

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.

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

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 $^{\circ}$ 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 \times 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.

25 **Supplementary Figure 5.** Effects of pinobanksin on composition of intestinal bacteria
26 in mice with colitis. A. Cladogram showing the impact of pinobanksin on the taxonomic
27 distribution of the bacteria in mice with colitis. A total of 15 differentially abundant
28 bacterial taxa were detected. Of those, 11 bacterial taxa were significantly
29 overrepresented in the DSS ctrl (DSS) group (blue) and 4 bacterial taxa were
30 overrepresented in the pinobanksin-treated DSS mice (PIN) group (red). B. Histogram

31 of the LDA scores computed for differentially abundant bacterial taxa between the DSS
32 and PIN groups. Only taxa with a LDA score (\log_{10}) > 4 and $P < 0.05$ are listed. C.
33 Clustering heat map at genus level of 16S rRNA between the DSS and PIN groups. D.
34 Taxonomic analysis of microbiota in fecal samples at the phylum and genus levels, $n=3$.
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