**S8 Table.** **Characteristics of genetic instruments for sphingolipids.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNP** | **Nearest gene** | **Chr** | **Position** | **EA** | **NEA** | **EAF** | **Exposure** | **T2D** |
| **β** | **SE** | ***P*** | ***F*** | **β** | **SE** | ***P*** |
| **Cer(d18:1/20:0)** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| rs76415391 | ***CERS4*** | 19 | 8318959 | T | C | 0.176  | -0.092  | 0.015  | **2.88×10-9** | 38  | -0.007  | 0.023  | 0.770  |
| rs79224144 | *GPR75-ASB3* | 2 | 53996555 | C | T | 0.078  | -0.100  | 0.020  | 1.08×10-6 | 25  | -0.013  | 0.017  | 0.470  |
| rs34192714 | *ATP9B* | 18 | 76958587 | C | T | 0.208  | 0.064  | 0.014  | 3.02×10-6 | 21  | 0.020  | 0.110  | 0.860  |
| rs1896315 | *RP11-411G2.2* | 12 | 115401716 | A | G | 0.248  | -0.058  | 0.012  | 3.64×10-6 | 23  | 0.000  | 0.006  | 0.990  |
| rs36114260 | *MAP6* | 11 | 75394429 | T | C | 0.072  | 0.096  | 0.021  | 3.68×10-6 | 21  | 0.002  | 0.010  | 0.810  |
| rs10054303 | *LOC101929710* | 5 | 95509602 | T | C | 0.259  | 0.058  | 0.012  | 4.30×10-6 | 23  | -0.001  | 0.007  | 0.930  |
| rs12189372 | *RP11-231G15.1* | 5 | 107907196 | C | G | 0.348  | -0.053  | 0.011  | 4.87×10-6 | 23  | -0.001  | 0.007  | 0.940  |
| rs13030314 | *GFPT1* | 2 | 69520795 | A | G | 0.248  | 0.061  | 0.013  | 4.88×10-6 | 22  | -0.011  | 0.006  | 0.085  |
| **Cer(d18:1/20:1)** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| rs11881630 | ***CERS4*** | 19 | 8319455 | T | C | 0.177  | -0.085  | 0.015  | **3.81×10-8** | 32  | -0.007  | 0.023  | 0.760  |
| rs6496103 | *LINC01197* | 15 | 95891921 | C | G | 0.364  | -0.055  | 0.011  | 6.92×10-7 | 25  | -0.015  | 0.008  | 0.045  |
| rs4838314 | *RP11-343J18.2* | 9 | 128796578 | G | T | 0.186  | -0.069  | 0.014  | 7.99×10-7 | 24  | -0.007  | 0.007  | 0.290  |
| rs11017173 | *DOCK1* | 10 | 129095694 | T | C | 0.045  | -0.128  | 0.027  | 2.86×10-6 | 22  | -0.025  | 0.011  | 0.024  |
| rs72897064 | *LRRC4C* | 11 | 40490450 | C | A | 0.138  | 0.073  | 0.016  | 4.00×10-6 | 21  | -0.002  | 0.009  | 0.860  |
| **SM C34:0** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| rs9889726 | ***LASP1*** | 17 | 37047658 | A | G | 0.287  | 0.038  | 0.007  | **1.18****×10-8** | 29  | -0.006  | 0.007  | 0.340  |
| rs1127267 | *ARNT2* | 15 | 80889953 | C | T | 0.122  | 0.044  | 0.009  | 1.76×10-6 | 24  | -0.005  | 0.012  | 0.690  |
| rs61746884 | *NFATC1* | 18 | 77306934 | T | C | 0.018  | -0.101  | 0.022  | 3.56×10-6 | 21  | 0.016  | 0.019  | 0.400  |
| rs11666165 | *IL12RB1* | 19 | 18167463 | A | G | 0.103  | -0.045  | 0.010  | 4.28×10-6 | 20  | -0.004  | 0.008  | 0.610  |
| **SM C36:0** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| rs79371681 | ***LRRC4C*** | 11 | 41434470 | A | C | 0.111  | -0.073  | 0.013  | **4.63×10-8** | 32  | -0.005  | 0.012  | 0.660  |
| rs11881630 | *CERS4* | 19 | 8319455 | T | C | 0.177  | -0.061  | 0.012  | 5.21×10-7 | 26  | -0.007  | 0.023  | 0.760  |
| rs76500530 | *CACHD1* | 1 | 64934264 | T | C | 0.024  | -0.133  | 0.028  | 1.81×10-6 | 23  | 0.009  | 0.022  | 0.700  |
| rs80032050 | *LOC101929147* | 1 | 119765192 | T | G | 0.048  | 0.097  | 0.020  | 1.81×10-6 | 24  | -0.013  | 0.009  | 0.150  |
| rs9889726 | *LASP1* | 17 | 37047658 | A | G | 0.287  | 0.042  | 0.009  | 4.31×10-6 | 22  | -0.006  | 0.007  | 0.340  |
| rs7174883 | *ARNT2* | 15 | 80904460 | A | G | 0.106  | 0.064  | 0.014  | 4.36×10-6 | 21  | -0.130  | 0.069  | 0.061  |

**S8 Table. Continued.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SNP** | **Nearest gene** | **Chr** | **Position** | **EA** | **NEA** | **EAF** | **Exposure** | **T2D** |
| **β** | **SE** | ***P*** | ***F*** | **β** | **SE** | ***P*** |
| **SM C34:1** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| rs72790056 | ***PCDHGA12*** | 5 | 140838943 | A | G | 0.033  | -0.136  | 0.024  | **1.39×10-8** | 32  | -0.015  | 0.019  | 0.430  |
| rs79224144 | *GPR75-ASB3* | 2 | 53996555 | C | T | 0.078  | -0.079  | 0.016  | 1.82×10-6 | 24  | -0.013  | 0.017  | 0.470  |
| rs588136 | *LIPC* | 15 | 58730498 | C | T | 0.358  | 0.043  | 0.009  | 2.49×10-6 | 23  | -0.004  | 0.008  | 0.580  |
| rs2354319 | *LINC00644* | 14 | 62603838 | C | T | 0.362  | 0.041  | 0.009  | 4.78×10-6 | 21  | 0.004  | 0.007  | 0.570  |
| rs73617300 | *CFAP61,C20orf26* | 20 | 20312119 | A | G | 0.239  | -0.046  | 0.010  | 4.92×10-6 | 21  | -0.220  | 0.270  | 0.410  |
| **SM C42:3** |  |  |  |  |  |  |  |  |  |  |  |  |  |
| rs174535 | ***MYRF*** | 11 | 61551356 | C | T | 0.356  | -0.024  | 0.003  | **3.30×10-13** | 64  | -0.028  | 0.007  | <0.001  |
| rs7125097 | *PKNOX2* | 11 | 125192524 | G | A | 0.165  | 0.021  | 0.004  | 1.01×10-6 | 28  | -0.012  | 0.020  | 0.530  |
| rs9785210 | *PLGRKT* | 9 | 5372048 | A | C | 0.378  | 0.016  | 0.003  | 1.14×10-6 | 28  | -0.002  | 0.007  | 0.780  |
| rs501981 | *NTM* | 11 | 131809462 | G | A | 0.050  | -0.035  | 0.007  | 1.58×10-6 | 25  | 0.003  | 0.007  | 0.670  |
| rs11086580 | *RP13-379L11.3* | 20 | 55478973 | C | T | 0.495  | -0.015  | 0.003  | 2.13×10-6 | 25  | -0.013  | 0.006  | 0.050  |
| rs111791140 | *AMN1* | 12 | 31858972 | T | C | 0.010  | 0.075  | 0.016  | 2.29×10-6 | 22  | 0.002  | 0.013  | 0.890  |
| rs2359181 | *RNU6-443P* | 18 | 41315375 | G | A | 0.084  | 0.027  | 0.006  | 3.63×10-6 | 20  | 0.580  | 0.350  | 0.094  |
| rs9822399 | *LMCD1-AS1* | 3 | 8388333 | A | G | 0.192  | 0.020  | 0.004  | 4.35×10-6 | 25  | -0.003  | 0.006  | 0.630  |
| **HexCer(18:1/20:1)** |  |  |  |  |  |  |  |  |  |  |  |  |
| rs13106043 | ***ATP10D*** | 4 | 47561141 | A | G | 0.234  | -0.093  | 0.014  | **1.03×10-10** | 44  | 0.001  | 0.006  | 0.830  |
| rs2648408 | *LHFPL4* | 3 | 9579609 | T | C | 0.015  | 0.233  | 0.048  | 1.24×10-6 | 24  | -0.003  | 0.013  | 0.820  |
| rs11339221 | *CDC14A* | 1 | 100826655 | T | A | 0.090  | 0.101  | 0.022  | 3.31×10-6 | 21  | 0.080  | 0.390  | 0.840  |
| rs151140560 | *CAMKMT* | 2 | 44754503 | T | C | 0.108  | 0.093  | 0.020  | 3.35×10-6 | 22  | 0.023  | 0.036  | 0.530  |
| rs16954224 | *RNU6-745P* | 15 | 70481307 | T | C | 0.273  | -0.069  | 0.015  | 3.36×10-6 | 21  | -0.005  | 0.008  | 0.490  |
| rs10411408 | *FAM90A28P* | 19 | 53808016 | T | C | 0.036  | 0.161  | 0.035  | 3.76×10-6 | 21  | 0.018  | 0.019  | 0.320  |
| rs899437 | *EMP1* | 12 | 13428022 | C | T | 0.460  | 0.057  | 0.012  | 4.22×10-6 | 23  | 0.002  | 0.007  | 0.740  |

Data are based on genome-wide significant SNPs using linear regression analysis under an additive genetic model, adjusted for age, sex, region (Beijing or Shanghai), and the first four principal components (PCs) (*n* = 1,976). Data source: diabetes case (*n* = 748)-control (*n* = 4,983) study based on the China Health and Nutrition Survey (CHNS).

Chr, chromosome; Cer, ceramide; EA, effect allele; EAF, effect allele frequency; HexCer, hexosylceramide; NEA, non-effect allele; SE, standard error; SNP, single nucleotide polymorphism; SM, sphingomyelin; SM (OH), hydroxyl-sphingomyelin with 1 additional hydroxyl; SM (2OH), hydroxyl-sphingomyelin with 2 additional hydroxyls; T2D, type 2 diabetes.