Supplemental Data for

Cationic Nanoparticles Induce Nanoscale Disruption in Living Cell Plasma Membranes

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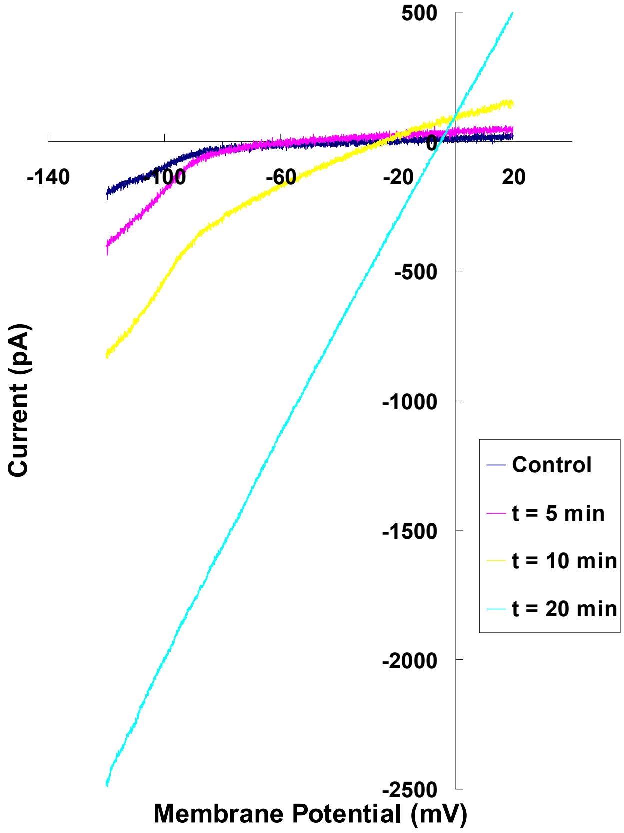
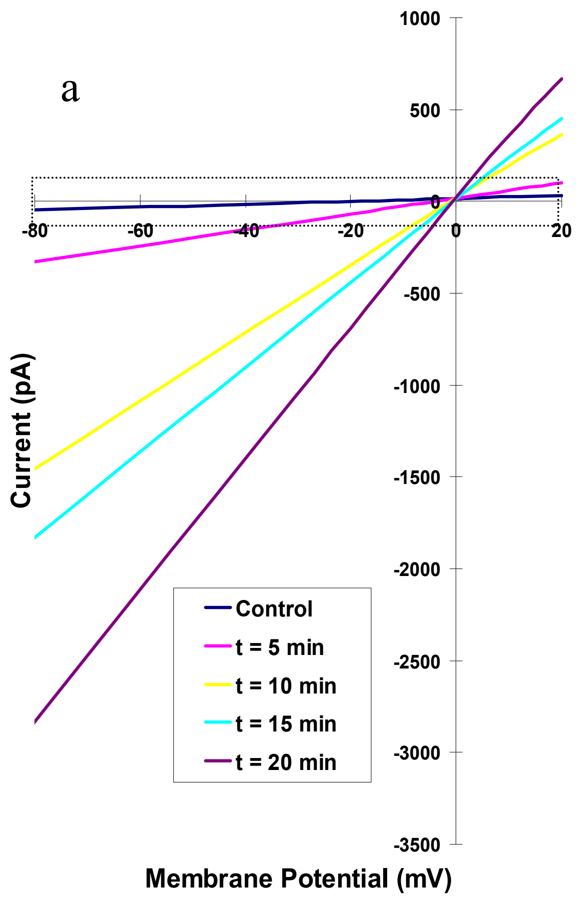
The calculation for the diameter of the formed defects provides an estimate between current step size and the hole size in the cell membrane based on several important assumptions. First, E_m is considered as the membrane holding potential (-70 mV). However, the true value of potential held across the cell membrane becomes less negative as the absolute value of the current becomes larger. This is due to an increasing voltage drop on the patch-clamp pipette. Knowing the maximum pipette resistance and absolute value of recorded current, one can conclude that, in the extreme cases, hole size is ~20% larger than provided in Figure 4. Other sources of potential error are the assumed solution resistivity, 50 Ωcm, (±50%) and membrane thickness (±20%). These errors lead to an uncertainty in the absolute accuracy of the calculated hole area of ±50%, or ±30% in the diameter. The calculated typical diameter of a hole produced in the membrane ranges from 2 – 10 nm.

S 1


500
-500
-1000
-1500
-2000
-2500
-140
-100
-60
-20
0
20
Current (pA)
Membrane Potential (mV)
Control
t = 5 min
t = 10 min
t = 20 min

S 2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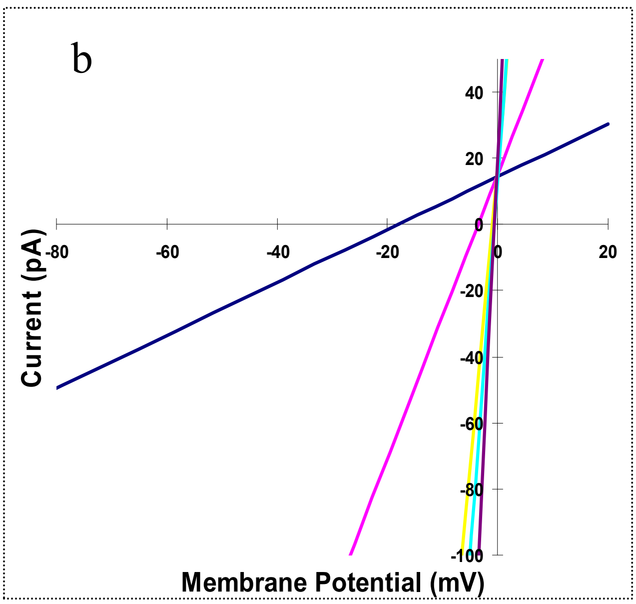
-1500
-2000
-2500
-3000
-3500
-80
-60
-40
-20
0
20
Current (pA)
Membrane Potential (mV)
Control
t = 5 min
t = 10 min
t = 15 min
t = 20 min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20
0
-20
-40
-60
-80
-100
-80
-60
-40
-20
0
20
Current (pA)
Membrane Potential (mV)

S1. Current-voltage relationships for KB cell at different exposure time (t) of 6 μg/mL PEI. Membrane potential was ramped from -120 to 20 mV in 2 sec. After stable recordings were obtained (usually ~5 minutes), external solution (Modified Tyrode, pH 7.4) containing PEI was applied. Before injection of PEI, the KB cell showed I-V behavior typical of inward-rectifier potassium ion channels with the reversal potential at ~-70 mV. After the PEI injection, the cell gradually lost its inward rectification and the reversal potential moved toward 0 mV while the conductance of the cell increased to ~20 nS.

S2. **(a)** Current-voltage relationships for 293A cell at different exposure time (t) of 30 μg/ml AMO-3 solution. Membrane potential was ramped from -80 to 20 mV in 2 sec. After stable recordings were obtained (usually ~5 minutes), external solution (Modified Tyrode, pH 7.4) containing AMO-3 was applied. Upon application the reversal potentials of the cell moved toward 0 mV, and the conductance of the cell increased to ~35 nS. **(b)** Expanded view of dashed box in **(a).** Nonexposed control cell (dark blue line) show a conductance of 0.8 nS and the reversal potential of -17.3 mV.

Table S1. Physical Properties of Polycationic Polymers Used in This Study

	Molecular Weight* (g/mol)	Polydispersity*	Shape of Chain
G5-NH_2	26530	1.02	Sphere-like
G7-NH_2	97020	1.07	Sphere-like
PEI	78220	3.44	Branched, flexible
PLL	11210	1.67	Linear, flexible

Molecular weight and polydispersity determined by GPC/light scattering as previously reported (*Bioconjugate Chemistry* **2006**, *17*, 728-734).