

† Electronic Supplementary Information (ESI) available:

External Temperature Control of Lymphatic Drainage of Thermo-sensitive Nanomaterials

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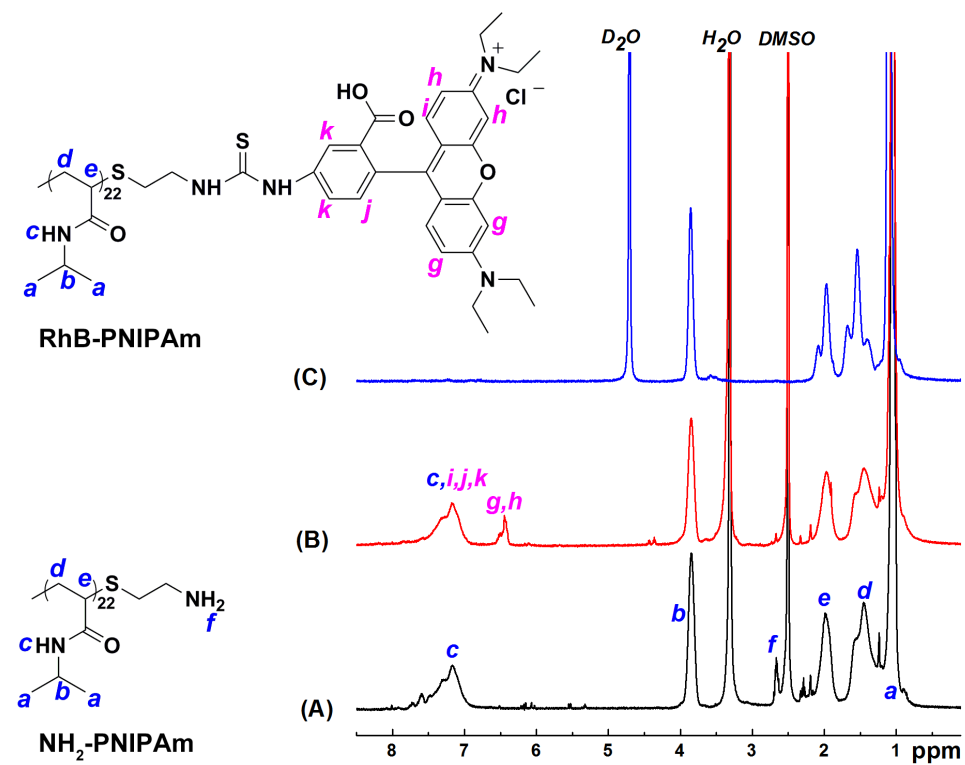


Fig. S1 ^1H NMR spectra of $\text{NH}_2\text{-PNIPAm}$ in $\text{DMSO-}d_6$ (A), and RhB-PNIPAm oligomer in $\text{DMSO-}d_6$ (B) and D_2O (C).

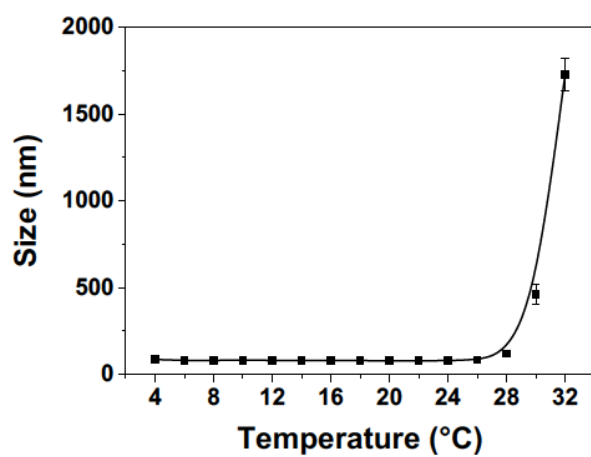


Fig. S2 Temperature-dependent changes of average particle size of RhB-PNIPAm in PBS.

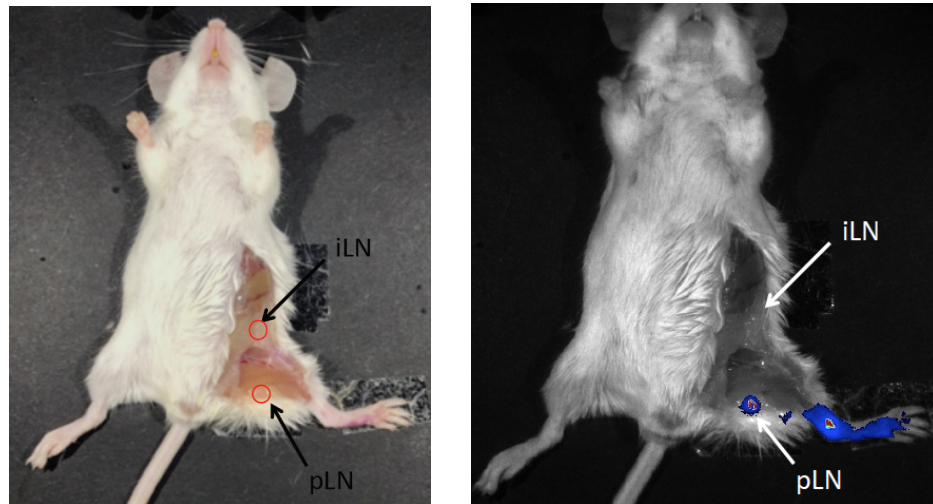


Fig. S3 Determination of the anatomical locations of the draining LNs after dissection (left). Draining of the fluorescently labeled polymer from the footpad to the pLN was visible (right), whereas the signal in the iLN was too weak to see.

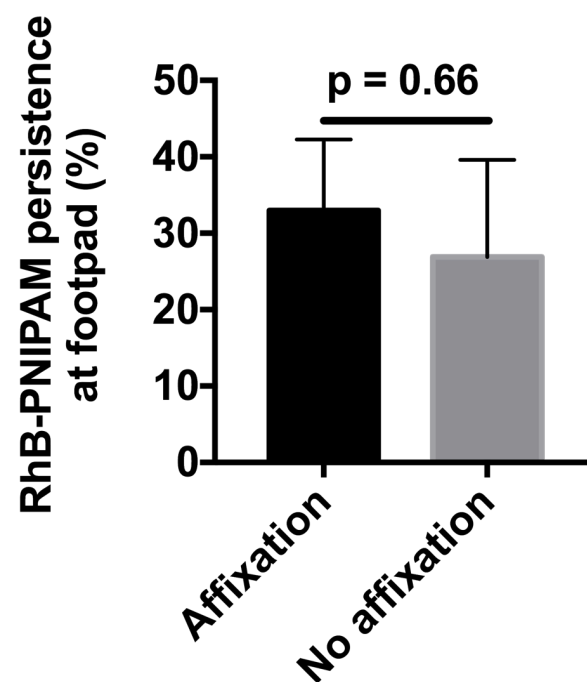


Fig. S4 Draining of the injection site was not affected by the affixation of the cooling device. Data represented as mean $\pm$ SD (n=4). Student's *t*-test.

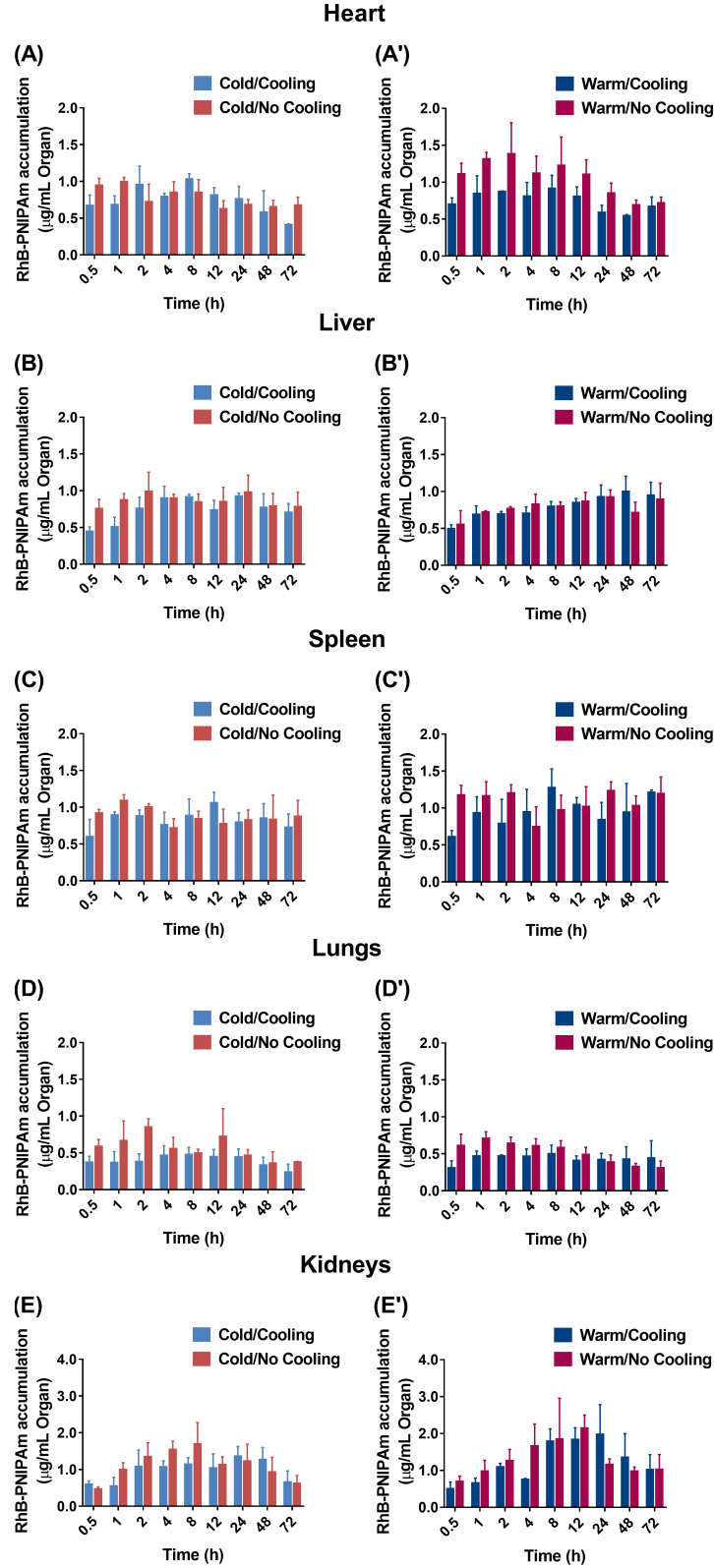


Fig. S5 Time-dependent changes of RhB-PNIPAm accumulation in the heart (A), liver (B), spleen (C), lungs (D), kidneys (E) of mice injected with either “cold” or “warm” polymer in the footpad with and without external cooling. Data represented as mean $\pm$ SD (n=3).

Table S1 PK parameters (C_{max} , AUC_{0-72} , T_{max}) of RhB-PNIPAm in the heart of mice and statistical comparison

Samples	C_{max} ($\mu\text{g/mL}$)	AUC_{0-72} ($\mu\text{g}\cdot\text{h/mL}$)	T_{max} (h)
(A) Cold/Cooling	1.03 ± 0.07	47.7 ± 10.3	8
(B) Cold/No Cooling	0.99 ± 0.06	49.2 ± 2.9	1
(C) Warm/Cooling	0.91 ± 0.18	46.4 ± 5.7	8
(D) Warm/No Cooling	1.38 ± 0.42	61.1 ± 2.2	2
Statistical comparisons	A = B (NS)	A = B (NS)	
	C = D (NS)	C < D **	
	A = C (NS)	A = C (NS)	
	B = D (NS)	B < D **	

Data represented as mean $\pm$ SD (n=3). ** p <0.01, Student's t -test.

Table S2 PK parameters (C_{max} , AUC_{0-72} , T_{max}) of RhB-PNIPAm in the liver of mice and statistical comparison

Samples	C_{max} ($\mu\text{g/mL}$)	AUC_{0-72} ($\mu\text{g}\cdot\text{h/mL}$)	T_{max} (h)
(A) Cold/Cooling	0.92 ± 0.04	57.5 ± 5.8	24
(B) Cold/No Cooling	0.99 ± 0.27	61.2 ± 11.0	2
(C) Warm/Cooling	0.99 ± 0.21	65.8 ± 5.8	48
(D) Warm/No Cooling	0.92 ± 0.10	58.9 ± 1.6	24
Statistical comparisons	A = B (NS)	A = B (NS)	
	C = D (NS)	C = D (NS)	
	A = C (NS)	A = C (NS)	
	B = D (NS)	B = D (NS)	

Data represented as mean $\pm$ SD (n=3).

Table S3 PK parameters (C_{max} , AUC_{0-72} , T_{max}) of RhB-PNIPAm in the spleen of mice and statistical comparison

Samples	C_{max} ($\mu\text{g/mL}$)	AUC_{0-72} ($\mu\text{g}\cdot\text{h/mL}$)	T_{max} (h)
(A) Cold/Cooling	1.10 ± 0.14	59.9 ± 6.2	12
(B) Cold/No Cooling	1.09 ± 0.08	59.7 ± 7.8	1
(C) Warm/Cooling	1.27 ± 0.25	70.7 ± 9.4	8
(D) Warm/No Cooling	1.23 ± 0.12	78.6 ± 4.5	24
Statistical comparisons	A = B (NS)	A = B (NS)	
	C = D (NS)	C = D (NS)	
	A = C (NS)	A = C (NS)	
	B = D (NS)	B < D *	

Data represented as mean $\pm$ SD (n=3). * p <0.05, Student's t -test.

Table S4 PK parameters (C_{max} , AUC_{0-72} , T_{max}) of RhB-PNIPAm in the lungs of mice and statistical comparison

Samples	C_{max} ($\mu\text{g/mL}$)	AUC_{0-72} ($\mu\text{g}\cdot\text{h/mL}$)	T_{max} (h)
(A) Cold/Cooling	0.48 ± 0.10	26.6 ± 2.2	8
(B) Cold/No Cooling	0.85 ± 0.12	32.9 ± 3.3	1
(C) Warm/Cooling	0.50 ± 0.12	30.8 ± 3.3	8
(D) Warm/No Cooling	0.70 ± 0.09	28.2 ± 2.7	2
Statistical comparisons	A < B **	A < B *	
	C < D *	C = D (NS)	
	A = C (NS)	A = C (NS)	
	B = D (NS)	B = D (NS)	

Data represented as mean $\pm$ SD (n=3). * p <0.05, ** p <0.01, Student's t -test.

Table S5 PK parameters (C_{max} , AUC_{0-72} , T_{max}) of RhB-PNIPAm in the kidneys of mice and statistical comparison.

Samples	C_{max} ($\mu\text{g/mL}$)	AUC_{0-72} ($\mu\text{g}\cdot\text{h/mL}$)	T_{max} (h)
(A) Cold/Cooling	1.36 ± 0.27	80.9 ± 8.3	24
(B) Cold/No Cooling	1.69 ± 0.59	75.0 ± 8.1	8
(C) Warm/Cooling	1.97 ± 0.81	106.4 ± 4.2	24
(D) Warm/No Cooling	2.14 ± 0.36	88.6 ± 10.7	12
Statistical comparisons	A = B (NS)	A = B (NS)	
	C = D (NS)	C > D *	
	A = C (NS)	A < C **	
	B = D (NS)	B = D (NS)	

Data represented as mean $\pm$ SD (n=3). * p <0.05, ** p <0.01, Student's t -test.