1 **Supplementary Figure 1.** Effects of pinobanksin on ferroptotic cell death of IEC-6 2 cells. IEC-6 cells incubated with ferroptosis inducer RSL3 for 48 hours to induce 3 ferroptotic cell death, then effects of pinobanksin, at different doses (5 μ M, 10 μ M, 25 4 μ M, 50 μ M, 125 μ M), on ferroptotic cell death of IEC-6 cell were measured, n=3.

Supplementary Figure 2. Effects of different doses of pinobanksin on DSS-induced 5 colitis in mice. Mice was were administrated with dextran sulfate sodium (DSS) for 9 6 consecutive days to induce colitis model, mice with colitis were gavaged with 7 pinobanksin (10 mg/kg, 25 mg/kg, 40 mg/kg, 80 mg/kg, 120 mg/kg) every day for 9 8 consecutive days respectively. (A)hematoxylin and eosin (HE)-staining analysis of 9 mice colonic tissue was performed (scale bar=500 µm). And (B) colon length, (C) 10 disease activity index of mice in different groups were measured. Data are expressed as 11 the mean \pm SD, n=3. 12

13 Supplementary Figure 3. Chromatography peak of pinobanksin standards or DSS-14 treated pinobanksin. Pinobanksin standards (PIN, 500 μ M) was incubated with 2.5% 15 dextran sulfate sodium (DSS) solution in 37 °C for 2 hours and were injected for HPLC 16 analysis. HPLC analysis was performed on a PM1000 series HPLC system (Hitachi, 17 Japan), and the separation was performed on an Innoval ODS-2 column (Agela 18 Technologies, USA, 250 mm × 4.6 mm, 5 μ m).

19 **Supplementary Figure 4.** Suppression effects of pinobanksin on erastin-induced 20 epithelial cell death. IEC-6 cells incubated with erastin (5 μ M) were established to 21 induce ferroptotic cell death *in vitro*, and si-RNA-mediated gene silencing was 22 performed to mimic knockdown of SLC7A11, then the influence of pinobanksin (50 23 μ M) on cell viability in erastin-treated wild type (A) and SLC7A11 depletion IEC-6 24 cells (B) were determined, n=3.

Supplementary Figure 5. Effects of pinobanksin on composition of intestinal bacteria in mice with colitis. A. Cladogram showing the impact of pinobanksin on the taxonomic distribution of the bacteria in mice with colitis. A total of 15 differentially abundant bacterial taxa were detected. Of those, 11 bacterial taxa were significantly overrepresented in the DSS ctrl (DSS) group (blue) and 4 bacterial taxa were overrepresented in the pinobanksin-treated DSS mice (PIN) group (red). B. Histogram of the LDA scores computed for differentially abundant bacterial taxa between the DSS and PIN groups. Only taxa with a LDA score $(log_{10}) > 4$ and P < 0.05 are listed. C. Clustering heat map at genus level of 16S rRNA between the DSS and PIN groups. D. Taxonomic analysis of microbiota in fecal samples at the phylum and genus levels, n=3.