

Appendix 1 Targeted lipidomic analysis

The detailed gradient elution conditions for mobile phases A and B were as follows: flow rate: 0.5 mL/min. 0 min—90% (A):10% (B); 0.5 min—90% (A):10% (B); 11 min—100% (B); 17 min—100% (B); 17.1 min—90% (A):10% (B); 20 min—90% (A):10% (B).

The ion source conditions were set as follows: temperature, 550 °C; curtain gas, 30 psi; ion source gas 1, 50 psi; ion source gas 2, 60 psi; ion spray voltage, 5,500 V in positive mode; declustering potential, 80 V; collision energy, 10 V for time-of-flight mass spectrometry (TOF-MS), and 35±15 V for TOF-MS/MS.

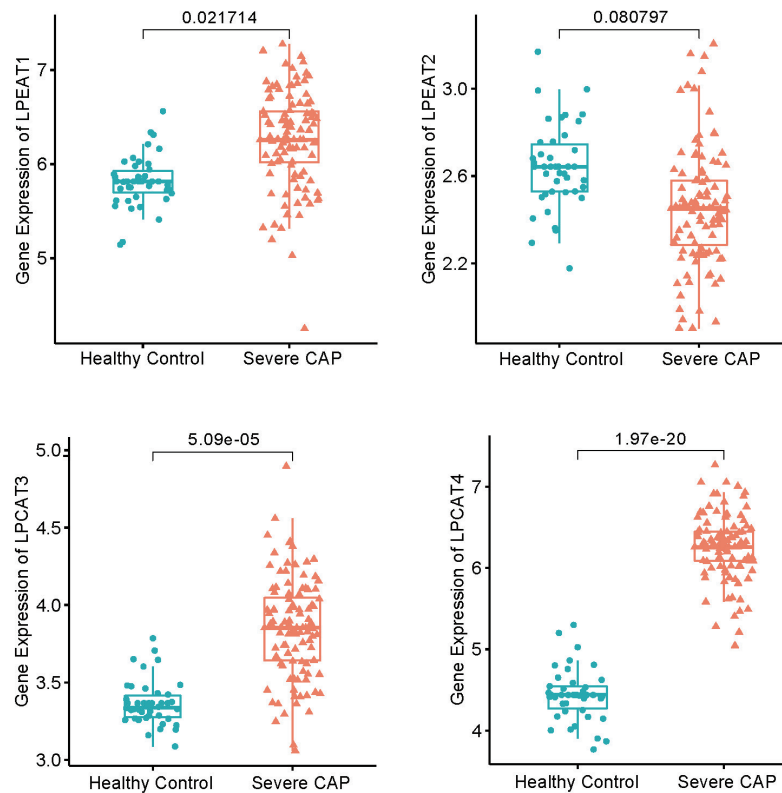


Figure S1 Gene expression levels of *LPEAT1-2* and *LPCAT3-4* in healthy controls and patients with severe CAP. LPCAT, lysophosphatidylcholine acyltransferase; LPEAT, lysophosphatidylethanolamine acyltransferase.

Table S1 Search conditions

| Parameter | Condition |
|--------------------------------|-----------|
| Retention time tolerance | 100 min |
| Accurate mass tolerance (MS1) | 0.01 Da |
| Accurate mass tolerance (MS2) | 0.05 Da |
| Identification score cut off | 90% |
| Use retention time for scoring | √ |

Table S2 Primers used for qRT-PCR analysis

| Gene | Forward sequence | Reverse sequence |
|---------------|-----------------------------|------------------------------|
| <i>LPCAT1</i> | 5'-ACCTATTCCGAGCCATTGACC-3' | 5'-CCTAATCCAGCTTCTTGCGAAC-3' |
| <i>LPCAT2</i> | 5'-TTGTTGCTGCCCTCATTCA-3' | 5'-GGGAATCCGGATCTACACGG-3' |

Table S3 Demographic characteristics of the study population (CAP vs. Control)

| Characteristic | CAP (n=58) | Control (n=11) | P value |
|------------------------|------------------|----------------|---------|
| Male sex | 38 (65.5) | 4 (36.4) | 0.095 |
| Age years | 68 (59.25,78.25) | 61.91±9.14 | 0.261 |
| Underlying diseases | | | |
| Chronic lung disease | 18 (31.0) | 0 | 0.055 |
| Hypertension | 17 (29.3) | 3 (27.3) | 1.000 |
| Diabetes | 8 (13.8) | 0 | 0.338 |
| Cardiovascular disease | 11 (19.0) | 4 (36.4) | 0.237 |
| Autoimmune disease | 3 (5.2) | 0 | 1.000 |

Categorical variables are presented as numbers (percentages). Normally distributed variables are presented as the mean ± standard deviation, and abnormally distributed continuous variables are expressed as the median and interquartile ranges (25th-75th). CAP, community-acquired pneumonia.

Table S4 Between-group comparisons of lipid groups

| Variable | PE | LPE | PC | LPC |
|--|-------------------------|------------------------|-------------------------|-------------------------|
| Relative abundances of four lipid groups | | | | |
| NC | -1.128 (-1.417, -0.723) | 0.233 (-0.477, 1.007) | -0.888 (-2.116, -0.060) | 1.292 (0.794, 1.894) |
| CAP | 0.215 (-0.648, 0.840) | -0.218 (-0.604, 0.375) | 0.250 (-0.218, 0.672) | -0.270 (-0.901, 0.327) |
| NSCAP | -0.350 (-0.722, 0.419) | -0.334 (-0.464, 0.344) | 0.136 (-0.134, 0.679) | -0.019 (-0.394, 0.369) |
| SCAP | 0.728 (-0.217, 1.362) | -0.135 (-1.024, 0.461) | 0.284 (-0.298, 0.665) | -0.723 (-1.108, -0.133) |
| Results of comparisons | | | | |
| All groups | P<0.001 | P=0.518 | P=0.004 | P<0.001 |
| NC vs. NSCAP | P=0.017 | - | P=0.009 | P=0.006 |
| NSCAP vs. SCAP | P=0.026 | - | P=1.000 | P=0.064 |
| NC vs. CAP | P<0.001 | P=0.003 | P<0.001 | P<0.001 |

Variables are presented as medians and interquartile ranges (25th-75th). PE, phosphatidylethanolamine; PC, phosphatidylcholine; LPE, lysophosphatidylethanolamine; LPC, lysophosphatidylcholine; CAP, community-acquired pneumonia; NC, nondisease control; NSCAP, nonsevere community-acquired pneumonia; SCAP, severe community-acquired pneumonia.

Table S5 Between-group comparisons of lipid ratios

| Variable | PC/LPC | PE/LPE |
|------------------------|----------------------|----------------------|
| Lipid ratios | | |
| NC | 16.11 (13.49, 19.10) | 14.83 (13.37, 19.45) |
| CAP | 30.54 (22.77, 46.37) | 24.29 (18.82, 33.54) |
| NSCAP | 26.43 (22.29, 32.73) | 22.49 (18.30, 28.53) |
| SCAP | 40.43 (28.20, 55.80) | 28.77 (19.76, 45.58) |
| Results of comparisons | | |
| All groups | P<0.001 | P<0.001 |
| NC vs. NSCAP | P=0.005 | P=0.024 |
| NSCAP vs. SCAP | P=0.073 | P=0.199 |
| NC vs. CAP | P<0.001 | P<0.001 |

Variables are presented as medians and interquartile ranges (25th-75th). PE, phosphatidylethanolamine; PC, phosphatidylcholine; LPE, lysophosphatidylethanolamine; LPC, lysophosphatidylcholine; CAP, community-acquired pneumonia; NC, nondisease control; NSCAP, nonsevere community-acquired pneumonia; SCAP, severe community-acquired pneumonia.

Table S6 Areas under the curves (AUCs) and thresholds for ROC analysis (NSCAP *vs.* SCAP)

| Variable | | Threshold | Sensitivity (%) | Specificity (%) | AUC | P value | 95% CI |
|---------------|----------------|-----------|-----------------|-----------------|-------|-------------------|----------------|
| CURB65 | | >1 | 53.57 | 93.33 | 0.782 | <0.0001 | 0.654 to 0.880 |
| PSI | | >92 | 67.86 | 80.00 | 0.781 | <0.0001 | 0.653 to 0.879 |
| Lipid groups | PE | >0.2669 | 60.71 | 80.00 | 0.726 | 0.0010 | 0.593 to 0.835 |
| | PC | >0.0746 | 57.14 | 60.00 | 0.530 | 0.7028 | 0.394 to 0.662 |
| | LPE | ≤-0.5284 | 35.71 | 83.33 | 0.504 | 0.9644 | 0.369 to 0.638 |
| | LPC | ≤-0.8148 | 50.00 | 96.67 | 0.708 | 0.0044 | 0.574 to 0.820 |
| | PE_CURB65 | >0.5517 | 71.43 | 86.67 | 0.848 | <0.0001 | 0.729 to 0.928 |
| | PC_CURB65 | >0.3961 | 53.57 | 93.33 | 0.782 | <0.0001 | 0.654 to 0.880 |
| | LPE_CURB65 | >0.3961 | 53.57 | 93.33 | 0.782 | <0.0001 | 0.654 to 0.880 |
| | LPC_CURB65 | >0.3961 | 53.57 | 93.33 | 0.782 | <0.0001 | 0.654 to 0.880 |
| | PE_PSI | >0.6124 | 60.71 | 86.67 | 0.799 | <0.0001 | 0.673 to 0.893 |
| | PC_PSI | >0.4907 | 67.86 | 80.00 | 0.781 | <0.0001 | 0.653 to 0.879 |
| | LPE_PSI | >0.4907 | 67.86 | 80.00 | 0.781 | <0.0001 | 0.653 to 0.879 |
| | LPC_PSI | >0.4907 | 67.86 | 80.00 | 0.781 | <0.0001 | 0.653 to 0.879 |
| Lipid ratios | PC/LPC | >40.4475 | 50.00 | 93.33 | 0.704 | 0.0056 | 0.569 to 0.816 |
| | PE/LPE | >33.6364 | 39.29 | 96.67 | 0.661 | 0.0323 | 0.525 to 0.780 |
| | PC/LPC_CURB65 | >0.6420 | 71.43 | 96.67 | 0.843 | <0.0001 | 0.723 to 0.925 |
| | PE/LPE_CURB65 | >0.5121 | 67.86 | 93.33 | 0.824 | <0.0001 | 0.701 to 0.911 |
| | PC/LPC_PSI | >0.6023 | 60.71 | 86.67 | 0.821 | <0.0001 | 0.699 to 0.910 |
| | PE/LPE_PSI | >0.3445 | 92.86 | 60.00 | 0.811 | <0.0001 | 0.686 to 0.902 |
| Lipid species | PE 36:1 | >0.39 | 67.86 | 93.33 | 0.836 | <0.0001 | 0.715 to 0.920 |
| | PE 36:4 | >0.55 | 89.29 | 70.00 | 0.811 | <0.0001 | 0.686 to 0.902 |
| | PE 36:1_CURB65 | >0.3610 | 92.86 | 86.67 | 0.928 | <0.0001 | 0.829 to 0.979 |
| | PE 36:4_CURB65 | >0.3070 | 89.29 | 76.67 | 0.905 | <0.0001 | 0.799 to 0.966 |
| | PE 36:1_PSI | >0.2955 | 92.86 | 73.33 | 0.886 | <0.0001 | 0.775 to 0.954 |
| | PE 36:4_PSI | >0.3742 | 89.29 | 76.67 | 0.858 | <0.0001 | 0.742 to 0.936 |

ROC analysis, receiver operating characteristic analysis; NSCAP, nonsevere community-acquired pneumonia; SCAP, severe community-acquired pneumonia; PE, phosphatidylethanolamine; PC, phosphatidylcholine; LPE, lysophosphatidylethanolamine; LPC, lysophosphatidylcholine; CURB-65, confusion, uremia, respiratory rate, blood pressure, and age ≥65 years old; PSI, pneumonia severity index.

Table S7 Comparisons of ROC curves (NSCAP vs. SCAP)

| Comparison | Standard Error ^a | 95% CI | Significance level |
|---------------------------|-----------------------------|-------------------|--------------------|
| Lipid groups | | | |
| PE_CURB65 vs. CURB65 | 0.0325 | 0.00180 to 0.129 | P=0.0439 |
| PE_CURB65 vs. PSI | 0.0678 | -0.0662 to 0.200 | P=0.3253 |
| PE_PSI vs. CURB65 | 0.0693 | -0.119 to 0.152 | P=0.8099 |
| PE_PSI vs. PSI | 0.0417 | -0.0638 to 0.0995 | P=0.6683 |
| Lipid ratios | | | |
| PC/LPC_CURB65 vs. CURB65 | 0.0414 | -0.0205 to 0.142 | P=0.1427 |
| PC/LPC_CURB65 vs. PSI | 0.0758 | -0.0867 to 0.210 | P=0.4142 |
| PE/LPE_CURB65 vs. CURB65 | 0.0370 | -0.0308 to 0.114 | P=0.2596 |
| PE/LPE_CURB65 vs. PSI | 0.0728 | -0.0999 to 0.186 | P=0.5562 |
| PC/LPC_PSI vs. CURB65 | 0.0670 | -0.0919 to 0.171 | P=0.5574 |
| PC/LPC_PSI vs. PSI | 0.0399 | -0.0377 to 0.119 | P=0.3101 |
| PE/LPE_PSI vs. CURB65 | 0.0671 | -0.103 to 0.160 | P=0.6703 |
| PE/LPE_PSI vs. PSI | 0.0335 | -0.0359 to 0.0954 | P=0.3742 |
| Lipid species | | | |
| PE 36:1 vs. CURB65 | 0.0802 | -0.104 to 0.211 | P=0.5041 |
| PE 36:1 vs. PSI | 0.0873 | -0.116 to 0.226 | P=0.5304 |
| PE 36:4 vs. CURB65 | 0.0840 | -0.136 to 0.193 | P=0.7338 |
| PE 36:4 vs. PSI | 0.0879 | -0.142 to 0.202 | P=0.7348 |
| PE 36:1_CURB65 vs. CURB65 | 0.0467 | 0.0543 to 0.237 | P=0.0018 |
| PE 36:1_CURB65 vs. PSI | 0.0705 | 0.00886 to 0.285 | P=0.0370 |
| PE 36:4_CURB65 vs. CURB65 | 0.0447 | 0.0357 to 0.211 | P=0.0058 |
| PE 36:4_CURB65 vs. PSI | 0.0697 | -0.0121 to 0.261 | P=0.0741 |
| PE 36:1_PSI vs. CURB65 | 0.0671 | -0.0280 to 0.235 | P=0.1230 |
| PE 36:1_PSI vs. PSI | 0.0566 | -0.00616 to 0.216 | P=0.0641 |
| PE 36:4_PSI vs. CURB65 | 0.0716 | -0.0642 to 0.217 | P=0.2876 |
| PE 36:4_PSI vs. PSI | 0.0514 | -0.0233 to 0.178 | P=0.1319 |

^a, DeLong *et al.*, 1988. ROC curves, receiver operating characteristic curves; NSCAP, nonsevere community-acquired pneumonia; SCAP, severe community-acquired pneumonia; PE, phosphatidylethanolamine; PC, phosphatidylcholine; LPE, lysophosphatidylethanolamine; LPC, lysophosphatidylcholine; CURB-65, confusion, uremia, respiratory rate, blood pressure, and age ≥ 65 years old; PSI, pneumonia severity index.

Table S8 67 lipid species as predictors of disease severity and mortality

| No. | Lipid | Formula | Reference m/z | Ontology | NSCAP vs. SCAP | | | Non-Survivors vs. Survivors | | |
|-----|----------------------|------------|---------------|----------|----------------|------------|-------|-----------------------------|------------|-------|
| | | | | | FDR | VIP | ROC | FDR | VIP | ROC |
| 1 | LPC 14:0/0:0 | C22H46NO7P | 468.3085 | LPC | 0.83563 | 0.793598 | 0.612 | 0.022973 | 1.38158 | 0.749 |
| 2 | LPC 15:0 | C23H48NO7P | 482.3241 | LPC | 0.19621 | 0.923794 | 0.643 | 0.011075 | 1.39135 | 0.783 |
| 3 | LPC 16:0 | C24H50NO7P | 496.33981 | LPC | 0.075358 | 0.935215 | 0.654 | 0.011075 | 1.33066 | 0.740 |
| 4 | LPC 16:1 | C24H48NO7P | 494.3241 | LPC | 0.48261 | 0.77831 | 0.614 | 0.015777 | 1.33353 | 0.733 |
| 5 | LPC 17:0 | C25H52NO7P | 510.35541 | LPC | 0.049975 | 1.2005 | 0.673 | 0.0081951 | 1.54735 | 0.773 |
| 6 | LPC 17:1 | C25H50NO7P | 508.33981 | LPC | 0.33353 | 0.769032 | 0.602 | 0.023985 | 1.15304 | 0.696 |
| 7 | LPC 18:0 | C26H54NO7P | 524.37109 | LPC | 0.049975 | 1.24612 | 0.689 | 0.0061942 | 1.53301 | 0.775 |
| 8 | LPC 18:1 | C26H52NO7P | 522.35541 | LPC | 0.24738 | 0.858686 | 0.640 | 0.015777 | 1.32437 | 0.738 |
| 9 | LPC 18:2/0:0 | C26H50NO7P | 520.33978 | LPC | 0.03284 | 0.981038 | 0.686 | 0.00055093 | 1.52466 | 0.819 |
| 10 | LPC 18:3/0:0 | C26H48NO7P | 518.3241 | LPC | 0.83563 | 0.530427 | 0.565 | 0.023985 | 1.25328 | 0.738 |
| 11 | LPC 20:0 | C28H58NO7P | 552.4024 | LPC | 0.03284 | 1.572 | 0.723 | 0.011075 | 1.66979 | 0.788 |
| 12 | LPC 20:1 | C28H56NO7P | 550.38672 | LPC | 0.39817 | 0.974651 | 0.650 | 0.17646 | 1.1212 | 0.686 |
| 13 | LPC 20:2 | C28H54NO7P | 548.37109 | LPC | 0.10697 | 1.2062 | 0.651 | 0.014959 | 1.52131 | 0.741 |
| 14 | LPC 20:3 | C28H52NO7P | 546.35541 | LPC | 0.45934 | 1.04493 | 0.604 | 0.034766 | 1.48429 | 0.729 |
| 15 | LPC 20:4 | C28H50NO7P | 544.33978 | LPC | 0.083065 | 1.11815 | 0.652 | 0.023913 | 1.37936 | 0.726 |
| 16 | LPC 20:5 | C28H48NO7P | 542.3241 | LPC | 0.1865 | 1.09937 | 0.588 | 0.26601 | 1.18821 | 0.635 |
| 17 | LPC 22:5 | C30H52NO7P | 570.35541 | LPC | 0.049975 | 0.860263 | 0.684 | 0.15529 | 1.11783 | 0.709 |
| 18 | LPC 22:6/0:0 | C30H50NO7P | 568.33978 | LPC | 0.049975 | 0.988376 | 0.625 | 0.046584 | 1.20703 | 0.717 |
| 19 | LPE 16:0 | C21H44NO7P | 454.29279 | LPE | 0.85856 | 0.178465 | 0.508 | 0.25502 | 0.474754 | 0.623 |
| 20 | LPE 18:0 | C23H48NO7P | 482.3241 | LPE | 0.82696 | 0.0551849 | 0.515 | 0.30499 | 0.52997 | 0.619 |
| 21 | LPE 18:1 | C23H46NO7P | 480.3085 | LPE | 0.83563 | 0.203683 | 0.527 | 0.30499 | 0.562532 | 0.628 |
| 22 | PC 28:0 | C36H72NO8P | 678.50677 | PC | 0.97368 | 0.534154 | 0.511 | 0.5295 | 0.249578 | 0.612 |
| 23 | PC 30:0 | C38H76NO8P | 706.53809 | PC | 0.6713 | 0.536389 | 0.515 | 0.70858 | 0.00560963 | 0.536 |
| 24 | PC 32:0 PC 16:0_16:0 | C40H80NO8P | 734.5694 | PC | 0.83563 | 0.611099 | 0.531 | 0.15529 | 0.442061 | 0.564 |
| 25 | PC 32:1 PC 16:0_16:1 | C40H78NO8P | 732.55377 | PC | 0.61017 | 1.03207 | 0.602 | 0.57029 | 0.417093 | 0.526 |
| 26 | PC 32:2 | C40H76NO8P | 730.53809 | PC | 0.71146 | 0.14117 | 0.568 | 0.040949 | 0.958506 | 0.711 |
| 27 | PC 33:1 | C41H80NO8P | 746.5694 | PC | 0.6653 | 1.21991 | 0.711 | 0.70858 | 0.583084 | 0.638 |
| 28 | PC 33:2 | C41H78NO8P | 744.55377 | PC | 0.79718 | 0.167913 | 0.517 | 0.20101 | 0.616444 | 0.665 |
| 29 | PC 34:0 | C42H84NO8P | 762.60071 | PC | 0.002639 | 0.8537 | 0.666 | 0.023913 | 1.14555 | 0.717 |
| 30 | PC 34:1 PC 16:0_18:1 | C42H82NO8P | 760.58508 | PC | 0.0013469 | 1.88253 | 0.796 | 0.0038959 | 1.07796 | 0.669 |
| 31 | PC 34:2 PC 16:0_18:2 | C42H80NO8P | 758.5694 | PC | 0.37919 | 0.766746 | 0.598 | 0.57195 | 0.0450517 | 0.515 |
| 32 | PC 34:3 | C42H78NO8P | 756.55377 | PC | 0.83665 | 0.448726 | 0.539 | 0.42663 | 0.468133 | 0.605 |
| 33 | PC 34:4 | C42H76NO8P | 754.53809 | PC | 0.72028 | 0.517448 | 0.581 | 0.065522 | 1.15962 | 0.707 |
| 34 | PC 35:1 PC 16:0_19:1 | C43H84NO8P | 774.60071 | PC | 0.78764 | 0.749997 | 0.671 | 0.47621 | 0.559 | 0.660 |
| 35 | PC 35:2 PC 17:0_18:2 | C43H82NO8P | 772.58508 | PC | 0.48366 | 0.0767404 | 0.528 | 0.96948 | 0.323908 | 0.678 |
| 36 | PC 35:4 | C43H78NO8P | 768.55377 | PC | 0.35556 | 0.491759 | 0.589 | 0.26601 | 0.822216 | 0.660 |
| 37 | PC 36:1 | C44H86NO8P | 810.59833 | PC | 0.049975 | 1.37514 | 0.710 | 0.47621 | 0.402855 | 0.549 |
| 38 | PC 36:1 PC 18:0_18:1 | C44H86NO8P | 788.61639 | PC | 0.049975 | 1.37514 | 0.710 | 0.47621 | 0.402855 | 0.549 |
| 39 | PC 36:2 PC 18:0_18:2 | C44H84NO8P | 786.60071 | PC | 0.049975 | 0.129804 | 0.517 | 0.036849 | 0.603332 | 0.667 |
| 40 | PC 36:3 PC 16:0_20:3 | C44H82NO8P | 784.58508 | PC | 0.25822 | 0.256825 | 0.544 | 0.12114 | 0.94292 | 0.654 |
| 41 | PC 36:4 PC 16:0_20:4 | C44H80NO8P | 782.5694 | PC | 0.51212 | 0.0189675 | 0.502 | 0.377 | 0.049348 | 0.514 |
| 42 | PC 36:4 PC 18:2_18:2 | C44H80NO8P | 782.5694 | PC | 0.034486 | 0.688094 | 0.664 | 0.000042994 | 1.34042 | 0.854 |
| 43 | PC 36:5 PC 16:0_20:5 | C44H78NO8P | 780.55377 | PC | 0.72028 | 0.474037 | 0.546 | 0.65071 | 0.484758 | 0.514 |
| 44 | PC 36:6 | C44H76NO8P | 778.53809 | PC | 0.21652 | 0.798896 | 0.604 | 0.036411 | 1.24251 | 0.692 |
| 45 | PC 37:2 PC 18:1_19:1 | C45H86NO8P | 800.61639 | PC | 0.45559 | 0.374756 | 0.558 | 0.65957 | 0.141989 | 0.517 |
| 46 | PC 37:6 | C45H78NO8P | 792.55377 | PC | 0.10697 | 0.885707 | 0.639 | 0.04828 | 1.0758 | 0.710 |
| 47 | PC 38:2 | C46H88NO8P | 836.61401 | PC | 0.93273 | 0.20337 | 0.561 | 0.49707 | 0.166121 | 0.504 |
| 48 | PC 38:3 PC 18:0_20:3 | C46H86NO8P | 812.61639 | PC | 0.61017 | 0.537317 | 0.556 | 0.28466 | 1.01933 | 0.644 |
| 49 | PC 38:4 PC 18:0_20:4 | C46H84NO8P | 810.60071 | PC | 0.057973 | 0.604517 | 0.619 | 0.7559 | 0.464577 | 0.586 |
| 50 | PC 38:5 PC 16:0_22:5 | C46H82NO8P | 808.58508 | PC | 0.027012 | 0.885151 | 0.643 | 0.70858 | 0.839523 | 0.619 |
| 51 | PC 38:6 PC 16:0_22:6 | C46H80NO8P | 806.5694 | PC | 0.10697 | 0.393498 | 0.608 | 0.44478 | 0.404371 | 0.647 |
| 53 | PC 38:7 | C46H78NO8P | 804.55377 | PC | 0.10751 | 0.6012 | 0.607 | 0.023985 | 0.973503 | 0.716 |
| 54 | PC 40:3 | C48H90NO8P | 840.64771 | PC | 0.03284 | 0.518565 | 0.659 | 0.15529 | 0.712402 | 0.656 |
| 55 | PC 40:5 | C48H86NO8P | 836.61639 | PC | 0.012156 | 0.773788 | 0.649 | 0.2959 | 0.817348 | 0.649 |
| 56 | PC 40:6 PC 18:0_22:6 | C48H84NO8P | 834.60071 | PC | 0.03284 | 0.732863 | 0.663 | 0.16367 | 0.719783 | 0.703 |
| 57 | PC 40:7 | C48H82NO8P | 832.58508 | PC | 0.049975 | 1.07401 | 0.600 | 0.12659 | 1.29611 | 0.672 |
| 59 | PC 42:8 | C50H84NO8P | 858.60071 | PC | 0.0033254 | 1.47184 | 0.747 | 0.049302 | 1.46965 | 0.732 |
| 60 | PE 34:1 PE 16:0_18:1 | C39H76NO8P | 718.53809 | PE | 0.1865 | 1.98995 | 0.816 | 0.023985 | 1.50987 | 0.785 |
| 61 | PE 34:2 PE 16:0_18:2 | C39H74NO8P | 716.52252 | PE | 0.0021878 | 2.13097 | 0.789 | 0.023985 | 1.24452 | 0.649 |
| 62 | PE 35:1 | C40H78NO8P | 732.55377 | PE | 0.72028 | 0.00401754 | 0.576 | 0.44478 | 0.26545 | 0.622 |
| 63 | PE 36:1 | C41H80NO8P | 746.5694 | PE | 0.0013469 | 2.13882 | 0.836 | 0.014959 | 1.25587 | 0.689 |
| 64 | PE 36:2 PE 18:1_18:1 | C41H78NO8P | 744.55377 | PE | 0.0094713 | 2.11736 | 0.780 | 0.11525 | 1.12754 | 0.598 |
| 65 | PE 36:4 | C41H74NO8P | 740.52252 | PE | 0.0044169 | 2.06769 | 0.811 | 0.015777 | 1.36878 | 0.698 |
| 66 | PE 37:2 | C42H80NO8P | 758.5694 | PE | 0.23914 | 0.0564084 | 0.532 | 0.87882 | 0.352906 | 0.581 |
| 67 | PE 38:2 | C43H82NO8P | 772.58508 | PE | 0.45934 | 0.383227 | 0.522 | 0.65957 | 0.298693 | 0.571 |
| 68 | PE 38:6 | C43H74NO8P | 764.52252 | PE | 0.12449 | 1.38928 | 0.668 | 0.29655 | 0.854962 | 0.563 |
| 69 | PE 40:6 | C45H78NO8P | 792.55377 | PE | 0.1502 | 1.3421 | 0.648 | 0.28466 | 0.861305 | 0.561 |

PE, phosphatidylethanolamine; PC, phosphatidylcholine; LPE, lysophosphatidylethanolamine; LPC, lysophosphatidylcholine; NSCAP, non-severe community acquired pneumonia; SCAP, severe community acquired pneumonia; VIP, variable importance on projection value; FDR, false discovery rate.

Table S9 Areas under the curves (AUCs) and thresholds for ROC analysis (30-day mortality)

| Variable | Threshold | Sensitivity (%) | Specificity (%) | AUC | P value | 95% CI | |
|---------------|-----------------------------|-----------------|-----------------|--------|---------------|-------------------|-------------------|
| CURB65 | >1 | 55.56 | 82.50 | 0.722 | 0.0013 | 0.588 to 0.831 | |
| PSI | >75 | 94.44 | 40.00 | 0.649 | 0.0402 | 0.513 to 0.770 | |
| Lipid groups | PE | >0.2669 | 72.22 | 75.00 | 0.725 | 0.0035 | 0.592 to 0.834 |
| | PC | >-0.2332 | 83.33 | 45.00 | 0.656 | 0.0429 | 0.519 to 0.775 |
| | LPE | ≤0.9095 | 100.00 | 20.00 | 0.560 | 0.4861 | 0.423 to 0.690 |
| | LPC | ≤0.3247 | 100.00 | 50.00 | 0.789 | <0.0001 | 0.662 to 0.885 |
| | PE_CURB65 | >0.2321 | 55.56 | 82.50 | 0.722 | 0.0013 | 0.588 to 0.831 |
| | PC_CURB65 | >0.2469 | 83.33 | 70.00 | 0.811 | <0.0001 | 0.687 to 0.902 |
| | LPE_CURB65 | >0.2321 | 55.56 | 82.50 | 0.722 | 0.0013 | 0.588 to 0.831 |
| | LPC_CURB65 | >0.3984 | 77.78 | 90.00 | 0.854 | <0.0001 | 0.737 to 0.933 |
| | PE_PSI | >0.3337 | 72.22 | 75.00 | 0.725 | 0.0035 | 0.592 to 0.834 |
| | PC_PSI | >0.2597 | 83.33 | 45.00 | 0.656 | 0.0429 | 0.519 to 0.775 |
| | LPE_PSI | >0 | 0.00 | 100 | 0.500 | 1.0000 | 0.366 to 0.634 |
| | LPC_PSI | >0.1682 | 100.00 | 50.00 | 0.789 | <0.0001 | 0.662 to 0.885 |
| | Lipid ratios | PC/LPC | >26.1709 | 100.00 | 50.00 | 0.788 | <0.0001 |
| PE/LPE | | >20.2685 | 94.44 | 47.50 | 0.742 | 0.0004 | 0.610 to 0.848 |
| PC/LPC_CURB65 | | >0.3601 | 77.78 | 90.00 | 0.838 | <0.0001 | 0.717 to 0.921 |
| PE/LPE_CURB65 | | >0.2586 | 77.78 | 75.00 | 0.797 | <0.0001 | 0.671 to 0.891 |
| PC/LPC_PSI | | >0.1914 | 100.00 | 50.00 | 0.788 | <0.0001 | 0.660 to 0.884 |
| PE/LPE_PSI | | >0.2125 | 94.44 | 47.50 | 0.742 | 0.0004 | 0.610 to 0.848 |
| Lipid species | PC 36:4 PC 18:2_18:2 | ≤1.636 | 66.67 | 95.00 | 0.854 | <0.0001 | 0.737 to 0.933 |
| | LPC 18:2/0:0 | ≤0.8014 | 88.89 | 67.50 | 0.819 | <0.0001 | 0.696 to 0.908 |
| | PC 36:4 PC 18:2_18:2_CURB65 | >0.2796 | 94.44 | 77.50 | 0.878 | <0.0001 | 0.765 to 0.949 |
| | LPC 18:2/0:0_CURB65 | >0.4318 | 77.78 | 90.00 | 0.856 | <0.0001 | 0.738 to 0.934 |
| | PC 36:4 PC 18:2_18:2_PSI | >0.5103 | 66.67 | 90.00 | 0.853 | <0.0001 | 0.735 to 0.932 |
| | LPC 18:2/0:0_PSI | >0.3704 | 83.33 | 75.00 | 0.822 | <0.0001 | 0.700 to 0.910 |

ROC analysis, receiver operating characteristic analysis; PE, phosphatidylethanolamine; PC, phosphatidylcholine; LPE, lysophosphatidylethanolamine; LPC, lysophosphatidylcholine; CURB-65, confusion, uremia, respiratory rate, blood pressure, and age ≥65 years old; PSI, pneumonia severity index.

Table S10 Comparisons of ROC curves (30-day mortality)

| Comparison | Standard Error ^a | 95% Confidence Interval | Significance level |
|--|-----------------------------|-------------------------|--------------------|
| Lipid groups | | | |
| LPC vs. CURB65 | 0.0834 | -0.0961 to 0.231 | P=0.4193 |
| LPC vs. PSI | 0.0794 | -0.0161 to 0.295 | P=0.0788 |
| PE vs. CURB65 | 0.102 | -0.197 to 0.204 | P=0.9729 |
| PE vs. PSI | 0.0937 | -0.108 to 0.259 | P=0.4191 |
| PC vs. PSI | 0.0996 | -0.189 to 0.201 | P=0.9500 |
| LPC_CURB65 vs. CURB65 | 0.0498 | 0.0350 to 0.230 | P=0.0078 |
| LPC_CURB65 vs. PSI | 0.0747 | 0.0585 to 0.351 | P=0.0061 |
| PC_CURB65 vs. CURB65 | 0.0412 | 0.00882 to 0.170 | P=0.0297 |
| PC_CURB65 vs. PSI | 0.0815 | 0.00199 to 0.322 | P=0.0472 |
| LPC_PSI vs. CURB65 | 0.0834 | -0.0961 to 0.231 | P=0.4193 |
| LPC_PSI vs. PSI | 0.0794 | -0.0161 to 0.295 | P=0.0788 |
| PE_PSI vs. CURB65 | 0.102 | -0.197 to 0.204 | P=0.9729 |
| PE_PSI vs. PSI | 0.0937 | -0.108 to 0.259 | P=0.4191 |
| Lipid ratios | | | |
| PC/LPC_CURB65 vs. CURB65 | 0.0484 | 0.0211 to 0.211 | P=0.0166 |
| PC/LPC_CURB65 vs. PSI | 0.0787 | 0.0340 to 0.342 | P=0.0167 |
| PE/LPE_CURB65 vs. CURB65 | 0.0407 | -0.00404 to 0.155 | P=0.0628 |
| PE/LPE_CURB65 vs. PSI | 0.0791 | 0.00712 to 0.303 | P=0.0615 |
| PC/LPC_PSI vs. CURB65 | 0.0843 | -0.0993 to 0.231 | P=0.4340 |
| PC/LPC_PSI vs. PSI | 0.0794 | -0.0173 to 0.294 | P=0.0816 |
| PE/LPE_PSI vs. CURB65 | 0.0849 | -0.146 to 0.187 | P=0.8125 |
| PE/LPE_PSI vs. PSI | 0.0867 | -0.0775 to 0.262 | P=0.2865 |
| Lipid species | | | |
| PC 36:4 PC 18:2_18:2 vs. CURB65 | 0.0775 | -0.0193 to 0.285 | P=0.0870 |
| PC 36:4 PC 18:2_18:2 vs. PSI | 0.0824 | 0.0433 to 0.366 | P=0.0130 |
| LPC 18:2/0:0 vs. CURB65 | 0.0724 | -0.0440 to 0.240 | P=0.1764 |
| LPC 18:2/0:0 vs. PSI | 0.0794 | 0.0145 to 0.326 | P=0.0321 |
| PC 36:4 PC 18:2_18:2_CURB65 vs. CURB65 | 0.0528 | 0.0527 to 0.260 | P=0.0031 |
| PC 36:4 PC 18:2_18:2_CURB65 vs. PSI | 0.0787 | 0.0743 to 0.383 | P=0.0037 |
| LPC 18:2/0:0_CURB65 vs. CURB65 | 0.0464 | 0.0431 to 0.225 | P=0.0039 |
| LPC 18:2/0:0_CURB65 vs. PSI | 0.0783 | 0.0528 to 0.360 | P=0.0084 |
| PC 36:4 PC 18:2_18:2_PSI vs. CURB65 | 0.0760 | -0.0176 to 0.280 | P=0.0840 |
| PC 36:4 PC 18:2_18:2_PSI vs. PSI | 0.0751 | 0.0562 to 0.351 | P=0.0068 |
| LPC 18:2/0:0_PSI vs. CURB65 | 0.0692 | -0.0349 to 0.236 | P=0.1457 |
| LPC 18:2/0:0_PSI vs. PSI | 0.0720 | 0.0318 to 0.314 | P=0.0163 |

^a, DeLong *et al.*, 1988. ROC curves, receiver operating characteristic curves; PE, phosphatidylethanolamine; PC, phosphatidylcholine; LPE, lysophosphatidylethanolamine; LPC, lysophosphatidylcholine; CURB-65, confusion, uremia, respiratory rate, blood pressure, and age ≥ 65 years old; PSI, pneumonia severity index.

Table S11 Demographic characteristics of the study population (GEO database)

| Characteristic | Severe CAP (n=108) | Healthy Control (n=42) | P value |
|--------------------------|--------------------|------------------------|------------------|
| Male sex-no. (%) | 63 (58.3) | 24 (57.1) | 1.000 |
| Age years-no. (%) | 63.5 (52,73) | 37 (30, 63.25) | <0.001 |
| 18-29 | 10 (9.3) | 9 (21.4) | <0.001 |
| 30-44 | 5 (4.6) | 15 (35.7) | |
| 45-59 | 21 (19.4) | 4 (9.5) | |
| 60-74 | 48 (44.4) | 10 (23.8) | |
| ≥75 | 24 (22.2) | 4 (9.5) | |
| Diabetes | 25/105 (23.8) | 0 | |
| 28-day mortality-no. (%) | 23/106 (21.7) | 0 | |

Categorical variables are presented as numbers (percentages). Abnormally distributed continuous variables are expressed as medians and interquartile ranges (25th-75th). CAP, community-acquired pneumonia.

Table S12 Demographic characteristics of the study population (qRT-PCR)

| Characteristic | NSCAP (n=5) | SCAP (n=5) | Control (n=5) | P value |
|-----------------------------|----------------------|----------------------|----------------------|---------|
| Male sex-no. (%) | 2 (40) | 2 (40) | 3 (60) | 1.000 |
| Age years | 66.00 (52.50, 72.00) | 51.00 (43.00, 71.50) | 35.00 (34.50, 56.50) | 0.079 |
| Underlying diseases no. (%) | | | | |
| Chronic lung disease | 0 | 1 (20) | 0 | 1.000 |
| Hypertension | 0 | 2 (40) | 0 | 0.286 |
| Diabetes | 1 (20) | 0 | 0 | 1.000 |
| Cardiovascular disease | 1 (20) | 0 | 0 | 1.000 |
| Autoimmune disease | 0 | 0 | 0 | |

Categorical variables are presented as numbers (percentages). Abnormally distributed continuous variables are presented as medians and interquartile ranges (25th-75th). NSCAP, nonsevere community-acquired pneumonia; SCAP, severe community-acquired pneumonia; qRT-PCR, quantitative real-time polymerase chain reaction.

Table S13 Differentially expressed genes involved in the inflammatory response

| SYMBOL | logFC | AveExpr | adj.P.Val | Description |
|----------|--------|---------|-----------|---|
| HP | 5.082 | 7.159 | 1.95E-15 | Haptoglobin |
| MMP8 | 4.307 | 5.515 | 5.90E-07 | Neutrophil collagenase |
| LCN2 | 3.534 | 8.584 | 2.58E-07 | Neutrophil gelatinase-associated lipocalin |
| IL1R2 | 3.338 | 10.014 | 2.04E-15 | Interleukin-1 receptor type 2 |
| VNN1 | 3.002 | 5.433 | 6.49E-14 | Pantetheinase |
| S100A12 | 2.964 | 10.996 | 5.27E-22 | Protein S100-A12 |
| MMP9 | 2.815 | 10.337 | 5.38E-11 | Matrix metalloproteinase-9 |
| TLR5 | 2.795 | 7.041 | 1.24E-15 | Toll-like receptor 5 |
| IL18R1 | 2.611 | 5.293 | 7.33E-13 | Interleukin-18 receptor 1 |
| PGLYRP1 | 2.56 | 5.917 | 4.68E-12 | Peptidoglycan recognition protein 1 |
| LILRA5 | 2.506 | 8.654 | 2.27E-18 | Leukocyte immunoglobulin-like receptor subfamily A member 5 |
| LY96 | 2.415 | 6.824 | 1.28E-09 | Lymphocyte antigen 96 |
| AIM2 | 2.282 | 6.7 | 1.87E-09 | Interferon-inducible protein AIM2 |
| IL18RAP | 2.158 | 6.807 | 1.11E-14 | Interleukin-18 receptor accessory protein |
| PLSCR1 | 2.117 | 7.354 | 4.92E-12 | Phospholipid scramblase 1 |
| MAPK14 | 2.092 | 7.327 | 1.35E-17 | Mitogen-activated protein kinase 14 |
| CD163 | 2.075 | 6.413 | 3.09E-06 | Scavenger receptor cysteine-rich type 1 protein M130 |
| TNFAIP6 | 1.998 | 8.617 | 1.77E-08 | Tumor necrosis factor-inducible gene 6 protein |
| IL1R1 | 1.966 | 6.456 | 1.46E-11 | Interleukin-1 receptor type 1 |
| NAIP | 1.946 | 7.067 | 9.38E-10 | Baculoviral IAP repeat-containing protein 1 |
| SOCS3 | 1.919 | 4.262 | 1.38E-10 | Suppressor of cytokine signaling 3 |
| ADM | 1.907 | 7.33 | 4.90E-12 | Pro-adrenomedullin |
| CST7 | 1.893 | 10.08 | 2.42E-13 | Cystatin-F |
| S100A8 | 1.738 | 12.405 | 8.30E-25 | Protein S100-A8 |
| C3AR1 | 1.699 | 8.244 | 2.71E-08 | C3a anaphylatoxin chemotactic receptor |
| HMGB2 | 1.6 | 5.182 | 1.79E-14 | High mobility group protein B2 |
| CASP5 | 1.582 | 3.847 | 0.00011 | Caspase-5 |
| ORM1 | 1.554 | 4.89 | 1.54E-05 | Alpha-1-acid glycoprotein 1 |
| BCL6 | 1.527 | 9.359 | 1.05E-08 | B-cell lymphoma 6 protein |
| LTB4R | 1.519 | 6.496 | 1.21E-12 | Leukotriene B4 receptor 1 |
| BST1 | 1.485 | 8.365 | 3.37E-10 | ADP-ribosyl cyclase/cyclic ADP-ribose hydrolase 2 |
| PROK2 | 1.483 | 8.874 | 2.71E-05 | Prokineticin-2 |
| FUT7 | 1.473 | 5.539 | 7.06E-09 | Fucosyltransferase 7 |
| NLRC4 | 1.443 | 4.248 | 3.55E-12 | NLR family CARD domain-containing protein 4 |
| JAK2 | 1.441 | 5.047 | 6.77E-07 | Tyrosine-protein kinase JAK2 |
| ANXA1 | 1.42 | 9.231 | 1.27E-08 | Annexin A1 |
| IL1RN | 1.414 | 6.831 | 1.38E-07 | Interleukin-1 receptor antagonist protein |
| ELANE | 1.375 | 4.41 | 0.00755 | Neutrophil elastase |
| SLC11A1 | 1.364 | 5.577 | 1.84E-09 | Natural resistance-associated macrophage protein 1 |
| IL4R | 1.345 | 4.481 | 4.27E-09 | Interleukin-4 receptor subunit alpha |
| MAC1R | 1.27 | 3.717 | 0.000125 | Macrophage immunometabolism regulator |
| ALOX5 | 1.227 | 7.746 | 6.66E-07 | Polyunsaturated fatty acid 5-lipoxygenase |
| TPST1 | 1.213 | 4.649 | 6.73E-05 | Protein-tyrosine sulfotransferase 1 |
| GBA | 1.192 | 5.133 | 4.41E-08 | Lysosomal acid glucosylceramidase |
| PTX3 | 1.19 | 3.208 | 0.000501 | Pentraxin-related protein PTX3 |
| THBS1 | 1.181 | 3.983 | 0.000128 | Thrombospondin-1 |
| TSPAN2 | 1.154 | 5.74 | 0.000181 | Tetraspanin-2 |
| TLR4 | 1.128 | 6.574 | 3.49E-06 | Toll-like receptor 4 |
| PPBP | 1.097 | 10.106 | 0.000378 | Platelet basic protein |
| TLR8 | 1.089 | 7.601 | 3.96E-05 | Toll-like receptor 8 |
| ACER3 | 1.076 | 3.619 | 2.80E-06 | Alkaline ceramidase 3 |
| TLR2 | 1.064 | 7.785 | 2.05E-05 | Toll-like receptor 2 |
| NMI | 1.063 | 7.506 | 7.38E-07 | N-myc-interactor |
| ORM2 | 1.053 | 3.882 | 0.000421 | Alpha-1-acid glycoprotein 2 |
| HGF | 1.027 | 3.071 | 0.001437 | Hepatocyte growth factor |
| P2RX1 | 1.02 | 6.049 | 7.90E-06 | P2X purinoceptor 1 |
| PIK3AP1 | 1.009 | 6.315 | 2.61E-05 | Phosphoinositide 3-kinase adapter protein 1 |
| OSM | 1 | 3.715 | 1.57E-08 | Oncostatin-M |
| PTGDR | -1.006 | 2.44 | 1.12E-12 | Prostaglandin D2 receptor |
| DROSHA | -1.011 | 3.208 | 3.95E-16 | Ribonuclease 3 |
| LIPA | -1.028 | 5.283 | 5.53E-05 | Lysosomal acid lipase/cholesteryl ester hydrolase |
| GPR68 | -1.05 | 3.673 | 1.82E-11 | Ovarian cancer G-protein coupled receptor 1 |
| LY75 | -1.119 | 5.141 | 0.00287 | Lymphocyte antigen 75 |
| MEF2C | -1.135 | 4.538 | 2.53E-07 | Myocyte-specific enhancer Factor 2C |
| PLCG1 | -1.151 | 2.937 | 3.68E-18 | 1-Phosphatidylinositol 4 |
| CCN3 | -1.187 | 2.751 | 1.26E-17 | CCN family member 3 |
| ABCF1 | -1.199 | 4.64 | 1.34E-14 | ATP-binding cassette subfamily F member 1 |
| LY86 | -1.206 | 5.908 | 0.001072 | Lymphocyte antigen 86 |
| STK39 | -1.236 | 4.548 | 2.75E-12 | STE20/SPS1-related proline-alanine-rich protein kinase |
| NLRP1 | -1.247 | 4.439 | 8.56E-07 | NLR Family Pyrin Domain Containing 1 |
| NRROS | -1.248 | 4.257 | 1.66E-12 | Transforming growth factor beta activator LRRC33 |
| NR1D2 | -1.287 | 2.895 | 1.91E-15 | Nuclear receptor subfamily 1 Group D member 2 |
| CCR5 | -1.289 | 3.275 | 1.37E-11 | C-C Chemokine receptor type 5 |
| CCR6 | -1.331 | 2.878 | 3.20E-21 | C-C Chemokine receptor type 6 |
| HNRNPA0 | -1.372 | 5.555 | 6.04E-15 | Heterogeneous nuclear ribonucleoprotein A0 |
| SMAD3 | -1.415 | 3.832 | 1.65E-17 | Mothers against decapentaplegic homolog 3 |
| NFATC3 | -1.484 | 5.639 | 4.90E-12 | Nuclear factor of activated T cells |
| ADA | -1.506 | 4.742 | 2.50E-10 | Adenosine deaminase |
| GATA3 | -1.509 | 3.574 | 9.10E-25 | Trans-acting T cell-specific transcription factor GATA-3 |
| APOL3 | -1.526 | 4.545 | 7.28E-14 | Apolipoprotein L3 |
| CD81 | -1.574 | 5.757 | 2.66E-11 | CD81 antigen |
| ETS1 | -1.576 | 5.657 | 1.58E-13 | Protein C-ets-1 |
| BIRC3 | -1.589 | 4.344 | 2.31E-09 | Baculoviral IAP repeat-containing protein 3 |
| RPS6KA5 | -1.599 | 4.207 | 4.54E-12 | Ribosomal protein S6 kinase alpha-5 |
| CCL5 | -1.672 | 8.963 | 1.40E-08 | C-C Motif chemokine 5 |
| FYN | -1.701 | 6.277 | 6.67E-11 | Tyrosine-protein kinase Fyn |
| BLNK | -1.707 | 3.796 | 1.03E-09 | B cell linker protein |
| LAT | -1.717 | 4.776 | 9.72E-17 | Linker for activation of T cells family member 1 |
| PTGER4 | -1.735 | 6.358 | 2.40E-06 | Prostaglandin E2 receptor EP4 subtype |
| CD96 | -1.737 | 3.368 | 1.07E-24 | T cell surface protein tactile |
| RASGRP1 | -1.754 | 4.195 | 2.67E-21 | RAS guanyl-releasing protein 1 |
| PRKCQ | -1.853 | 3.659 | 4.69E-20 | Protein kinase C theta type |
| CD6 | -1.915 | 3.483 | 9.56E-22 | T cell differentiation antigen CD6 |
| IL23A | -1.989 | 6.113 | 1.61E-14 | Interleukin-23 subunit alpha |
| HLA-DRB1 | -2.259 | 8.675 | 5.65E-11 | HLA class II histocompatibility antigen |
| RORA | -2.262 | 4.003 | 6.67E-16 | Nuclear receptor ROR-alpha |
| NLRC3 | -2.392 | 5.203 | 4.23E-20 | NLR family CARD domain-containing protein 3 |
| CHI3L1 | -2.44 | 6.44 | 2.12E-05 | Chitinase-3-like protein 1 |
| CCR7 | -2.463 | 6.686 | 6.14E-11 | C-C Chemokine receptor type 7 |
| CX3CR1 | -2.494 | 8.461 | 1.14E-09 | CX3C Chemokine receptor 1 |
| KLRG1 | -2.644 | 4.079 | 2.43E-16 | Killer cell lectin-like receptor subfamily G member 1 |
| CCR3 | -3.268 | 4.553 | 1.03E-17 | C-C Chemokine receptor type 3 |