Electronic Supplementary Material (ESI) for Biomaterials Science.

Supplementary Information

Redox-responsive interleukin-2 nanogel specifically and safely promotes the proliferation and memory precursor differentiation of tumor-reactive T-cells

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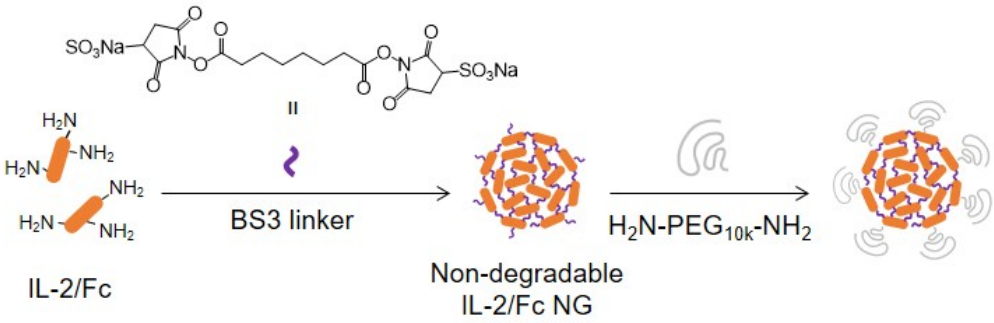

Figure S1 Scheme of synthesis of non-degradable IL-2/Fc NG using bis(sulfosuccinimidyl) suberate (BS3) linker.

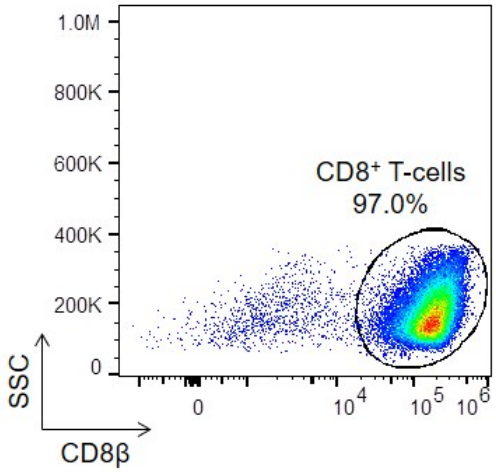

Figure S2 Representative flow cytometric analysis of activated pmel-1 $CD8^+$ T-cells.

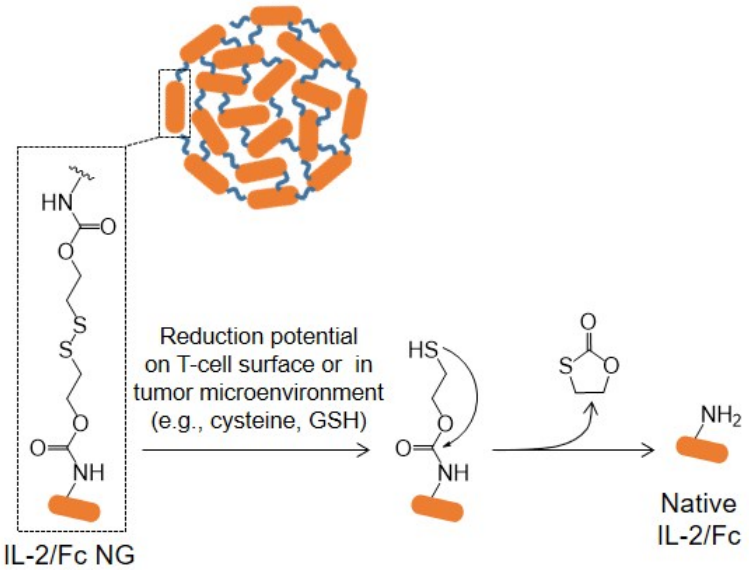

Figure S3 Traceless covalent conjugation results in the release of native cytokine without any chemical residues.

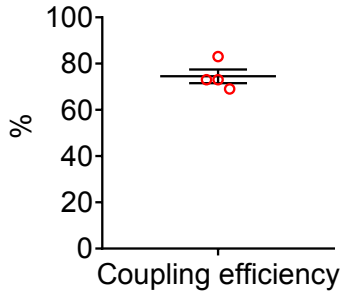

Figure S4 Coupling efficiency of IL-2/Fc NGs onto the plasma membrane of T-cells. Data represent the mean ± s.e.m. (n = 4/group).

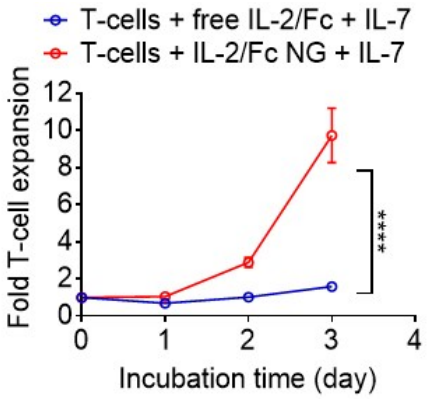

Figure S5 IL-2/Fc NGs promote $CD8^+$ memory precursor differentiation by increasing the sensitivity to IL-7 signaling. Activated pmel-1 $CD8^+$ T-cells (1.0×10^4) were cultured in the presence of free IL-2/Fc (0.1 μg) or backpacked with IL-2/Fc NGs (0.1 μg) for 3 days; both are supplemented with IL-7 (1 ng/mL). Fold change of alive $CD8^+$ T-cells in the presence of IL-7 at indicated days. Data represent the mean ± s.e.m. (n = 3/group). *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$ by Two-Way ANOVA and Tukey's tests.

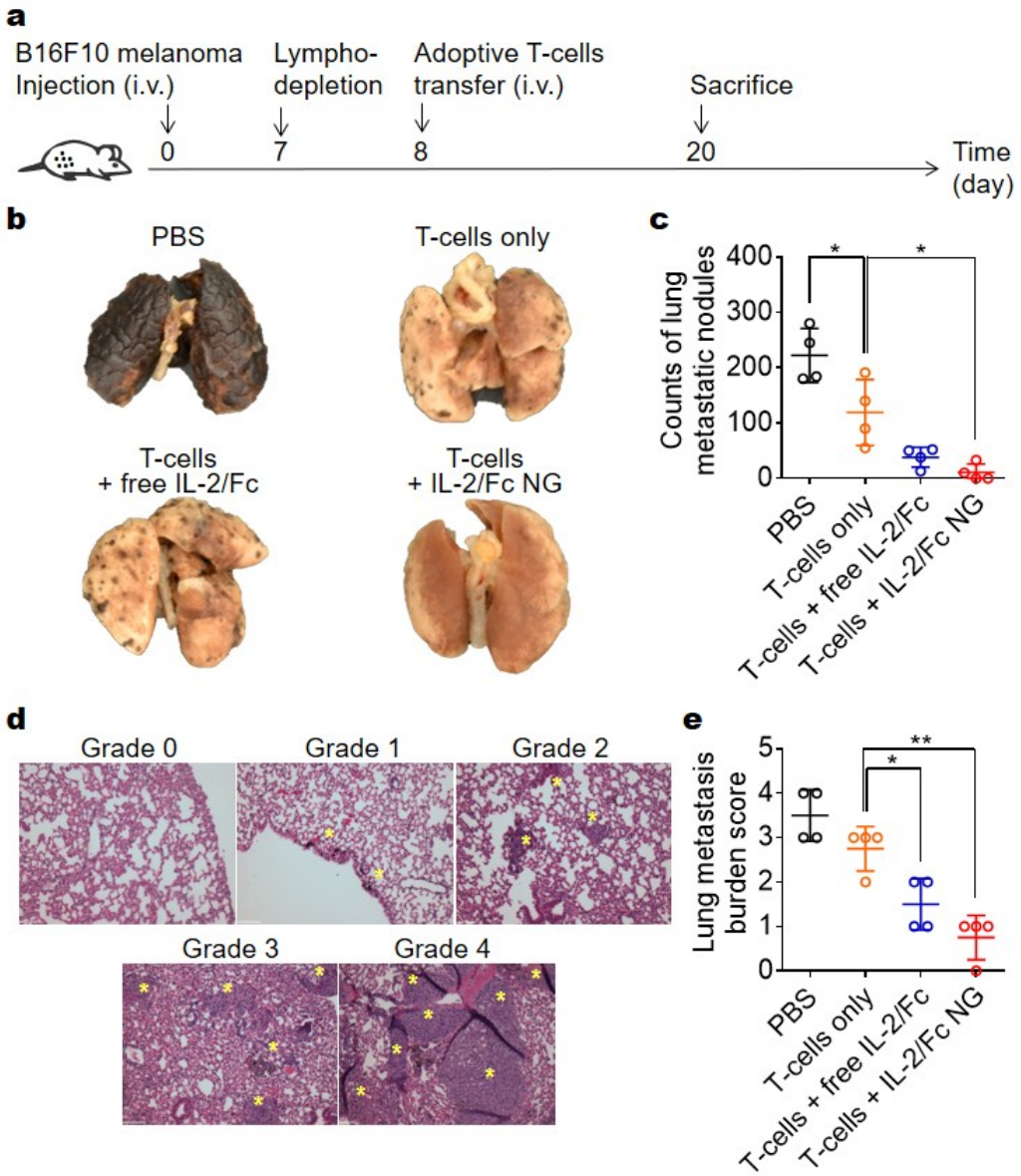

Figure S6 IL-2/Fc NG backpacks improve the efficacy of adoptive T-cell therapy. B16F10 melanoma cells (1.0×10^6) were i.v. injected into C57Bl/6 mice and allowed to establish pulmonary metastasis for 7 days. Mice were then sublethally lymphodepleted by irradiation at day 7, followed by i.v. infusion of activated pmel-1 $CD8^+$ T-cells (1.0×10^7) at day 8. Mice received injections of PBS, T-cells only, T-cells followed by i.v. injection of free IL-2/Fc (60 μg), or T-cells backpacked with IL-2/Fc NGs at the same dose. Pulmonary melanoma metastases were histologically analyzed with H&E staining when the mice were sacrificed at day 20. (a) Experimental timeline. (b) Representative images for pulmonary melanoma metastases. (c) Counts of lung metastatic nodules. (d) Representative tissue sections of each grade for metastatic burden scoring. (e) Scores of metastatic burden. Data represent the mean ± s.e.m. (n = 4/group). *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$; ****, $p < 0.0001$ by One-Way ANOVA and Tukey's tests; n.s., not significant.