

## Figure Legends

**Figure 1. Schematic of the Wnt/ $\beta$ -catenin signal transduction pathway.** The pathway is inactive in the absence of Wnt (**A**, “Wnt OFF”) and active upon Wnt binding (**B**, “Wnt ON”). Abbreviations: Frizzled (FZD), low-density lipoprotein-related protein (LRP), Glycogen synthase kinase (GSK), Adenomatous polyposis coli (APC), Casein kinase 1 (CK1),  $\beta$ -transduction repeat-containing protein ( $\beta$ -TrCP),  $\beta$ -catenin ( $\beta$ -cat), T-cell factor/lymphocyte enhancer factor (TCF).

**Figure 2. Establishing intestinal epithelium organoids.** **A:** A diagram representation of the intestinal epithelium with crypts and villi. The intestinal stem cells (green) are flanked by Paneth cells (red) at the base of the crypts. Several crypts feed cells onto one villus, which is a finger-like projection into the lumen. **B:** An isolated crypt from the Lgr5-EGFP-IRES-Cre mouse shows the green (EGFP<sup>+</sup>) stem cells (this is a fresh crypt preparation). **C:** After one day in culture, the isolated crypts form cysts with stem cells (green cells) polarized to one end of the cyst. **D:** Over several days the cells generated by the stem cells then self-organize into an organoid with domains that represent the crypt and villus of the epithelium.

**Figure 3. LIM-1863-Mph: a colon cancer tumour morphogenesis model.** **A:** A differential interference contrast (DIC) image of a LIM1863-Mph monolayer patch undergoing MET and tumour organoid formation. Assembled organoids that are about to dislodge from the patch (arrow) are generated by monolayer cells (arrow-heads) that spontaneously re-organize at the centre of the monolayer patch (along the white dashed line, scale bar is 100  $\mu$ ). **B:** The transition between organoid and monolayer is readily detected using immunofluorescence confocal microscopy to detect ZO-1 (red). The organoid lumen is lined by the apical surface of the cells and thus ZO-1 staining is seen as a tight rosette (shown are stacked Z-sections at

the cross section of organoid). This is in stark contrast to the monolayer cells where it shows the cell outline. Nuclei are are blue (DAPI stained).