Supporting Information

Nontoxic organic solvents identified using an *a priori* approach with Hansen solubility parameters

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Theoretical details regarding Hansen solubility parameters

Hansen solubility parameters (HSP) constitute a substance-specific set of three-partitioned cohesive energy densities, δD, δP, and δH, based on London dispersion, polar, and hydrogen-bonding molecular interactions, respectively. HSP have been proposed to effectively deal with polar materials and their solubility by partitioning Hildebrand solubility parameter that is applicable only to apolar materials. Although HSP cannot be applicable to some cases which Lewis acid-base interaction is critical (e.g. chloroform-ketones cases), the substances with greater Lewis acidity than Lewis basicity should be very rare (less than 5% of whole substances). Therefore, HSP still work very well in most cases.

The HSP values of organic solvents and other compounds are available from databases, the literature, and by estimation using commercial software. The compatibility (solubility, dispersibility, or wettability) of two substances/materials with the HSPs [δD_1, δP_1, δH_1] and [δD_2, δP_2, δH_2] [unit: $(\mathrm{J/cm^3})^{1/2}$] is determined by the HSP distance R_a calculated using the following equation:[1]

$$R_\mathrm{a} = \sqrt{4\times(\delta D_1 - \delta D_2)^2 + (\delta P_1 - \delta P_2)^2 + (\delta H_1 - \delta H_2)^2}\ . \quad (1)$$

The smaller R_a is, the better the compatibility (soluble, dispersible, or wettable) of two substances.

Seven major cell constituents were considered in the analysis (cell-constituent IDs: C1–C7); they were C1: cholesterol, C2: DNA, C3: phosphatidylcholine, C4: phosphatidylethanolamine, C5: sphingomyelin, C6:

phosphatidylserine, and C7: water. Table S1 summarizes the chemical structures and HSPs of these cell constituents. The HSPs of C1, C2 and C7 were available from the literature,[1, 2] and the others (C3–C6: cell-membrane constituents) were estimated using commercial software (HSPiP v4.1.03).[3] The values for R_0 listed in Table S1 are interaction radii and indicate thresholds for the constituents to dissolve into (or uptake) solvents when the R_a values between the constituents and solvents are smaller than the R_0 values.[1] The term "HSP sphere" of a material (polymer, powder, or any substance) refers to a sphere with a center determined by the material's HSP values [δD, δP, δH] and with a radius of R_0 in HSP space (with the Cartesian coordinates δD, δP and δH). The positional relationship between HSP spheres (and/or HSPs) of different materials in HSP space helps visually grasp interactions between different materials.

To systemically compare the interactions between test solvents and cell constituents (*i.e.,* to investigate the cytotoxic factors), the relative energy differences (RED) of nontoxic/cytotoxic test-solvent HSPs with respect to the cell-constituent HSP spheres (C1–C7) were calculated using the following equation:[1]

$$\mathrm{RED} = R_a / R_0 , \qquad (2)$$

where R_a is the HSP distance between the cell-constituent and solvent HSPs, calculated using Eq. 1, and R_0 is the cell-constituent interaction radius listed in Table S1. A RED < 1.0 means that a test solvent potentially dissolves or diffuses into a corresponding cell constituent, *i.e.,* the test solvent should be cytotoxic.

Table S1 HSP values of major cell constituents

ID	Cell constituent	SMILES	HSP [(J/cm^3)$^{1/2}$]*			
			δD	δP	δH	R_0
C1	Cholesterol	CC(C)CCCC(C)C1CCC2C1(CCC3C2CC=C4C3(CCC(C4)O)C)C	20.4	2.8	9.4	12
C2	DNA	-	19	20	11	11
C3	Phosphatidylcholine	C[N+](C)(C)CCOP([O-])(=O)OCC(OC(=O)CCCCCCC=CCCCCCCCC)COC(=O)CCCCCCCCCCCCCCC	*16.1*	*6.4*	*9.1*	*10*
C4	Phosphatidylethanolamine	C(OP(OCCN)(O)=O)C(OC(CCC=CCC=CCCCCCCCC)=O)COC(CCCCCCCCCCCCCCC)=O)	*16.2*	*7.1*	*9.8*	*10*
C5	Sphingomyelin	CCCCCCCCCCCCCCCC(=O)NC(COP(=O)([O-])OCC[N+](C)(C)C)C(C=CCCCCCCCCCCCCCC)O	*16.1*	*9.6*	*11.4*	*10*
C6	Phosphatidylserine	CCCC(=O)OC(COC(=O)CC)COP(=O)(O)OCC(C(=O)O)N	*17.6*	*12.5*	*18.7*	*10*
C7	Water (1% soluble in water)	[H]O[H]	15.1	20.4	16.5	18.1

* HSP values written in Roman have been experimentally obtained, and those in *Italic* were estimated using HSPiP v4.1.03 (their interaction radii are tentatively set by 10).

Materials and Methods

Potential nontoxic solvents (25 test solvents, IDs S1–S25) and their HSPs are listed in Table S2 and S3, respectively, and their cytotoxicities were investigated using the direct-contact test described in Fig. S1. In addition to the test solvents, the positive controls (known cytotoxic solvents) water, ethanol, acetone and diethylether (IDs: P1–P4) and the known nontoxic solutions RPMI-1640 cell culture medium with 0.5 vol% fetal bovine serum (FBS), phosphate buffered saline (PBS), and physiological saline (saline) (IDs: N1–N3) were also tested for comparison and normalization of the resultant cell survival rates.

The direct-contact tests were carried out by soaking human airway epithelial cells[4] [BEAS-2B (ATCC® CRL-9609™)[5]] in test wells with pure (non-diluted) test solvents for 10 s to 2 h (typically 2 h). First, the BEAS-2B cells were seeded into 96-well test plates at a density of 1 x 10^5 cells/cm^2, then incubated for 1 night in RPMI-1640 with 10 vol%-FBS growth medium in a CO_2 incubator [37 °C, relative humidity (RH): 95%, CO_2: 5%]. Next, the liquid growth medium was replaced with the test solvent (200 μL/well, 4 wells per solvent), then the test wells were sealed with adhesive tape to prevent evaporation of the test solvents. S1–S11 were tested in plate #1, S12–S21 in plate #2, S22 in plate #3, and S23–S25 in plate #4. The positive controls P1 and P2, as well as the nontoxic solutions N1–N3, were tested in all plates. The positive controls P3 and P4 were tested in plate #4. The direct-contact tests with plates #1, #2 and #4 were carried out by placing them in a CO_2 incubator (37 °C, RH: 95%, CO_2: 5%) for 2 h, whereas the test with plate #3 was conducted at ambient conditions (22 °C) for 1 h to prevent boiling of S22 (boiling point: 34 °C). Tests with P3 and P4 were conducted at ambient conditions (22 °C) for 10 s to prevent breach of the test plate (P3 and P4 can dissolve test plates made of polystyrene). After the direct-contact tests, the test solvents were replaced with RPMI-1640 culture medium containing 0.5 vol%-FBS and the plates were post-test incubated for 20 h to detect delayed cytotoxicity.

Next, the dehydrogenase activity test[6] (WST-8 assay) was conducted to evaluate cell survival rates and optical-microscope observations of cell morphologies were carried out. The cell survival rates were calculated using the arithmetic mean of 4-well results and normalized using the result obtained from nontoxic solution N1 (which provided the maximum cell survival rate). The errors for the cell survival rates were evaluated by standard errors from the dispersion of the 4-well results. In addition, after the WST-8 assay for test solvents S2, S5, S11, S17, S18, S23–S25, P1–P4 and N1–N3, live/dead cells were observed using live/dead staining[7] (Live/Dead Cell Staining Kit II, PromoKine, #PK-CA707-30002).

Table S2 Summary of test solvents (including positive controls and nontoxic solutions) and test conditions.

ID	Solvent name	CAS No.	SMILES or structural formula	BP (°C)	MWt (g/mol)	Plate No.	Remarks
S1	1,3-Bis(Trifluoromethyl) Benzene	402-31-3	C1=CC(=CC(=C1)C(F)(F)F)C(F)(F)F	116	214	1	
S2	Perfluorohexane	355-42-0	FC(F)(C(F)(C(F)(C(F)(C(F)(C(F)(F)F)F)F)F)F)F	60	338	1	
S3	AE-3000	406-78-0	FC(OCC(F)(F)F)(C(F)F)F	50	200	1	
S4	1H,1H,7H-Dodecafluoro -1-heptanol	335-99-9	FC(C(F)(F)C(F)(F)CO)(F)C(F)(F)C(F)(F)C(F)F	170	332	1	
S5	Novec649	756-13-8	O=C(C(C(F)(F)F)(C(F)(F)F)F)C(F)(C(F)(F)F)F	49	316	1	2h in CO_2
S6	HFE-7100	163702-07-6	COC(C(C(C(F)(F)F)(F)F)(F)F)(F)F	61	250	1	incubator
S7	HFE-7200	163702-06-5, 163702-05-4	C(F)(F)(F)C(F)(F)C(F)(F)C(F)(F)OCC, C(F)(F)(F)C(F)(C(F)(F)(F))C(F)(F)OCC	76	264	1	(37°C, RH: 95%, 5% -CO_2)
S8	HFE-7300	132182-92-4	FC(F)(C(F)(F)C(F)(F)C(F)(F)C(F)(F)F)C(F)(F)OC	98	350	1	
S9	GALDEN HT55	Mixture	CF_3-[(O-CF-CF_2)$_1$-(O-CF_2)$_{0.3}$]-O-CF_3 └CF_3	55	340	1	
S10	GALDEN HT80	Mixture	CF_3-[(O-CF-CF_2)$_{1.17}$-(O-CF_2)$_{1.24}$]-O-CF_3 └CF_3	80	430	1	
S11	GALDEN HT110	Mixture	CF_3-[(O-CF-CF_2)$_2$-(O-CF_2)$_{1.42}$]-O-CF_3 └CF_3	110	580	1	
S12	GALDEN HT135	Mixture	CF_3-[(O-CF-CF_2)$_{2.21}$-(O-CF_2)$_{1.36}$]-O-CF_3 └CF_3	135	610	2	
S13	GALDEN HT170	Mixture	CF_3-[(O-CF-CF_2)$_3$-(O-CF_2)$_{1.63}$]-O-CF_3 └CF_3	170	760	2	
S14	GALDEN HT200	Mixture	CF_3-[(O-CF-CF_2)$_4$-(O-CF_2)$_{0.79}$]-O-CF_3 └CF_3	200	870	2	
S15	GALDEN HT230	Mixture	CF_3-[(O-CF-CF_2)$_4$-(O-CF_2)$_{3.06}$]-O-CF_3 └CF_3	230	1020	2	2h in CO_2
S16	GALDEN HT270	Mixture	CF_3-[(O-CF-CF_2)$_6$-(O-CF_2)$_{6.06}$]-O-CF_3 └CF_3	270	1550	2	incubator (37°C, RH: 95%, 5% -CO_2)
S17	Hexamethyldisiloxane	107-46-0	C[Si](C)(C)O[Si](C)(C)C	100	162	2	
S18	Octamethyltrisiloxane	107-51-7	C[Si](C)(C)O[Si](C)(C)O[Si](C)(C)C	153	237	2	
S19	Decamethyltetrasiloxane	141-62-8	C[Si](C)(C)O[Si](C)(C)O[Si](C)(C)O[Si](C)(C)C	194	311	2	
S20	Decamethylcyclopentasiloxane	541-02-6	[Si]1(C)(C)O[Si](C)(C)O[Si](C)(C)O[Si](C)(C)O[Si](O1)(C)C	210	371	2	
S21	1-Bromoperfluorooctane	423-55-2	FC(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)C(F)(F)Br	142	499	2	
S22	HFE-7000	375-03-1	COC(F)(C(F)(C(F)(F)F)F)F	34	200	3	1h in atm. (22°C)
S23	Hexadecane	544-76-3	CCCCCCCCCCCCCCCC	287	227	4	2h in CO_2
S24	Octadecane	593-45-3	CCCCCCCCCCCCCCCCCC	317	255	4	incubator
S25	PAO6 (poly-α-olefin 6cSt)	68037-01-4	CC(CCCCCCCC)CC(CCCCCCCC)CC(CCCCCCCC)CC(CCCCCCCC)	514	563	4	(37°C, RH: 95%, 5% -CO_2)
P1	Water	7732-18-5	[H]O[H]	100	18	1, 2, 3, 4	Positive control
P2	Ethanol	64-17-5	CCO	78	46	1, 2, 3, 4	Positive control
P3	Acetone	67-64-1	CC(C)=O	56	58	4	Positive control
P4	Diethylether	60-29-7	CCOCC	34	74	4	Positive control
N1	0.5% FBS RPMI-1640	-	-	-	-	1, 2, 3, 4	Culture medium
N2	Phosphate buffered saline (PBS)	-	-	-	-	1, 2, 3, 4	Nontoxic buffer solution
N3	Saline	-	-	-	-	1, 2, 3, 4	Nontoxic buffer solution

Table S3 HSP and molar volumes of test solvents and positive controls.

Solvent ID	Solvent name	HSP [$(J/cm^3)^{1/2}$]*			Molar volume (cm^3/mol)
		δD	δP	δH	
S1	1,3-Bis(Trifluoromethyl)Benzene	17	6.8	0	155.2
S2	Perfluorohexane	12.1	0	0	201.2
S3	AE-3000	*14*	*4.9*	*3.9*	136.3
S4	1H,1H,7H-Dodecafluoro-1-Heptanol	*13.6*	*4.6*	*8.1*	196.4
S5	Novec649	*12.4*	*3.6*	*1.3*	189.3
S6	HFE-7100	13.7	2.2	1	164.5
S7	HFE-7200	*13*	*2.9*	*2*	182
S8	HFE-7300	*12.8*	*2.6*	*2.1*	216.6
S9	GALDEN HT55	*12.1*	*4.2*	*2.2*	201.8
S10	GALDEN HT80	*11.8*	*4.7*	*2.5*	249.2
S11	GALDEN HT110	*10.9*	*4.4*	*2.1*	328.5
S12	GALDEN HT135	*10.7*	*4.3*	*2*	344.4
S13	GALDEN HT170	*9.9*	*4.3*	*1.8*	423.7
S14	GALDEN HT200	*9.3*	*3.7*	*1.1*	482.1
S15	GALDEN HT230	*8.6*	*4.9*	*2*	560.9
S16	GALDEN HT270	-	-	-	-
S17	Hexamethyldisiloxane	12.6	2	0	212.4
S18	Octamethyltrisiloxane	12.2	1.8	0	288.4
S19	Decamethyltetrasiloxane	11.7	2.4	0	363.8
S20	Decamethylcyclopentasiloxane	12.9	1.3	1	388.7
S21	1-Bromoperfluorooctane	12.9	1.9	1.3	260.9
S22	HFE-7000	13	4.2	1	141.9
S23	Hexadecane	16.3	0	0	294.2
S24	Octadecane	16.4	0	0	328.2
S25	PAO6 (poly-α-olefin 6cSt)	*16.1*	*0*	*0*	689.6
P1	Water (1% solubility in water)	15.1	20.4	16.5	18
P2	Ethanol	15.8	8.8	19.4	58.6
P3	Acetone	15.5	10.4	7	73.8
P4	Diethylether	14.5	2.9	4.6	104.7

*HSP values written in Roman are from official HSPs, and those in *Italic* were estimated using HSPiP v4.1.03.

-: Too large molecular size of S16 to estimate the HSP values using the software.

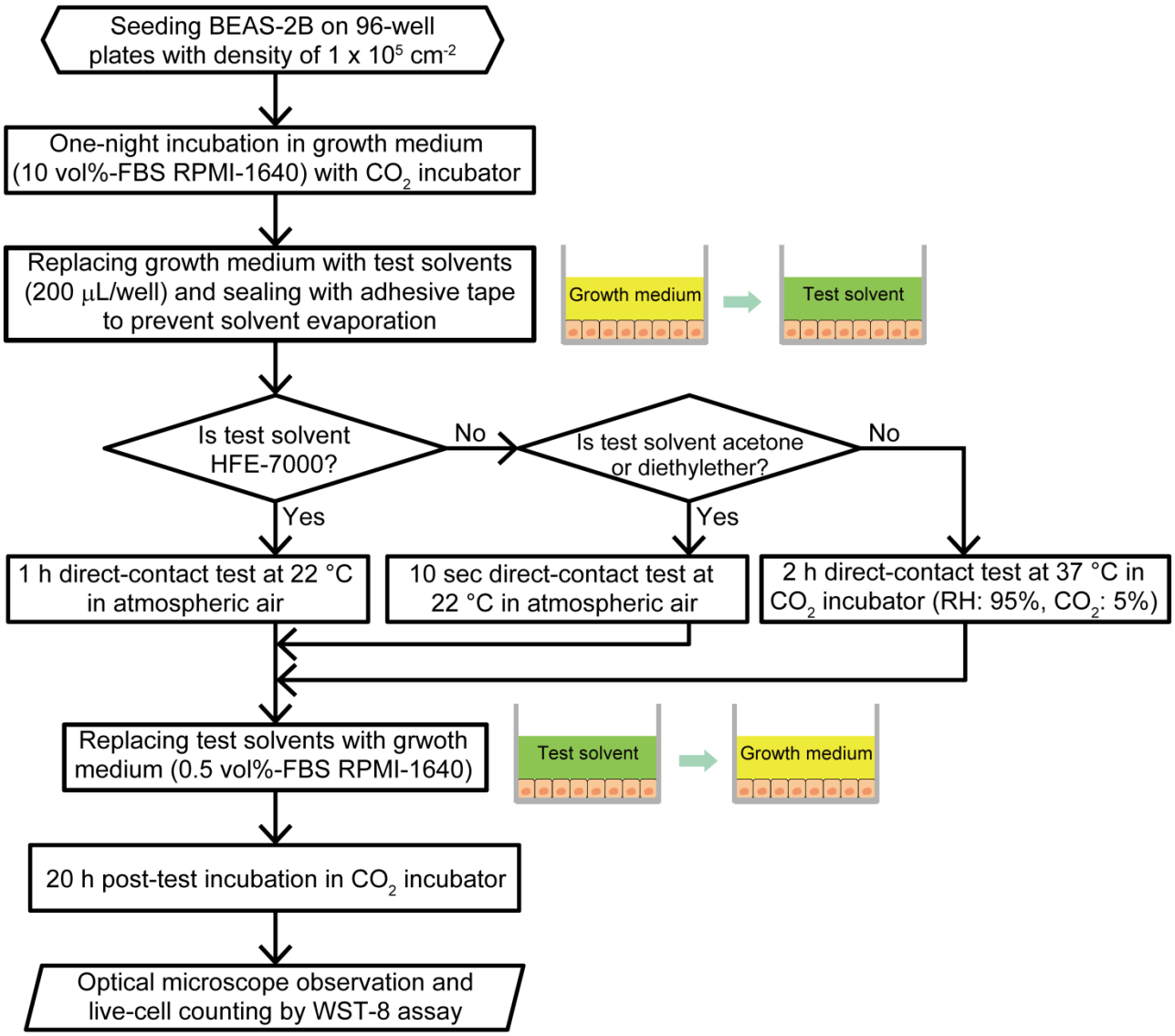

Fig. S1 Flow chart showing the experimental procedures for the direct-contact cytotoxicity test.

Supplementary results (1): Cell morphologies and live/dead cell observation

The survival rate of cells exposed to N1 was used as the baseline for normalizing the other test results because N1 provided the highest cell survival of the 3 nontoxic solutions tested. The difference in cell survival rate provided by the nontoxic solutions is attributed to large areas of cells detaching from the well surface. The cell morphologies after the direct-contact test show a homogeneous and dense distribution of cells following exposure to N1 (Fig. S2a), whereas detached cells were observed following exposure to N2 (Fig. S2b). This detachment suggests that the relatively low cell survival rates observed following exposure to N2 and N3 are due to the detachment of cells during the solvent/culture-medium replacement procedure. This detachment may be due to decreased cell adhesion resulting from a lack (elution) of bivalent ions since N2: PBS and N3: saline do not contain bivalent ions such as Ca^{2+} which are essential for cell adhesion. In addition, significant cell detachment was also observed following exposure to S16 and may be due to the high viscosity of S16 and the accompanying shear stress during the solvent/culture-medium replacement procedure. Therefore, we excluded the results obtained using S16 from our detailed analysis/discussion.

Supplementary data showing cell morphologies and live/dead cell observation after the direct-contact test (other than the results presented in the main figures) are shown in Fig. S3, S4, S5, S6 and S7 for reference.

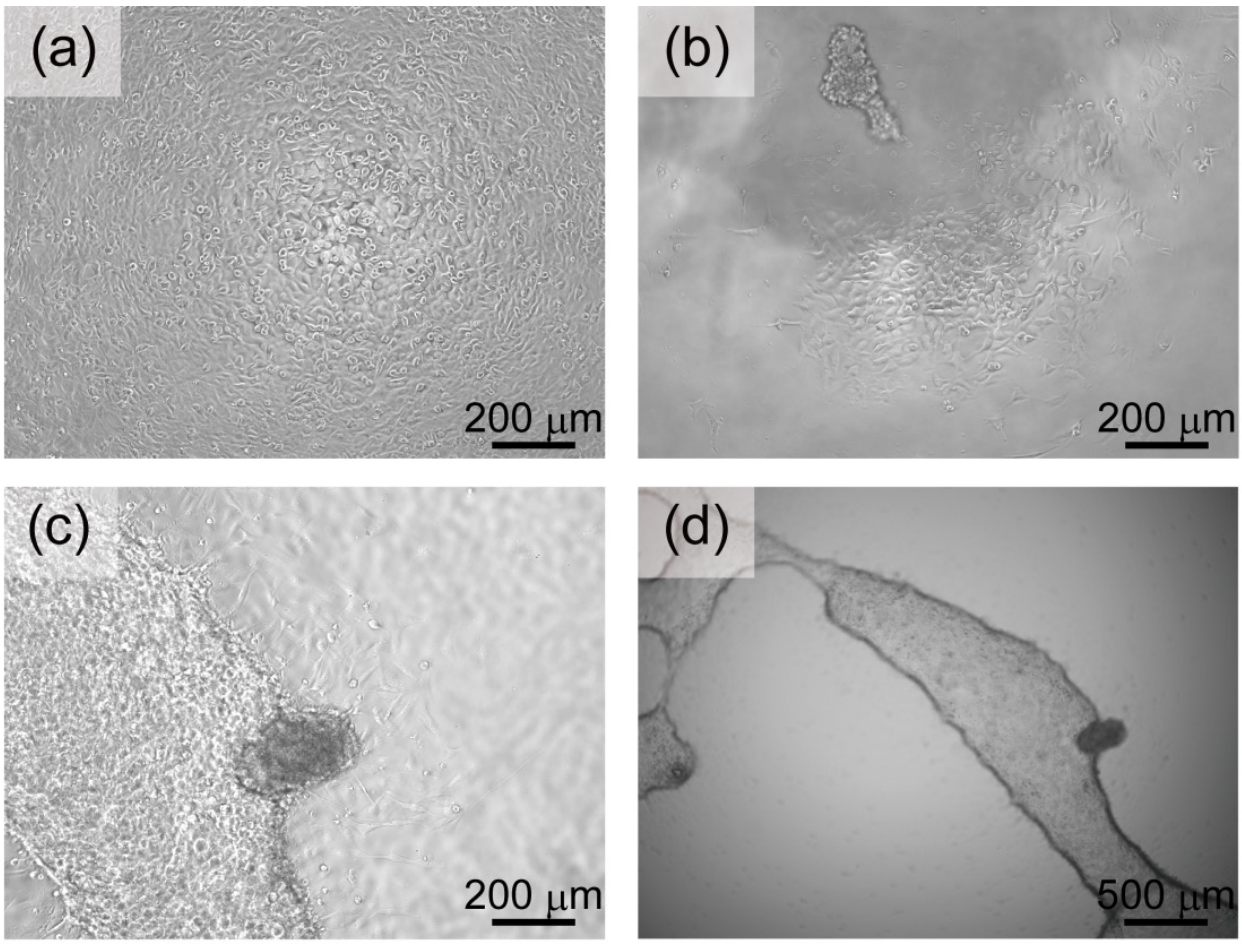

Fig. S2 Comparison of the detachment of cells after the direct-contact test to solvents (a) N1: RPMI-1650 culture medium with 0.5 vol%-FBS (objective lens: x10), (b) N2: PBS (x10) and (c, d) S16: GALDEN HT270 (x10, x4). The results obtained using N2 and S16 show large areas of detached cells, resulting in a misleading decrease in cell survival rates.

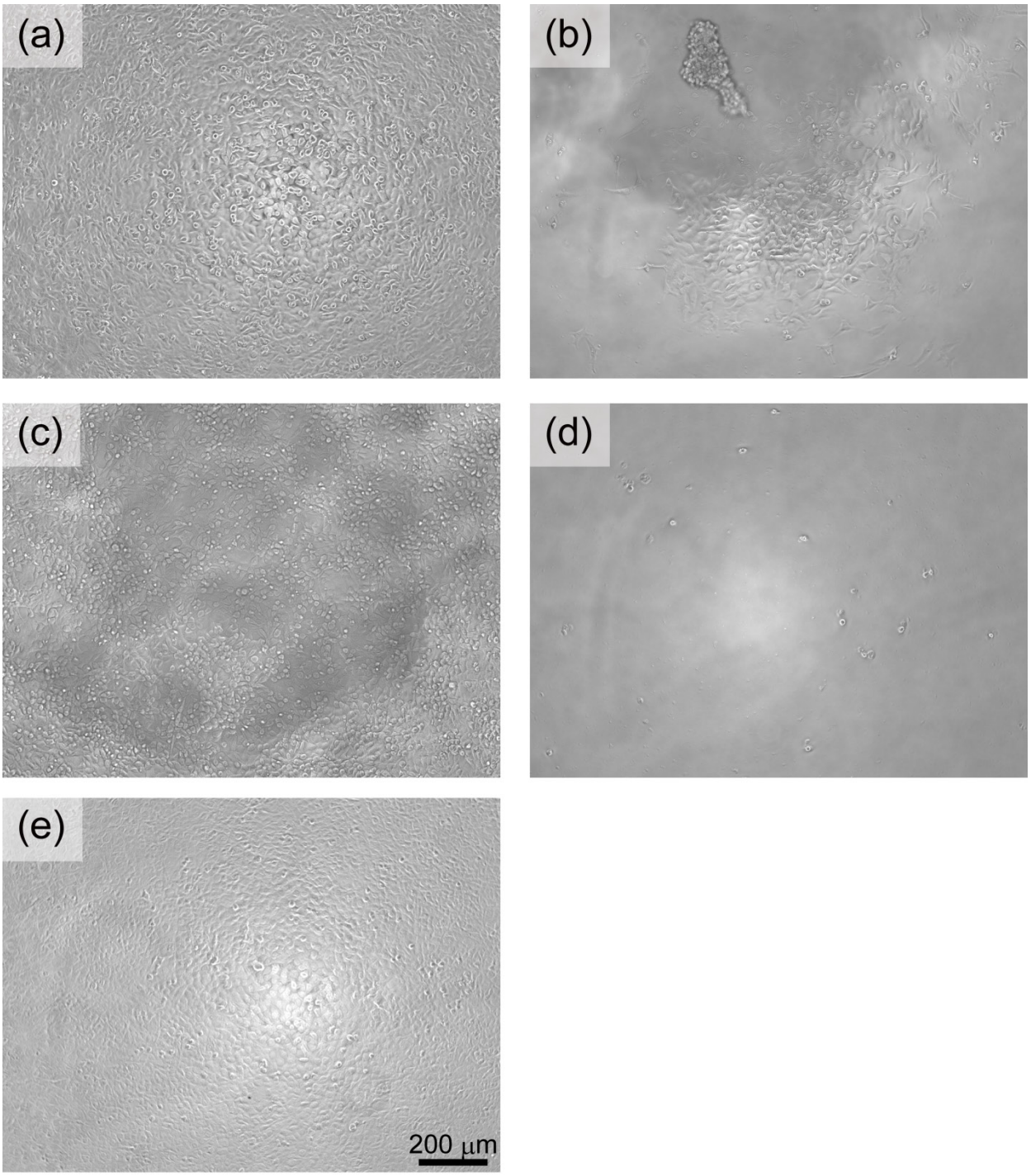

Fig. S3 Optical micrographs of cells after the direct-contact test to known nontoxic solutions and known cytotoxic solvents (a) N1: RPMI-1650 culture medium with 0.5 vol%-FBS, (b) N2: PBS, (c) N3: saline, (d) P1: water and (e) P2: ethanol.

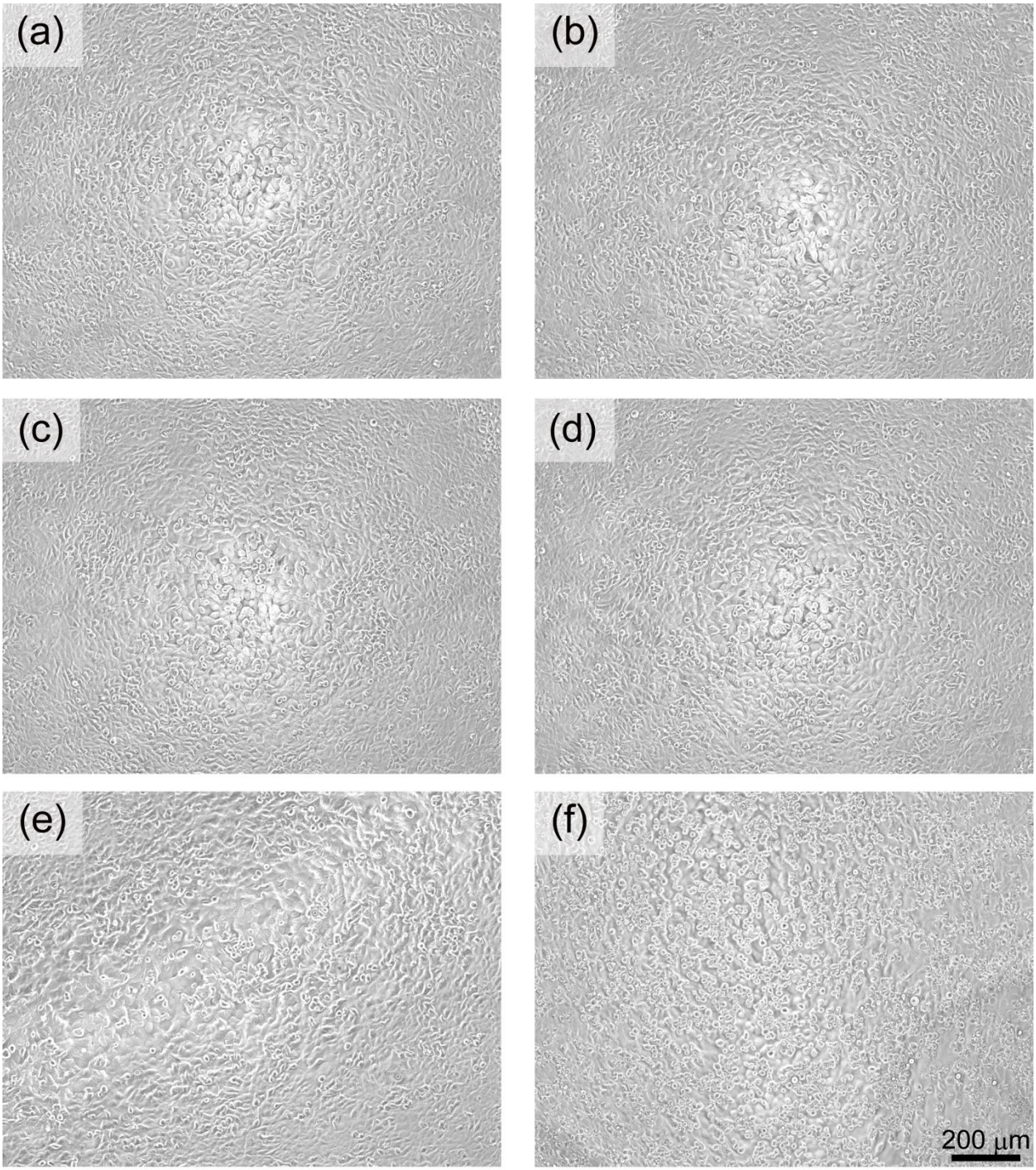

Fig. S4 Optical micrographs of cells after the direct-contact test to identified nontoxic test solvents (a) S6: HFE-7100, (b) S8: HFE-7300, (c) S9: GALDEN HT55, (d) S10: GALDEN HT80, (e) S13: GALDEN HT170 and (f) S15: GALDEN HT230.

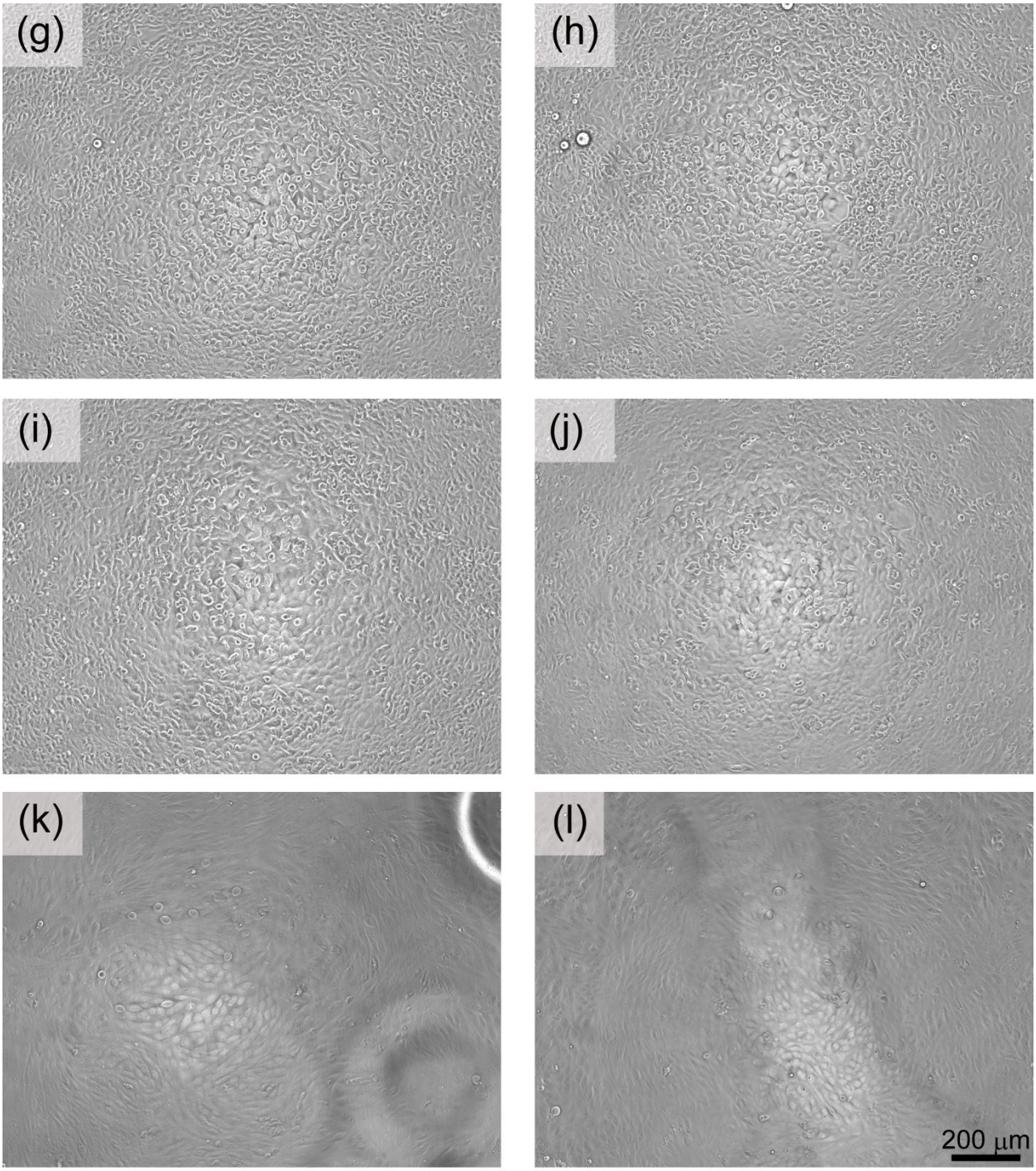

Fig. S4 (continued) Optical micrographs of cells after the direct-contact test to identified nontoxic test solvents (g) S19: decamethyltetrasiloxane, (h) S20: decamethylcyclopentasiloxane, (i) S21: 1-bromoperfluorooctane, (j) S22: HFE-7000, (k) S23: hexadecane and (l) S25: PAO6.

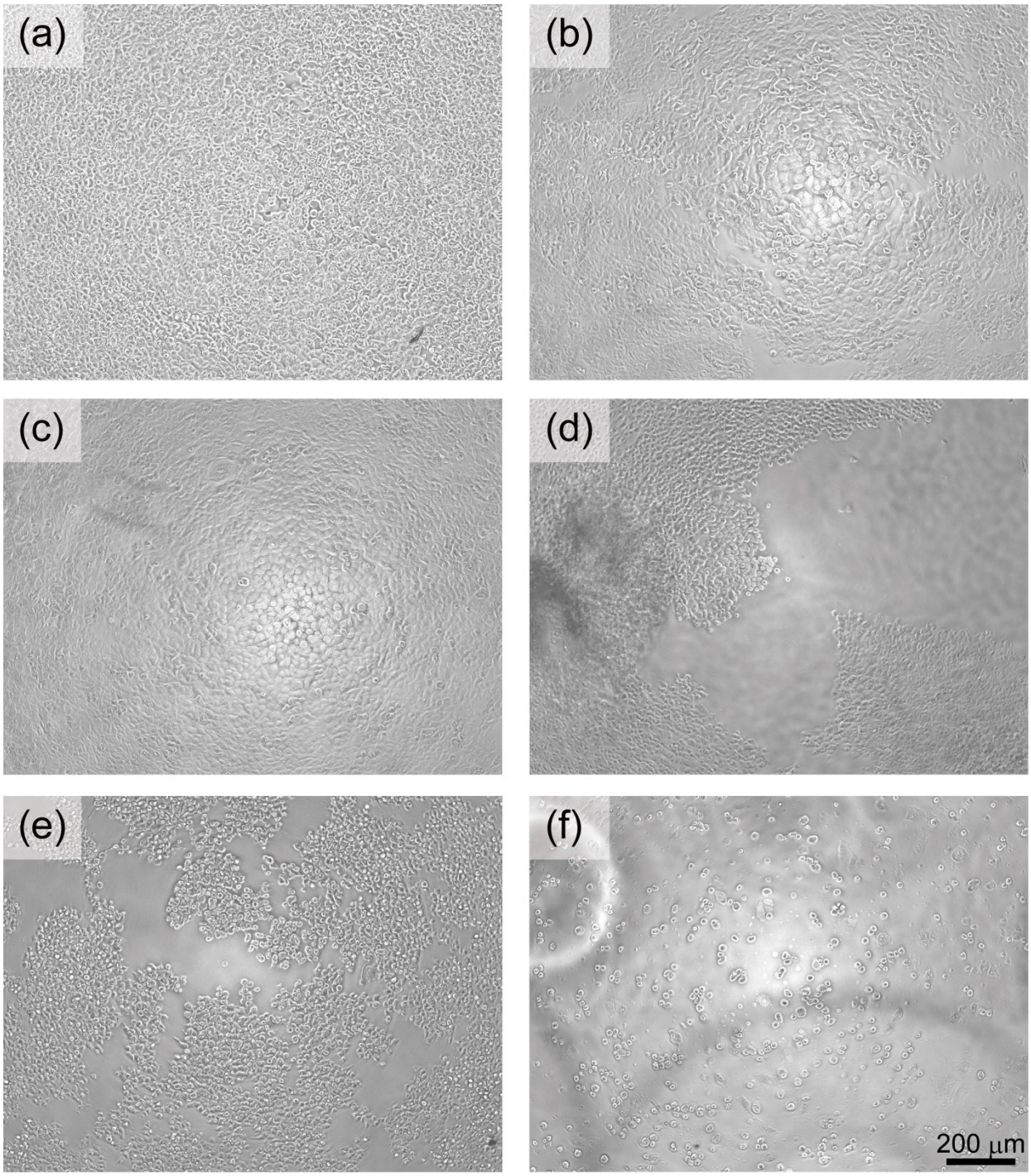

Fig. S5 Optical micrographs of cells after the direct-contact test to cytotoxic test solvents (a) S2: perfluorohexane, (b) S3: AE-3000, (c) S5: Novec649, (d) S17: hexamethyldisiloxane, (e) S18: octamethyltrisiloxane and (f) S24: octadecane.

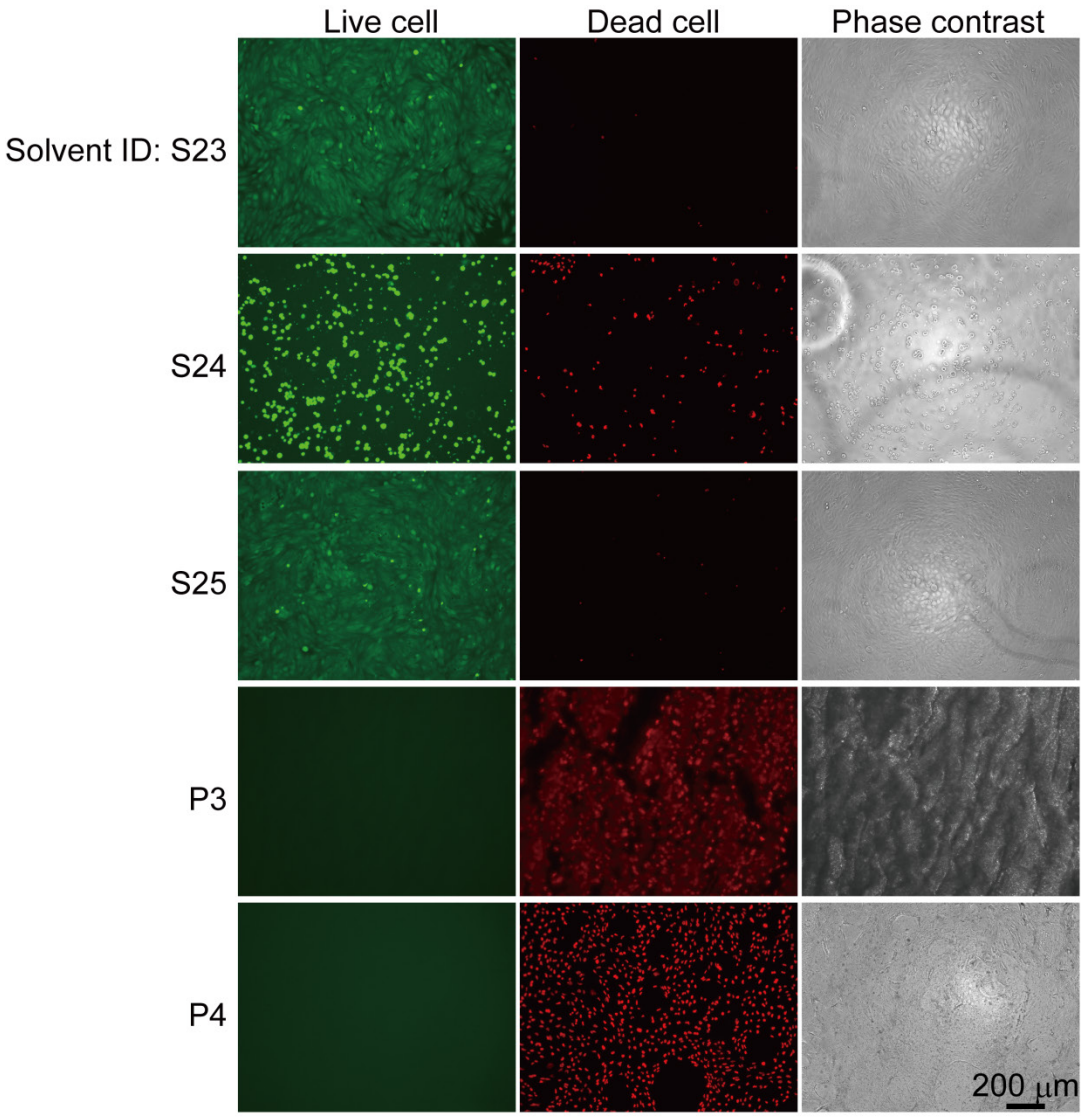

Fig. S6 Optical micrographs of cells after the direct-contact test to solvents (IDs: S23, S24, S25, P3 and P4) in plate #4 stained using Live/Dead Cell Staining Kit II (PromoKine). The test wells of plate #4 were coated with iMatrix-511 to enhance the adhesion between the cells and the test wells (to prevent the detachment of cells).

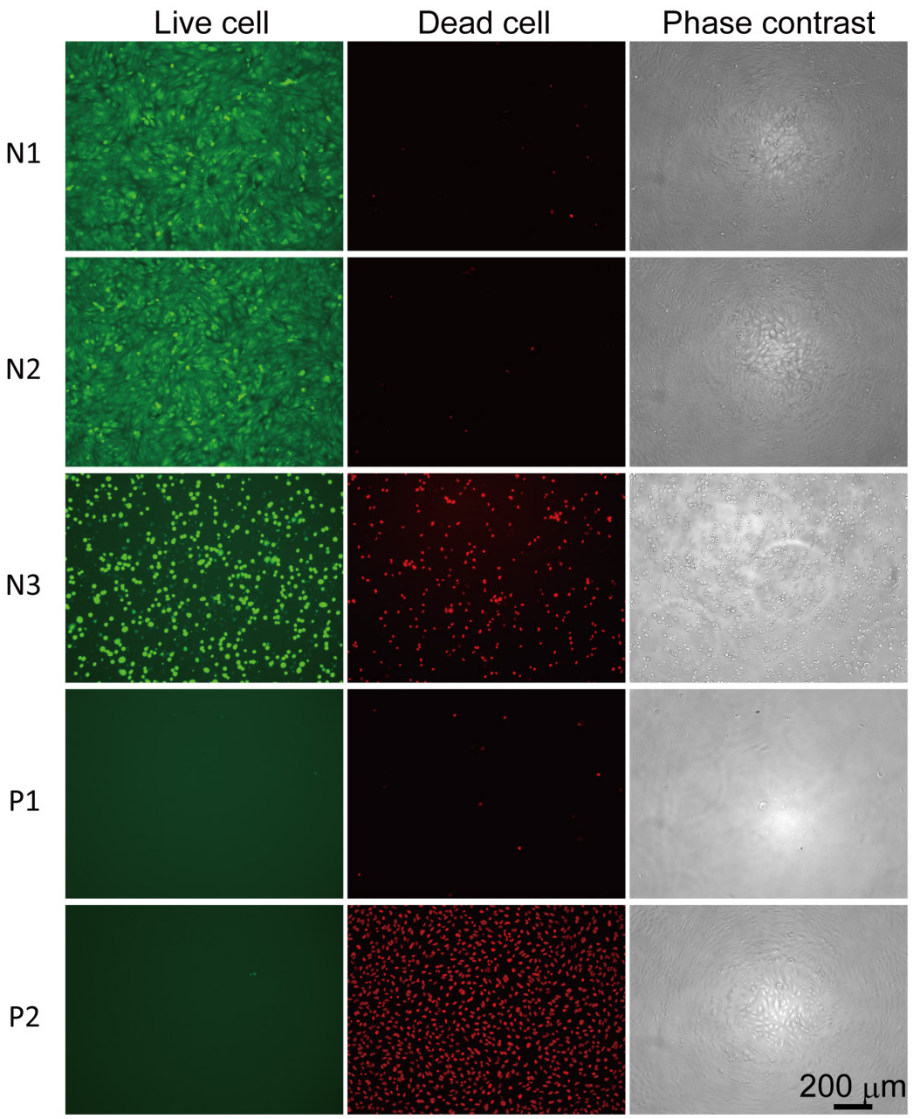

Fig. S6 (continued) Optical micrographs of cells after the direct-contact test to solvents (IDs: N1, N2, N3, P1 and P2) in plate #4 stained using Live/Dead Cell Staining Kit II (PromoKine). The detachment of cells exposed to N2 appears to be suppressed by coating with i-Matrix511, as compared to the result shown in Fig. S3b.

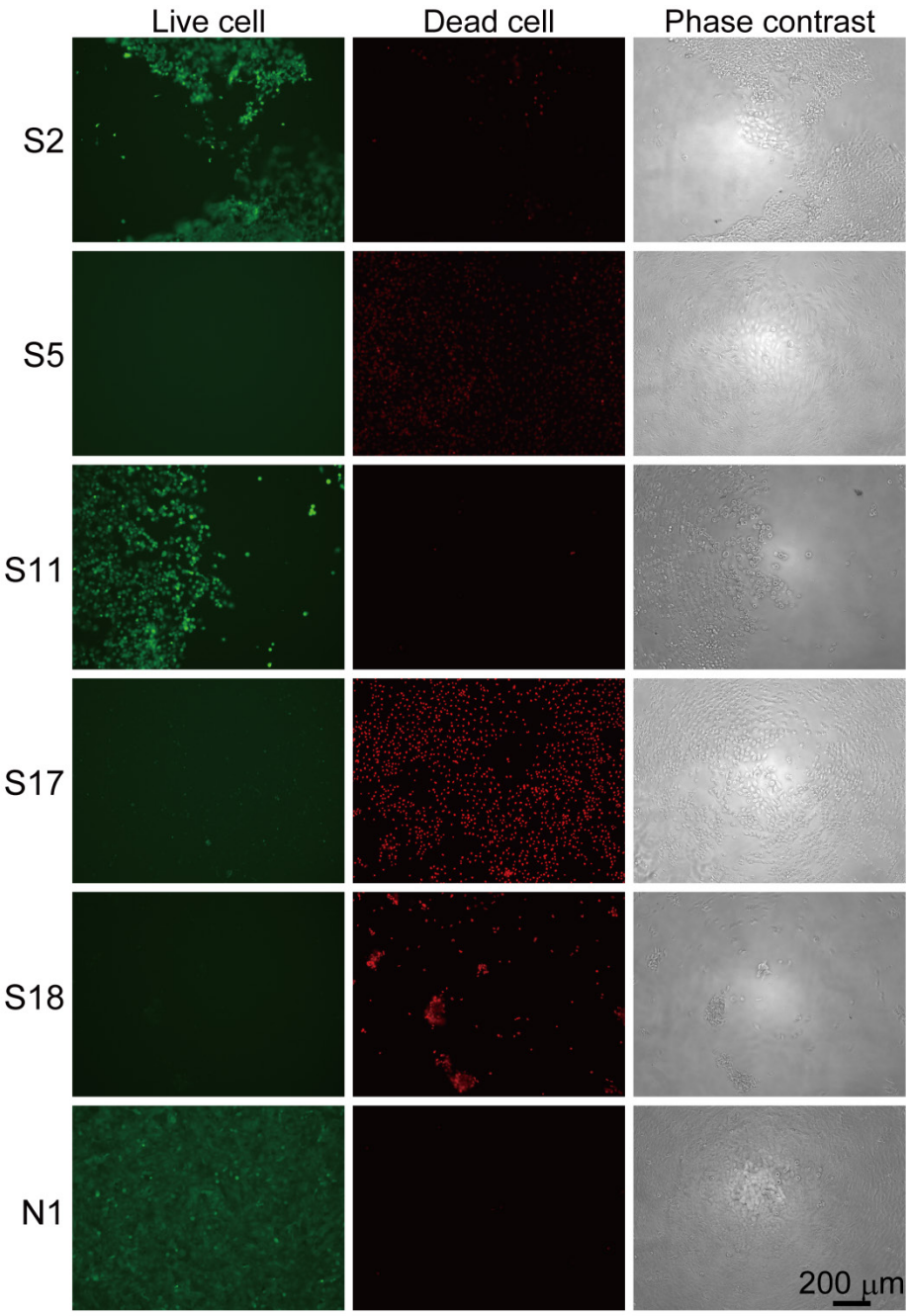

Fig. S7 Optical micrographs of cells after the direct-contact test to solvents (IDs: S2, S5, S11, S17, S18 and N1) stained using Live/Dead Cell Staining Kit II (PromoKine).

Supplementary results (2): Validity assessment of estimated HSP values and the interaction radius for cell-membrane constituents

Since cell membranes consist of a mixture of various biomolecules (glycerophospholipids), the full experimental determination of HSPs of all the cell-membrane glycerophospholipids is unrealistic. This is why we utilized the estimated HSPs of representative glycerophospholipids (C3–C6 in Table S1) as the cell membrane constituents. Here, the validity of HSPs of cell-membrane constituents is assessed through comparison with its experimentally-obtained HSP.

As proposed in the main text, we hypothesized that HSPs of nontoxic organic solvents should locate outside cell-constituents HSPs, which means that nontoxic organic solvents should have their HSPs in smaller HSP region than cell-membrane constituents. As seen from Fig. 1 and Table S1, the HSP of phosphatidylcholine locates in the smallest HSP region among cell-membrane constitutes, which indicates that the smaller-HSP-region boundary position of HSP sphere of phosphatidylcholine should be the most critical to determine cytotoxicity/nontoxicity of organic solvents. Therefore, experimental assessment of HSP values and its interaction radius [δD, δP, δH, R_0] of phosphatidylcholine should be primarily important in order to support our cytotoxicity/nontoxicity hypothesis based on HSP consideration.

HSPs of materials can be determined through their dissolution experiment in 20–80 probe liquids and subsequent fitting by SPHERE method[1]. Although the dissolution experiment typically requires ~10 g of target materials as a test sample, pure material of phosphatidylcholine is too expensive for us to prepare the required amount of them. Thus, lecithin from egg (containing phosphatidylcholine at a composition of >80%)[8] was substituted for pure phosphatidylcholine as a test sample for the dissolution experiment. The dissolution experiment was carried out by mixing 0.2 g of the lecithin with 4 mL of selected 39 probe liquids in each vial. After hand-shake mixing for 1–60 min (dependent on the viscosity and molar volume of probe liquids), the solutions were observed by the naked eye and sorted out the 39 probe liquids as good (totally soluble) or poor (insoluble or partially-soluble) solvents for dissolving the lecithin (detailed results will be published elsewhere).

Figure S8 shows HSP plots of good (blue circle: 21 probe liquids) and poor (red square: 18 probe liquids) solvents for the lecithin in quasi-3D view. HSP sphere of the lecithin determined by SPHERE method are shown by green wire frame. As shown in Fig. S8, the obtained HSP sphere of lecithin efficiently divide good solvents (inside the HSP sphere) from poor solvents (outside the HSP sphere) in HSP space. The FIT value[1] to represent efficiency of SPHERE fitting (FIT = 1 indicates perfect fitting without anomalies) was 0.945, which confirms that the obtained HSP sphere for the lecithin is quite probable. The obtained HSP values and R_0 of lecithin were listed in Table S4 along

with the estimated values of phosphatidylcholine for comparison. Although the experimentally-obtained HSP values of lecithin are quite similar to estimated values of phosphatidylcholine, there exists non-negligible deviation in δP values. This deviation might be attributed to the amphipathic nature of lecithin, which means that the HSP region of lecithin might be described by dual HSP spheres[1] of hydrophilic and hydrophobic portions (not by conventional single HSP sphere). The more detailed analysis on the lecithin HSP values to be obtained by dissolution experiment with a larger number of probe liquids is under consideration to clarify cause of the δP deviation and to obtain more reasonable HSP values of lecithin.

To compare the smaller-HSP-region boundaries of HSP spheres of phosphatidylcholine (estimated values) and lecithin (experimentally-obtained values), both HSP spheres were drawn in projection views as shown in Fig. S9. Although there exists the deviation in their center positions of HSP spheres, their boundaries at the smaller HSP region well correspond to each other when R_0 = 10 $(\mathrm{J/cm^3})^{1/2}$ was assumed for phosphatidylcholine. Furthermore, REDs of nontoxic and cytotoxic solvents with respect to lecithin were calculated and compared to those with respect to phosphatidylcholine (Table S5 and S6). The RED values of phosphatidylcholine and lecithin also show quite good correspondence to each other. Therefore, we conclude that estimated HSPs and assumed R_0 for cell-membrane constituents were valid to appropriately screen cytotoxic/nontoxic solvents.

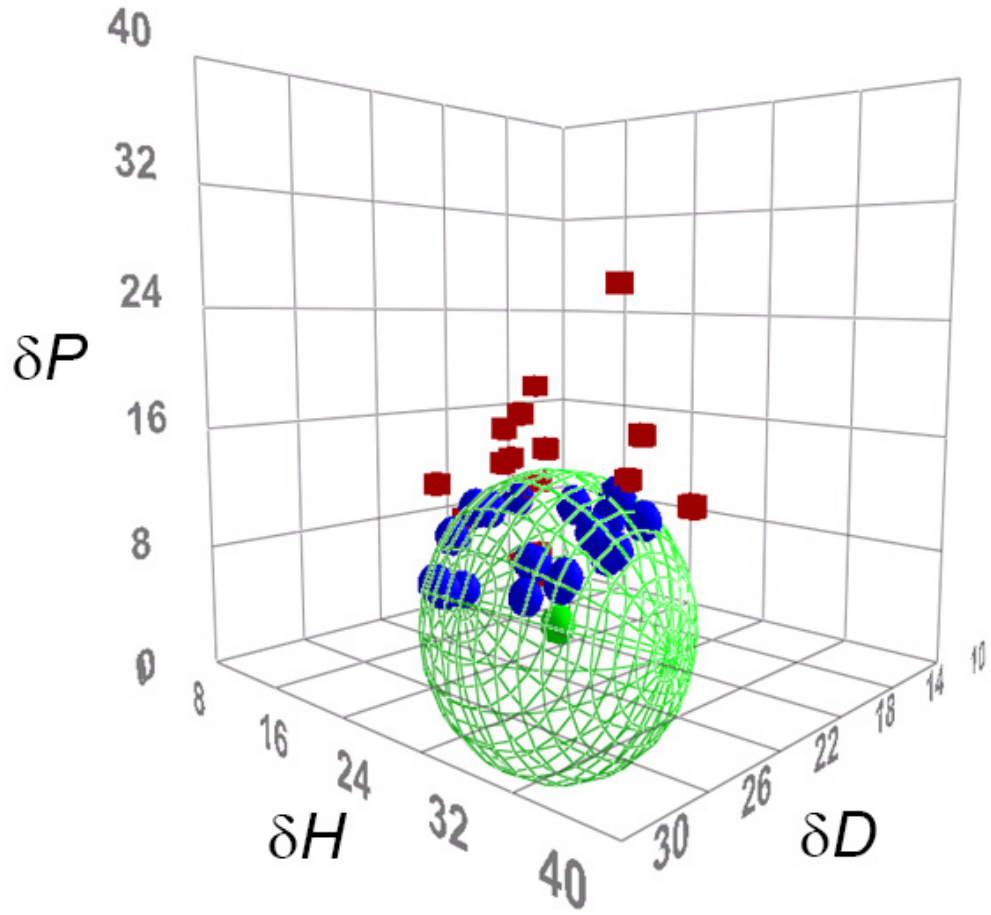

Fig. S8 HSP plots of good solvents (blue solid circle) and poor solvents (red solid square) for dissolving the lecithin from egg in quasi-3D view. HSP values and R_0 of the lecithin determined by SPHERE method are shown by green solid circle and green wire frame, respectively.

Table S4 Comparison of HSP values and R_0 for phosphatidylcholine (estimated values) and lecithin (experimental values).

Cell-membrane constiituet	HSP ($[J/cm^3]^{1/2}$)			
	δD	δP	δH	R_0
Phosphatidylcoline (estimation)	*16.1*	*6.4*	*9.1*	*10*
Lecithin from egg (solubility experiment)	17.2	0.2	12.3	12.0

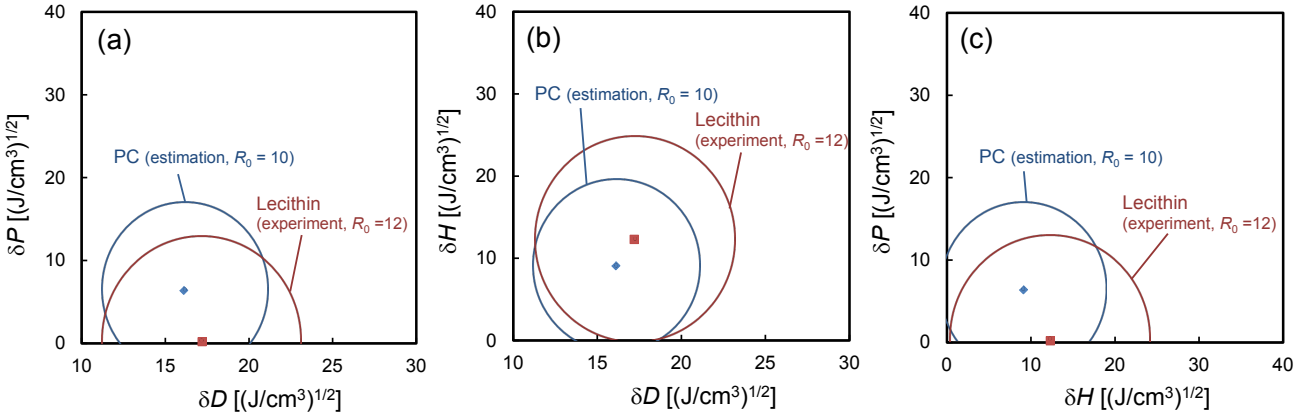

Fig. S9 Comparison of HSP spheres for phosphatidylcholine (estimated values) and lecithin (experimental values) in projection views.

Table S5 Relative energy differences (REDs) of nontoxic solvents with respect to phosphatidylcholine (estimated values) and lecithin (experimental values).

Solvent ID	Anti-cytotoxic solvent	Relative energy difference (RED) to:	
		C3: Phosphatidylcholine	Lecithin from egg
S6	HFE-7100	1.03	1.12
S7	HFE-7200	1.01	1.13
S8	HFE-7300	1.04	1.14
S9	GALDEN HT55	1.07	1.24
S10	GALDEN HT80	1.10	1.27
S12	GALDEN HT135	1.31	1.42
S13	GALDEN HT170	1.46	1.54
S14	GALDEN HT200	1.61	1.64
S15	GALDEN HT230	1.67	1.72
S19	Decamethyltetrasiloxane	1.33	1.39
S20	Decamethylcyclopentasiloxane	1.15	1.19
S21	1-Bromoperfluorooctane	1.10	1.17
S22	HFE-7000	1.04	1.22
S23	Hexadecane	1.11	1.04
S25	PAO6	1.11	1.04

Table S6 REDs of cytotoxic solvents with respect to phosphatidylcholine (estimated values) and lecithin (experimental values).

Solvent ID	Cytotoxic solvent	Relative energy difference (RED) to:	
		C3: Phosphatidylcholine	Lecithin from egg
S1	1,3-Bis(Trifluoromethyl)Benzene	0.93	1.16
S2	Perfluorohexane	1.37	1.33
S3	AE-3000	0.69	0.96
S4	1H,1H,7H-Dodecafluoro-1-heptanol	0.54	0.79
S5	Novec649, Novec1230	1.11	1.25
S11	GALDEN HT110	1.27	1.40
S17	Hexamethyldisiloxane	1.23	1.29
S18	Octamethyltrisiloxane	1.28	1.33
S24	Octadecane	1.11	1.03
P1	Water	1.60	1.75
P2	Ethanol	1.06	0.96
P3	Acetone	0.47	1.00
P4	Diethyl ether	0.65	0.82

Supplementary results (3): LC-MS analysis on solvents after direct-contact test

If the dissolution of cell-membrane constituents (glycerophospholipids) into solvents is a main cytotoxic factor of organic solvents, the evidence (glycerophospholipids solutes in cytotoxic solvents soaked to cells) might be detected by liquid chromatography mass spectrometry (LC-MS). To attain the evidence, we selected 5 cytotoxic (S1, S3, S4, P3, and P4) and 2 nontoxic solvents (S7 and S8) as the test and reference solvents to identify glycerophospholipids solutes in the solvents after the direct-contact test by LC-MS.

After soaking the test solvents to the cells by following the protocol described in Fig. S1, the test solvents with solutes were dried in vacuum, subsequently the solutes were re-dissolved in methanol (carrier fluid for LC-MS), and then the solutes in methanol were analyzed by LC-MS (negative ions, error in *m/z* value: ±3–5 ppm). Because the S1 and S4 were too low-volatile to replace solvents with methanol, LC-MS analysis on the S1 was carried out without solvent replacement, and that on the S4 was with x20 dilution in methanol. The obtained *m/z* spectra were subtracted backgrounds, and the mass of proton was added to significantly-detected *m/z* values (since the negative ions are generated mainly via deficit of proton), which are compared to lipid database[9] to identify possible lipids (within 5 ppm deviation from their exact mass) originating from the cells.

Figures S10(a, b) show *m/z* spectra (backgrounds subtracted) obtained from solutes in cytotoxic and nontoxic test solvents, respectively. The *m/z* spectra from solutes in cytotoxic solvents (especially S4, P3, and P4) exhibited a variety of signals while those in nontoxic solvents exhibited limited number of signals. The possible lipids originating from cell membrane (glycerophosholipids: GP1–GP30) and lipids other than glycerophosholipids (L1–L12) identified by comparing significantly-detected *m/z* (plus proton mass) values with the lipid database were summarized in Table S7. Figures S11(a, b) show LC-MS signal intensities of possible cell-membrane lipids (GP1–GP30) from solutes in cytotoxic and nontoxic solvents, respectively. Figures S12 also show the signal intensities of lipids other than cell-membrane lipids (L1–L12) from solutes in cytotoxic and nontoxic solvents for reference. As clearly shown in Fig. S11, possible cell-membrane lipids were dissolved into cytotoxic solvents (especially S4, P3, and P4) while no possible cell-membrane lipids were detected in nontoxic solvents. Therefore, we conclude that the dissolution of cell-membrane constituents should be, at least, one of the main cytotoxic factors of organic solvents. As for the S1 and S3 cytotoxic solvents, no cell-membrane lipids were dissolved into them. Although these solvents might lack dissolving power for cell-membrane lipids, they might still have other cytotoxic factors such as diffusion into cell interior and accompanying denaturalization of cell-interior proteins. The diffusion of solvents into the cell interior should be a remaining main cytotoxic factor to be assessed by other analytical techniques.

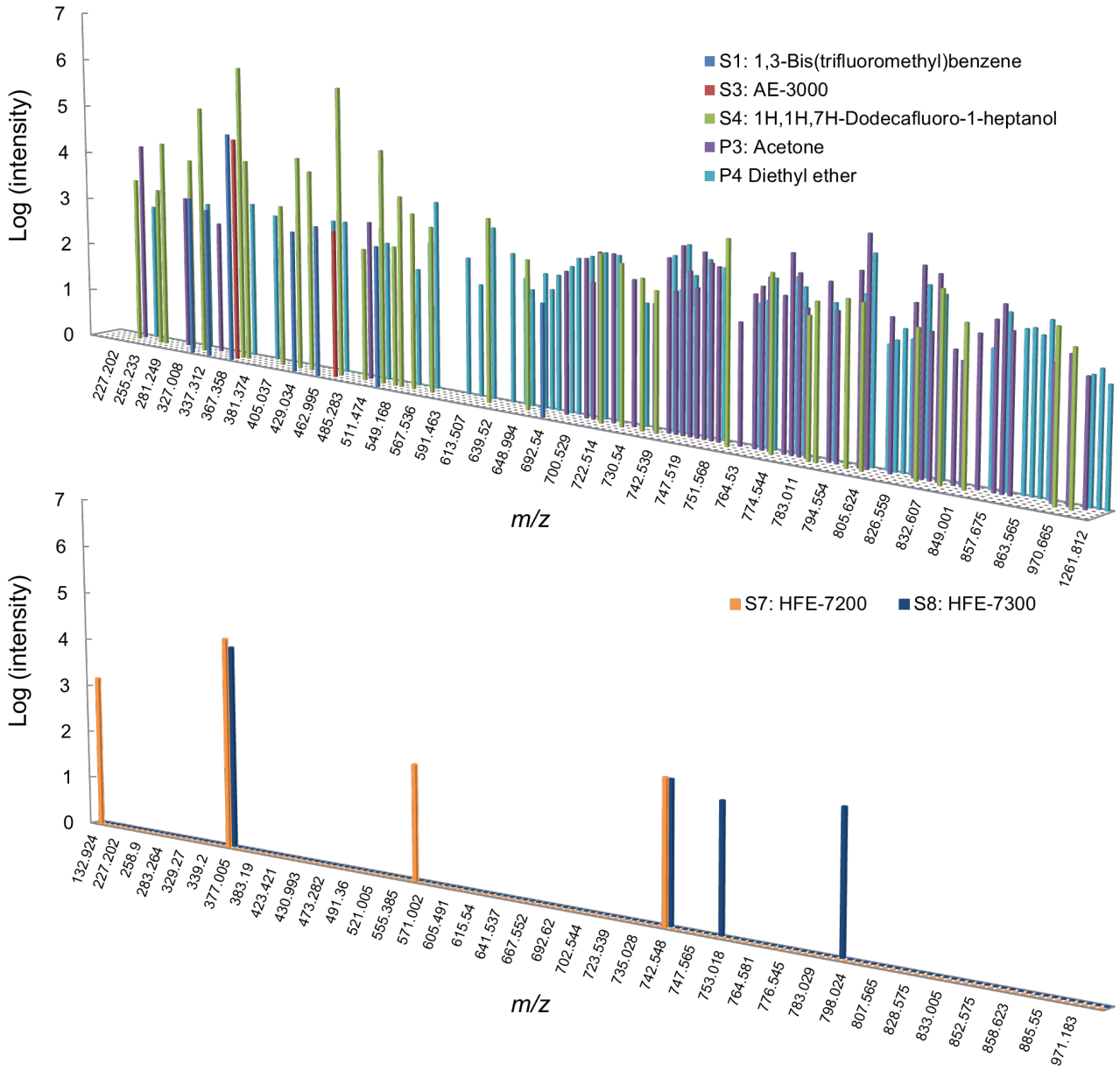

Fig. S10 LC-MS spectra (with respect to *m/z*) obtained from solutes in; (a) cytotoxic and (b) nontoxic solvents after the direct-contact test to the cells.

Table S7 List of possible glycerophospholipids (GP1–GP30) and possible lipids other than glycerophospholipids (L1–L12) detected in the LC-MS spectra obtained from solutes in the solvents after the direct-contact test to the cells.

ID	*m/z* + proton	Exact mass (g/mol)	Formula	Common name or systematic name of possible lipid
GP1	675.5218	675.5203	C37H74NO7P	PC(P-16:0/13:0), PE(O-16:0/16:1(9Z)), PE(O-18:0/14:1(9Z)), PE(P-16:0/16:0), PE(P-18:0/14:0), PE(P-20:0/12:0)
GP2	701.5368	701.5359	C39H76NO7P	PC(P-16:0/15:1(9Z)), PE(O-16:0/18:2(9Z,12Z)), PE(P-18:0/16:1(9Z)), PE(P-20:0/14:1(9Z)), PE(P-16:0/18:1(9Z)), PnE(16:0/18:1(9Z))
GP3	703.5518	703.5516	C39H78NO7P	PC(O-16:0/15:1(9Z)), PC(P-16:0/15:0), PC(P-18:0/13:0), PE(O-16:0/18:1(9Z)), PE(O-20:0/14:1(9Z)), PE(O-18:0/16:1(9Z)), PE(P-16:0/18:0), PE(P-18:0/16:0), PE(P-20:0/14:0)
GP4	717.5318	717.5309	C39H76NO8P	PC(16:0/15:1(14)), PC(17:0/14:1(9Z)), PC(15:0/16:1(9Z)), PC(12:0/19:1(9Z)), PC(13:0/18:1(9Z)), PC(14:0/17:1(9Z)), PC(14:1(9Z)/17:0), PC(15:1(9Z)/16:0), PC(16:0/15:1(9Z)), PC(16:1(9Z)/15:0), PC(17:1(9Z)/14:0), PC(18:1(9Z)/13:0), PC(19:1(9Z)/12:0), PE(16:0/18:1(9Z)), PE(16:0/18:1(11Z)), PE(18:1(9Z)/16:0), PE(16:0/18:1(7Z)), PE(12:0/22:1(11Z)), PE(14:0/20:1(11Z)), PE(14:1(9Z)/20:0), PE(15:0/19:1(9Z)), PE(15:1(9Z)/19:0), PE(16:1(9Z)/18:0), PE(17:0/17:1(9Z)), PE(17:1(9Z)/17:0), PE(19:0/15:1(9Z)), PE(19:1(9Z)/15:0), PE(20:0/14:1(9Z)), PE(20:1(11Z)/14:0), PE(22:1(11Z)/12:0), PE(18:0/16:1(9Z))
GP5	723.5218	723.5203	C41H74NO7P	PE(O-16:0/20:5(5Z,8Z,11Z,14Z,17Z)), PE(P-18:0/18:4(6Z,9Z,12Z,15Z)), PE(P-16:0/20:4(5Z,8Z,11Z,14Z))
GP6	729.5678	729.5672	C41H80NO7P	PC(O-16:0/17:2(9Z,12Z)), PC(P-16:0/17:1(9Z)), PC(P-18:0/15:1(9Z)), PE(O-16:0/20:2(11Z,14Z)), PE(O-18:0/18:2(9Z,12Z)), PE(P-18:0/18:1(9Z)), PE(P-16:0/20:1(11Z)), PE(P-20:0/16:1(9Z))
GP7	731.5478	731.5465	C40H78NO8P	PC(14:0/18:1(11Z)), PC(14:0/18:1(9Z)), PC(16:0/16:1(9Z)), PC(18:1(9Z)/14:0), PC(12:0/20:1(11Z)), PC(13:0/19:1(9Z)), PC(14:1(9Z)/18:0), PC(15:0/17:1(9Z)), PC(15:1(9Z)/17:0), PC(16:1(9Z)/16:0), PC(17:0/15:1(9Z)), PC(17:1(9Z)/15:0), PC(18:0/14:1(9Z)), PC(19:1(9Z)/13:0), PC(20:1(11Z)/12:0), PC(18:1(11Z)/14:0), PE-NMe(16:0/18:1(9Z)), PE-NMe(18:1(9Z)/16:0), PE(13:0/22:1(11Z)), PE(14:1(9Z)/21:0), PE(15:0/20:1(11Z)), PE(15:1(9Z)/20:0), PE(16:0/19:1(9Z)), PE(16:1(9Z)/19:0), PE(17:1(9Z)/18:0), PE(18:0/17:1(9Z)), PE(18:1(9Z)/17:0), PE(19:0/16:1(9Z)), PE(19:1(9Z)/16:0), PE(20:0/15:1(9Z)), PE(20:1(11Z)/15:0), PE(21:0/14:1(9Z)), PE(22:1(11Z)/13:0), PE(17:0/18:1(9Z))
GP8	743.5468	743.5465	C41H78NO8P	PC(15:0/18:2(9Z,12Z)), PC(13:0/20:2(11Z,14Z)), PC(14:1(9Z)/19:1(9Z)), PC(15:1(9Z)/18:1(9Z)), PC(16:0/17:2(9Z,12Z)), PC(16:1(9Z)/17:1(9Z)), PC(17:1(9Z)/16:1(9Z)), PC(17:2(9Z,12Z)/16:0), PC(18:1(9Z)/15:1(9Z)), PC(18:2(9Z,12Z)/15:0), PC(19:1(9Z)/14:1(9Z)), PC(20:2(11Z,14Z)/13:0), PE(18:1(9E)/18:1(9E)), PE(18:0/18:2(9Z,12Z)), PE(18:1(9Z)/18:1(9Z)), PE(18:1(6Z)/18:1(6Z)), PE(14:0/22:2(13Z,16Z)), PE(14:1(9Z)/22:1(11Z)), PE(16:0/20:2(11Z,14Z)), PE(16:1(9Z)/20:1(11Z)), PE(17:1(9Z)/19:1(9Z)), PE(17:2(9Z,12Z)/19:0), PE(19:0/17:2(9Z,12Z)), PE(19:1(9Z)/17:1(9Z)), PE(20:1(11Z)/16:1(9Z)), PE(20:2(11Z,14Z)/16:0), PE(22:1(11Z)/14:1(9Z)), PE(22:2(13Z,16Z)/14:0), PE(18:2(9Z,12Z)/18:0)
GP9	745.5628	745.5622	C41H80NO8P	PC(15:0/18:1(11Z)), PC(16:0/17:1(9Z)), PC(13:0/20:1(11Z)), PC(14:0/19:1(9Z)), PC(14:1(9Z)/19:0), PC(15:0/18:1(9Z)), PC(15:1(9Z)/18:0), PC(16:1(9Z)/17:0), PC(17:0/16:1(9Z)), PC(17:1(9Z)/16:0), PC(18:0/15:1(9Z)), PC(18:1(9Z)/15:0), PC(19:0/14:1(9Z)), PC(19:1(9Z)/14:0), PC(20:1(11Z)/13:0), PE(18:0/18:1(9Z)), PE(18:1(9Z)/18:0), PE(18:0/18:1(7Z)), PE(16:0/20:1(11Z)), PE-NMe2(16:0/18:1(9Z)), PE-NMe2(18:1(9Z)/16:0), PE(14:0/22:1(11Z)), PE(14:1(9Z)/22:0), PE(15:1(9Z)/21:0), PE(16:1(9Z)/20:0), PE(17:0/19:1(9Z)), PE(17:1(9Z)/19:0), PE(19:0/17:1(9Z)), PE(19:1(9Z)/17:0), PE(20:0/16:1(9Z)), PE(20:1(11Z)/16:0), PE(21:0/15:1(9Z)), PE(22:0/14:1(9Z)), PE(22:1(11Z)/14:0)
GP10	747.5208	747.5203	C43H74NO7P	PE(P-16:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))
GP11	748.5268	748.5254	C40H77O10P	PG(16:0/18:1(9Z)), PG(16:0/18:1(11Z)), PG(12:0/22:1(11Z)), PG(14:0/20:1(11Z)), PG(14:1(9Z)/20:0), PG(15:0/19:1(9Z)), PG(15:1(9Z)/19:0), PG(16:1(9Z)/18:0), PG(17:0/17:1(9Z)), PG(17:1(9Z)/17:0), PG(19:0/15:1(9Z)), PG(19:1(9Z)/15:0), PG(20:0/14:1(9Z)), PG(20:1(11Z)/14:0), PG(22:1(11Z)/12:0), PG(18:0/16:1(9Z)), PG(18:1(9Z)/16:0), PG(16:0/18:1(9Z)), LBPA(16:0/18:1(9Z))
GP12	751.5518	751.5516	C43H78NO7P	PE(O-16:0/22:5(4Z,7Z,10Z,13Z,16Z)), PE(O-16:0/22:5(7Z,10Z,13Z,16Z,19Z)), PE(O-18:0/20:5(5Z,8Z,11Z,14Z,17Z)), PE(P-18:0/20:4(5Z,8Z,11Z,14Z)), PE(P-16:0/22:4(7Z,10Z,13Z,16Z)), PE(P-20:0/18:4(6Z,9Z,12Z,15Z))
GP13	767.5478	767.5465	C43H78NO8P	PC(18:2(9Z,12E)/17:2(9Z,11E)), PC(13:0/22:4(7Z,10Z,13Z,16Z)), PC(15:0/20:4(5Z,8Z,11Z,14Z)), PC(15:1(9Z)/20:3(8Z,11Z,14Z)), PC(17:0/18:4(6Z,9Z,12Z,15Z)), PC(17:1(9Z)/18:3(6Z,9Z,12Z)), PC(17:1(9Z)/18:3(9Z,12Z,15Z)), PC(17:2(9Z,12Z)/18:2(9Z,12Z)), PC(18:2(9Z,12Z)/17:2(9Z,12Z)), PC(18:3(6Z,9Z,12Z)/17:1(9Z)), PC(18:3(9Z,12Z,15Z)/17:1(9Z)), PC(18:4(6Z,9Z,12Z,15Z)/17:0), PC(20:3(8Z,11Z,14Z)/15:1(9Z)), PC(20:4(5Z,8Z,11Z,14Z)/15:0), PC(22:4(7Z,10Z,13Z,16Z)/13:0), PE(20:0/18:4(6Z,9Z,12Z,15Z)), PE(18:1(9Z)/20:3(5Z,8Z,11Z)), PE(16:0/22:4(7Z,10Z,13Z,16Z)), PE(18:0/20:4(5Z,8Z,11Z,14Z)), PE(18:0/20:4(5E,8E,11E,14E)), PE(18:1(9Z)/20:3(8Z,11Z,14Z)), PE(18:2(9Z,12Z)/20:2(11Z,14Z)), PE(18:3(6Z,9Z,12Z)/20:1(11Z)), PE(18:3(9Z,12Z,15Z)/20:1(11Z)), PE(18:4(6Z,9Z,12Z,15Z)/20:0), PE(20:1(11Z)/18:3(6Z,9Z,12Z)), PE(20:1(11Z)/18:3(9Z,12Z,15Z)), PE(20:2(11Z,14Z)/18:2(9Z,12Z)), PE(20:3(8Z,11Z,14Z)/18:1(9Z)), PE(20:4(5Z,8Z,11Z,14Z)/18:0), PE(22:4(7Z,10Z,13Z,16Z)/16:0), PE(P-18:0/20:4(5Z,8Z,10E,14Z)(12OH[S])), PE(P-18:0/20:4(5Z,8Z,11Z,13E)(15OH[S])), PE(P-18:0/20:4(6E,8Z,11Z,14Z)(5OH[S]))
GP14	775.5518	775.5516	C45H78NO7P	PE(P-18:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))
GP15	777.5528	777.552	C41H80NO10P	PS(13:0/22:0), PS(14:0/21:0), PS(15:0/20:0), PS(18:0/17:0), PS(20:0/15:0), PS(22:0/13:0), PS(21:0/14:0), PS(17:0/18:0), PS(19:0/16:0), PS(16:0/19:0)
GP16	779.5838	779.5829	C45H82NO7P	PE(O-20:0/20:5(5Z,8Z,11Z,14Z,17Z)), PE(P-18:0/22:4(7Z,10Z,13Z,16Z)), PE(P-20:0/20:4(5Z,8Z,11Z,14Z))
GP17	791.6038	791.604	C43H86NO9P	PS(O-16:0/21:0), PS(O-18:0/19:0), PS(O-20:0/17:0)
GP18	803.5688	803.5676	C43H82NO10P	PT(18:0/18:1(9Z)), PS(15:0/22:1(11Z)), PS(15:1(9Z)/22:0), PS(16:1(9Z)/21:0), PS(17:0/20:1(11Z)), PS(17:1(9Z)/20:0), PS(18:0/19:1(9Z)), PS(18:1(9Z)/19:0), PS(19:0/18:1(9Z)), PS(19:1(9Z)/18:0), PS(20:0/17:1(9Z)), PS(20:1(11Z)/17:0), PS(21:0/16:1(9Z)), PS(22:0/15:1(9Z)), PS(22:1(11Z)/15:0)
GP19	805.5838	805.5833	C43H84NO10P	PS(15:0/22:0), PS(16:0/21:0), PS(18:0/19:0), PS(20:0/17:0), PS(21:0/16:0), PS(22:0/15:0), PS(19:0/18:0), PS(17:0/20:0)
GP20	817.5838	817.5833	C44H84NO10P	PS(16:0/22:1(11Z)), PS(16:1(9Z)/22:0), PS(17:1(9Z)/21:0), PS(19:0/19:1(9Z)), PS(19:1(9Z)/19:0), PS(20:1(11Z)/18:0), PS(21:0/17:1(9Z)), PS(22:0/16:1(9Z)), PS(22:1(11Z)/16:0), PS(20:0/18:1(9Z)), PS(18:1(9Z)/20:0), PS(18:0/20:1(11Z))

Table S7 (continued) List of possible glycerophospholipids (GP1–GP30) and possible lipids other than glycerophospholipids (L1–L12) detected in LC-MS spectra obtained from solutes in the solvents after the direct-contact test to the cells.

GP21	819.5998	819.5989	C44H86NO10P	PS(17:0/21:0), PS(21:0/17:0), PS(22:0/16:0), PS(19:0/19:0), PS(20:0/18:0), PS(18:0/20:0), PS(16:0/22:0)
GP22	827.5668	827.5676	C45H82NO10P	PS(17:1(9Z)/22:2(13Z,16Z)), PS(17:2(9Z,12Z)/22:1(11Z)), PS(18:3(6Z,9Z,12Z)/21:0), PS(18:3(9Z,12Z,15Z)/21:0), PS(19:0/20:3(8Z,11Z,14Z)), PS(19:1(9Z)/20:2(11Z,14Z)), PS(20:2(11Z,14Z)/19:1(9Z)), PS(20:3(8Z,11Z,14Z)/19:0), PS(21:0/18:3(6Z,9Z,12Z)), PS(21:0/18:3(9Z,12Z,15Z)), PS(22:1(11Z)/17:2(9Z,12Z)), PS(22:2(13Z,16Z)/17:1(9Z))
GP23	829.5828	829.5833	C45H84NO10P	PS(17:0/22:2(13Z,16Z)), PS(17:1(9Z)/22:1(11Z)), PS(17:2(9Z,12Z)/22:0), PS(18:2(9Z,12Z)/21:0), PS(19:0/20:2(11Z,14Z)), PS(19:1(9Z)/20:1(11Z)), PS(20:1(11Z)/19:1(9Z)), PS(20:2(11Z,14Z)/19:0), PS(21:0/18:2(9Z,12Z)), PS(22:0/17:2(9Z,12Z)), PS(22:1(11Z)/17:1(9Z)), PS(22:2(13Z,16Z)/17:0)
GP24	831.5988	831.5989	C45H86NO10P	PS(17:0/22:1(11Z)), PS(17:1(9Z)/22:0), PS(18:1(9Z)/21:0), PS(19:0/20:1(11Z)), PS(19:1(9Z)/20:0), PS(20:0/19:1(9Z)), PS(20:1(11Z)/19:0), PS(21:0/18:1(9Z)), PS(22:0/17:1(9Z)), PS(22:1(11Z)/17:0)
GP25	833.6148	833.6146	C45H88NO10P	PS(17:0/22:0), PS(18:0/21:0), PS(19:0/20:0), PS(20:0/19:0), PS(22:0/17:0), PS(21:0/18:0)
GP26	853.5828	853.5833	C47H84NO10P	PS(19:0/22:4(7Z,10Z,13Z,16Z)), PS(20:4(5Z,8Z,11Z,14Z)/21:0), PS(21:0/20:4(5Z,8Z,11Z,14Z)), PS(22:4(7Z,10Z,13Z,16Z)/19:0)
GP27	859.6308	859.6302	C47H90NO10P	PS(19:0/22:1(11Z)), PS(19:1(9Z)/22:0), PS(20:1(11Z)/21:0), PS(21:0/20:1(11Z)), PS(22:0/19:1(9Z)), PS(22:1(11Z)/19:0)
GP28	862.5568	862.5571	C45H83O13P	PI(14:0/22:2(13Z,16Z)), PI(14:1(9Z)/22:1(11Z)), PI(16:0/20:2(11Z,14Z)), PI(16:1(9Z)/20:1(11Z)), PI(17:1(9Z)/19:1(9Z)), PI(17:2(9Z,12Z)/19:0), PI(19:0/17:2(9Z,12Z)), PI(19:1(9Z)/17:1(9Z)), PI(20:1(11Z)/16:1(9Z)), PI(20:2(11Z,14Z)/16:0), PI(22:1(11Z)/14:1(9Z)), PI(22:2(13Z,16Z)/14:0), PI(18:2(9Z,12Z)/18:0), PI(18:0/18:2(9Z,12Z))
GP29	864.5728	864.5728	C45H85O13P	PI(14:0/22:1(11Z)), PI(14:1(9Z)/22:0), PI(15:1(9Z)/21:0), PI(16:1(9Z)/20:0), PI(17:0/19:1(9Z)), PI(17:1(9Z)/19:0), PI(19:0/17:1(9Z)), PI(19:1(9Z)/17:0), PI(20:0/16:1(9Z)), PI(20:1(11Z)/16:0), PI(21:0/15:1(9Z)), PI(22:0/14:1(9Z)), PI(22:1(11Z)/14:0), PI(18:1(9Z)/18:0), PI(16:0/20:1(11Z)), PI(18:0/18:1(9Z))
GP30	886.5578	886.5571	C47H83O13P	PI(18:0/20:4(5Z,8Z,11Z,14Z)), PI(18:1(9Z)/20:3(8Z,11Z,14Z)), PI(18:2(9Z,12Z)/20:2(11Z,14Z)), PI(18:3(6Z,9Z,12Z)/20:1(11Z)), PI(18:3(9Z,12Z,15Z)/20:1(11Z)), PI(18:4(6Z,9Z,12Z,15Z)/20:0), PI(20:1(11Z)/18:3(6Z,9Z,12Z)), PI(20:1(11Z)/18:3(9Z,12Z,15Z)), PI(20:2(11Z,14Z)/18:2(9Z,12Z)), PI(20:3(8Z,11Z,14Z)/18:1(9Z)), PI(20:4(5Z,8Z,11Z,14Z)/18:0), PI(22:4(7Z,10Z,13Z,16Z)/16:0), PI(20:0/18:4(6Z,9Z,12Z,15Z)), PI(16:0/22:4(7Z,10Z,13Z,16Z)), Glc-GP(18:0/20:4(5Z,8Z,11Z,14Z))
L1	238.0989	238.0994	C16H14O2	4'-Methoxychalcone
L2	330.2778	330.277	C19H38O4	MG(16:0/0:0/0:0)[rac], MG(16:0/0:0/0:0), MG(0:0/16:0/0:0)
L3	649.6378	649.6373	C42H83NO3	Cer(d18:1/24:0), Cer(d18:0/24:1(15Z))
L4	743.5558	743.5548	C41H77NO10	Termitomycesphin A
L5	1262.8198	1262.8227	C65H118N2O21	NeuAcalpha2-3Galbeta1-4Glcbeta-Cer(d18:1/24:1(15Z))
L6	338.3198	338.3185	C22H42O2	n-Butyl Oleate, cis-cetoleic acid, cis-erucic acid, trans-brassidic acid
L7	528.4568	528.4542	C35H60O3	32,35-anhydrobacteriohopaneterol
L8	606.4988	606.5012	C41H66O3	1-(6-[5]-ladderane-hexanyl)-2-(8-[3]-ladderane-octanyl)-sn-glycerol

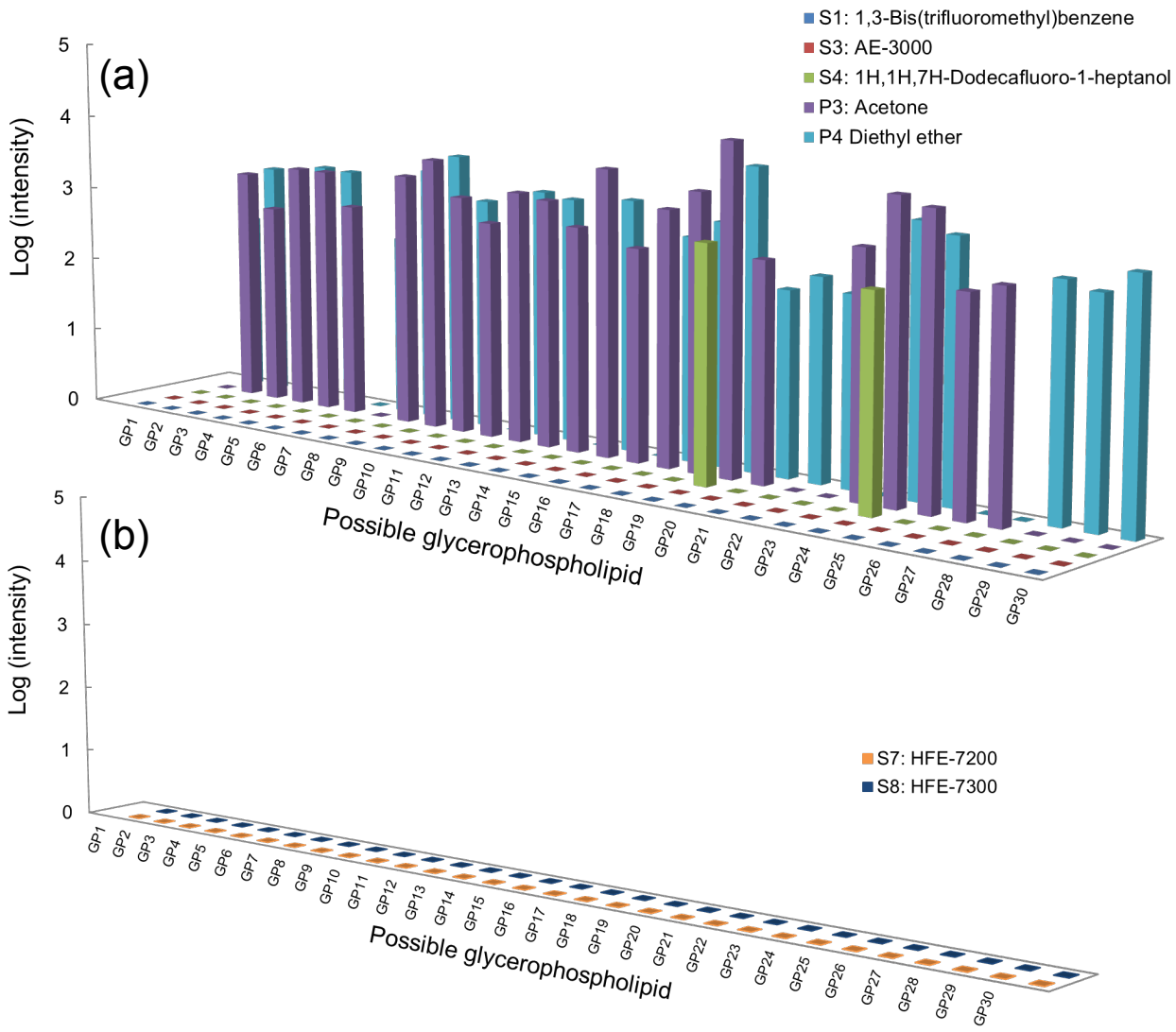

Fig. S11 Comparison of possible glycerophospholipids detected in the LC-MS spectra obtained from solutes in; (a) cytotoxic and (b) nontoxic solvents after the direct-contact test to the cells.

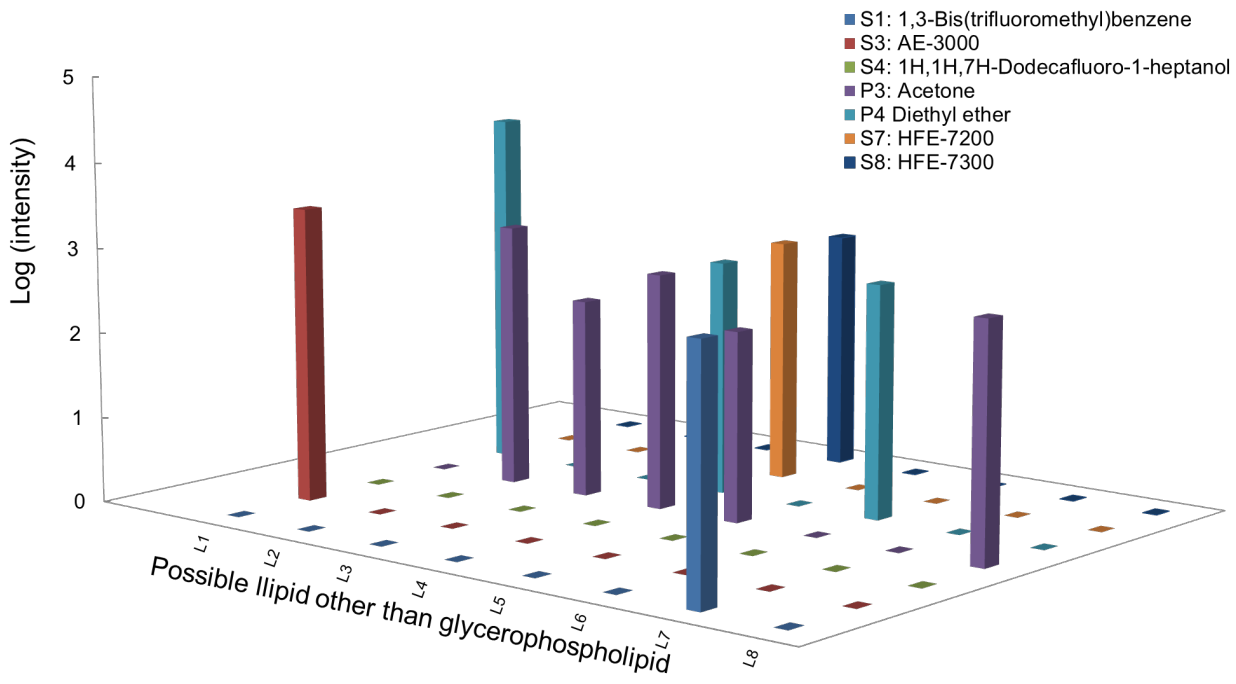

Fig. S12 Comparison of possible lipids other than glycerophospholipids detected in the LC-MS spectra obtained from solutes in the solvents after the direct-contact test to the cells.

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