1   *Supporting Information*

2   **Targeted Delivery of Cytotoxic Proteins via Lipid-based Nanoparticles to**

3   **Langerhans cells**

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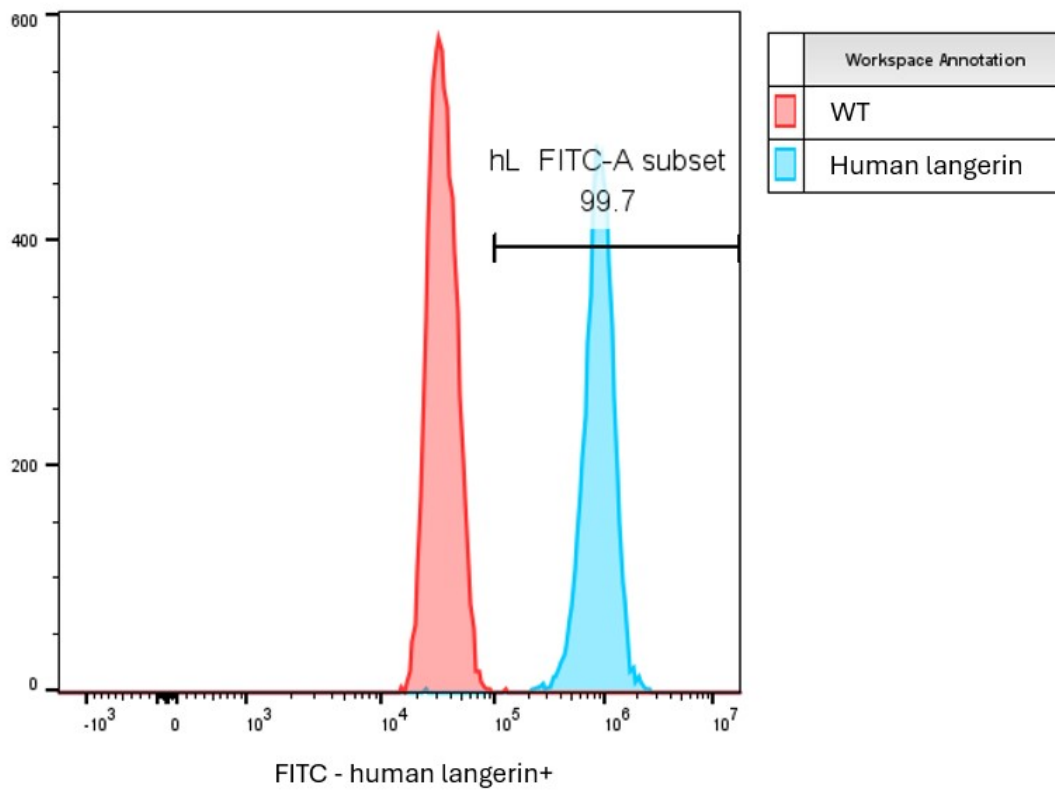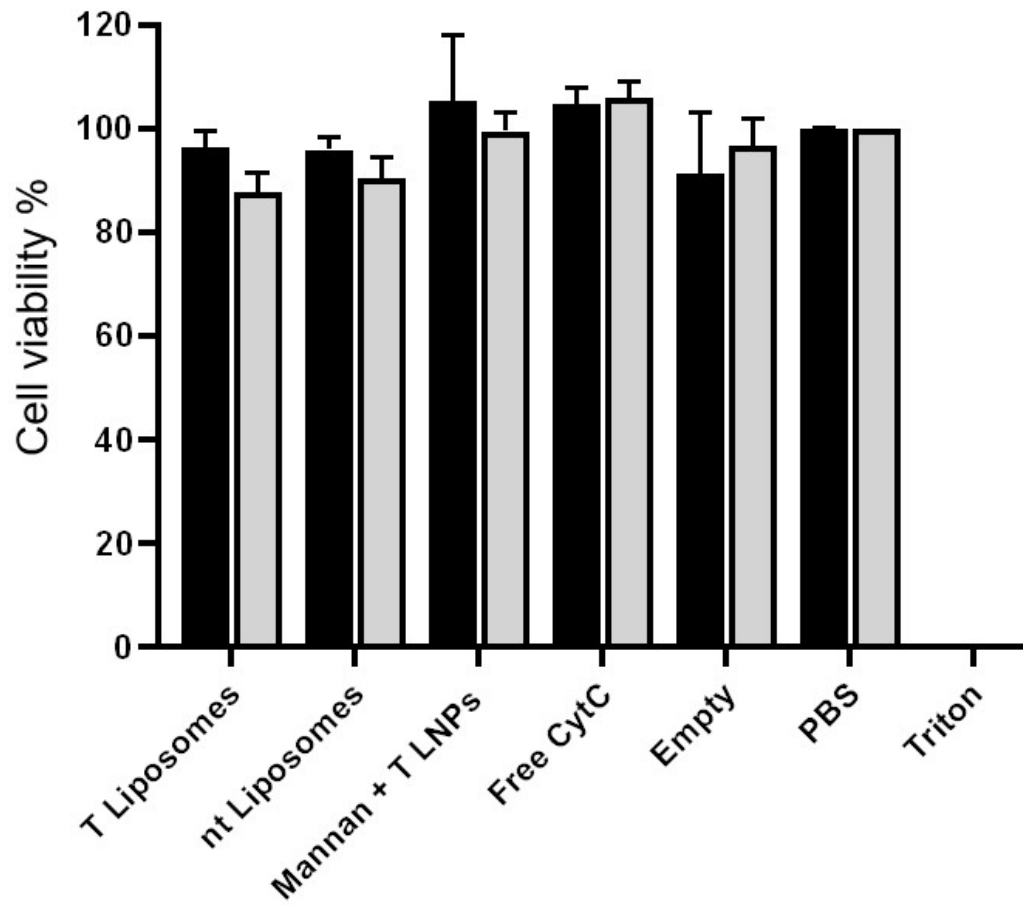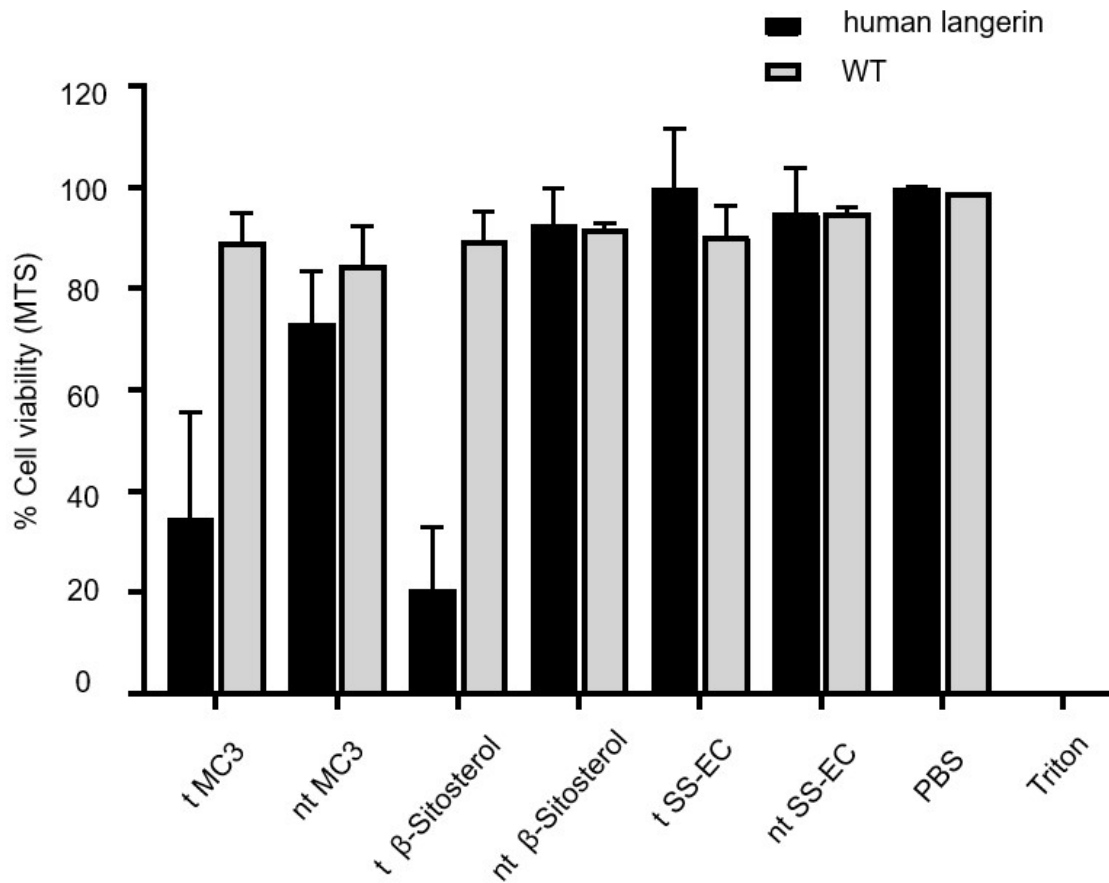
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Figure S1. Representative staining for human langerin expression on Raji cells as analyzed by flow cytometry.

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Figure S2 *In-vitro* cell proliferation on wild-type (WT) and human langerin (hL) expressing Raji cells. MTS assay for cells treated with t and nt liposomes encapsulating Cyt C (25 µg/mL of the protein loaded in the nanoparticles), Cyt C protein (250 µg/mL of the free protein), empty targeted (et) LNPs, for 24 hours.
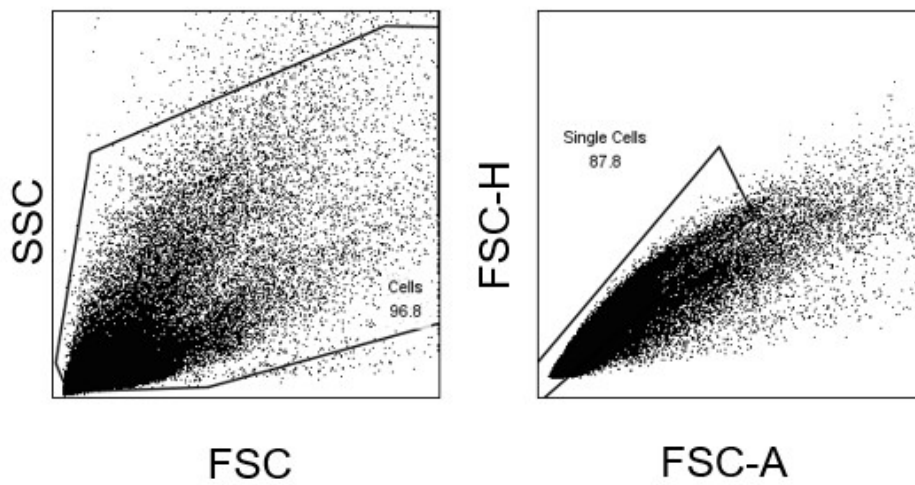
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Figure S3 *In-vitro* cell proliferation assay (MTS) for altered composition of LNPs on WT and hL expressing Raji cells. values in this graph are from one representative of three independent measurements. Cells were treated with 25 µg/mL of the protein loaded in the nanoparticles Cyt C for 24 hours.
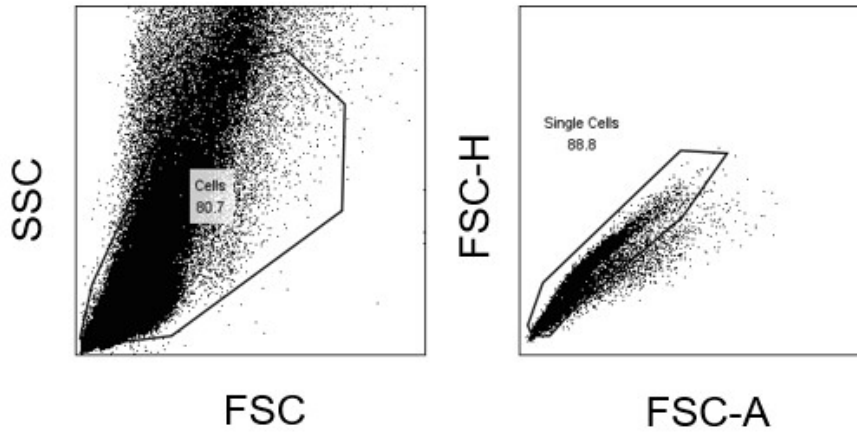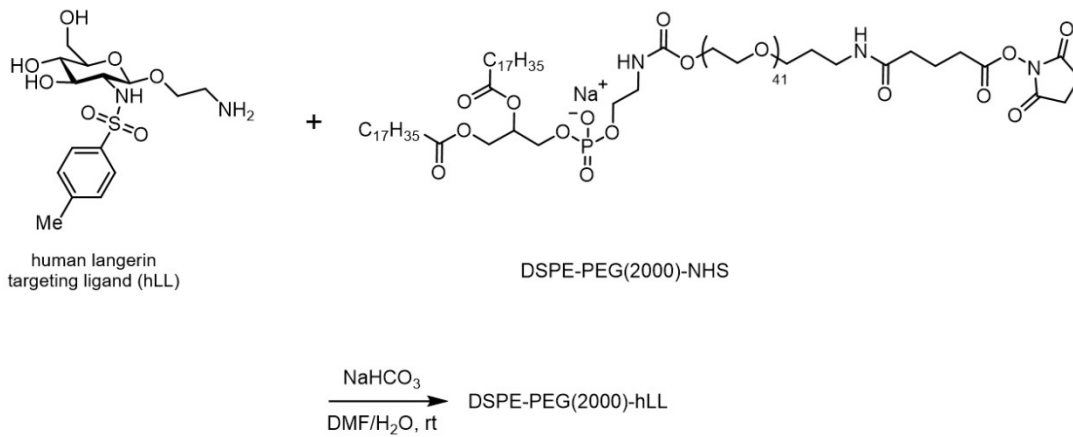
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Figure S4 Representative dot plots for the gating of epidermal single cell suspensions prepared from the skin of human langerin DTR C56BL/6 mice (n=3), identifying cells based on forward scatter (FSC) and side scatter (SSC) to select single cells.

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Figure S5 Representative dot plots for the gating of epidermal single cell suspensions prepared from healthy adult human skin (n=3), identifying single cells based on forward scatter (FSC) and side scatter (SSC) to select single cells.

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Figure S6. Schematic overview of the conjugation strategy for the human langerin targeting ligand (hLL) to DSPE-PEG-NHS

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Table 1 Characterization of lipid-based nanoparticles

Saporin	Size (nm)	Zeta potential (mV)	PDI	Loading efficiency % (starting from 1 mg/ml)
t LNPs	129	-14.6	0.2	31.9
nt LNPs	126	-15.6	0.22	21.9
t liposomes	112	-8.2	0.29	34.8
nt liposomes	142	-6.6	0.12	33.4
Cyt C	Size (nm)	Zeta potential (mV)	PDI	Loading efficiency % (starting from 2.5 mg/ml)
t LNPs (MC3)	136	-12.6	0.18	6.5
nt LNPs (MC3)	124	-12.3	0.16	6.9
t LNPs (SS)	169	-12.6	0.08	3.7
nt LNPs (SS)	184	-11.2	0.10	3.4
t LNPs (β-sitosterol)	174	-13.6	0.11	3.5
nt LNPs (β-sitosterol)	198	-12.2	0.11	3.5
t liposomes	91	-9.7	0.13	3.4
nt liposomes	105	-11	0.1	3.4
et LNPs	116	n/a	0.2	