Electronic Supplementary Material (ESI) for Chemical Science.

Supplementary Information

Antigenically shielded universal red blood cells by polydopamine-based cell surface engineering

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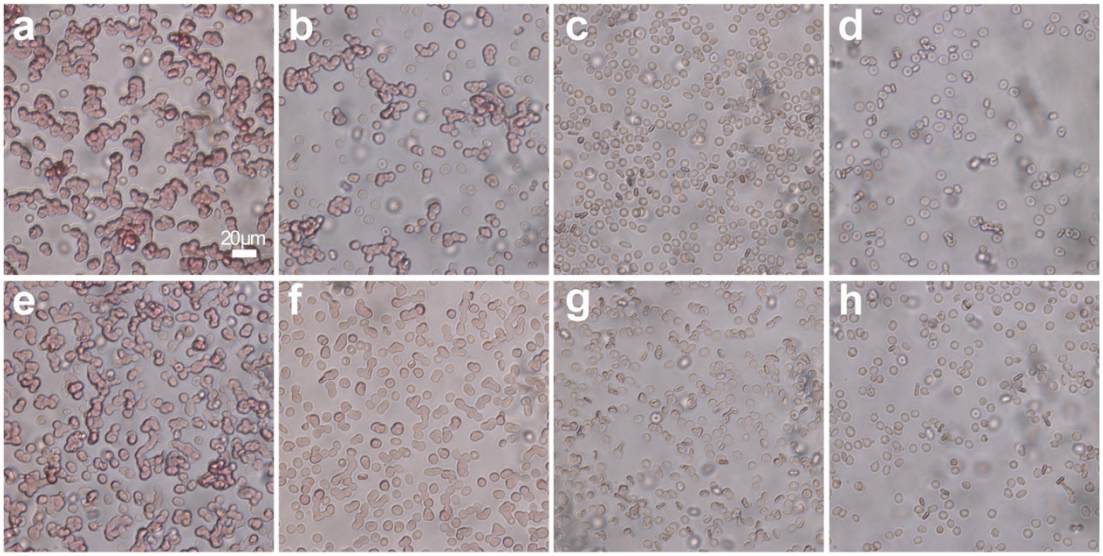

Fig. S1 Cell surface engineering with different reaction concentrations of dopamine, and different reaction time. (a) Human type A RBCs are getting agglomerate in the anti-A serum. (b) The agglomerate phenomenon could be prevented sharply after treatment with 1 mg/mL dopamine for 45 min. However, there are still some conglomerations left in the field of vision shows that this treatment could not shelter the antigen sites on the cell surface completely. (c) Antibody-mediated aggregation can be prevented completely by treatment of 2 mg/mL dopamine. (d) High concentration of dopamine, for example, 4 mg/mL can also shield the surface antigens of RBCs, however, results in cell hemocytolysis seriously. It can be seen that cell concentration decreased after treatment of 4 mg/mL. (e) Human type AB RBCs are inclined to aggregate together in the anti-A serum. (f) Antibody-mediated aggregation is prevented partially after treatment of 2 mg/mL dopamine for 30 minutes. (g) As reported before, antibody-sites could be sheltered and their mediated gather could be impeded by 45 minutes treatment of 2 mg/mL dopamine. (h) 60 minutes treatment can also result in nice sheltering effect for antibody-sites on the RBC surface, however, lead to cell fractures and decline of cell concentration.

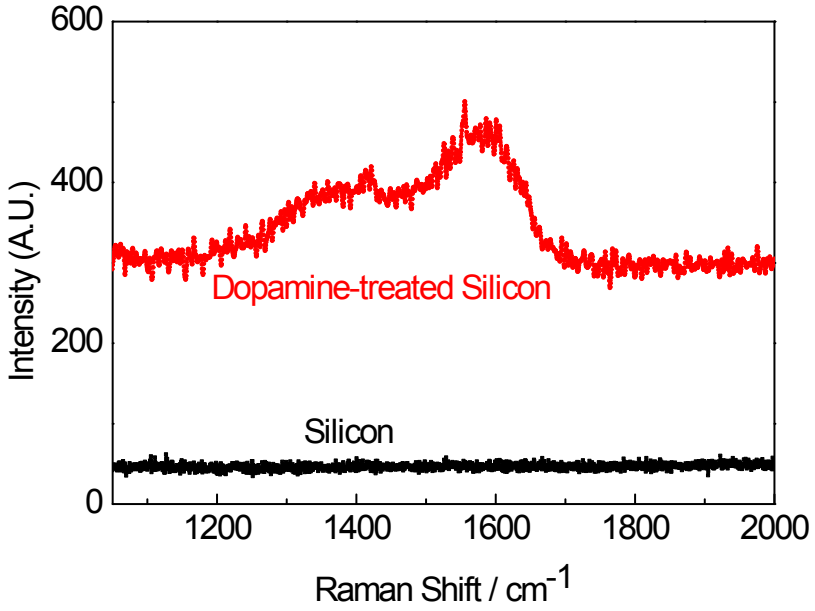

Fig. S2 The Raman spectra of polydopamine (PDA) modified silicon wafer and unmodified silicon substrate. There are two peaks, 1370 and 1600 cm^{-1} for PDA-engineered silicon, showing that PDA signal, compared with smooth curve for bare silicon at 1100 – 2000 cm^{-1}.

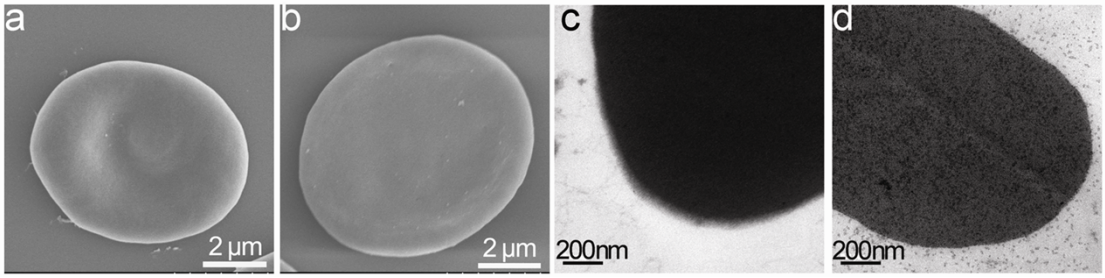

Fig. S3 PDA modification is a universal method for cell modification. **(**a) SEM images of human RBC and (b) PDA-modified RBC (PDA-RBC). A larger magnification of view shows that PDA-RBC is morphologically normal. (c) TEM image of the native human RBC. The surface of red blood cells is covered by sugar chains fine hairs, which give a pretty blurry boundary of native ones. (d) TEM images of ultrathin sectional PDA-RBC showing the details of morphology change. Surface engineering endows RBCs with well-defined boundary and spots on the cell surface.

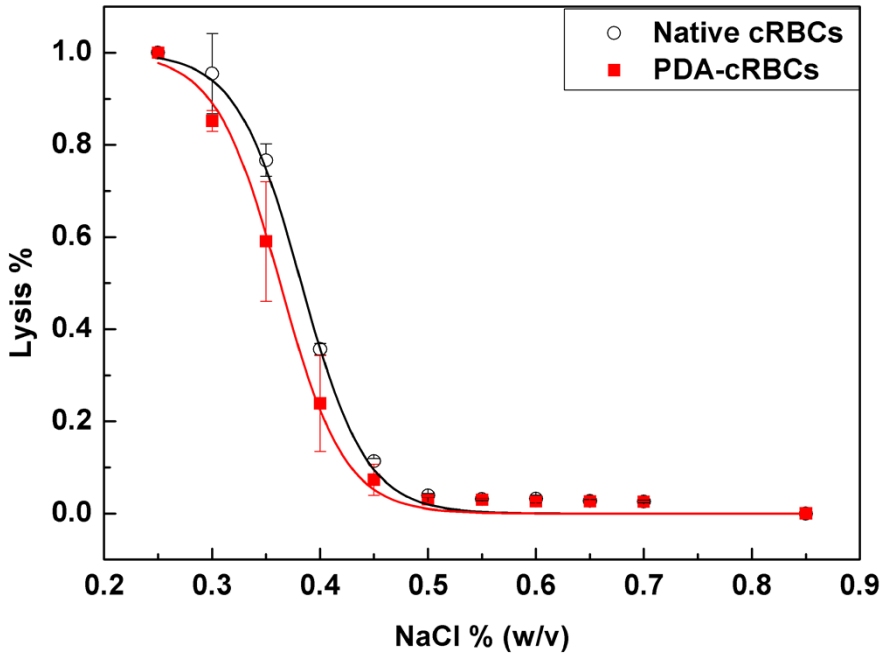

Fig. S4 Chicken erythrocyte (chicken red blood cells, cRBCs) stability is minimally affected by chemical modification of PDA; however, osmotic fragility of PDA-cRBCs is even increased slightly. Shown are representative osmotic fragility profiles of the native and PDA-cRBCs for 45 min.

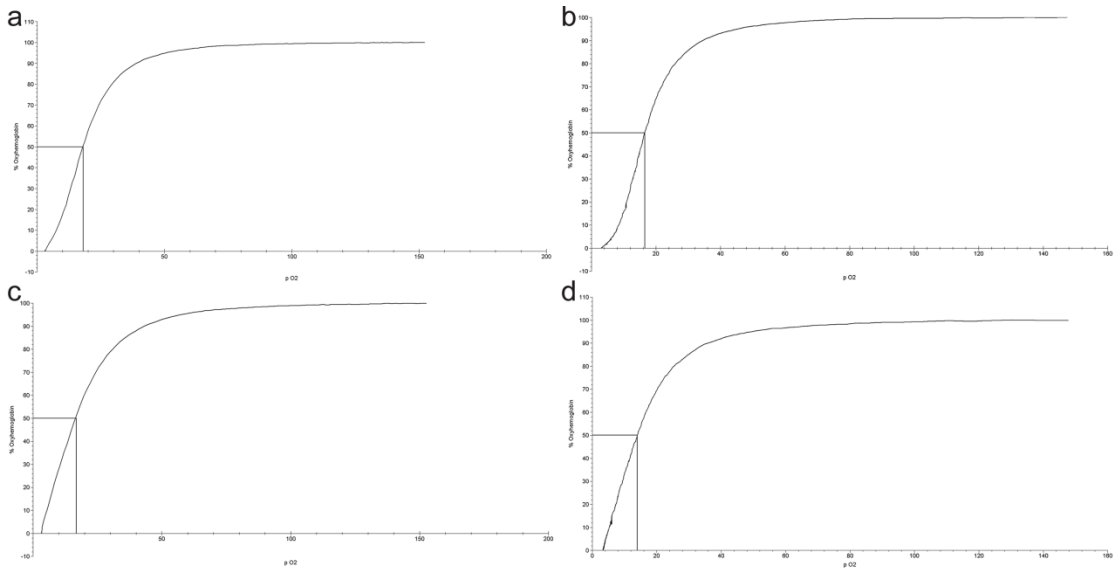

Fig. S5 Oxygen Equilibrium Curves of the native and PDA-RBCs. (a) Tonometric oxygen binding curves of native RBCs at 37°C in 10 mM HEPES buffer (pH 7.4) containing 150 mM NaCl, and (b) PDA-RBCs. (c) The oxygen dissociation curve of the original RBCs and (d) the PDA-engineered ones.

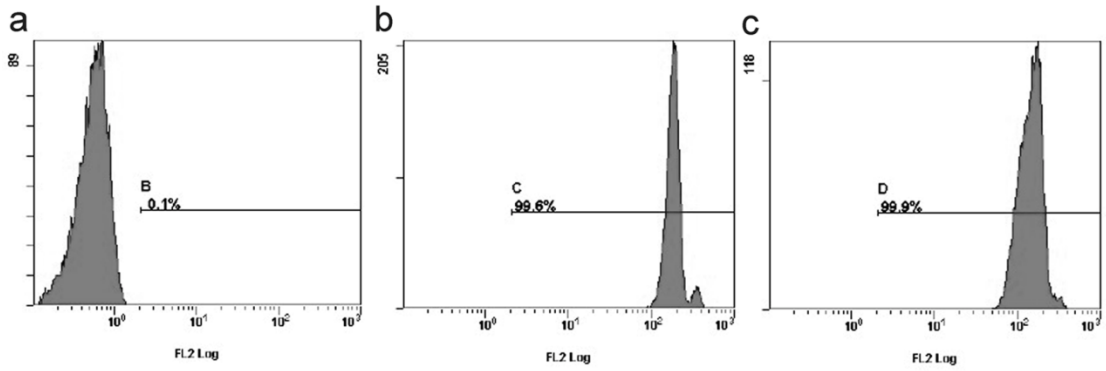

Fig. S6 Fluorescent labeled mouse RBCs by PKH26. The PKH26 fluorescent cell linker kits (Sigma) use proprietary membrane labeling technology to stably incorporate a yellow-orange fluorescent dye with long aliphatic tails (PKH26) into lipid regions of the cell membrane. (Horan PK, Melnicoff MJ, Jensen BD, Slezak S, Fluorescent cell labeling for in vivo and in vitro cell tracking, Academic Press, 1990) PKH26 fluoresces in the yellow-orange region of the spectrum and has been found to be useful for in vitro and in vivo cell tracking applications in a wide variety of systems. Due to its extremely stable fluorescence, PKH26 is the cell linker dye of choice for in vivo cell tracking studies, particularly when labeled cells are to be followed for periods longer than a few months. Compared with native mouse RBCs (a), the PKH26-labelled native mouse RBCs (b) and PDA surface-engineered mouse RBCs (c) all have above 99.5% fluorescence ratio, which confirmed that fluorescent labeling was not obstructed by the PDA surface engineering.

Table S1 Routine blood test and body weights assay of the native and PDA-RBCs transfused mice.

Samples		Saline Transfused	Native RBCs	PDA-RBCs
Body weight [g]	Initial	19.35±0.69	19.75±1.25	19.45±0.66
	Final	35.25±0.90	36.2±1.01	36.63±0.54
White blood cells (WBC) [10^9/L]	Before injection	0. 67±0.98	2.97±0.85	4.1±1.15
	4 h after injection	5.47±1.80	7.87±1.27	7.6±1.56
Red blood cells (RBC) [10^{12}/L]	Before injection	3.57±4.19	5.47±1.80	7.53±2.14
	4 h after injection	6.23±0.78	5.47±1.80	6.27±0.58
Hematocrit (HCT) [%]	Before injection	21.27±25.75	45.27±11.80	55.07±3.17
	4 h after injection	37.9±4.78	37.73±0.96	40.7±1.76
Mean corpuscular volume (MCV) [fl]	Before injection	58±2.65	60.33±3.21	59.67±0.58
	4 h after injection	61	60.67±3.79	60
Mean corpuscular hemoglobin (MCH) [pg]	Before injection	16.33±3.05	22±4.58	17
	4 h after injection	16	16.33±0.58	16.33±0.58
Mean corpuscular hemoglobin concentration (MCHC) [g/L]	Before injection	280.33±49.41	360±64.71	285±3.61
	4 h after injection	262.67±3.79	264.67±10.69	273.67±5.69
Hemoglobin [Hb] [g/L]	Before injection	58.33±69.89	158±12.49	157±8.72
	4 h after injection	99.67±13.87	100±6.08	111.33±4.04
Platelet [PLT] [10^9/L]	Before injection	106±123.09	260.67±100.32	315±94.03
	4 h after injection	471±55.43	530.67±118.01	448±73.65

Table S2 Routine blood test and body weights assay of the native and PDA-RBCs three-transfused mice.

Samples		Saline Transfused	Native RBCs	PDA-RBCs
Body weight [g]	Initial	26.3±2.70	28.73±1.15	28.1±0.87
	Final	36.06±1.66	41.23±2.74	42±2.61
White blood cells (WBC) [10^9/L]	Before injection	4. 57±0.15	3.53±0.75	3.16±0.76
	4 h after injection	3.5±1.41	2.5±0.5	3.0±0
Red blood cells (RBC) [10^{12}/L]	Before injection	7.73±0.32	7.83±0.90	6.05±0.92
	4 h after injection	3.75±1.06	5.0±0.5	5.0±2.29
Hematocrit (HCT) [%]	Before injection	54.17±2.32	55.83±6.83	26.8.±23.55
	4 h after injection	23.75±7.42	31.83±6.21	26.5±11.17
Mean corpuscular volume (MCV) [fl]	Before injection	70±1	71±1.73	66.5±0.71
	4 h after injection	61±1.41	57±3	54.33±0.58
Mean corpuscular hemoglobin (MCH) [pg]	Before injection	17.67±0.58	12.33±7.23	18.5±0.71
	4 h after injection	18	16.33±0.58	15.67±0.58
Mean corpuscular hemoglobin concentration (MCHC) [g/L]	Before injection	252±2.65	176±108.43	272.5±4.95
	4 h after injection	295±2.83	284.67±15.28	290.67±11.72
Hemoglobin [Hb] [g/L]	Before injection	136.67±7.37	101.67±65.55	110.33±9.61
	4 h after injection	99.67±13.87	100±6.08	111.33±4.04
Platelet [PLT] [10^9/L]	Before injection	544.33±59.07	342.67±91.18	595.5±147.79
	4 h after injection	1157.5±81.32	488.33±42.52	696.67±150.11