Electronic Supplementary Material (ESI) for RSC Advances.

SUPPLEMENTAL FIGURES

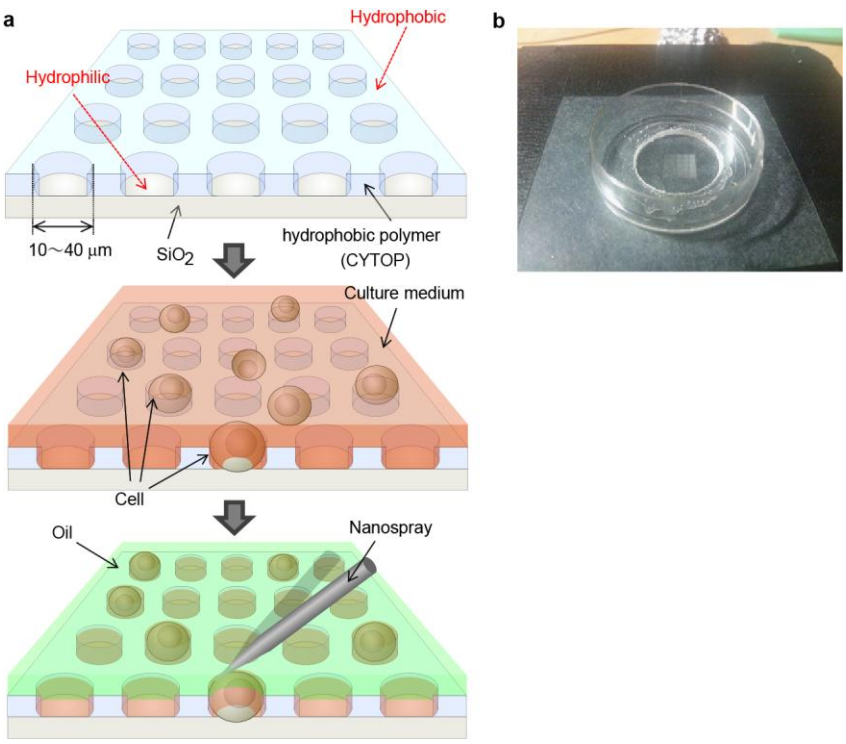

Figure S1. Micro-well array in which micro-droplets trap cells.

(**a**) Procedure of trapping individual cells within micro-droplets. Cells were washed twice with HEPES buffer and diluted to 1.0×10^5 cells/ml. Then, 500 μl of cell suspension was dropped onto the micro-well array, which was made of CYTOP, and given 5 min so that cells could sink to the bottom of the dish. Cells were then covered with oil (FC-40). Buffer surrounding each cell was collected with a glass micro-needle and applied to mass spectrometry analysis. (**b**) Photograph of a cell culture dish with a micro-well array at the bottom.

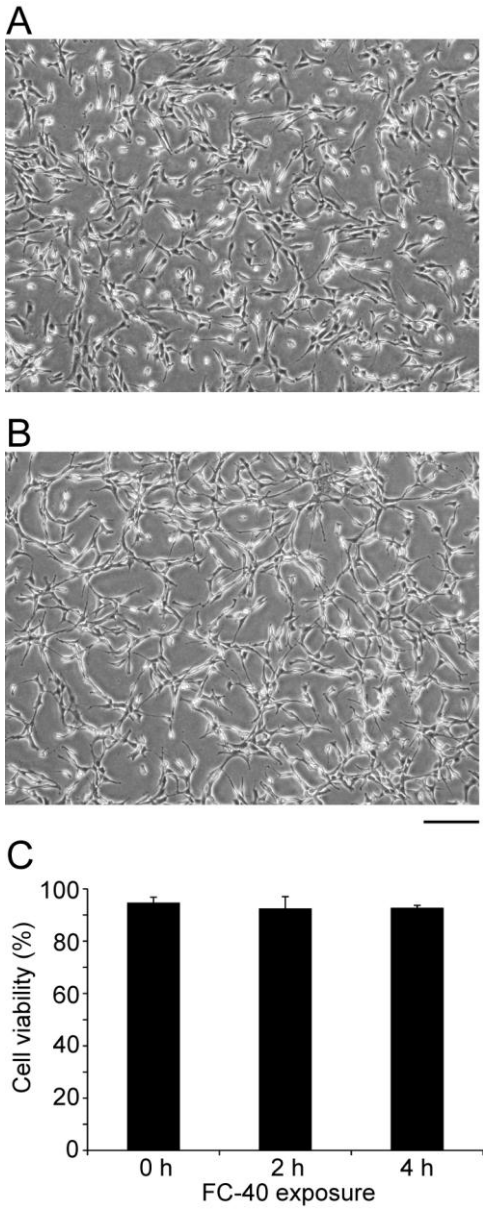

Figure S2. Cytotoxicity of FC-40.

NIH3T3 cells were exposed to 20 % FC-40 in culture medium for 2-4 h and cell viability was measured. (A) Phase contrast image of cells without FC-40 exposure. (B) Phase contrast image of cells after 4 h exposure to FC-40. Scale bar, 200 μm. (C) Cell viability after exposure to FC-40. Cell viability was assessed by trypan blue.

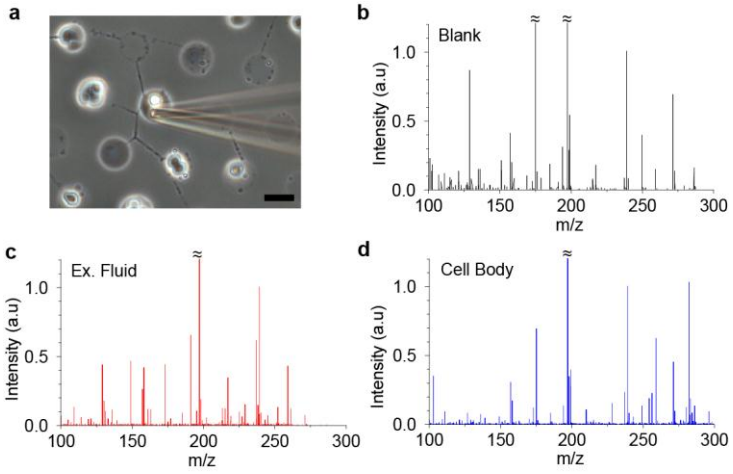

Figure S3. Example of single cell secretomics of a T-cell.

(**a**) Phase contrast image of a T-cell in a micro-well and glass micro-needle for sample collection. (**b**) Typical mass spectrum from the buffer of a micro-droplet without any cells. (**c,d**) Typical mass spectrum from the buffer surrounding a T-cell (**c**) and single cell body (**d**).

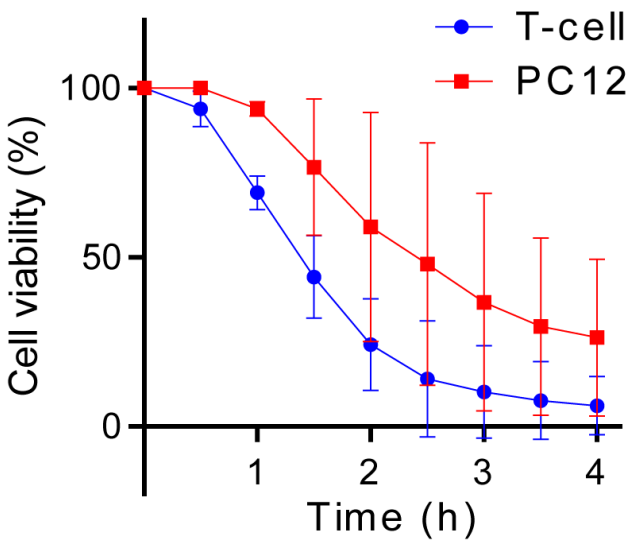

Figure S4. Cell viability after cells were trapped in micro-well.

T-cell and PC12 cells were trapped in a micro-well with diameter of 15 μm and cell viability was monitored for 4 h using propidium iodide under fluorescent microscope.

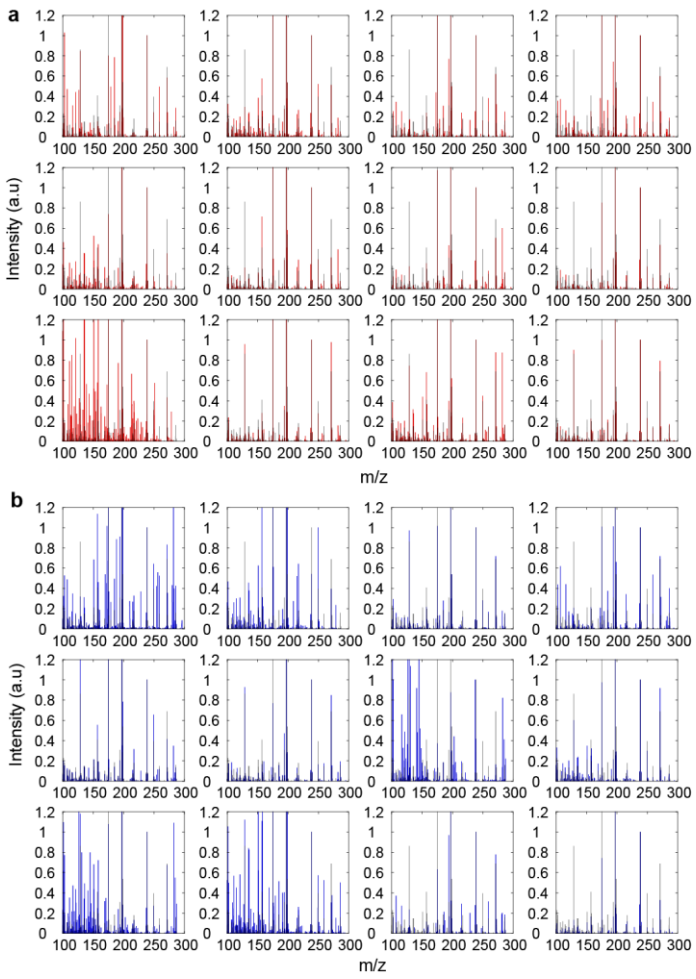

Figure S5. Heterogeneity of chemical releasates.

(**a, b**) Typical examples of mass spectra of releasates from 12 T-cells (**A**) and B-cells (**B**), respectively. The spectrum of a blank (buffer collected from micro-wells without cells) is shown in gray.

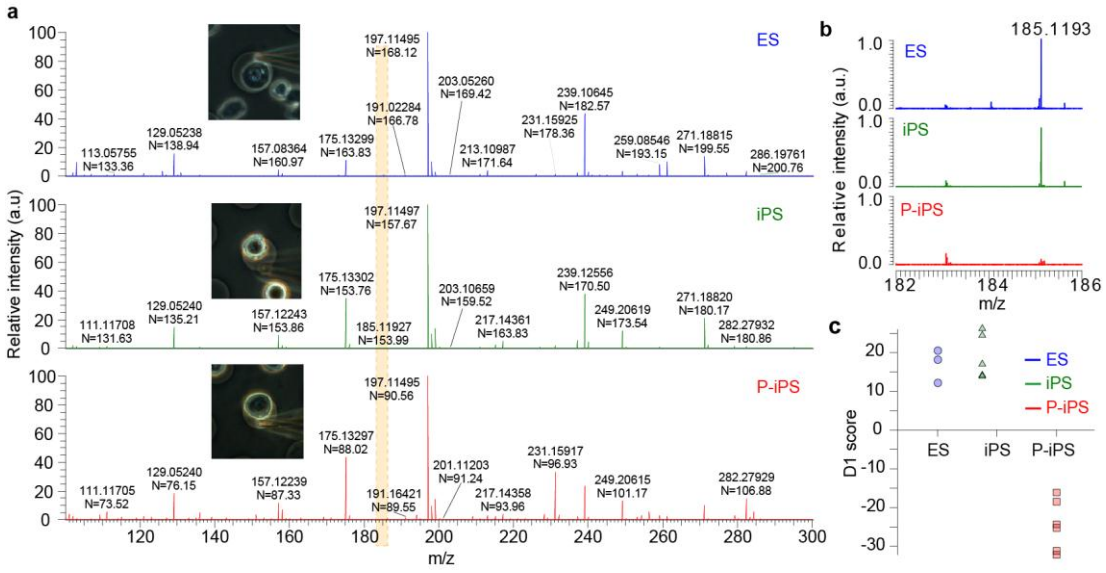

Figure S6. Discrimination of fully reprogrammed and partially reprogrammed iPS cells at the single cell level. (**a**) Typical mass spectrum of releasates from an ES cell (upper), fully reprogramed iPS cell (iPS, middle), and partially reprogramed iPS cell (P-iPS, lower). Insertions are phase contrast images of the cells inside micro-wells and the glass micro-needle used for sample collection. (**b**) Examples of mass spectrum from the ES cell (blue), fully reprogramed iPS cell (green), and partially reprogramed iPS cell (red) in the region of m/z = 182.0~186.0. The secretion of the unknown chemical releasate at 185.1193 m/z was confirmed with conventional mass spectrometry using culture medium where cells were cultured 48 h before sample collection (Fig. S7). The most likely candidate of this compound as predicted from exact mass was indanamin. (**c**) One dimensional visualization of DAPC results against ES cells (blue), fully reprogramed iPS cells (green), and partially reprogrammed iPS cells (red).

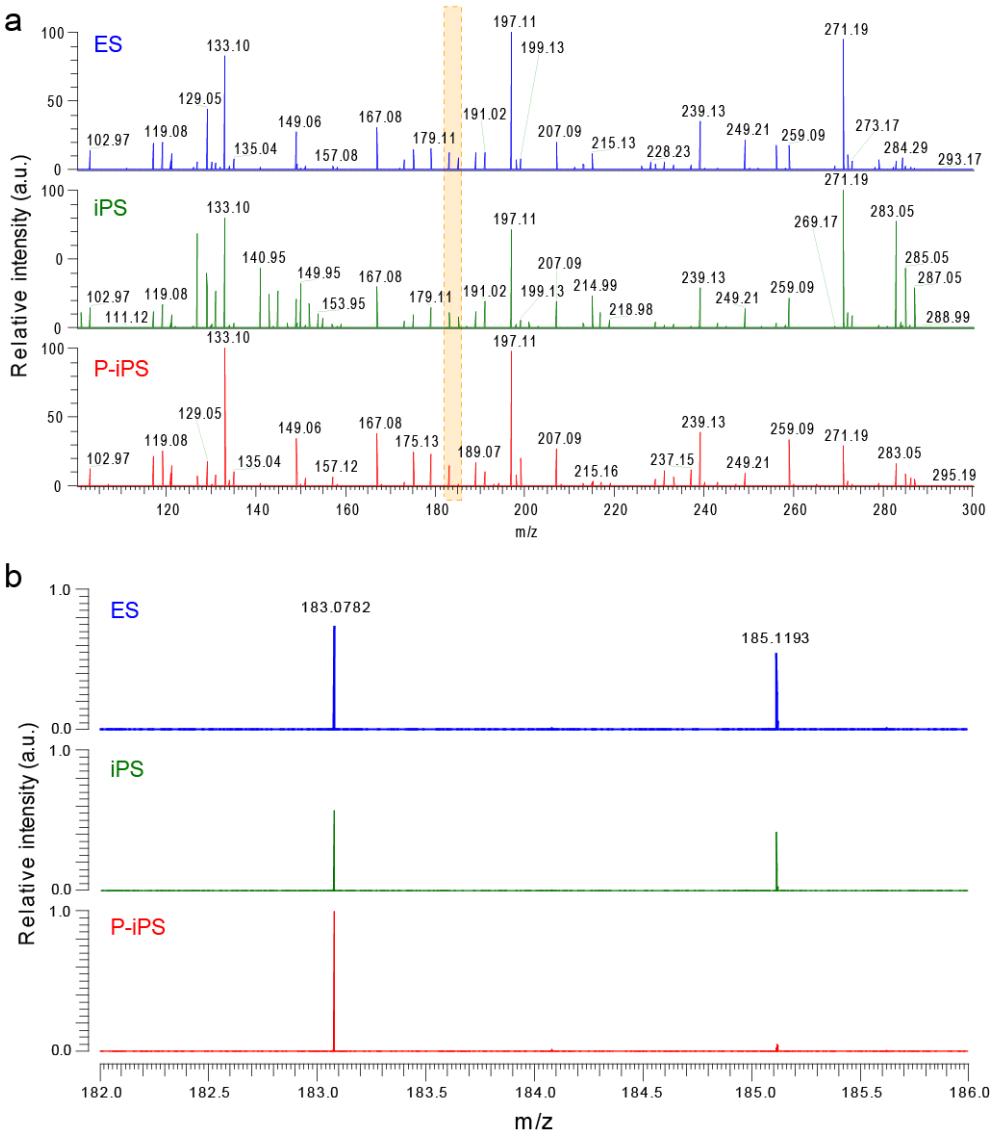

Figure S7. Discrimination of fully reprogramed and partially reprogrammed iPS cells using a huge number of cells.

(**a**) Typical mass spectrum of culture medium from an ES cell (upper), fully reprogramed iPS cell (iPS, middle), and partially reprogramed iPS cell (P-iPS, lower). Cells were cultured 48 h without medium exchange before sample collection. (**b**) Examples of mass spectrum from the ES cell (blue), fully reprogramed iPS cell (green), and partially reprogramed iPS cell (red) in the region of m/z = 182.0~186. 0.