                                                                        |                                     |                            |                             |
|------------------------------------------------------------------------|-------------------------------------|----------------------------|-----------------------------|
| In Situ Cell Death Detection Kit, Fluorescein                          |                                     | 11684795910                | Roche Life Science Products |
| Pierce BCA protein assay kit                                           |                                     | 23225                      | Thermo Scientific           |
| Proteinase K                                                           | 20 µg/mL                            | AM2546                     | Thermo Scientific           |
| DAPI                                                                   | 1:1000                              | 62248                      | Thermo Scientific           |
| <b>Antibodies</b>                                                      |                                     |                            |                             |
| CK20, mouse mAb, clone Ks20.8                                          | 1:1000 auto / 1:150 manual staining | M7019, RRID:AB_2133718     | Dako Agilent                |
| Ki67 mouse mAb, clone MIB-1                                            | 1:600 auto /1:50 manual staining    | M7240, RRID:AB_2631211     | Dako Agilent                |
| LGR5 mouse mAb, clone OTI2A2                                           | 1:1000                              | MA5-25644, RRID:AB_2723318 | Thermo Scientific           |
| EphB2 goat pAb                                                         | 1:1000                              | AF467, RRID:AB_355375      | R&D Systems                 |
| Phospho-MLKL (Ser358) rabbit mAb, clone E7G7P                          | 1:1000                              | 18640S                     | Cell Signaling Technology   |
| MLKL mouse mAb, clone E7v4W                                            | 1:1000                              | 26539                      | Cell Signaling Technology   |
| Caspase-3 rabbit mAb, clone D3R6Y (also recognizing cleaved caspase-3) | 1:1000                              | 14220, RRID:AB_2798429     | Cell Signaling Technology   |
| GAPDH XP rabbit mAb, clone D16H11                                      | 1:5000                              | 5174, RRID:AB_10622025     | Cell Signaling Technology   |
| Goat anti-mouse IgG, DyLight800                                        | 1:5000                              | SA5-35521, RRID:AB_2556774 | Thermo Scientific           |
| Goat anti-mouse IgG, DyLight680                                        | 1:5000                              | 35518, RRID:AB_614942      | Thermo Scientific           |
| Goat anti-rabbit IgG, DyLight800                                       | 1:5000                              | SA5-35571, RRID:AB_2556775 | Thermo Scientific           |
| Goat anti-rabbit IgG, DyLight680                                       | 1:5000                              | 35569, RRID:AB_1965957     | Thermo Scientific           |
| Donkey anti-goat Donkey anti-Goat IgG, Alexa Fluor™ 647                | 1:5000                              | A-21447, RRID:AB_2535864   | Thermo Scientific           |
| <b>Multiplex and ELISA kits</b>                                        |                                     |                            |                             |
| Bio-Plex Pro Human Chemokine Panel, 40-plex                            |                                     | 171ak99mr2                 | Bio-Rad laboratories        |
| Human CXCL2/GRO beta DuoSet ELISA                                      |                                     | DY276-05                   | R&D systems                 |
| Human CXCL5/ENA-78 DuoSet ELISA                                        |                                     | DY254-05                   | R&D systems                 |
| Human CXCL11/I-TAC DuoSet ELISA                                        |                                     | DY672                      | R&D systems                 |
| <b>Softwares</b>                                                       |                                     |                            |                             |

|                                   |                                          |
|-----------------------------------|------------------------------------------|
| Fiji                              | RRID:SCR_002285, Schindelin et al., 2012 |
| QuPath 3.0                        | RRID:SCR_018257, Bankhead et al., 2017   |
| Rstudio                           | RRID:SCR_001905                          |
| Graphpad Prism 9                  | RRID:SCR_002798, GraphPad Software Inc.  |
| LI-COR Odyssey Fc Imager, v3.0.25 | RRID:SCR_023227, LI-COR Biotechnology    |
| LI-COR Image Studio Lite, v3.1    | RRID:SCR_013715, LI-COR Biotechnology    |

\*Comprehensive protocol in Gopalakrishnan, S., et al., *Comprehensive protocols for culturing and molecular biological analysis of IBD patient-derived colon epithelial organoids*. Frontiers in Immunology, 2023. **14**.

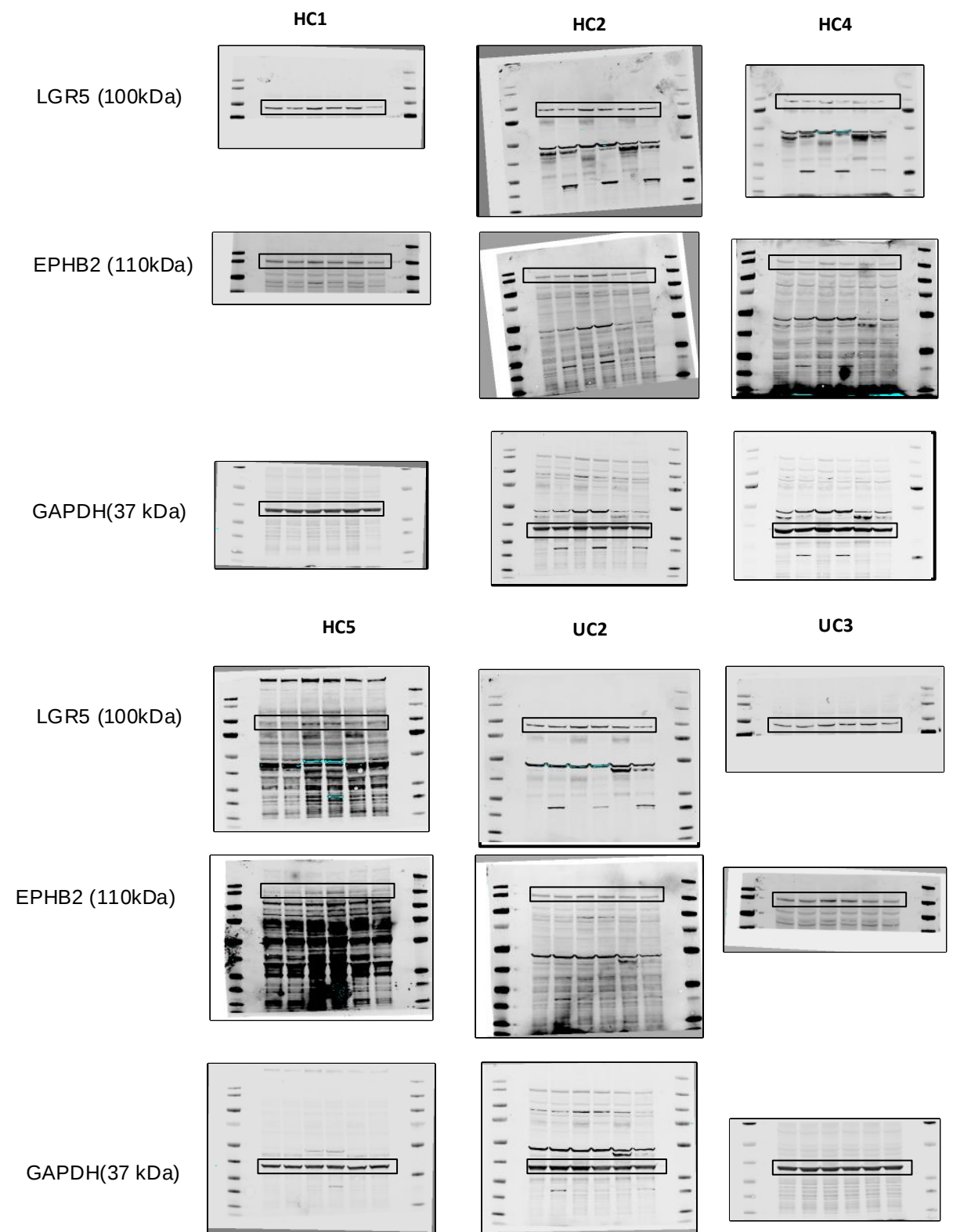


Figure S1. Full blot images with boxes indicating the respective immunoblot bands shown in Figure 6

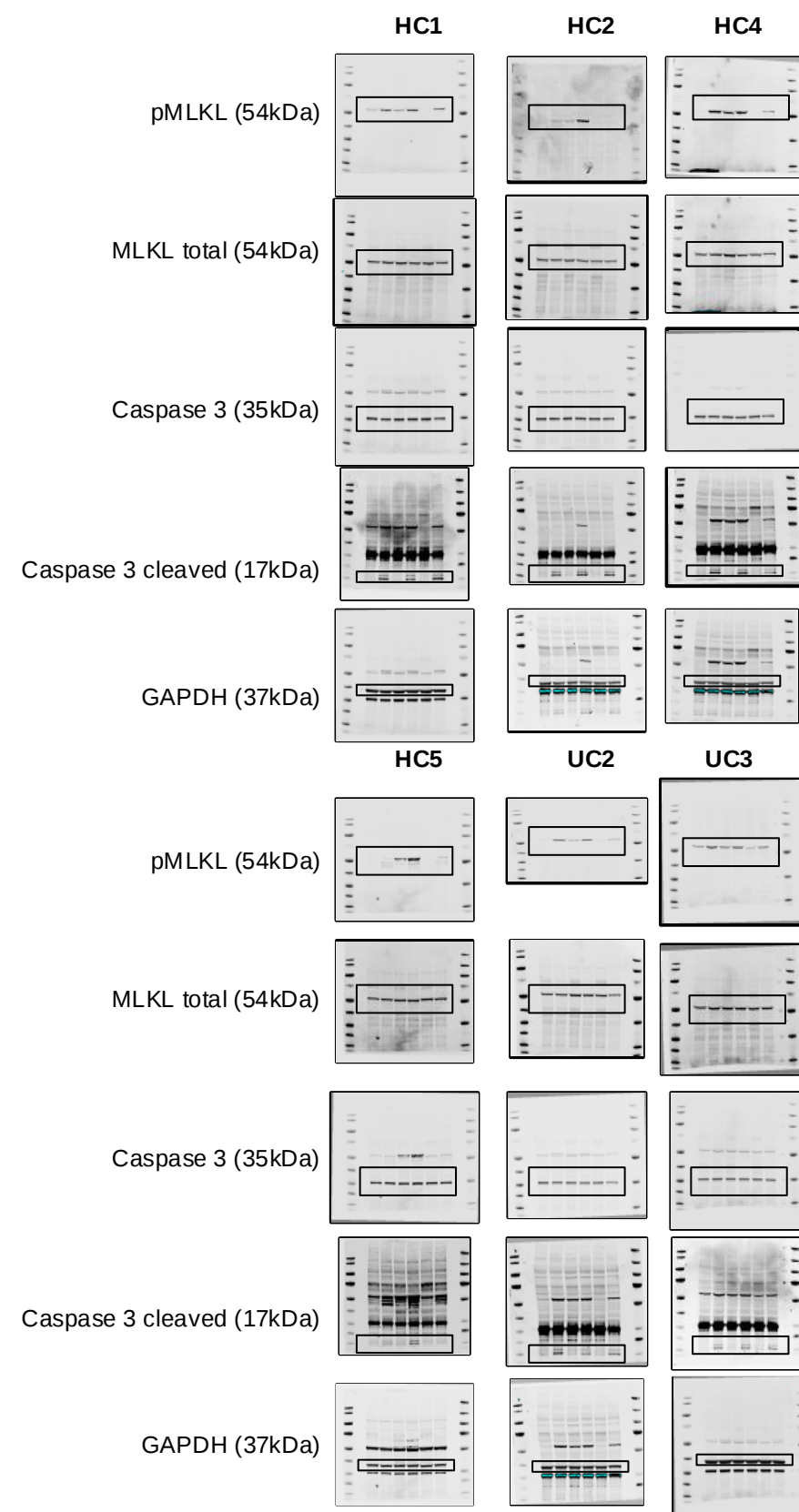


Figure S2. Full blot images with boxes indicating the respective immunoblot bands shown in Figure 8.