**Whole-mount organoid immunofluorescence, DNA damage quantification and scanning electron microscopy**

Organoids co-cultured with pks+ or pksΔclbQ E. coli21 were collected in cell recovery solution (Corning) and incubated at 4 °C for 30 min with regular shaking in order to free them from BME. For FANCD2 staining, organoids were pre-permeabilized with 0.2% Triton-X (Sigma) for 10 min at room temperature. Then, organoids were fixed in 4% formalin overnight at 4 °C. Subsequently, organoids were permeabilized with 0.5% Triton-X (Sigma), 2% donkey serum (BioRad) in PBS for 30 min at 4 °C and blocked with 0.1% Tween-20 (Sigma) and 2% donkey serum in PBS for 15 min at room temperature. Organoids were incubated with mouse anti-γH2AX (Millipore; clone JBW301; 1:1,000 dilution) or rabbit anti-FANCD2 (affinity purified as described36; 1 mg/ml) primary antibody overnight at 4 °C. Then, organoids were washed four times with PBS and incubated with either secondary goat anti-mouse AF-647 (Thermo Fisher, catalogue number A-21235, 1:500 dilution) or goat anti-rabbit AF-488 (Life Technologies, catalogue number A21206, 1:500 dilution) antibodies, respectively, for 3 h at room temperature in the dark and washed again with PBS. Organoids were imaged using an SP8 confocal microscope (Leica). Fluorescent microscopic images of γH2AX foci were quantified as follows: nuclei were classified as containing either no foci or one or more foci. The fraction of nuclei containing foci over all nuclei is displayed as one datapoint per organoid.