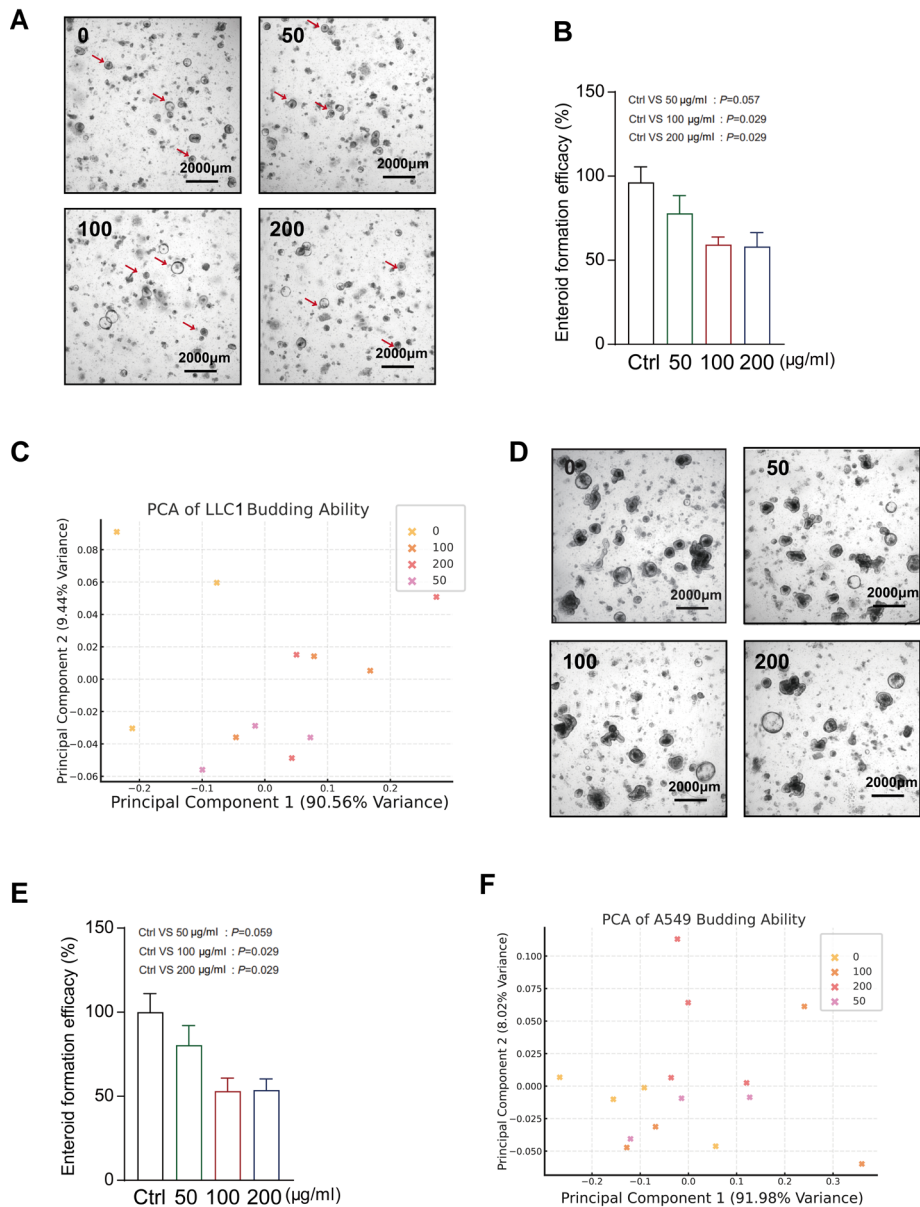


**Figure S1** LLC1-CM and A549-CM impaired the enteroids formation and differentiation. (A) Representative images of enteroids in control group and LLC1-CM groups after 72 h culture (bar = 200  $\mu$ m). (B) Normalized enteroid formation efficacy at 72 h in different groups (LLC1-CM) (n=4 wells each group). (C) Normalized enteroid differentiation efficacy at 72h in different groups (the differentiation between Ctrl group and 25% LLC1-CM group and 50% LLC1-CM group didn't show significance) (n=4 wells each group). (D) Representative images of enteroids in control group and A549-CM groups after 24 h culture (bar =200  $\mu$ m). The red arrows indicated representative enteroids in day 1. (E) Normalized enteroid formation efficacy at 72h in different groups (n=4 wells each group). (F) Representative images of enteroids in control group and A549-CM groups after 72 h culture (bar =200  $\mu$ m). (G) Normalized enteroid formation efficacy at 72 h in different groups (A549-CM) (n=4 wells each group). (H) Normalized enteroid differentiation efficacy at 72h in different groups (the differentiation between Ctrl group and 25% A549-CM group and 50% A549-CM group didn't show significance) (n=4 wells each group). LLC1-CM, Lewis lung carcinoma cell conditional medium; A549-CM, A549 human lung adenocarcinoma cells conditional medium.



**Figure S2** LCCDEs inhibited the formation of intestinal organoids in vitro. (A,B) Higher concentrations of A549 LCCDEs caused more significant impairment on small intestinal organoid proliferation at day 1. The red arrows indicated representative enteroids in day 1. (C) PCA of LLC1 LCCDEs differentiation ability didn't show significant of differentiation in the four groups. (D,E) Higher concentrations of A549 LCCDEs caused more significant impairment of small intestinal organoid proliferation at day 3. (F) PCA didn't show a significant change in the differentiation in enteroids treated by A549 LCCDEs at D3 (n=4). LCCDEs, lung cancer cell derived exosomes; PCA, principal components analysis; A549, A549 human lung adenocarcinoma cells.