

Supplemental Digital Content 2

Table 1. Summary of significant spectral regions of postulated metabolites and their relative amounts from the control and the VILI groups (¹H-NMR Spectroscopy).

Sample	Bucket position (ppm)	Postulated metabolites	Relative intensity		P value
			Control	VILI	
Lung tissue	1.34	Lactate	42.6 ± 0.4	55.0 ± 0.5	<0.0001
	1.37	Lactate	36.5 ± 0.2	48.6 ± 0.5	<0.0001
	3.22	Glucose	32.2 ± 0.2	27.3 ± 0.2	0.0005
	3.26	Glucose	35.6 ± 0.2	28.5 ± 0.2	<0.0001
	3.30	Glucose	72.9 ± 0.5	59.1 ± 0.4	0.0006
	3.41	Glucose	47.2 ± 0.4	38.6 ± 0.3	<0.0001
	4.45	Glucose	71.8 ± 0.8	56.3 ± 0.5	<0.0001
	3.57	Glycine	93.6 ± 0.8	75.8 ± 0.8	<0.0001
	3.80	Glucose	22.7 ± 0.4	18.5 ± 0.3	0.0002
BAL fluid	1.20	Hydroxybutyrate	3.4 ± 0.1	11.8 ± 0.2	0.0002
	1.22	Hydroxybutyrate	3.1 ± 0.1	11.2 ± 0.2	0.0005
	1.23	Hydroxybutyrate	2.6 ± 0.1	8.5 ± 0.6	0.0023
	1.33	Lactate	14.1 ± 0.8	45.2 ± 0.9	0.0002
	1.35	Lactate	14.1 ± 0.8	45.2 ± 0.9	0.0002
	1.94	Acetate	11.5 ± 0.7	55.2 ± 0.9	0.0017
	2.45	Hydroxybutyrate	0.6 ± 0.0	1.8 ± 0.0	0.0017
	3.05	Creatine	3.2 ± 0.1	8.7 ± 0.2	0.0041
	3.25	Glucose	1.6 ± 0.3	4.6 ± 0.4	0.0050
	3.28	Glucose	1.5 ± 0.1	5.2 ± 0.3	0.0014
	3.30	Glucose	2.7 ± 0.3	9.0 ± 0.5	0.0028
	3.42	Glucose	1.7 ± 0.2	6.8 ± 0.3	0.0073
	3.49	Glucose	1.5 ± 0.1	8.1 ± 0.2	0.0076
	3.51	Glucose	2.4 ± 0.3	10.1 ± 0.4	0.0051
3.55	Glucose	1.9 ± 0.2	4.0 ± 0.2	0.0032	

	3.56	Glucose	2.3 ± 0.3	4.7 ± 0.3	0.0049
	3.84	Glucose	1.8 ± 0.2	5.2 ± 0.2	0.0061
	3.96	Glucose	2.6 ± 0.3	7.0 ± 0.3	0.0020
	4.12	Lactate	1.3 ± 0.1	3.0 ± 0.1	0.0030
	4.14	Lactate	2.4 ± 0.2	9.5 ± 0.3	0.0012
	4.15	Lactate	2.5 ± 0.2	9.7 ± 0.3	0.0010
	4.16	Lactate	1.0 ± 0.0	3.7 ± 0.2	0.0010
	4.17	Hydroxybutyrate	0.9 ± 0.0	3.6 ± 0.1	0.0027
	4.18	Hydroxybutyrate	0.6 ± 0.0	1.8 ± 0.1	0.0004
	4.69	Glucose	2.4 ± 0.6	7.4 ± 0.1	0.0056
	5.25	Glucose	1.3 ± 0.3	4.4 ± 0.2	0.0058

BAL, bronchoalveolar lavage. NMR, Nuclear Magnetic Resonance. VILI, ventilator induced lung injury.

Values are mean ± SD. Signal intensities were normalized to total sum of the spectral regions to calculate the relative intensity.

Table 2. Identified compounds that are significantly different in serum samples from the control and the VILI groups (mass spectrometry).

Compound	RT (min)	Measured mass (Da)	Mass error (ppm)	Identification	% change	CV for QCs (%)
Olemide (18:1)	28.35	281.2719	0.16	Standard	73.1	29.47
C16 Sphingosine (16:1)	11.57	271.2506	-1.95	272.1963, 254.2467, 114.0937, 100.0747	-40.5	24.14
C17 Sphinganine (17:1)	9.80	287.2821	-1.09	288.0801, 106.084, 88.0727, 57.0705	40.5	(†)
LysoPC (20:0)	28.30	551.3939	-2.16	552.4012, 184.0739, 104.1076, 86.0974	-26.6	18.75
PC (20:2/18:1)	34.47	795.6228	-15.69	796.5992, 309.2772, 184.0723	49.4	57.22
Lysine	0.57	146.1033	-15.25	Database isotopic distribution	50.0	17.36
Oxoisotretinoin	7.26	314.1879	-0.94	315.1943, 297.1007, 269.1889, 109.1007	-50.5	27.14
Hydroxy-oxo-cholenic acid	8.75	388.2605	-2.17	389.2555, 371.2583, 355.2620, 149.0227, 71.06, 57.07	40.7	26.04
LysoPC (15:0)	16.86	481.3159	-1.88	482.3212, 184.0731, 104.1066, 86.0966	-25.6 *	29.54
LysoPC (18:0)	21.21	509.3476	-1.06	510.3538, 184.0725, 104.1068, 86.9063	-17.8 *	19.18
LysoPC (20:3)	18.94	545.3425	-10.34	546.3473, 184.0731, 104.1072, 86.0971	-22.9 *	26.41
Oxo-hexadecenal (16:1)	13.95	252.2083	-2.5	253.2127, 209.1879, 141.09, 71.0859, 43.05	10.5 *	6.15
Ethyl-dodecanoic acid (12:0)	26.38	228.209	0.35	229.1355, 89.0603, 87.0456, 43.0557	-16.6 *	22.08
Octadecadienol (18:2)	31.87	266.2631	8.03	267.269, 85.1008, 71.0855, 57.0705, 43.0551	-0.9 *	20.49
Deoxycortisol	6.54	346.2137	-1.99	Database isotopic distribution	21.9 *	19.37

* Compounds found from Jack-knifing.

† The CV for C17-sphinganine is not included, because dilution caused by the QCs preparation limited the detection range of less concentrated metabolites.

CV, coefficient of signal variation. Da: Dalton. PC, phosphatidylcholine. QCs, quality control samples. RT, retention time. VILI, ventilator induced lung injury.