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## Rational design of Polymeric Hybrid Micelles To Overcome Lymphatic And Intracellular Delivery Barriers In Cancer Immunotherapy

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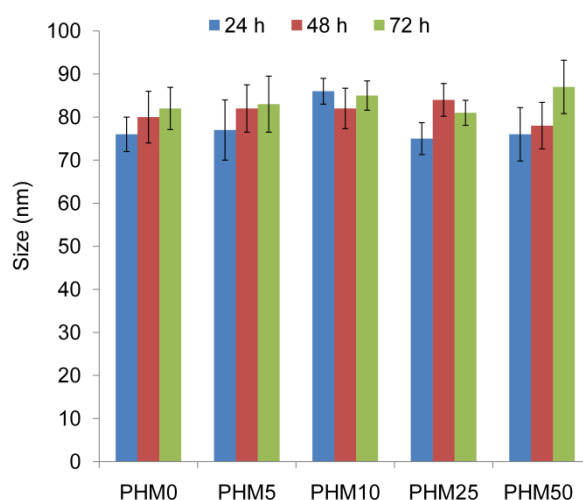
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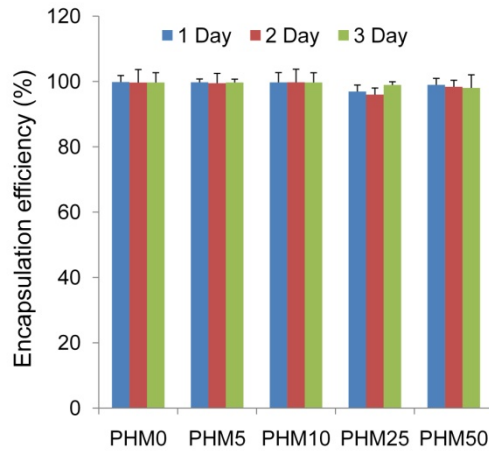
### SUPPLEMENTARY TABLES AND FIGURES

**Table S1.** The composition of various PHMs with different weight ratio of PCL-PEI to PCL-PEG.

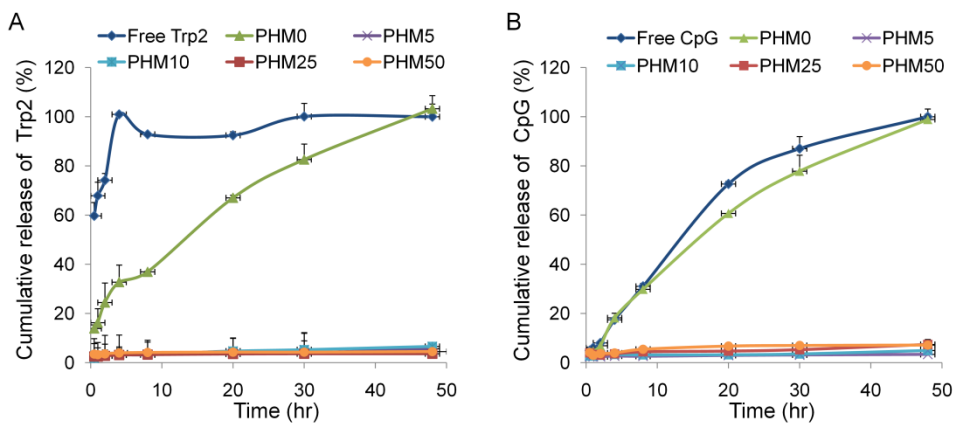
	Trp2/PHM-0/CpG	Trp2/PHM-5/CpG	Trp2/PHM-10/CpG	Trp2/PHM-25/CpG	Trp2/PHM-50/CpG
PCL-PEG	100	95	90	75	50
PCL-PEI	0	5	10	25	50



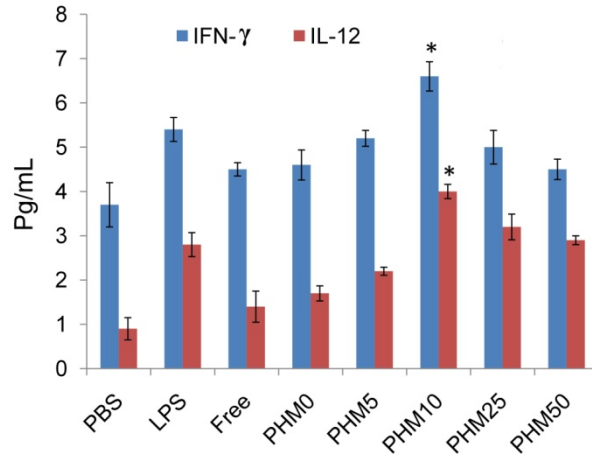
**Figure S1.** The stability of various Trp2/PHM/CpG nanoparticle after storage at 4 °C for 72 h.



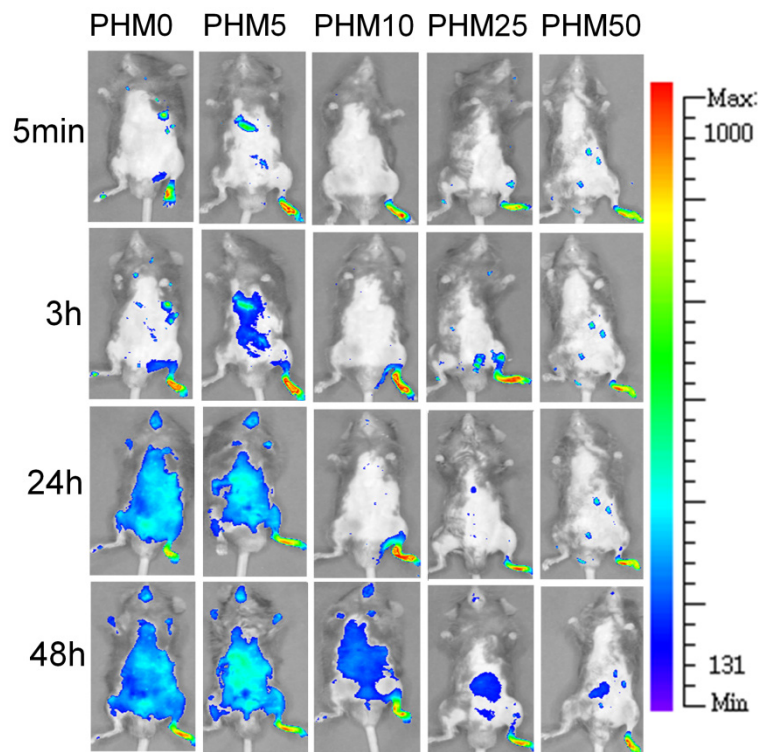
**Figure S2.** The encapsulation efficiency of various Trp2/PHM/CpG nanoparticle after storage at 4 °C for 72 h.



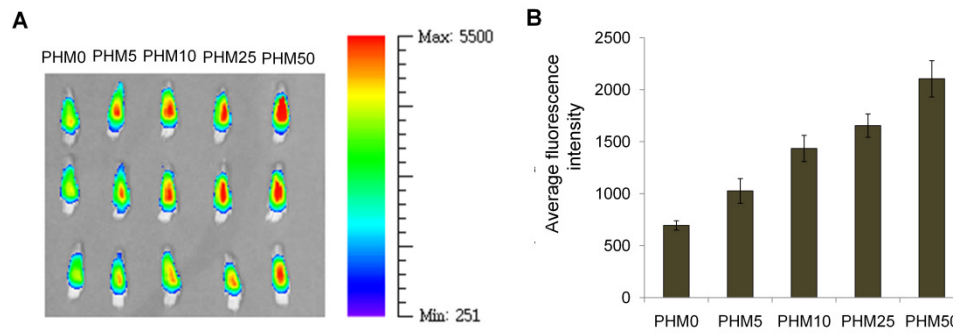
**Figure S3 .** Release profiles of Trp2 (A) and CpG (B) from various Trp2/PHM/CpG formulation in PBS (PH=7.4).



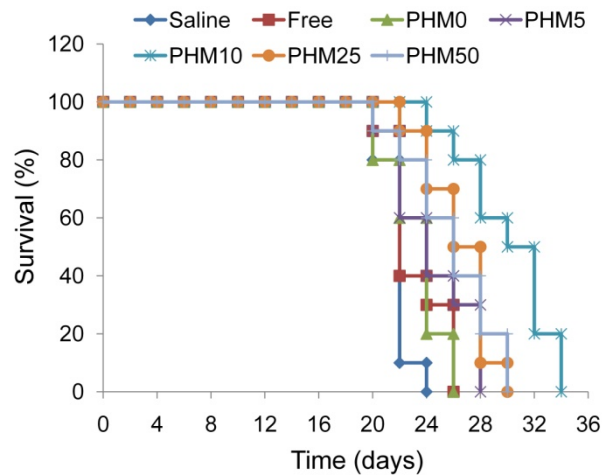
**Figure S4.** Secretion levels of IFN- $\gamma$  and IL-12 from BMDCs after treated by various Trp2/PHM/CpG formulations. Cells were treated with PHM formulations at 37 °C for 24 h. The concentrations of IFN- $\gamma$  and IL-12 were measured by ELISA. Results are shown as mean  $\pm$  SD (n = 5). Statistical comparisons were made relative to PBS. \*P < 0.05.



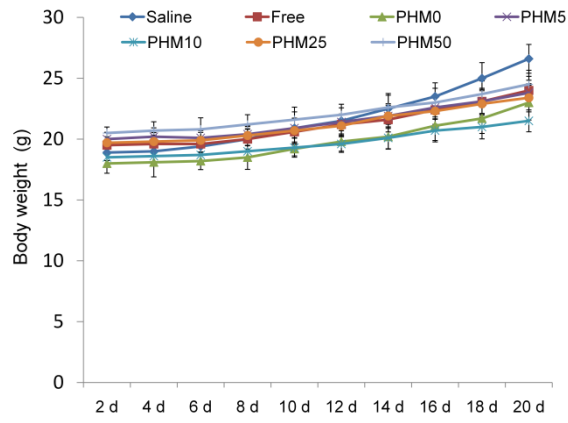
**Figure S5.** Whole-body imaging of mice at 5 min, 3 h, 24 h and 48 h after subcutaneous injection.



**Figure S6.** The retarding of DiD in the injected foot pad. **(A)** *Ex vivo* imaging of the injected foot pad after 24 h. **(B)** The average fluorescence intensity for the DiD retarding in the injected foot pad after 24 h.



**Figure S7.** Survival analysis of mice bearing B16F10 tumors. C57BL/6 mice were inoculated with B16F10 cells ( $1 \times 10^5$ ) subcutaneously on day 0. Animals were vaccinated with saline, Trp2/CpG, Trp2/PHM0/CpG, Trp2/PHM5/CpG, Trp2/PHM10/CpG, Trp2/PHM25/CpG or Trp2/PHM50/CpG (16  $\mu$ g Trp2, 1.6  $\mu$ g CpG) on days 4, 11 and 18. Dates of the animal death were recorded every 2 days to draw the survival curve (n=10).



**Figure S8.** Body weight of mice bearing B16F10 subcutaneous tumor during the vaccination therapy with saline, Trp2/CpG, Trp2/PHM-0/CpG, Trp2/PHM-5/CpG, Trp2/PHM-10/CpG, Trp2/PHM-25/CpG and Trp2/PHM-50/CpG. Body weight were measured every 2days.