

## Supplementary Information

### **An ionic liquid-based delivery system of small interfering RNA targeting Bcl-2 for melanoma therapy**

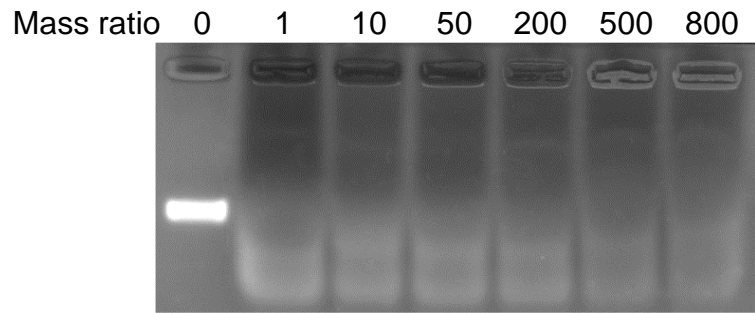
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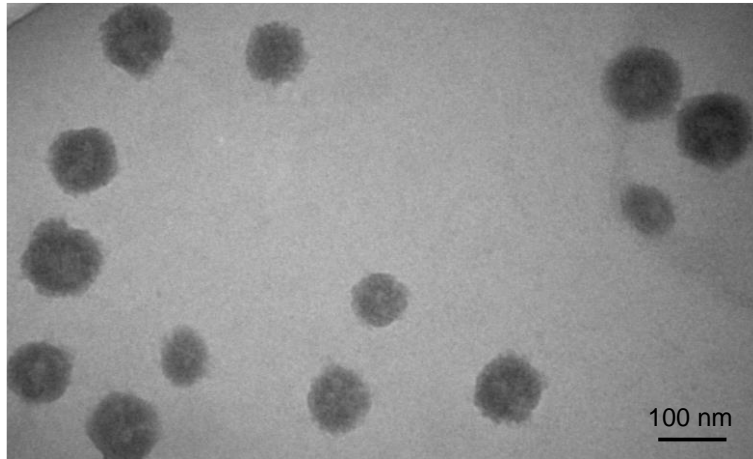
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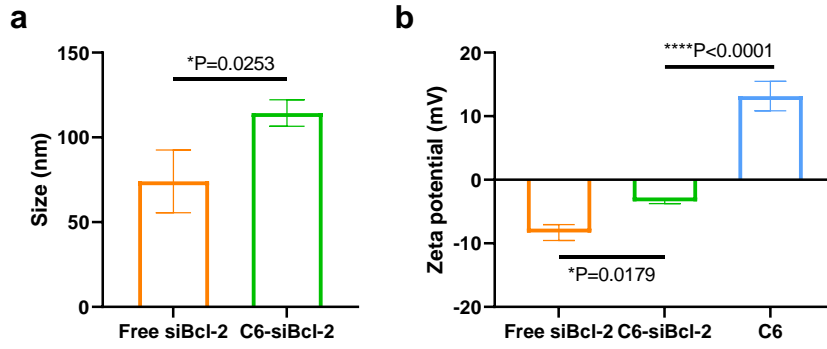
<sup>d</sup>School of Chemical & Environmental Engineering, China University of Mining and Technology (Beijing), Beijing 100083, P. R. China.



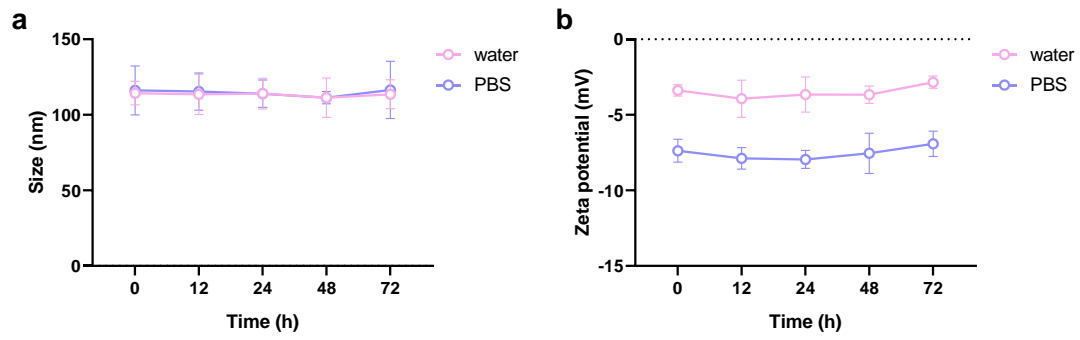
**Supplementary Fig. 1** Agarose gel electrophoresis retardation assessment of C6-siBcl-2 using formulations of 0, 1, 10, 50, 200, 500, and 800 mass ratios (C6: siBcl-2, w/w).



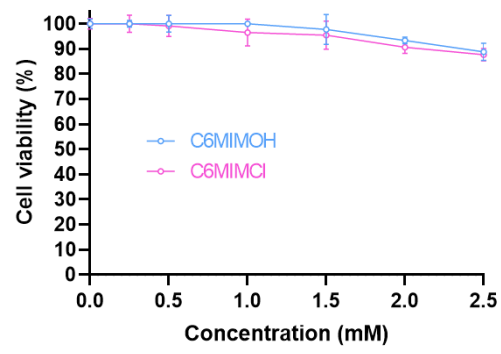
**Supplementary Fig. 2** TEM images of C6-siBcl-2.



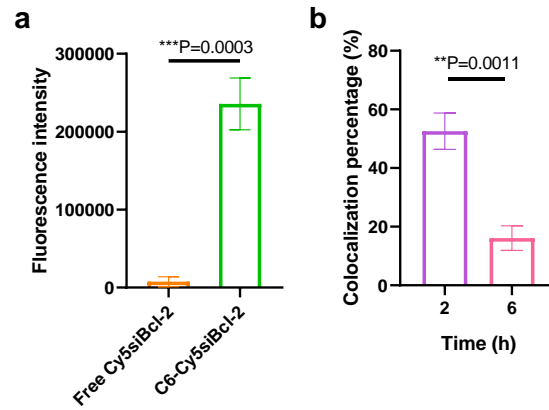
**Supplementary Fig. 3 Characterization of C6-siBcl-2.** (a and b) The particle diameter (a) and zeta potential (b) of indicated formulations. Data in (a and b) represent the mean  $\pm$  SD (n = 3). Statistical analysis was performed by Student's *t* test (a) or one-way ANOVA (b).



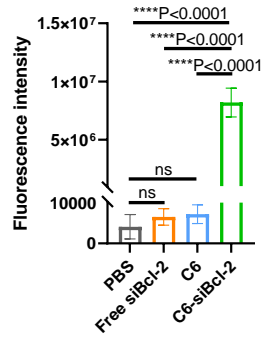
**Supplementary Fig. 4 The stability of C6-siBcl-2.** (a and b) The particle diameter (a) and zeta potential (b) of the delivery system in water and PBS for different time periods. Data in (a and b) represent the mean  $\pm$  SD (n = 3).



**Supplementary Fig. 5** The cytotoxicity of IL carriers before and after ion exchange at different concentrations determined by the CCK-8 assay. Data represent the mean  $\pm$  SD (n = 3).

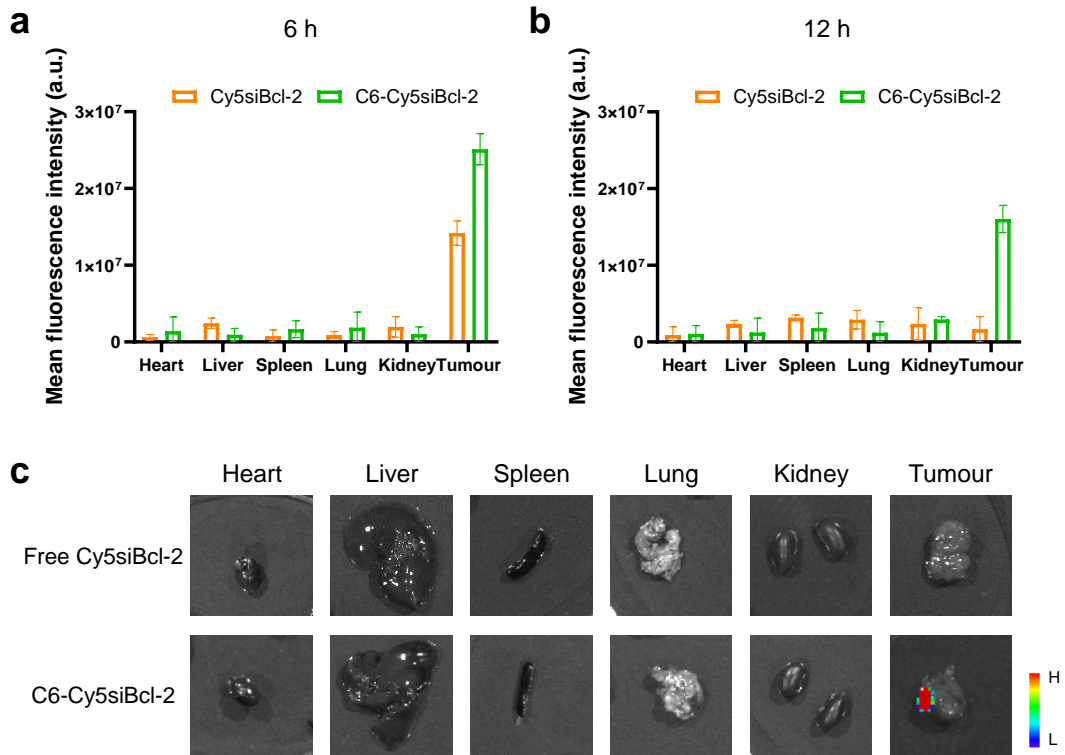


**Supplementary Fig. 6 Cell uptake and lysosome escape of delivery system.** (a) Fluorescence intensity of Cy5siBcl-2 in free Cy5siBcl-2 and C6-Cy5siBcl-2 groups for Fig. 2. (b) Colocalization analysis of lysosomes (LysoTracker, green) and C6-Cy5siBcl-2 (red) fluorescence signals in B16F10 cells treated with C6-Cy5siBcl-2 for 2 h and 6 h in Fig. 3. Data in (a and b) represent the mean  $\pm$  SD (n = 3). Statistical analysis was performed by Student's *t* test (a and b).



**Supplementary Fig. 7** Quantitative analysis of ROS production in B16F10 cells after incubation with PBS, free siBcl-2, C6, or C6-siBcl-2 for 6 h in Fig. 4a. Data represent the mean  $\pm$  SD (n = 3). Statistical analysis was performed by one-way ANOVA.

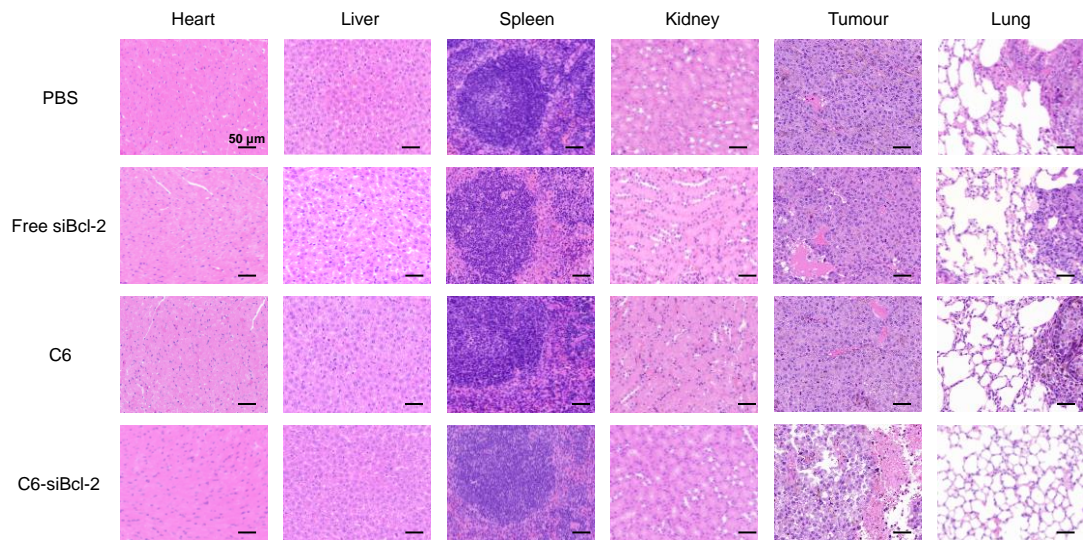




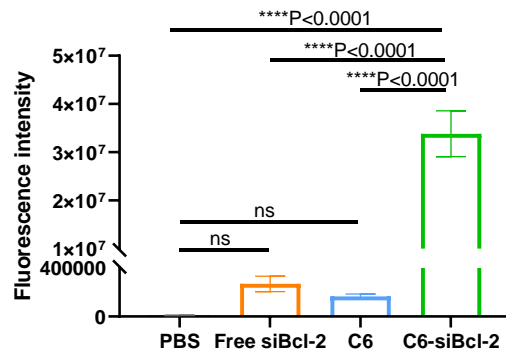
**Supplementary Fig. 8 Biodistribution assessment of delivery system on melanoma-bearing mice.**

(a and b) Quantitative analysis of the siBcl-2 distribution signals after 6 h (a) and 12 h (b) of injection.

(c) Representative fluorescence images of the excised organs after 12 h injection of free Cy5siBcl-2 and C6-Cy5siBcl-2. Data in (a and b) represent the mean  $\pm$  SD (n = 3).



**Supplementary Fig. 9** Representative H&E images of major organs and tumours of melanoma-bearing mice treatment with PBS, free siBcl-2, C6, or C6-siBcl-2.



**Supplementary Fig. 10** Quantitative analysis of TUNEL immunofluorescence staining in tumour tissues from mice with different treatments for Fig. 7e. Data represent the mean ± SD (n = 3). Statistical analysis was performed by one-way ANOVA.