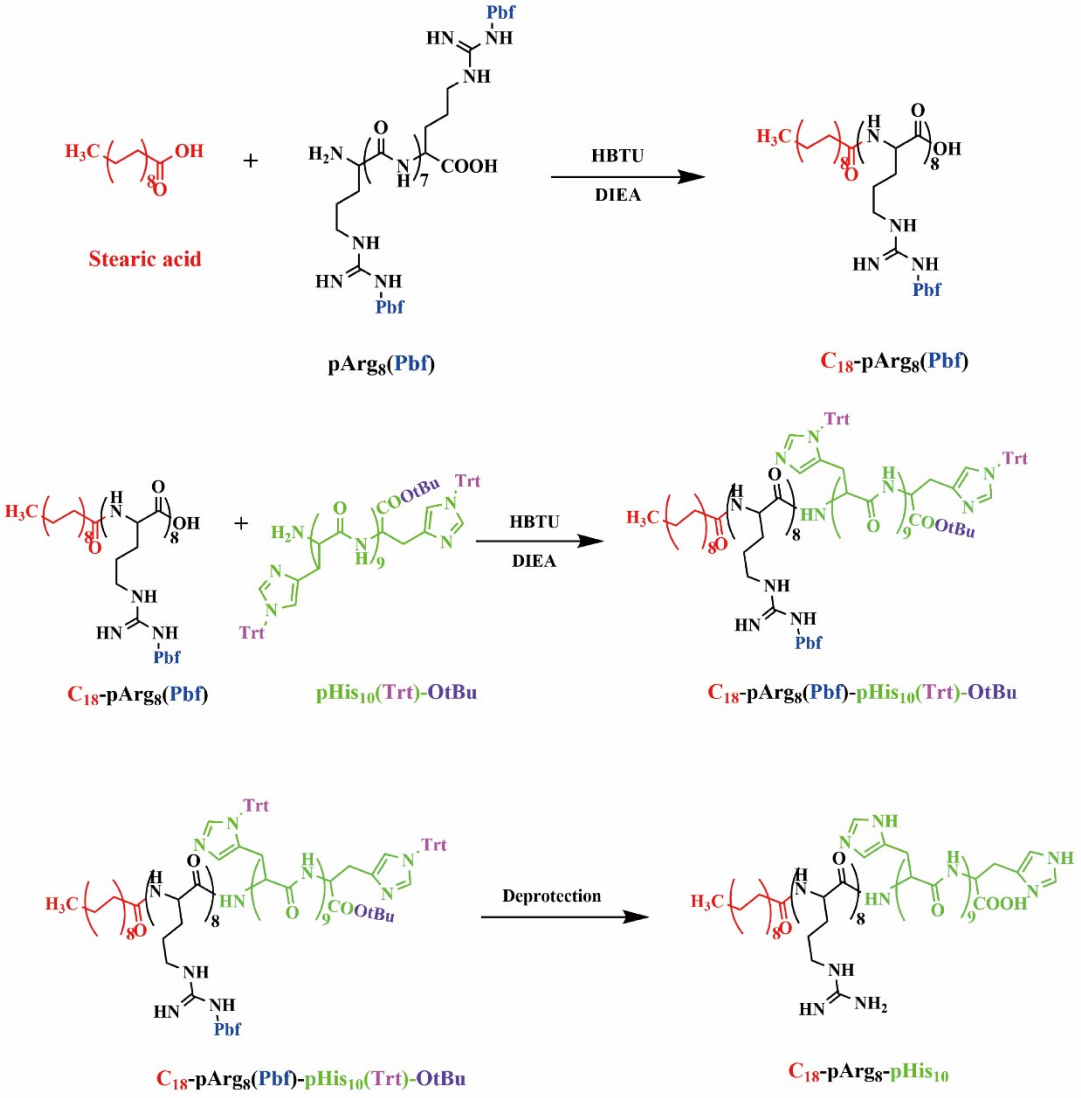


Fig. S1. Synthetic route of the amphiphilic lipopeptide C_{18}-$pArg_8$-$pHis_{10}$

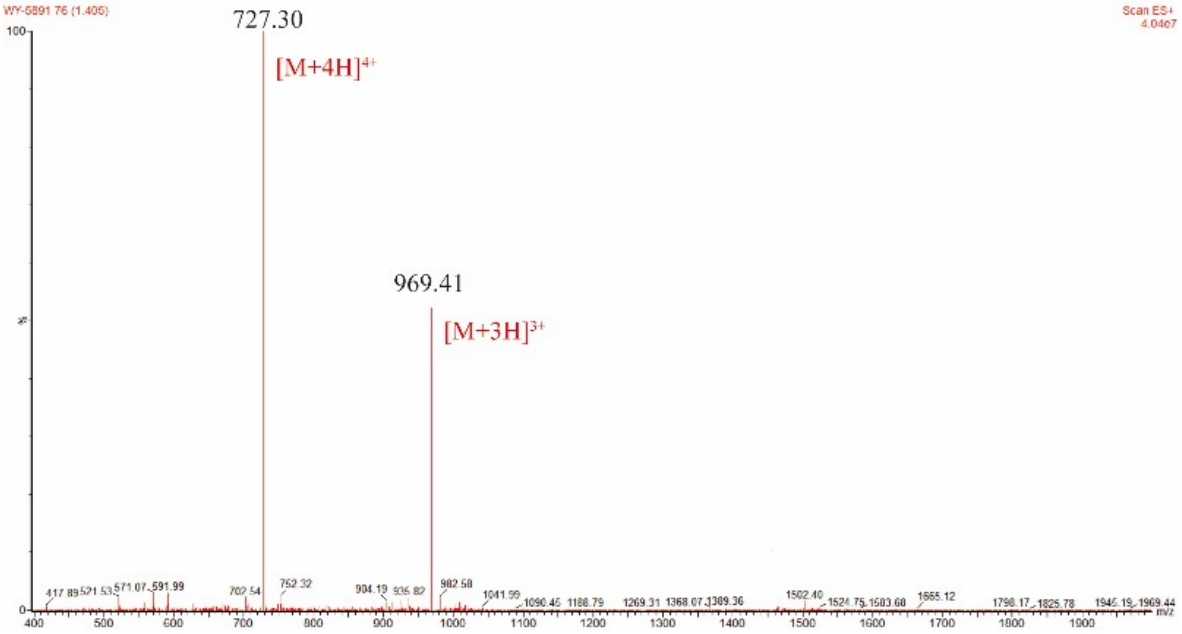


Fig. S2. MS spectrum of the C_{18}-pArg_8-pHis_{10} lipopeptide

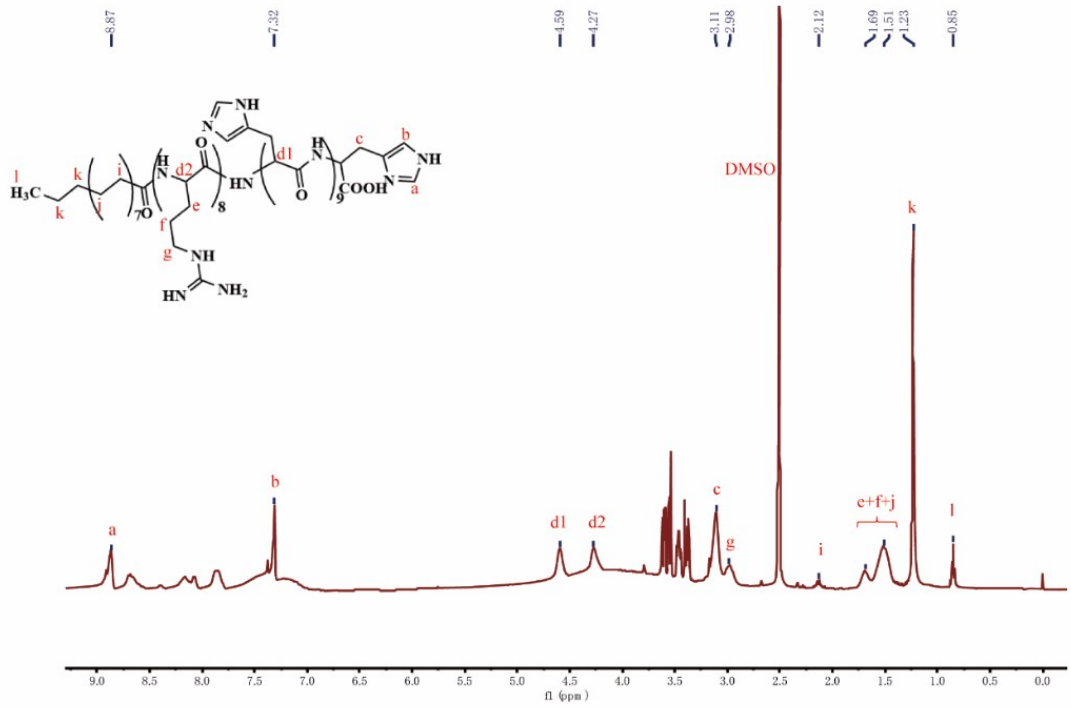


Fig. S3. ^{1}H-NMR spectrum of the C_{18}-pArg$_8$-pHis$_{10}$ lipopeptide

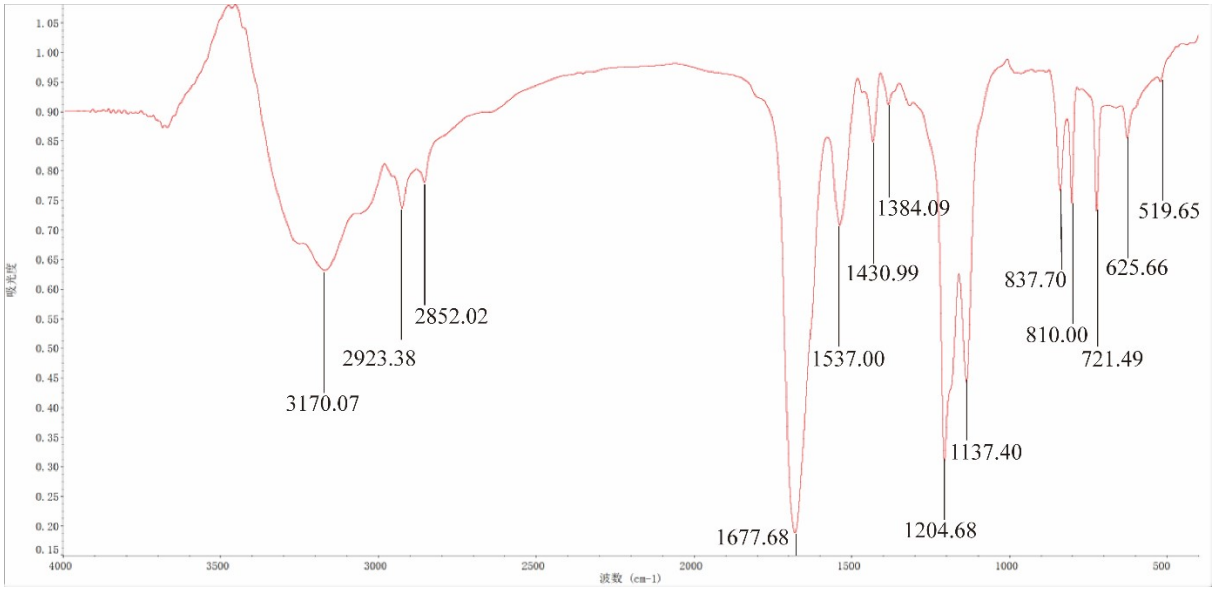
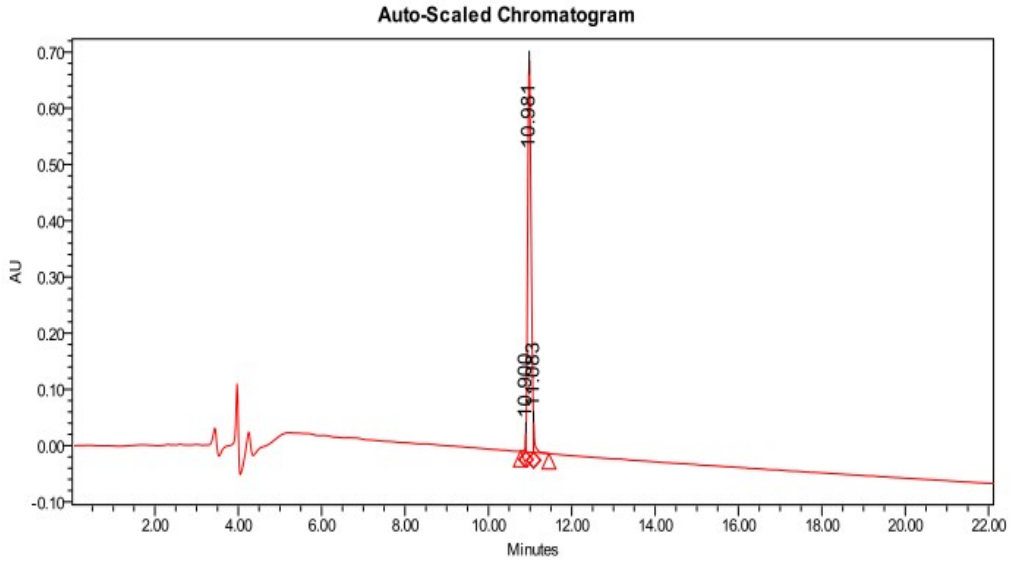


Fig. S4. FT-IR resolved map of C_{18}-pArg_8-pHis_{10}



	RT（min）	Height	Area	%Area
1	10.900	31867	30161	0.73
2	10.981	694557	3994294	96.63
3	11.083	52014	109228	2.64

Fig. S5. The purity of the C_{18}-pArg_8-pHis_{10} lipopeptide analyzed by HPLC

Tab. S6. Effect of different ratio of lipopeptide to $PLGA_{5k}$-PEG_{2k} (n = 3)

	EE% (Res)	DL% (Res)	Size (nm)	PDI	ZP (mV)
1：0 (Unstable)	96.27±0.52	2.35±0.05	24.58±2.12	0.306±0.162	24.8±2.7
2：1 (Clear)	98.34±0.63	6.45±0.11	93.47±1.23	0.308±0.120	14.3±1.2
1：1 (Clear)	99.48±1.26	8.24±0.21	103.52±2.31	0.144±0.072	7.6±0.9
1：2 (Clear)	99.36±1.87	9.05±0.17	126.48±2.56	0.099±0.095	-3.7±0.2
0：1 (Clear)	99.54±1.62	9.56±0.18	114.21±1.11	0.056±0.057	-13.9±1.5

Tab. S7. Characterization of different preparations (N/P = 15)

Preparations	Size (nm)	PDI	ZP (mV)	EE (%) (Res)	EE (%) (siP)	DL (%) (Res)	DL (%) (siP)
Blank SLNP	105.4±1.7	0.14±0.02	7.68±0.74	—	—	—	—
Res@SLNP	113.6±1.6	0.10±0.01	6.23±1.12	99.56±1.47	—	8.37±0.24	—
Res/siP@SLNP	127.9±1.8	0.12±0.02	0.90±0.06	99.23±1.13	92.19±1.01	7.93±0.19	2.53±0.05

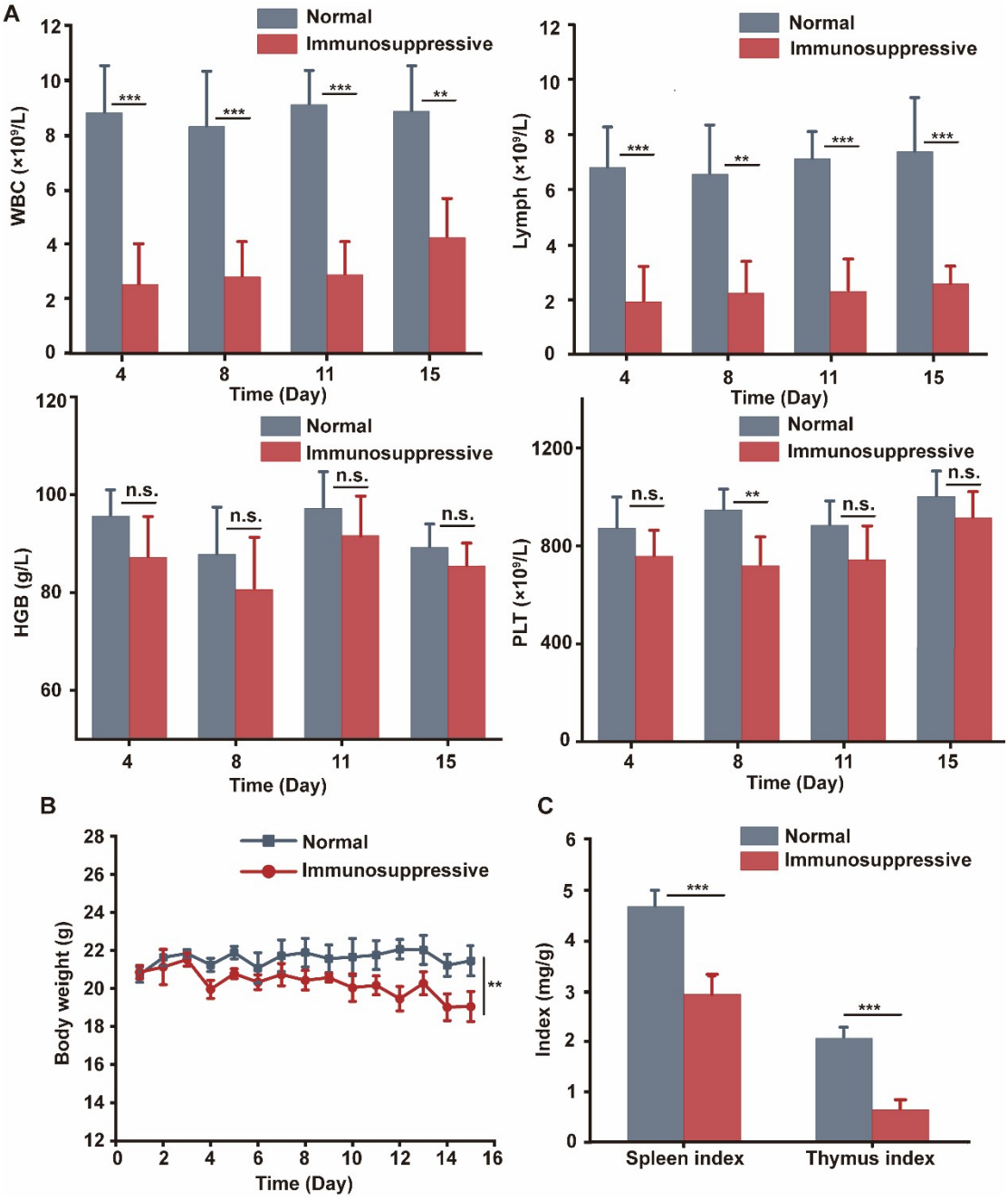


Fig. S8. Indicators of immunity in the immunosuppressed mouse model. (A) The counts of peripheral blood cells (leukocytes, lymphocytes, hemoglobin and platelets) (n=5) (B) Changes in body weight of mice (n=5) (C) immune organ index in the immunosuppressed group and the normal group (n=5). Dates are shown as mean±SD, n.s.: not significant, **p < 0.01, ***p < 0.001.

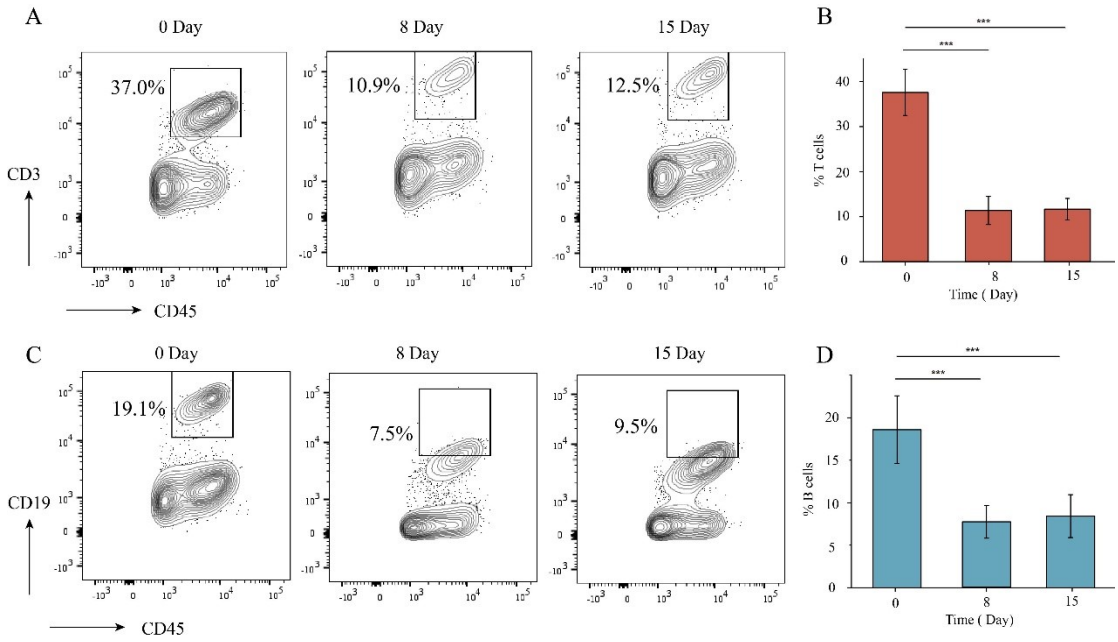


Fig. S9. The percentages of T cells and B cells in the peripheral blood of immunosuppressed mice during the experiment. (A) Representative contour plot and (B) statistical analysis of T cells percentage gated on white blood cells. (C) Representative contour plot and (D) statistical analysis of B cells percentage gated on white blood cells Dates are shown as mean ± SD, ***$p < 0.001$.

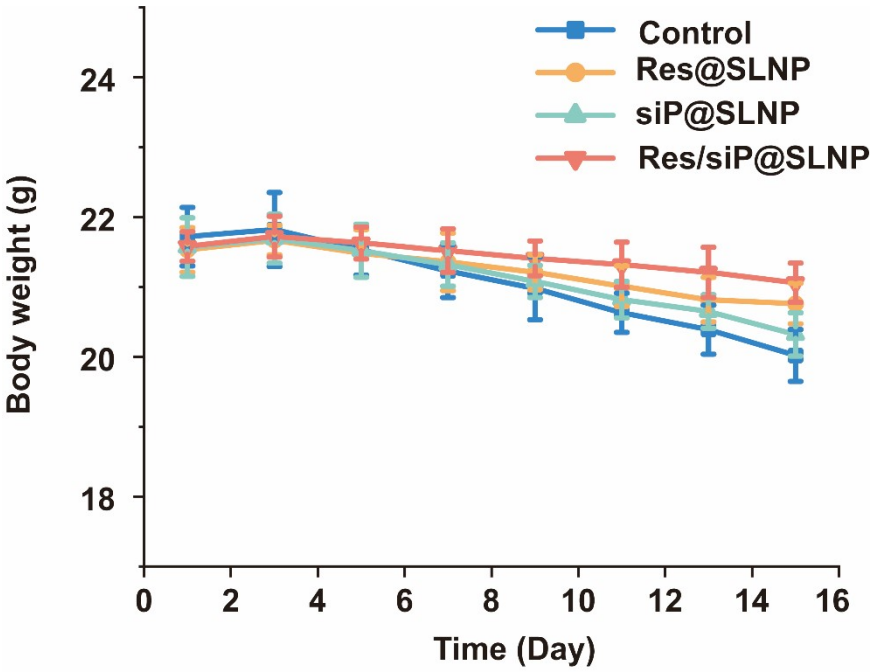


Fig. S10. Changes in mice body weight during treatment in the immunosuppressed model (n = 5)**.**

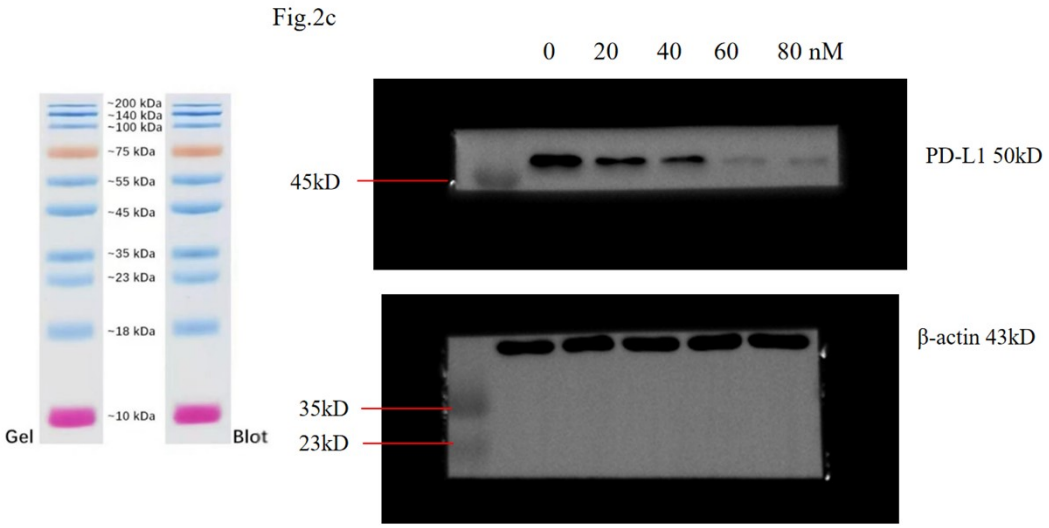


Fig. S11. Raw wb data for Fig.2c.

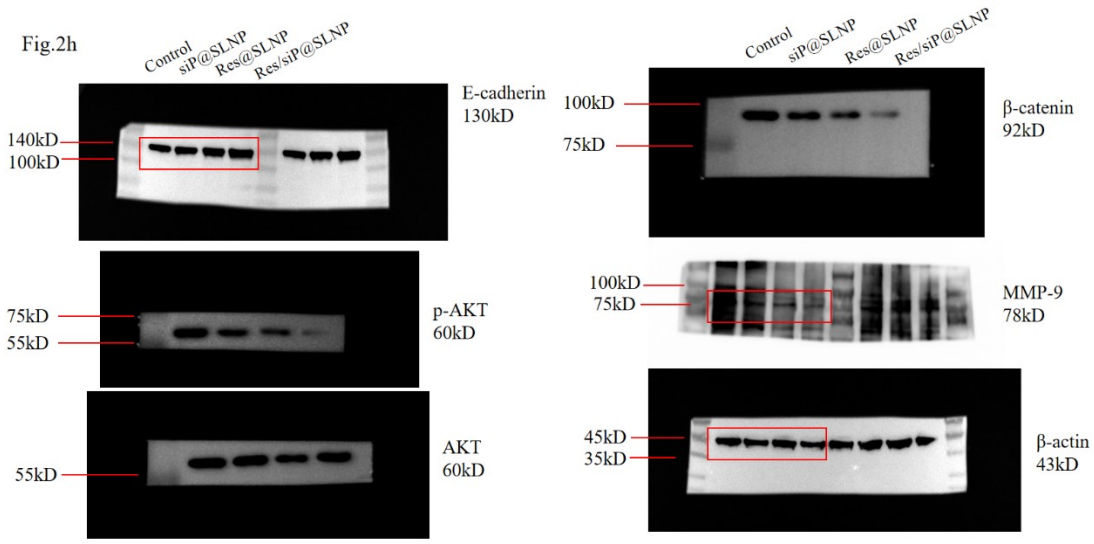


Fig. S12. Raw wb data for Fig.2h.

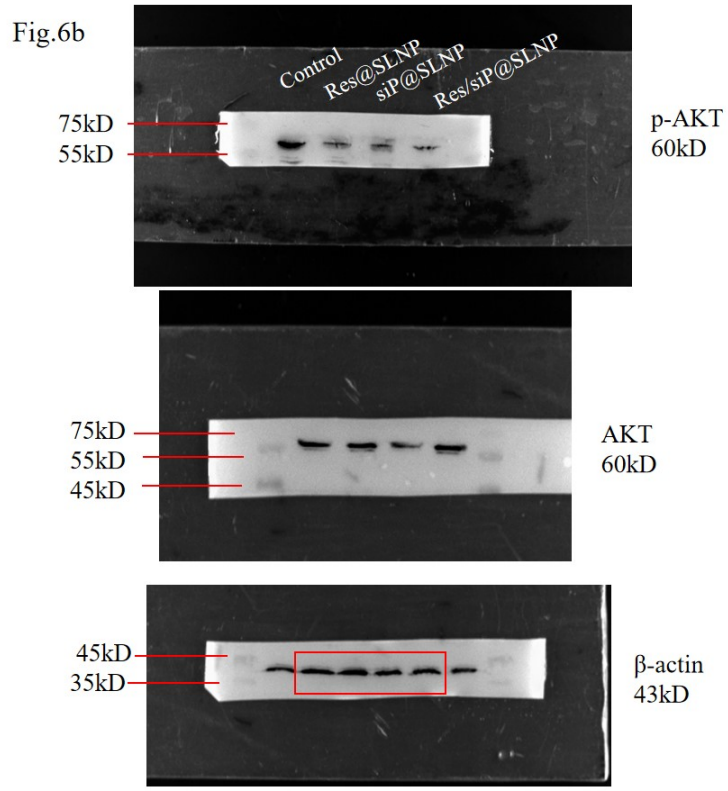


Fig. S13. Raw wb data for Fig.6b.

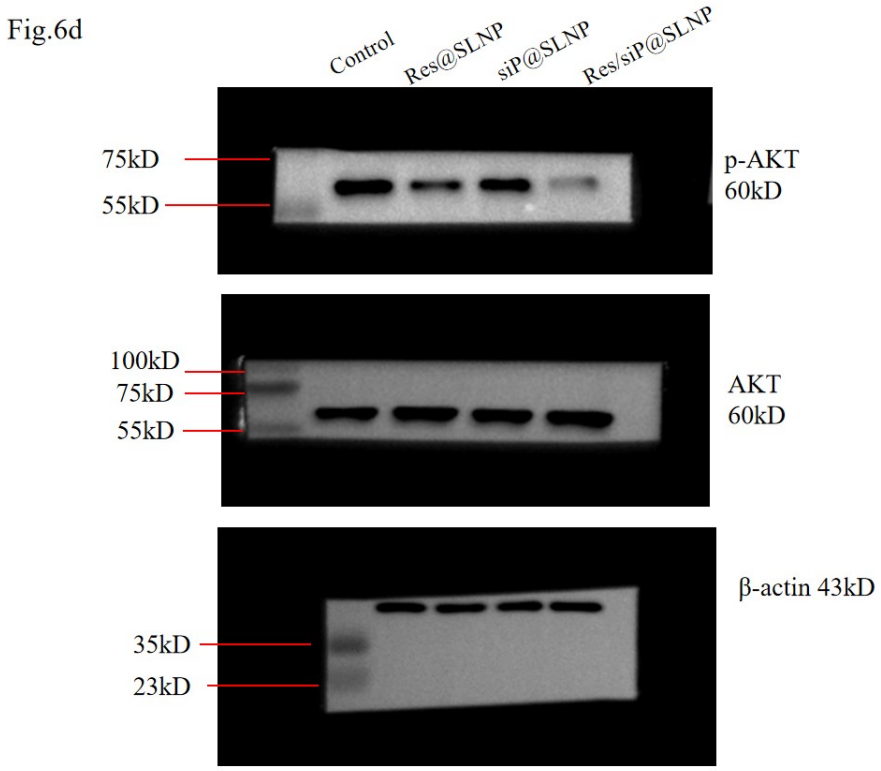


Fig. S14. Raw wb data for Fig.6d.

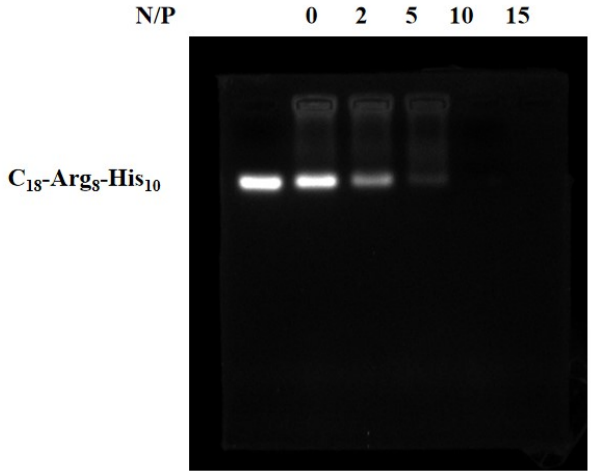


Fig. S15. Raw electrophoresis image for Fig.1c.

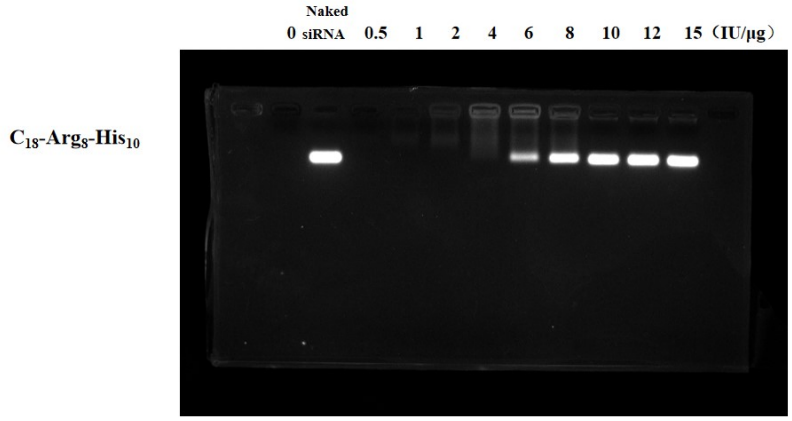


Fig. S16. Raw electrophoresis image for Fig.1d.

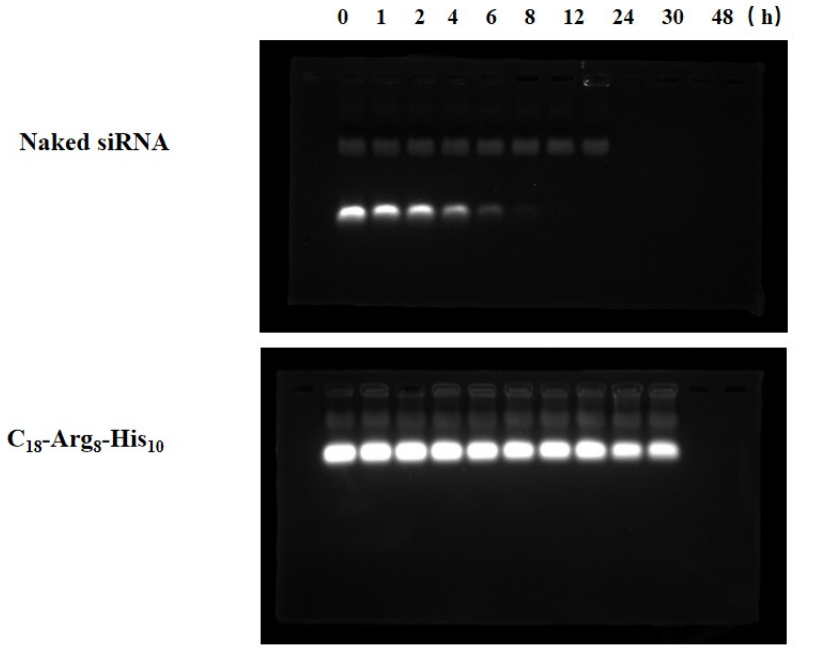


Fig. S17. Raw electrophoresis image for Fig.1e.