

Supplementary Fig. 2  $Mn^{2+}$  is a potent chemotherapeutic agent without detectable toxicity to mice. a The WT mice were treated with saline or 5 mg/kg MnCl<sub>2</sub> intratumorally (i.t.) at day 8, 10, 12, 14 after subcutaneous inoculation of  $3 \times 10^5$  B16-OVA cells in the right groin (Con, n=32; Mn<sup>2+</sup>, n=23), the sizes of tumor were recorded. No mice (0/32) in the control group and 13 mice (13/23) in Mn<sup>2+</sup>-treated group survived over 40 days. **b**, **c** The WT mice were subcutaneously inoculated with  $1.5 \times 10^5$  B16-OVA cells in both left and right groin respectively, one side of tumors was treated with saline or 5 mg/kg MnCl<sub>2</sub> i.t. at day 8, 10, 12, 14 after inoculation (Con, n=10; Mn<sup>2+</sup>, n=10), the sizes of tumors on the non-treated side were recorded (b). Their survival rates were monitored everyday (c). **d**, **e** The WT mice (n=6) were left untreated (NC) or treated with saline (Con, n=6) or 5mg/kg MnCl<sub>2</sub> (Mn<sup>2+</sup>, n=6) i.n. on day 0, 2, 4, 6, 8, 10 and 12. Their body weights (**d**) were monitored every two days and their survival rates (**e**) were monitored every day. **f-k** On day 40, hearts (**f**), livers (**g**), spleens (**h**), lungs (**i**), kidneys (**j**) and brains (**k**) were removed

and organ weights were recorded. **l** HE staining of livers, lungs, kidneys, and brains dissected from (**g**, **i**, **j**, **k**). Data represent analyses of the indicated n mice per group, mean  $\pm$  SEM. Data are representative of three independent experiments. ns, not significant; \*\*\*\*p <0.0001.