

# **SUPPLEMENTAL DATA**

## **Salinomycin Nanoparticles Interfere with Tumor Cells Growth and the Tumor Microenvironment in an Orthotopic Model of Pancreatic Cancer**

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### **Synthesis of PLGA-mPEG**

1500 mg PLGA ( $M_w=15$  kDa, 0.1 mmol), 378 mg mPEG-NH<sub>2</sub>, Trifluoroacetic acid ( $M_w=3000$ , 0.126 mmol), and 88  $\mu$ L (0.5 mmol) *N,N*-diisopropylethylamine (DIPEA) were dissolved in 6 mL dichloromethane. Afterwards, 156  $\mu$ L *N,N*-diisopropylcarbodiimide (DIC) (1.0 mmol) was added into the mixture. Twenty-four hours later, the solution was purified by precipitation into methanol and washed twice by methanol. The final product was dried to yield 1200 mg, 64 wt%.

### **In vivo Safety evaluation of SAL NPs**

The body weights of all mice (n=10, five in each group) were weekly monitored during the three weeks of *in vivo* experiment. SAL NPs were administered intravenously into the tail vein (200  $\mu$ L of solution containing 3.5mg of SAL per Kg body weight every two days). The control group just received normal saline 0.9% during the course of treatment.

The hematotoxicity was studied on both SAL-treated and control groups having three mice per group. After nine IV injections, the mice were sacrificed and blood samples were provided from the inferior vena cava. The red blood cell (RBC), white blood cell (WBC), granulocyte (Gc) and monocyte (Mc) counts were carried out on blood samples collected in EDTA coated tubes. Additional blood samples were centrifuged and the plasma was used for biochemistry assays

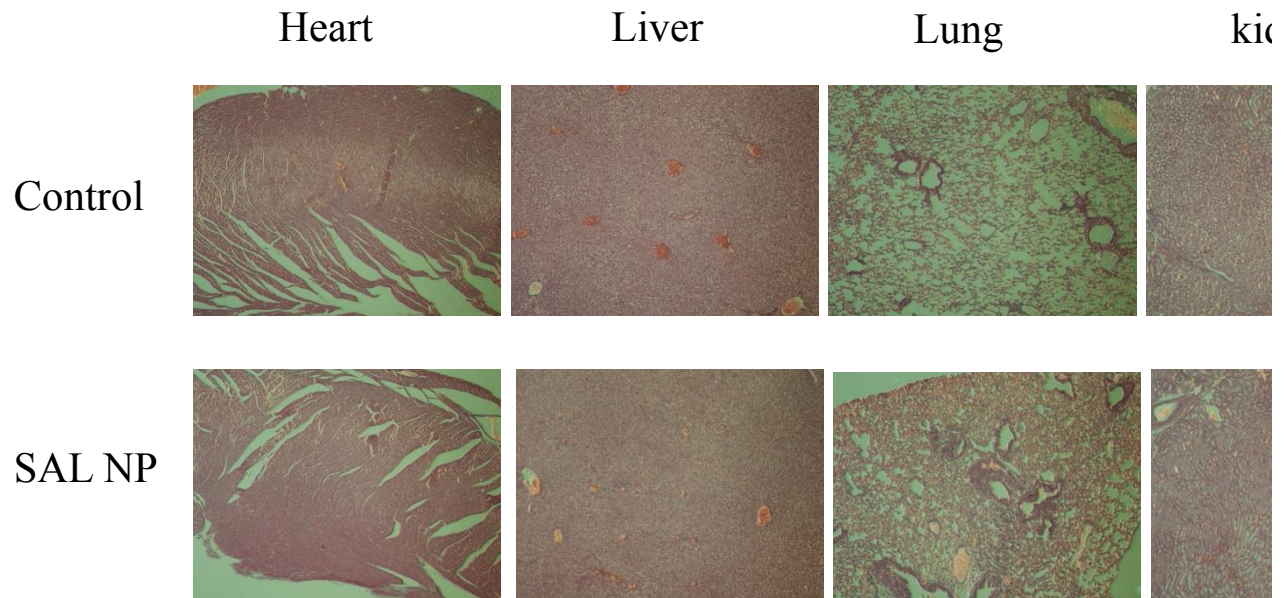
including aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), and creatinine (Cr). These tests were executed by routine clinical laboratory tests.

Histological examination of liver, heart, lung, spleen, and kidney specimens were done by fixing in 10% formalin and then embedding in paraffin. The 5-6  $\mu\text{m}$  sections were stained with hematoxylin-eosin (H&E) and examined by light microscopy.

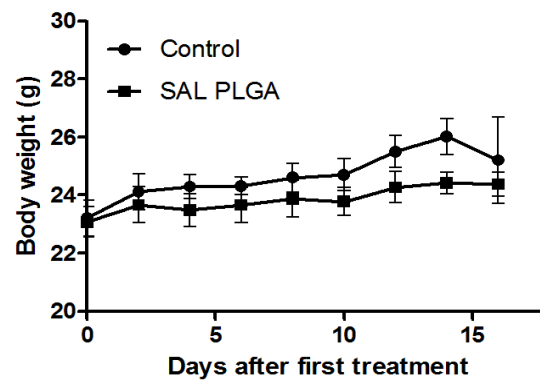
Table S1. Blood cell counts and biochemistry assays in nude mice following 3 weeks treatment with SAL NP versus control group. Values are presented as mean  $\pm$  SD ( $n = 3$ ).

| Assays            | Sample                           | Control         | SAL NP           |
|-------------------|----------------------------------|-----------------|------------------|
| Blood cell counts | RBC ( $\text{mil}/\mu\text{L}$ ) | $9.8 \pm 0.3$   | $9.8 \pm 1.3$    |
|                   | WBC ( $1000/\mu\text{L}$ )       | $10.9 \pm 2.7$  | $9.4 \pm 3.9$    |
|                   | Gc ( $1000/\mu\text{L}$ )        | $6.5 \pm 2.5$   | $4.8 \pm 2.1$    |
|                   | Mc ( $1000/\mu\text{L}$ )        | $0.8 \pm 0.3$   | $1.7 \pm 1.2$    |
| Biochemistry      | BUN ( $\text{mg}/\text{dL}$ )    | $15 \pm 4.4$    | $13.7 \pm 3.8$   |
|                   | Cr ( $\text{mg}/\text{dL}$ )     | $0.2 \pm 0.05$  | $0.13 \pm 0.06$  |
|                   | AST ( $\text{IU}/\text{L}$ )     | $146.7 \pm 4.7$ | $154.3 \pm 14.2$ |
|                   | ALT ( $\text{IU}/\text{L}$ )     | $36.3 \pm 5.5$  | $45.3 \pm 4.1$   |

A



B



**Figure S1.** Safety evaluation of the SAL NP treatment. (A) H&E photomicrograph of sections of various organs of nude mice treated with 3.5 mg/kg SAL NP versus control group. Duration: 21 days.