

Table S1 The fatty acids composition of PLs in human milk and IF

Milk type	Area	PL subclass	Unit	Major molecular species and Content	Reference
Human	Weihai	PC	mg/g of lipid	PC(16:0/18:2, 0.38 ± 0.07), PC(16:0/18:1, 0.42 ± 0.11), PC(16:0/18:0, 0.18 ± 0.08), PC(16:0/20:3, 0.22 ± 0.05), PC(18:0/18:2, 1.01 ± 0.20), PC(18:0/18:1 0.48 ± 0.12).	1
		PE	mg/g of lipid	PE(16:0/18:1, 0.14 ± 0.03), PE(18:0/18:2, 1.29 ± 0.25), PE(18:0/18:1 0.39 ± 0.09), PE(18:0/20:4, 0.14 ± 0.04).	
		PI	mg/g of lipid	PI(16:0/22:6, 0.05 ± 0.01), PI(18:0/18:2, 0.05 ± 0.01).	
		SM	mg/g of lipid	SM(d18:1/16:0, 0.30 ± 0.12), SM(d18:1/18:0, 0.24 ± 0.00), SM(d18:1/20:0, 0.45 ± 0.11), SM(d18:1/22:1, 0.22 ± 0.04), SM(d18:1/22:0, 1.30 ± 0.31), SM(d18:1/24:1, 0.33 ± 0.41), SM(d18:1/24:0, 0.48 ± 0.15).	
Human milk	Jinhua	PC	mg/g of lipid	PC(16:0/18:2, 0.15 ± 0.06), PC(16:0/18:1, 0.21 ± 0.08), PC(16:0/18:0, 0.32 ± 0.12), PC(16:0/20:5, 0.25 ± 0.12), PC(18:0/18:1, 0.53 ± 0.22), PC(18:0/18:0, 0.33 ± 0.12).	1
		PE	mg/g of lipid	PE(18:0/18:2, 0.43 ± 0.2), PE(18:0/18:1, 0.15 ± 0.06).	
		PI	mg/g of lipid	PI(16:0/22:6, 0.06 ± 0.03)	
		SM	mg/g of lipid	SM(d18:1/16:0, 0.30 ± 0.13), SM(d18:1/18:0, 0.41 ± 0.17), SM(d18:1/20:0, 0.44 ± 0.17), SM(d18:1/22:1, 0.15 ± 0.06), SM(d18:1/22:0, 0.83 ± 0.32), SM(d18:1/24:1, 0.53 ± 0.22), SM(d18:1/24:0, 0.33 ± 0.12).	
Human milk	Wuxi	SM	%	SM(d18:1/24:0, 16.23 ± 3.41), SM(d18:1/18:0, 10.23 ± 2.14), SM(d18:1/20:0, 9.88 ± 0.91), SM(d18:1/22:0, 17.22 ± 2.72), SM(d18:1/24:1, 14.90 ± 5.33), SM(d18:1/24:0, 16.23 ± 3.41).	2
		PC	%	PC(16:0/18:2, 13.92 ± 1.51), PC(16:0/18:1, 11.72 ± 1.67), PC(18:1/18:2 7.97 ± 1.39), PC(18:1/18:1, 30.86 ± 3.44), PC(18:0/18:1, 7.52 ± 0.95).	
		PE	%	PE(18:1/18:2, 12.18 ± 4.20), PE(18:2/18:0, 33.97 ± 10.35), PE(18:1/18:0, 11.36 ± 3.56), PE(18:0/20:4, 5.78 ± 2.70).	
		PS	%	PS(18:0/18:2, 53.07 ± 5.13), PS(18:0/18:1, 19.92 ± 1.84).	
		PI	%	PI(16:0/18:1, 6.28 ± 1.36), PI(18:1/18:2, 5.57 ± 1.29), PI(18:0/18:2, 47.00 ± 6.09), PI(18:0/18:1, 16.22 ± 3.68), PI(18:0/20:4, 9.59 ± 6.04), PI(18:0/20:3, 5.78 ± 2.53).	
		PG	%	PG(16:0/18:2, 9.70 ± 7.52), PG(16:0/18:1, 22.17 ± 4.45), PG(18:1/18:2, 10.75 ± 6.60), PG(18:0/18:2, 19.20 ± 5.15), PG(18:0/18:1, 38.18 ± 8.84).	
Human milk	Shanghai	SM	ng/mL	SM(d18:1/18:0, 13830.3±4241.5), SM(d18:1/20:0, 12913.1±4236.3), SM(d18:1/22:0, 57330.3±901.2), SM(d18:1/24:1, 17517.4±441.3),	3

				SM(d18:1/24:0, 47227.7±955.7).	
		PC	ng/mL	PC(16:0/16:0, 4778.8±14.9), PC(16:0/18:2, 6664.7±22), PC(18:1/18:1; 18:0/18:2; 18:2/18:0, 23418.8±249.3)	
		PE	ng/mL	PE(16:0/18:0, 327.2±7.8)	
		PS	ng/mL	PS(18:0/18:2; 18:2/18:0; 18:1/18:1, 3202.1±210.6)	
		PI	ng/mL	PI(18:1/18:1; 18:2/18:0; 18:0/18:2, 4251.4±114.9), PI(18:0/18:1; 18:1/18:0, 2137.4±52)	
Human milk	Chengdu	PC	mg/g of lipid	PC(16:0/18:2, 0.34 ± 0.05), PC(16:0/18:1, 0.49 ± 0.09), PC(16:0/18:0, 0.21 ± 0.07), PC(16:0/20:3, 0.25 ± 0.06), PC(18:0/18:2, 1.03 ± 0.18), PC(18:0/18:1 0.43 ± 0.08).	3
		PE	mg/g of lipid	PE(16:0/18:1, 0.15 ± 0.03), PE(18:0/18:2, 1.25 ± 0.27), PE(18:0/18:1, 0.41 ± 0.09), PE(18:0/20:4, 0.14 ± 0.04).	
		PI	mg/g of lipid	PI(16:0/22:6, 0.05 ± 0.01), PI(18:0/18:2, 0.05 ± 0.01).	
		SM	mg/g of lipid	SM(d18:1/16:0, 0.30 ± 0.09), SM(d18:1/18:0, 0.43 ± 0.13), SM(d18:1/20:0, 0.53 ± 0.11), SM(d18:1/22:1, 0.24 ± 0.05), SM(d18:1/22:0, 1.04 ± 0.22), SM(d18:1/24:2, 0.10 ± 0.03), SM(d18:1/24:1, 0.89 ± 0.35), SM(d18:1/24:0, 0.29 ± 0.08).	
Human milk	Chongqing	PC	mg/L	PC(36:2, 45.38±32.99), PC(36:3, 21.24±14.09).	4
		PE	mg/L	PE(36:0, 15.28±9.16), PE(36:1, 11.28±5.34), PE(36:2, 13.05±8.76), PE(38:1, 15.51±10.96), PE(38:2, 16.35±13.18).	
		SM	mg/L	SM(d36:1, 10.25±5.48), SM(d36:2, 22.87±15.59), SM(d38:2, 5.60±3.10 13.10±5.60 1), SM(d40:1, 14.70±9.63), SM(d42:2, 22.24±12.16).	
		PS	mg/L	PS(38:4, 8.68±5.10)	
		PI	mg/L	PI(36:2, 7.66±3.69)	
Human milk	Beijing	PC	mg/g of lipid	PC(16:0/18:2, 0.24 ± 0.06), PC(16:0/18:1, 0.32 ± 0.08), PC(16:0/18:0, 0.15 ± 0.05), PC(16:0/20:3, 0.15 ± 0.04), PC(18:0/18:2, 0.70 ± 0.17), PC(18:0/18:1, 0.40 ± 0.14).	1
		PE	mg/g of lipid	PE(18:0/18:2, 0.77 ± 0.25), PE(18:0/18:1, 0.22 ± 0.06).	
		PI	mg/g of lipid	PI(16:0/18:1 0.05 ± 0.03), PI(16:0/22:6, 0.08 ± 0.04).	
		SM	mg/g of lipid	SM(d18:1/16:0, 0.26 ± 0.10), SM(d18:1/18:0, 0.33 ± 0.16), SM(d18:1/20:0, 0.43 ± 0.16), SM(d18:1/22:1, 0.19 ± 0.05), SM(d18:1/22:0, 0.10 ± 0.38), SM(d18:1/24:1, 0.29 ± 0.10), SM(d18:1/24:0, 0.37 ± 0.15).	

Human milk	Harbin	PC	mg/g of lipid	PC(16:0/18:2, 0.41 ± 0.10), PC(16:0/18:1, 0.52 ± 0.14), PC(16:0/18:0, 0.22 ± 0.07), PC(16:0/20:3, 0.20 ± 0.04), PC(18:0/18:2, 1.11 ± 0.27), PC(18:0/18:1 0.57 ± 0.014).	1
		PE	mg/g of lipid	PE(18:0/18:2, 1.03 ± 0.32)	
		SM	mg/g of lipid	SM(d18:1/16:0, 0.36 ± 0.11), SM(d18:1/18:0, 0.50 ± 0.13), SM(d18:1/20:0, 0.58 ± 0.12), SM(d18:1/22:1, 0.21 ± 0.05), SM(d18:1/22:0, 1.39 ± 0.33), SM(d18:1/23:0, 0.13 ± 0.04), SM(d18:1/24:2, 0.13 ± 0.04), SM(d18:1/24:1, 0.52 ± 0.19), SM(d18:1/24:0, 0.55 ± 0.15).	
Human milk	Lanzhou	PC	mg/g of lipid	PC(16:0/18:1, 0.12 ± 0.05), PC(16:0/18:0, 0.20 ± 0.09), PC(16:0/20:5, 0.14 ± 0.07), PC(18:0/18:1, 0.34 ± 0.16), PC(18:0/18:0, 0.21 ± 0.11).	1
		PE	mg/g of lipid	PE(18:0/18:2, 0.34 ± 0.15), PE(18:0/18:1, 0.11 ± 0.05).	
		PI	mg/g of lipid	PI(16:0/22:6, 0.06 ± 0.03)	
		SM	mg/g of lipid	SM(d18:1/16:0, 0.15 ± 0.09), SM(d18:1/18:0, 0.21 ± 0.12), SM(d18:1/20:0, 0.28 ± 0.14), SM(d18:1/22:1, 0.10 ± 0.05), SM(d18:1/22:0, 0.53 ± 0.27), SM(d18:1/24:1, 0.36 ± 0.25), SM(d18:1/24:0, 0.20 ± 0.10).	
Human milk	Zhengzhou	PC	mg/g of lipid	PC(16:0/18:2, 0.47 ± 0.09), PC(16:0/18:1, 0.56± 0.08), PC(16:0/18:0, 0.23 ± 0.05), PC(16:0/20:3, 0.10 ± 0.02), PC(18:0/18:2, 0.24 ± 0.05a), PC(18:0/18:1 1.21 ± 0.04).	1
		PE	mg/g of lipid	PE(16:0/18:2, 0.10 ± 0.02), PE(16:0/18:1, 0.14 ± 0.03), PE(18:0/18:2, 1.26 ± 0.31), PE(18:0/18:1, 0.38 ± 0.08), PE(18:0/20:4, 0.14 ± 0.03).	
		SM	mg/g of lipid	SM(d18:1/16:0, 0.36 ± 0.10), SM(d18:1/18:0, 0.41 ± 0.12), SM(d18:1/20:0, 0.62 ± 0.15), SM(d18:1/22:1, 0.27 ± 0.09), SM(d18:1/22:0, 1.52 ± 0.37), SM(d18:1/23:0, 0.11 ± 0.03), SM(d18:1/24:2, 0.11 ± 0.03), SM(d18:1/24:1, 0.55 ± 0.19), SM(d18:1/24:0, 0.64 ± 0.18).	
Human milk	Wuhan	SM	%	SM(34:1, 13.38 ± 1.4), SM(36:1, 14.40 ± 2.64), SM(38:1, 13.05 ± 1.29), SM(40:1, 29.29 ± 5.15), SM(42:2, 12.34 ± 0.54), SM(42:1, 11.21 ± 1.70).	5
		PC	%	PC(34:2, 15.82 ± 1.08), PC(34:2, 10.45 ± 0.92), PC(36:2, 33.45 ± 0.79).	
		PS	%	PS(36:2, 75.49 ± 4.06), PS(36:1, 21.90 ± 3.97).	
		PE	%	PE(36:3, 12.8 ± 0.33), PE(36:2, 50.02 ± 1.27), PE(36:1, 11.11 ± 0.42).	
		PI	%	PI(34:1, 12.21 ± 3.35), PI(36:2, 50.26 ± 4.11), PI(36:1, 14.75 ± 1.00).	
		LPC	%	LPC(16:0, 35.57 ± 1.22), LPC(18:2, 50.64 ± 1.79), LPC(18:1, 13.79 ± 0.92a).	
Human milk	Huangpu	SM	ng/mL	SM(d18:1/18:0, 27022.9±450.8), SM(d18:1/20:0, 25987±432.6), SM(d18:1/22:0, 57330.3±901.2), SM(d18:1/24:1, 17517.4±441.3), SM(d18:1/24:0, 47227.7±955.7).	3

		PC	ng/mL	PC(16:0/16:0, 4778.8±14.9), PC(16:0/18:2, 6664.7±22), PC(18:1/18:1; 18:0/18:2; 18:2/18:0, 23418.8±249.3)	
		PE	ng/mL	PE(16:0/18:0, 565±151.7)	
		PS	ng/mL	PS(18:0/18:2; 18:2/18:0; 18:1/18:1, 3082.8±50.2)	
		PI	ng/mL	PI(18:1/18:1; 18:2/18:0; 18:0/18:2, 6341.6±331.4), PI(18:0/18:1; 18:1/18:0, 2307.8±88.2)	
Human milk	Guangzhou	PC	mg/g of lipid	PC(16:0/18:1, 0.12 ± 0.05), PC(16:0/18:0, 0.20 ± 0.09), PC(18:0/18:2, 0.23 ± 0.09), PC(18:0/18:1, 0.23 ± 0.10).	1
		PE	mg/g of lipid	PE(18:0/18:2, 0.19 ± 0.09)	
		SM	mg/g of lipid	SM(d18:1/16:0, 0.14 ± 0.08), SM(d18:1/18:0, 0.19 ± 0.10), SM(d18:1/20:0, 0.24 ± 0.11), SM(d18:1/22:0, 0.59 ± 0.27), SM(d18:1/24:1, 0.15 ± 0.07), SM(d18:1/24:0, 0.24 ± 0.11).	
IF1		PC	ng/mL	PC(14:0/16:0, 27573.8±637.1), PC(14:0/18:1; 16:0/16:1, 9698.4±300.2), PC(16:0/16:0, 31314.3±829.1), PC(16:0/18:2, 31890.4±586.5, PC(16:0/18:1, 44847.2±1194.3), PC(16:0/18:0, 11282.2±206.4), PC(18:2/18:2; 18:1/18:3, 26940.4±870.3), PC(18:2/18:1; 18:1/18:2, 24029.8±540.2), PC(18:1/18:1; 18:0/18:2; 18:2/18:0, 33085.6±963.6), PC(18:0/18:1; 18:1/18:0, 17294.8±462.4)	3
		PE	ng/mL	PE(16:0/18:0, 1117.2±49.4)	
		PS	ng/mL	PS(18:0/18:2; 18:2/18:0; 18:1/18:1, 456.4±139.5), PS(18:0/18:1; 18:1/18:0, 619.9±23.2)	
		PI	ng/mL	PI(16:0/18:2, 1402.8±12.7), PI(18:1/18:1; 18:2/18:0; 18:0/18:2, 1069.4±8.9), PI(18:0/18:1; 18:1/18:0, 984±7.8)	
		PG	ng/mL	PG(16:0/18:2; 16:1/18:1, 5598.2 ± 138.3)	
IF2		PC	ng/mL	PC(14:0/16:0, 31622.9±683.8), PC(14:0/18:1; 16:0/16:1, 11600.3±308), PC(16:0/16:0, 34046.3±952.3), PC(16:0/18:2, 61185.1±1548), PC(16:0/18:1, 59781.5±1560), PC(16:0/18:0, 10730.9±260.3), PC(18:2/18:2; 18:1/18:3, 53761.4±1795.5), PC(18:2/18:1; 18:1/18:2, 56969.3±1696), PC(18:1/18:1; 18:0/18:2; 18:2/18:0, 47000.7±1364.6), PC(18:0/18:1; 18:1/18:0, 17455.2±570.8)	3
		PE	ng/mL	PE(16:0/18:0, 1901.9±21)	
		PS	ng/mL	PS(18:0/18:2; 18:2/18:0; 18:1/18:1, 590±38), PS(18:0/18:1; 18:1/18:0, 854.2±56.4)	
		PI	ng/mL	PI(16:0/18:2, 2749±41), PI(18:1/18:1; 18:2/18:0; 18:0/18:2, 790±4.3), PI(18:0/18:1; 18:1/18:0; 984±7.8)	
		PG	ng/mL	PG(16:0/18:2; 16:1/18:1, 10273.7 ± 105.1)	

		SM	ng/mL	SM(d18:1/16:0, 39618.1±17591.9), SM(d18:1/21:0 419.7±315.8, 18327.3±8054.3), SM(d18:1/23:0, 20155±8871.9), SM(d18:1/24:0, 13768.4±5990.1)	
IF3		PC	ng/mL	PC(14:0/16:0, 6870.4±140.7), PC(14:0/18:1; 16:0/16:1, 2631.8±79), PC(16:0/16:0, 7650.2±275.2), PC(16:0/18:2, 5454.4±96), PC(16:0/18:1, 13189.7±192.4), PC(16:0/18:0, 2768.3±54.3), PC(18:2/18:2; 18:1/18:3, 2595.1±57.7), PC(18:2/18:1; 18:1/18:2, 4359.4±92.8), PC(18:1/18:1; 18:0/18:2; 18:2/18:0, 7360.8±91.9), PC(18:0/18:1; 18:1/18:0, 4201.6±81.9)	3
		PE	ng/mL	PE(16:0/18:0, 362.2±7.5)	
		PS	ng/mL	PS(18:0/18:2; 18:2/18:0; 18:1/18:1, 2864.3±190), PS(18:0/18:1; 18:1/18:0, 3633±284)	
		PI	ng/mL	PI(16:0/18:2, 685.3±23.5), PI(18:1/18:1; 18:2/18:0; 18:0/18:2, 972.5±12.6), PI(18:0/18:1; 18:1/18:0, 1190±36.8)	
		PG	ng/mL	PG(16:0/18:2; 16:1/18:1, 324.8 ± 8.6)	
		SM	ng/mL	SM(d18:1/16:0, 8871.5±96), SM(d18:1/21:0, 3407.9±1384.2), SM(d18:1/23:0, 9 3850.1±1456.4), SM(d18:1/24:0, 3003.8±63.7)	
IF4		PC	ng/mL	PC(14:0/16:0, 7435.6±331.8), PC(14:0/18:1; 16:0/16:1, 2773.8±158.2), PC(16:0/16:0, 9809.2±59.6), PC(16:0/18:2, 26552.3±444.1), PC(16:0/18:1, 19045.8±273.4), PC(16:0/18:0, 3702.2±161.4), PC(18:2/18:2; 18:1/18:3, 26194±302.2), PC(18:2/18:1; 18:1/18:2, 20644.6±80.8), PC(18:1/18:1; 18:0/18:2; 18:2/18:0, 14702.5±106.5), PC(18:0/18:1; 18:1/18:0, 5575.2±19.8)	3
		PE	ng/mL	PE(16:0/18:0, 475±47.1)	
		PS	ng/mL	PS(18:0/18:2; 18:2/18:0; 18:1/18:1, 3546.3±455.4), PS(18:0/18:1; 18:1/18:0, 3516.8±422.1)	
		PI	ng/mL	PI(16:0/18:2, 2324.3±48), PI(18:1/18:1; 18:2/18:0; 18:0/18:2, 537.5±12.8), PI(18:0/18:1; 18:1/18:0, 326.7±9.1)	
		PG	ng/mL	PG(16:0/18:2; 16:1/18:1, 5975.1 ± 114.7)	
		SM	ng/mL	SM(d18:1/16:0, 9896.8±46.6), SM(d18:1/21:0, 4251.2±20.6), SM(d18:1/23:0, 4669.6±66.5), SM(d18:1/24:0, 3022.3±79.9)	

Note: PC (34:2) provides overall carbon number and saturation information for the fatty acid chains, PC (16:0/18:2) indicates the specific composition of the two fatty acid chains, including their carbon number and saturation.

References:

- 1 H. Zhu, X. Wang, W. Zhang, J. Pan, Y. Zhang, Y. Wang, C. Jiang, Q. Wei, X. Si, S. Jiang, J. Lu and J. Lv, Comparison of glycerophospholipid and sphingolipid in

mature milk from different sampled regions in the Chinese human milk project (CHMP) study, *Food Chem.*, 2023, **410**, 135311.

2 W. Wei, D. Li, C. Jiang, X. Zhang, X. Zhang, Q. Jin, X. Zhang and X. Wang, Phospholipid composition and fat globule structure II: Comparison of mammalian milk from five different species, *Food Chem.*, 2022, **388**, 132939.

3 C. Jiang, B. Ma, S. Song, O. M. Lai and L. Z. Cheong, Fingerprinting of Phospholipid Molecular Species from Human Milk and Infant Formula Using HILIC-ESI-IT-TOF-MS and Discriminatory Analysis by Principal Component Analysis, *J. Agric. Food Chem.*, 2018, **66**, 7131–7138.

4 D. Ding, X. He, I. E. Agarry, Y. Wang, F. Zhou, Y. Li, J. Kan, T. Cai and K. Chen, Profile of Human Milk Phospholipids at Different Lactation Stages with UPLC/Q-TOF-MS: Characterization, Distribution, and Differences, *J. Agric. Food Chem.*, 2023, **71**, 6326–6337.

5 S. Li, Y. Chen, B. Han, T. Xu, T. Liu, H. Yi, X. Zhou, L. Zhang, P. Liu, C. Ma, Y. Li, J. Pan and S. Jiang, Composition and variability of phospholipids in Chinese human milk samples, *INT. DAIRY J.*, 2020, **110**, 104782.

Table S2 Study nutritional results of PLs.

NO.	Study design and Model	Intervention component	Groups	Nutritional finding	Reference
1.	Randomised animal experiment, 30 Eight-week-old C57BL/6J male mice	PC	The control group: standard diet (AIN-93M) and distilled water. The LPS group (lipopolysaccharide-induced mice): LPS (0.25 mg/kg body weight/day) and standard diet (AIN-93M). The PC group (LPS + PC): LPS (0.25 mg/kg body weight/day) and PC (60 mg/kg body weight/day) mixed in the standard diet (AIN-93M).	PC could regulate the expression of neurotrophic factors and synaptic proteins, mitigating nerve damage and synaptic dysfunction induced by lipopolysaccharide. It also enhances gut barrier integrity, regulates gut gene expression, and promotes gut health via the cell adhesion molecule pathway. Moreover, PC adjusts the gut microbiome in LPS-exposed mice, boosting the presence of Rikenellaceae and Lachnospiraceae. PC also increased short-chain fatty acid production, which alleviates brain inflammation.	¹
2.	Observational, prospective clinical study (NCT03221127), 482 men aged 42-60.	Intake of total choline and PC		Higher phosphatidylcholine intake is associated with lower risk of dementia and better cognitive performance (including better performance in verbal fluency and memory functions).	²
3.	Randomised animal experiment, 48 18-month-old rats.	PL concentrates of krill oil (PCKO) and buttermilk (PCBM)	Standard diet: EURodent Diet 22%. 1: 70mg refined olive oil daily, 2: 70mg PCBM daily, 3: 70mg PCKO daily, 4: 70mg PCBM +70mg PCBM daily.	Supplementation with PL concentrates modulated the expression of specific cognitively relevant miRNAs and hippocampus gene expression Supplementation with PL increased brain-derived neurotrophic factor levels which are necessary for synaptic plasticity.	^{3, 4}
4.	Double-blind, placebo-controlled, crossover design, 10 healthy male subjects.	PS	600 mg PS or placebo per day.	PS supplementation blunted increases in cortisol levels and combated exercise induced stress effectively.	⁵
5.	Randomised, double-blind, placebo-controlled clinical trial, 40 children (4–14 years old) with ADHD.	PS	200 mg of soy derived PS or placebo per day.	PS significantly improved ADHD symptoms and short-term auditory memory in children	⁶
6.	Randomised animal experiment (SPXY2019031), 16 senescence-accelerated mouse-prone 8 mice.	EPA-PC and EPA-PE	AIN-93M rodent feed formula. 1: high fat group, 2: containing 1% (w/w) EPA-PC, 3: containing 1% (w/w) EPA-PE.	EPA-PE and EPA-PC could restore the lipid homeostasis of dementia mice to a certain degree, including significantly decrease the level of DPA-containing PS as well as increase the levels of AA-containing PI and PS in cerebral cortex.	⁷
7.	Mouse neuroblastoma derived cells, Neuro-2A (cell number: IFO50081), and astrocyte-derived cells A1 (cell number: IFO50519).	Plasmalogens	Control: Pls were dissolved in 99.5% ethanol to the concentration 5-20 µg/ml. Study: ethanol at the same concentration without Pls	Plasmalogens inhibited primary mouse hippocampal neuronal cell death induced by nutrient deprivation.	⁸
8.	Control, animal experiments, the GNPAT gene was knocked out to reduce the synthesis of endogenous Pls	Plasmalogens	Control food Plasmalogens (0.01 % w/v)—containing food	Plasmalogens can regulate memory-related gene expression in the hippocampus, including enhanced recruitment of CREB transcription factor onto the murine brain-derived neurotrophic factor promoter region via upregulating ERK-Akt signaling pathways in neuronal cells.	⁹
9.	Randomised animal experiment, 50 male Sprague-Dawley rats (9 week old).	TAG-DHA, PC-DHA, LPC-DHA	Fed ad lib standard laboratory chow. 1: 10 mg (30.4 µmol) /day TAG-DHA, 2: 10 mg (30.4 µmol) /day di-DHA PC, 3: 10 mg (30.4 µmol) /day LPC-DHA. An additional dose of 5 mg DHA (15.2 µmol) was included for LPC-DHA to be	LPC-DHA increased brain DHA by up to 100%. Dietary DHA from TAG or from natural PC (sn-2 position) is not suitable for brain enrichment, whereas DHA from LPC (at either sn-1 or sn-2 position) or from sn-1 position of PC efficiently enriches the brain, and is functionally effective.	¹⁰

			equivalent to 10 mg di-DHA PC.		
10.	Randomised, control animal experiment, preterm pigs were obtained via caesarean section at gestation day 105(which corresponds to 91% of 115-day term).	PS-DHA	Experimental group: the milk with PS-DHA at a concentration of 190 mg per 100 mL. Control group: the milk with sunflower oil at a concentration of 190 mg per 100 mL.	PS-DHA may support cerebellar development in preterm subjects by enhancing proliferation of granule cells, a process specifically inhibited by preterm birth, and increasing the survival of granule cells in the internal granule cell layer.	11
11.	Randomised, animal experiment, 15 male mice (8-week-old).	Milk polar lipid	1: Control group: milk polar lipid (21 % palm oil +1.4% of anhydrous milk fat). 2: High fat - milk polar lipid 1 group: (21 % palm oil +0.7 % of anhydrous milk fat +1.9 % of milk polar lipid-rich ingredient). 3: High fat - milk polar lipid 2 (21 % palm oil +3.8 % of milk polar lipid -rich ingredient). MPL-rich ingredient).	Milk polar lipid can limit high fat-induced body weight gain and modulate gut physiology and the abundance in microbiota of bacteria of metabolic interest.	12
12.	Randomised, animal experiment, 30 male mice (8-week-old).	SM	1: High fat diet control. 2: High fat diet with 0.25 % of milk SM added by weight. 3: High fat diet with 0.25 % of egg SM.	Milk SM is more effective than egg SM at combating the detrimental effects of a high fat diet in mice. Distal gut microbiota is altered with milk SM.	13
13.	Randomised, animal experiment, 90 male mice.	SM	Study 1: High fat, semi-purified diet without or with 0.3 %, 0.6 % or 1.2 % (wt/wt) pure chicken egg-derived SM. Study 2: High fat diet or a high fat diet supplemented with 1.2 % (wt/wt) pure SM. Study 3: (i) normal chow diet, (ii) normal chow diet supplemented with 1.2 % (wt/wt) egg SM, (iii) normal chow diet plus antibiotics, or (iv) normal chow diet supplemented with 1.2 % (wt/wt) egg SM and antibiotics.	Dietary SM is anti-atherogenic in chow-fed mice.	14
14.	Randomised, animal experiment, 30 male apoE ^{-/-} mice.	SM	Control: a base high fat diet without SM. Experiment: a base high fat diet supplemented with 0.1 % (w/w) of purified SM-containing diets(>99 %).	Dietary SM improved atherosclerosis and modulation of gut microbiota.	15
15.	Randomised, animal experiment, 40 male mice.	Ethanolamine	The control group without ethanolamine supplements, and three treatment groups that were supplemented with 250, 500 and 1000 µM ethanolamine (99.0 %).	Predominant microbes including Bacteroidetes, Proteobacteria, Elusimicrobia and Tenericutes were altered by different levels of ethanolamine.	16
16.	Caco-2/TC7 intestinal cells.	Milk PL	Study 1: Milk PL rich ingredient or milk sphingomyelin were added at the corresponding concentration off0.2 or 0.4 mM of SM into the micelles in culture medium. Study 2: milk sphingomyelin was added into the micelles at the corresponding	Effect of milk SM on intestinal tight junction expression and that this may be mediated by IL-8.	17

			concentration of 0.2, 0.4 and 0.6 mM in culture medium. independent experiments; (ii) MSM was added into the micelles at the corresponding concentration of 0.2, 0.4 and 0.6 mM in culture medium. mRNA levels were performed on three independent experiments and IL-8 secretion were performed on five independent experiments.		
17.	CRISPR-Cas9 cell	PS	1: Normal human cell. 2: CRISPR-Cas9 cell. 3: CRISPR-Cas9 cell cultured with PS	PS controls the final step of LDL cholesterol from lysosome to plasma membrane to endoplasmic reticulum.	¹⁸
18.	Baby hamster kidney (BHK)-21 clone 13 cells.	PI	Control: a semisynthetic diet supplemented 7 % soybean oil Experiment: a semisynthetic diet supplemented with 5 % soybean oil plus 2 % soybean PI.	PI normalises cholesterol metabolism by promoting faecal bile acid excretion in rats with a model of metabolic syndrome.	¹⁹
19.	Human colon carcinoma cell line (Caco-2 cells)	PL	2 µCi/mL [1,2- ³ H (N)]-cholesterol, 100 µmol/L cholesterol, 1 mmol/L oleic acid, 0.5 mmol/L mono-olein 6.6 mmol/L sodium taurocholate including 0.1 mmol/L soy PC, or 0.3, 0.6, or 1.2 mmol/L phospholipids (soy PC/egg-yolk PC/PE/LPC/SM).	SM and PC attenuate cholesterol absorption in Caco-2 Cells.	²⁰
20.	Randomised, animal experiment, 40 five-week-old male C57BL/6 mice	SM	A high-fat semi-purified diet with SM or without egg SM.	SM reduces liver lipid levels and inhibits intestinal cholesterol absorption in high-fat-fed mice.	²¹
21.	Randomised, animal experiment,, female heterozygous 6-mo-old <i>APOE*3</i> Leiden transgenic mice	SM	First, 3 wk the same diet without or with 0.1% (by wt) PS, sphingosine, sphinganine, cerebroside, ceramide III, or SM. Then, the SM to 0.2% (by wt) for 3 wk. Finally, SM to 0.4% (by wt) for 3 wk.	SM lowers plasma cholesterol and triacylglycerols and protects the liver from fat and cholesterol induced steatosis.	²²
22.	HeLa, HEK293, and human fibroblasts (6)	Plasmalogen	Plasmalogen level in HeLa and HEK293 cells was increased by adding 5 µM or 2 µM ethanolamine.	Plasmalogens regulate cholesterol synthesis.	²³

References:

- 1 M. P. T. Ylilauri, S. Voutilainen, E. Lönnroos, H. E. K. Virtanen, T. P. Tuomainen, J. T. Salonen and J. K. Virtanen, Associations of dietary choline intake with risk of incident dementia and with cognitive performance: The Kuopio ischaemic Heart Disease Risk Factor Study, *Am. J. Clin. Nutr.*, 2019, **110**, 1416–1423.
- 2 M. P. T. Ylilauri, S. Voutilainen, E. Lönnroos, H. E. K. Virtanen, T. P. Tuomainen, J. T. Salonen and J. K. Virtanen, Associations of dietary choline intake with risk of incident dementia and with cognitive performance: The Kuopio ischaemic Heart Disease Risk Factor Study, *Am. J. Clin. Nutr.*, 2019, **110**, 1416–1423.

- 3 M. C. Crespo, J. Tomé-Carneiro, D. Gómez-Coronado, E. Burgos-Ramos, A. García-Serrano, R. Martín-Hernández, S. Baliyan, J. Fontechá, C. Venero, A. Dávalos and F. Visioli, Modulation of miRNA expression in aged rat hippocampus by buttermilk and krill oil, *Sci. Rep.*, 2018, **8**, 3993.
- 4 J. Tomé-Carneiro, M. C. Carmen Crespo, E. Burgos-Ramos, C. Tomas-Zapico, A. García-Serrano, P. Castro-Gómez, C. Venero, I. Pereda-Pérez, S. Baliyan, A. Valencia, J. Fontechá, A. Dávalos and F. Visioli, Buttermilk and krill oil phospholipids improve hippocampal insulin resistance and synaptic signaling in aged rats, *Mol. Neurobiol.*, 2018, **55**, 7285–7296.
- 5 M. A. Starks, S. L. Starks, M. Kingsley, M. Purpura and R. Jäger, The effects of phosphatidylserine on endocrine response to moderate intensity exercise, *J. Int. Soc. Sports Nutr.*, 2008, **5**, 11.
- 6 S. Hirayama, K. Terasawa, R. Rabeler, T. Hirayama, T. Inoue, Y. Tatsumi, M. Purpura and R. Jäger, The effect of phosphatidylserine administration on memory and symptoms of attention-deficit hyperactivity disorder: A randomised, double-blind, placebo-controlled clinical trial, *J. Hum. Nutr. Diet.*, 2014, **27** Supplement 2, 284–291.
- 7 C. Zhang, M. M. Zhou, T. T. Zhang, P. X. Cong, J. Xu, C. H. Xue, T. Yanagita, Z. H. Wei and Y. M. Wang, Effects of Dietary Supplementation with EPA-enriched phosphatidylcholine and phosphatidylethanolamine on glycerophospholipid Profile in Cerebral Cortex of SAMP8 Mice fed with High-fat Diet, *J. Oleo Sci.*, 2021, **70**, 275–287.
- 8 M. S. Hossain, M. Ifuku, S. Take, J. Kawamura, K. Miake and T. Katafuchi, Plasmalogens rescue neuronal cell death through an activation of AKT and ERK survival signaling, *PLOS ONE*, 2013, **8**, e83508.
- 9 M. S. Hossain, S. Mawatari and T. Fujino, Plasmalogens, the vinyl ether-linked glycerophospholipids, enhance learning and memory by regulating brain-derived neurotrophic factor, *Front. Cell Dev. Biol.*, 2022, **10**, 828282.
- 10 D. Sugasini, P. C. R. Yalagala, A. Goggin, L. M. Tai and P. V. Subbaiah, Enrichment of brain docosahexaenoic acid (DHA) is highly dependent upon the molecular carrier of dietary DHA: Lysophosphatidylcholine is more efficient than either phosphatidylcholine or triacylglycerol, *J. Nutr. Biochem.*, 2019, **74**, 108231.
- 11 D. Chizhikov, R. K. Buddington and I. Y. Iskusnykh, Effects of phosphatidylserine source of docosahexaenoic acid on cerebellar development in preterm pigs, *Brain Sci.*, 2020, **10**, 12.
- 12 M. Milard, F. Laugerette, A. Durand, C. Buisson, E. Meugnier, E. Loizon, C. Louche-Pelissier, V. Sauvinet, L. Garnier, S. Viel, K. Bertrand, F. Joffre, D. Cheillan, L. Humbert, D. Rainteau, P. Plaisancié, L. B. Bindels, A. M. Neyrinck, N. M. Delzenne and M. C. Michalski, Milk polar lipids in a high-fat diet can prevent body weight gain: Modulated abundance of gut bacteria in relation with fecal loss of specific fatty acids, *Mol. Nutr. Food Res.*, 2019, **63**, e1801078.
- 13 G. H. Norris, C. Jiang, J. Ryan, C. M. Porter and C. N. Blesso, Milk sphingomyelin improves lipid metabolism and alters gut microbiota in high fat diet-fed mice, *J. Nutr. Biochem.*, 2016, **30**, 93–101.

- 14 R. W. S. Chung, Z. N. Wang, C. A. Bursill, B. J. Wu, P. J. Barter and K. A. Rye, Effect of long-term dietary sphingomyelin supplementation on atherosclerosis in mice, *PLOS ONE*, 2017, **12**, e0189523.
- 15 C. L. Millar, G. H. Norris, A. Vitols, C. Garcia, S. Seibel, L. Anto and C. N. Blesso, Dietary egg sphingomyelin prevents aortic root plaque accumulation in apolipoprotein-E knockout mice, *Nutrients*, 2019, **11**.
- 16 J. Zhou, X. Xiong, K. X. Wang, L. J. Zou, P. Ji and Y. L. Yin, Ethanolamine enhances intestinal functions by altering gut microbiome and mucosal anti-stress capacity in weaned rats, *Br. J. Nutr.*, 2018, **120**, 241–249.
- 17 M. Milard, A. Penhoat, A. Durand, C. Buisson, E. Loizon, E. Meugnier, K. Bertrand, F. Joffre, D. Cheillan, L. Garnier, S. Viel, F. Laugerette and M. C. Michalski, Acute effects of milk polar lipids on intestinal tight junction expression: Towards an impact of sphingomyelin through the regulation of IL-8 secretion?, *J. Nutr. Biochem.*, 2019, **65**, 128–138.
- 18 M. N. Trinh, M. S. Brown, J. L. Goldstein, J. Han, G. Vale, J. G. McDonald, J. Seemann, J. T. Mendell and F. R. Lu, Last step in the path of LDL cholesterol from lysosome to plasma membrane to ER is governed by phosphatidylserine, *Proc. Natl Acad. Sci. U. S. A.*, 2020, **117**, 18521–18529.
- 19 B. Shirouchi, K. Nagao, K. Furuya, N. Inoue, M. Inafuku, M. Nasu, K. Otsubo, S. Koga, H. Matsumoto and T. Yanagita, Effect of Dietary phosphatidylinositol on cholesterol Metabolism in Zucker (fa/fa) Rats, *J. Oleo Sci.*, 2009, **58**, 111–115.
- 20 F. Yang, G. X. Chen, M. H. Ma, N. Qiu, L. J. Zhu and J. Li, Egg-yolk sphingomyelin and phosphatidylcholine attenuate cholesterol absorption in Caco-2 cells, *Lipids*, 2018, **53**, 217–233.
- 21 R. W. S. Chung, A. Kamili, S. Tandy, J. M. Weir, R. Gaire, G. Wong, P. J. Meikle, J. S. Cohn and K. A. Rye, Dietary sphingomyelin lowers hepatic lipid levels and inhibits intestinal cholesterol absorption in high-fat-fed mice, *PLOS ONE*, 2013, **8**, e55949.
- 22 I. Duivenvoorden, P. J. Voshol, P. C. N. Rensen, W. van Duyvenvoorde, J. A. Romijn, J. J. Emeis, L. M. Havekes and W. F. Nieuwenhuizen, Dietary sphingolipids lower plasma cholesterol and triacylglycerol and prevent liver steatosis in APOE*3Leiden mice 1–3, *Am. J. Clin. Nutr.*, 2006, **84**, 312–321.
- 23 M. Honsho, Y. Abe and Y. Fujiki, Dysregulation of plasmalogen homeostasis impairs cholesterol biosynthesis, *J. Biol. Chem.*, 2015, **290**, 28822–28833.

Table S3 PLs content in commercial MFGM-enriched materials.

Product	Brief	PL content	Reference
Lacprodan® MFGM-10	Origin: Whey protein concentrate. Function: Significant clinical effects within cognitive development, immune and gastrointestinal health in infants. Main nutrients: Unique composition of proteins and lipids including gangliosides and phospholipids like sphingomyelin.	PL 6.0-10.0 %	Product specification
Lacprodan® PL-20	Function: Supports cognitive performance and brain development. Main nutrients: Natural source of choline, phosphatidylserine and other biological important lipids such as the sialic acid containing gangliosides, and sphingomyelin.	PC 4.3%, PE 3.5%, PS 1.9%, PI 1.3%, SM 4.3%. PC (16:0/18:1, 23 mol%), PE (18:1/18:1, 34 mol%), PI (18:0/18:1, 39 mol%), PS (18:0/18:1, 38 mol%).	Product specification and Sokol et al. ¹
Hilmar MFGM	Origin: Whey protein concentrate. Function: High nutritional value, especially designed for infant and child nutrition and clinical nutritional products, as well as for use in population-specific supplement formulations and sports nutrition products. Main nutrients: Biologically active proteins and phospholipids.	PC 2.45%, PE 1.57%, PS 1.46%, PI 0.84%, SM 1.77%.	Product specification
Hilmar™ 7500	Origin: Whey protein concentrate derived from sweet whey. Function: Designed for a variety of food and nutritional applications especially infant formula nutritional supplement formulations and sports nutrition products.	PL 6.5 %	Product specification
Vivinal® MFGM	Origin: Whey protein concentrate is enriched in MFGM components obtained during the mild processing of pasteurized cheese whey. Main nutrients: Bioactive proteins and lipids like IgG and lactoferrin, phospholipids and gangliosides.	PL 7.4 %	Product specification
SureStart™ MFGM Lipid 70	Origin: Whey from cheese products. Function: Suitable for reconstitution and processing into paediatric applications. Main nutrients: Elevated levels of phospholipids.	PL 6.3 g/100g PC 26.4%, PE 26.6%, PI, 8.4%, PS 12.7%, SM 25.0%	Product specification
NZMP SureStart™ MFGM Lipid 100	Origin: Buttermilk from cream. Function: Suitable for dry blending paediatric products for children greater than 6 months of age. Main nutrients: Elevated levels of phospholipids and gangliosides.	PL 7.6 g/100g PC 26.9%, PE 31.8%, PI, 8.3%, PS 11.8%, SM 21.0%	Product specification

Reference:

- 1 E. Sokol, T. Ulven, N. J. Færgeman and C. S. Ejsing, Comprehensive and quantitative profiling of lipid species in human milk, cow milk and a phospholipid-enriched milk formula by GC and MS/MS^{ALL}, *Euro J Lipid Sci & Tech*, 2015, **117**, 751–759.