Supplementary Information

Improvement of Therapeutic Index by Combination of Enhanced Peptide Cationicity and Proline Introduction

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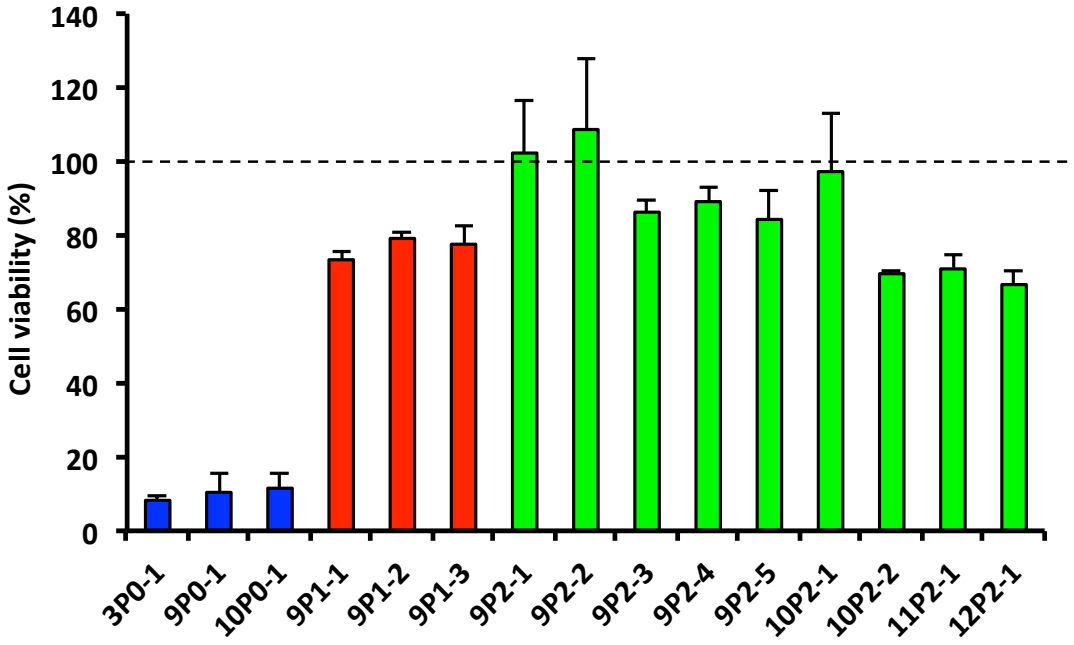

Figure S1. Cytotoxicity of the peptides against HUVEC cells. The percent cell viability values at 100 μM are presented (mean ± S.D., n = 3). Peptides are color-coded according to the number of Pro residues (0, blue; 1, red; 2, green).

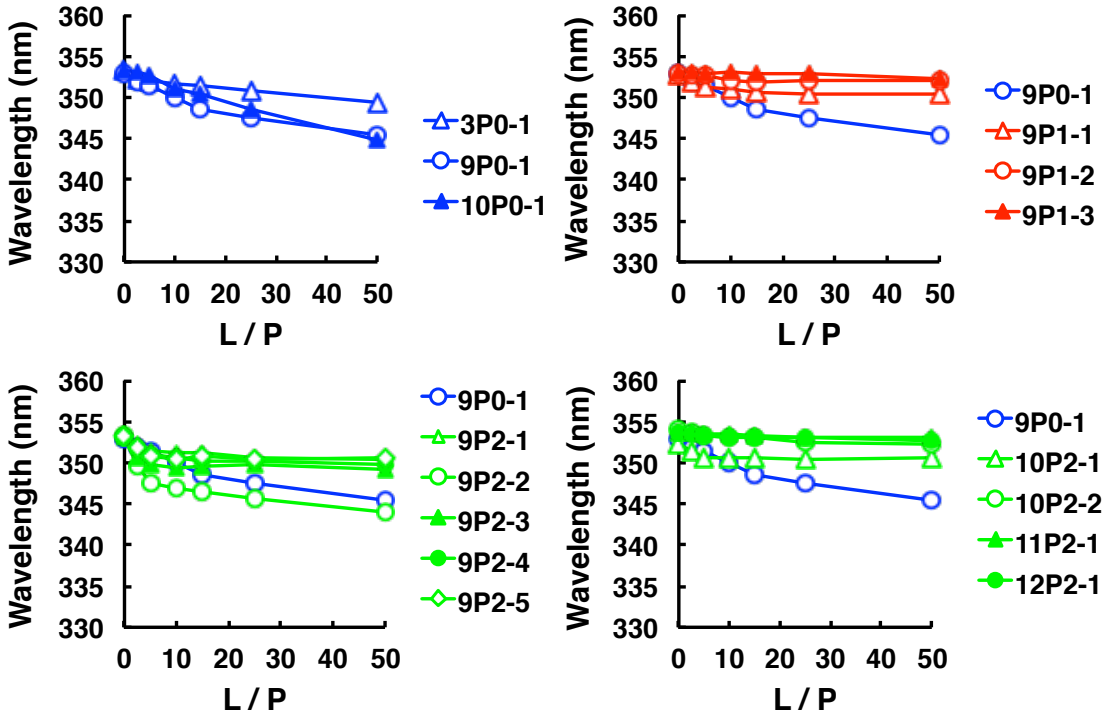

Figure S2. Binding of the peptides to mammalian cell-mimicking POPC/POPS/cholesterol (8 : 1: 1) bilayers. A peptide solution was titrated with LUVs while monitoring Trp fluorescence at 30 °C. The wavelength of maximal intensity is plotted as a function of the lipid-to-peptide molar ratio (L/P). Peptides are color-coded according to the number of Pro residues (0, blue; 1, red; 2, green). The S.D. values for 2–3 measurements were 0.9 nm on average at an L/P value of 25.

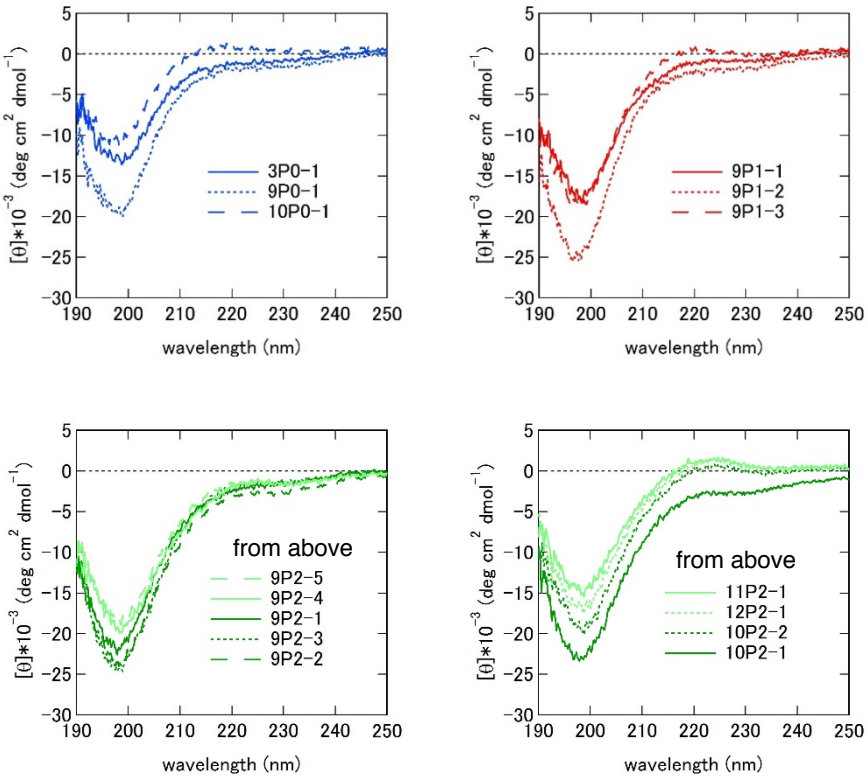

Figure S3. CD spectra of the peptides (20 μM) in 10 mM Tris/150 mM NaF/1 mM EDTA, pH 7.4 buffer at 30 ºC. Peptides are color-coded according to the number of Pro residues (0, blue; 1, red; 2, green).

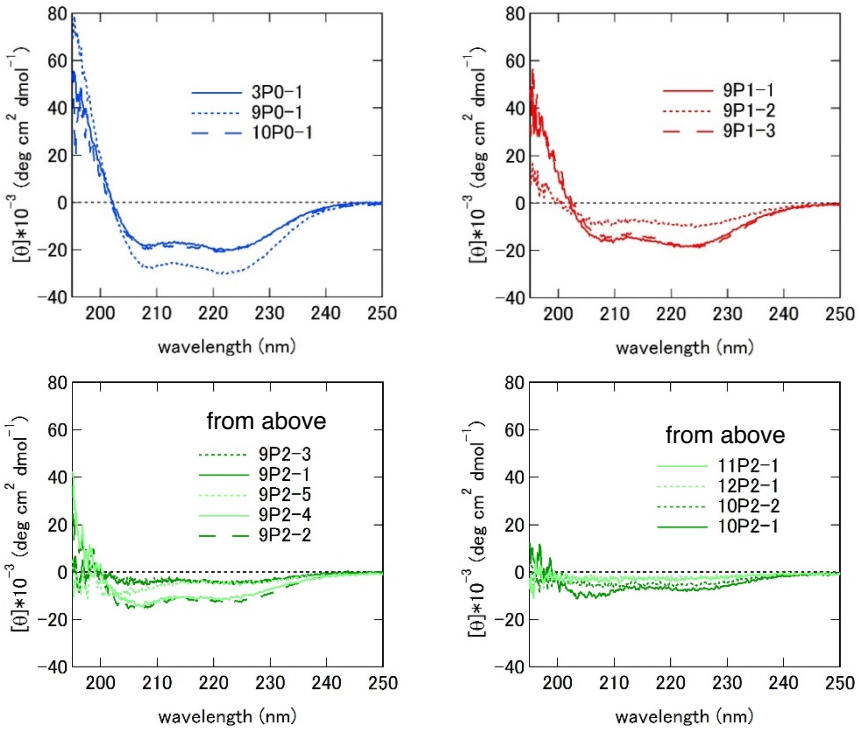

Figure S4. CD spectra of the peptides (20 μM) in thr presence of 2 mM POPG/POPC (1:1) liposomes at 30 ºC. Peptides are color-coded according to the number of Pro residues (0, blue; 1, red; 2, green).

Table S1. Peptide mass by MALDI-MS and purity by HPLC

peptide	MW $[M + H]^+$	observed	purity
3P0-1 (MG)	2506.0[a]	2504.7[b]	> 97 %
9P0-1	2705.3	2704.5	> 97 %
10P0-1	2731.5	2730.9	> 99 %
9P1-1	2730.4	2730.6	> 97 %
9P1-2	2654.4	2754.6	> 97 %
9P1-3	2744.5	2744.1	> 99 %
9P2-1	2680.4	2680.4	> 99 %
9P2-2	2770.5	2770.9	> 99 %
9P2-3	2694.4	2694.1	> 95 %
9P2-4	2714.4	2715.9	> 95 %
9P2-5	2728.4	2726.2	> 99 %
10P2-1	2811.6	2811.7	> 95 %
10P2-2	2755.5	2778.1[c]	> 99 %
11P2-1	2752.5	2774.5[c]	> 99 %
12P2-1	2766.5	2768.3	> 99 %

[a]exact mass [M]

[b]observed [M] measured by ESI-MS

[c]detected as $[M + Na]^+$