Supplementary Information

Micro/extended-nano Sampling Interface from Living Single Cell

Ling Lin,[a] Kazuma Mawatari,[a] Kyojiro Morikawa,[a] Yuriy Pihosh, [a] Ayumi Yoshizaki,[b]

Takehiko Kitamori,[a*]

a. *Department of Applied Chemistry, School of Engineering, The University of Tokyo, 7-3-1 Hongo, Bunkyo, Tokyo 113–8656, Japan*

b. *Department of Dermatology, Graduate School of Medicine and Faculty of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo, Tokyo 113–8656, Japan*

S1 Lipid bilayer modification

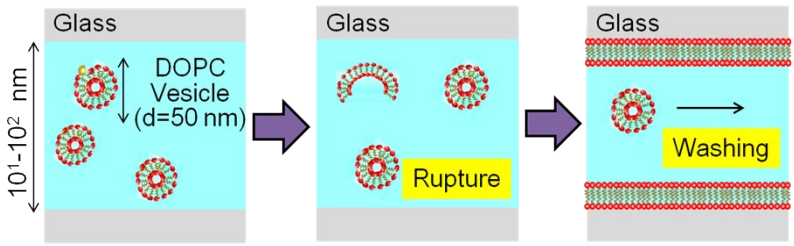

Figure S1. Lipid bilayer modification in an extended-nano channel using a vesicle fusion method.

S2 Evaluation of Sampling Volume

The precision of the volume of the extended-nano channel was evaluated by measuring its cross section at several positions using a scanning electron microscope (SEM) (JEOL JSM-7001J) as shown in Figure S1a. Figures S1a and S1b are plots of the width and depth, respectively, of the extended-nano channel and the differences between the widths and depths were within 1%.

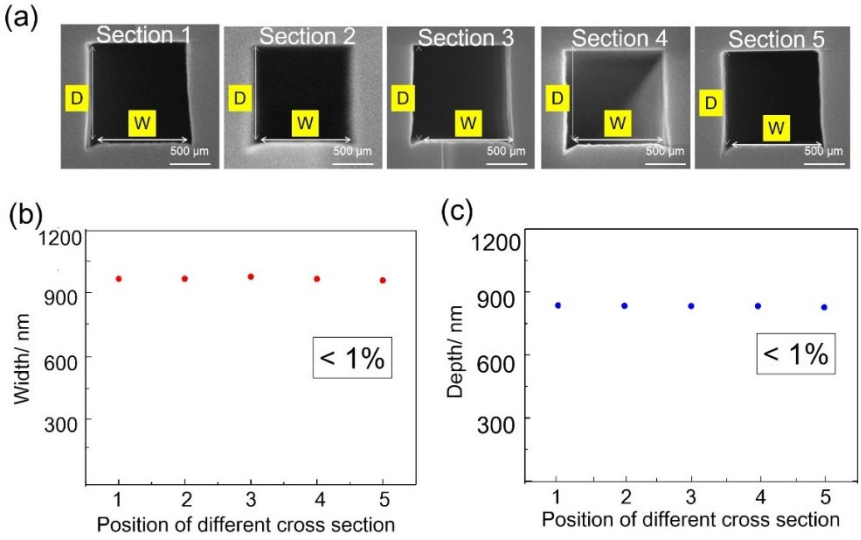

Figure S2. a, SEM images of the cross section at different positions. **b**, Plot of the widths. **c**, Plot of the depths.

S3 Effects of applied pressure on lipid fusion measured using a fluorescence microscope

The effect of different pressures on lipid fusion was investigated prior to confirming femtoliter sampling from a living single cell. The model comprised single HAECs and the cytoplasm was stained with a fluorescent dye (Calcein AM) for observation using a fluorescence microscope. A cell suspension (more than 1×10^7 cells/mL) was prepared using phosphate buffered saline, introduced into the microchannel, and a single cell was trapped in the single-cell chamber by applying a ~5 kPa pressure, resulting in little damage to the cell membrane. The solution in the microchannel was replaced with PBS solution to flush out excess cells. Then, a 0–70 kPa pressure was applied to the isolated cells to induce lipid fusion. As shown in Figure S2, no cytoplasm entered the extended-nano channel when the pressure was 0–50 kPa but cytoplasm was observed when the pressure was more than 70 kPa.

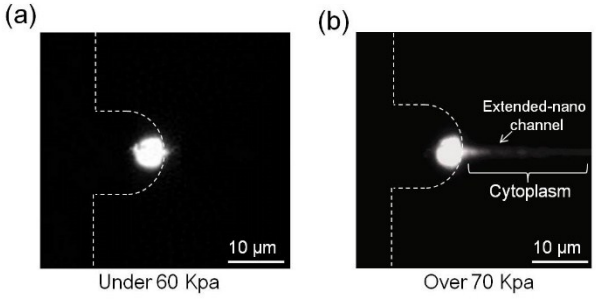

Figure S3. Effects of applied pressure. **a**, Fluorescence image at 50 kPa. **b**, Fluorescence image at 70 kPa.

S4 Effects of applied pressure on lipid fusion measured by the extended-nano patch clamp

The extended-nano patch clamp technique was used to observe the pressure dependence of lipid fusion and to verify the results obtained by fluorescence microscopy. Figure S3 shows that the ion current changed little in the range of 0–50 kPa but significantly dropped at pressures above 60 kPa. These results were consistent with those shown in Figure S2.

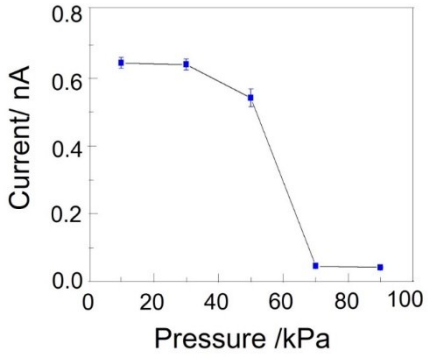

Figure S4. Effects of applied pressure measured by the extended-nano patch clamp technique.