Supplemental Table 1. Top 65 associated SNP pairs.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| SNP1 | SNP2 | GENEVA |  | IPM |  | Combined*P*a |
| OR | *P* |  | OR | *P* |  |
| rs4947941 | rs7785013 | 0.914 | 9.41E-07 |  | 0.851 | 1.61E-04 |  | 3.97E-09 |
| rs729715 | rs797518 | 1.168 | 1.37E-06 |  | 1.152 | 8.34E-02 |  | 2.90E-07 |
| rs12668947 | rs10240204 | 0.867 | 2.94E-06 |  | 0.900 | 1.58E-01 |  | 1.07E-06 |
| rs7108496 | rs4298915 | 0.868 | 6.96E-07 |  | 0.981 | 7.17E-01 |  | 1.62E-06 |
| rs16854403 | rs7652606 | 1.186 | 1.72E-06 |  | NA | NA |  | 1.72E-06 |
| rs17377867 | rs2289843 | 0.852 | 9.02E-06 |  | 0.895 | 1.99E-01 |  | 3.96E-06 |
| rs2741366 | rs6022643 | 0.875 | 4.22E-07 |  | 1.041 | 5.63E-01 |  | 4.85E-06 |
| rs17193049 | rs11624333 | 1.140 | 2.27E-05 |  | 1.132 | 1.01E-01 |  | 5.58E-06 |
| rs895394 | rs660721 | 1.064 | 6.54E-06 |  | NA | NA |  | 6.54E-06 |
| rs17193049 | rs17828907 | 1.148 | 6.66E-06 |  | NA | NA |  | 6.66E-06 |
| rs2754820 | rs13200680 | 0.851 | 1.75E-05 |  | 0.894 | 1.89E-01 |  | 7.23E-06 |
| rs6856354 | rs11100039 | 1.097 | 2.71E-06 |  | 0.999 | 9.88E-01 |  | 1.01E-05 |
| rs12481033 | rs3843773 | 1.121 | 3.91E-05 |  | 1.104 | 1.11E-01 |  | 1.04E-05 |
| rs4978374 | rs2439649 | 0.937 | 3.59E-05 |  | 0.952 | 1.44E-01 |  | 1.17E-05 |
| rs12928191 | rs7201173 | 1.145 | 4.16E-06 |  | 1.009 | 8.96E-01 |  | 1.19E-05 |
| rs9484785 | rs12528289 | 0.925 | 3.21E-05 |  | 0.945 | 1.75E-01 |  | 1.23E-05 |
| rs1078868 | rs619429 | 0.934 | 1.25E-05 |  | NA | NA |  | 1.25E-05 |
| rs9676784 | rs12608562 | 1.089 | 1.69E-05 |  | 1.038 | 3.47E-01 |  | 1.25E-05 |
| rs2371864 | rs2036072 | 1.075 | 1.35E-05 |  | NA | NA |  | 1.35E-05 |
| rs12554508 | rs10974470 | 1.091 | 1.42E-05 |  | NA | NA |  | 1.42E-05 |
| rs13270346 | rs17740942 | 1.099 | 1.66E-05 |  | NA | NA |  | 1.66E-05 |
| rs4376484 | rs7015740 | 0.939 | 1.72E-05 |  | NA | NA |  | 1.72E-05 |
| rs7494050 | rs12101174 | 0.897 | 2.04E-05 |  | NA | NA |  | 2.04E-05 |
| rs17149180 | rs17819187 | 1.195 | 2.86E-05 |  | 1.069 | 3.58E-01 |  | 2.14E-05 |
| rs4472929 | rs11021956 | 1.114 | 2.08E-05 |  | 1.050 | 4.75E-01 |  | 2.14E-05 |
| rs16875546 | rs2281449 | 1.130 | 1.00E-05 |  | 1.014 | 8.16E-01 |  | 2.25E-05 |
| rs658854 | rs6134038 | 0.932 | 2.43E-05 |  | 0.972 | 4.50E-01 |  | 2.34E-05 |
| rs2684289 | rs9283561 | 1.133 | 3.01E-05 |  | NA | NA |  | 3.01E-05 |
| rs7552202 | rs2805452 | 0.934 | 3.08E-05 |  | NA | NA |  | 3.08E-05 |
| rs1055640 | rs10742177 | 0.924 | 1.85E-06 |  | 1.037 | 3.05E-01 |  | 3.35E-05 |
| rs917880 | rs7788786 | 1.092 | 3.38E-05 |  | NA | NA |  | 3.38E-05 |
| rs6808352 | rs2686315 | 1.141 | 3.41E-05 |  | NA | NA |  | 3.41E-05 |
| rs12429883 | rs3794376 | 0.914 | 2.84E-05 |  | 0.972 | 5.60E-01 |  | 3.49E-05 |
| rs12545416 | rs6988366 | 1.069 | 1.11E-05 |  | 0.998 | 9.60E-01 |  | 3.75E-05 |
| rs11062544 | rs10491966 | 0.876 | 4.39E-06 |  | 1.040 | 5.13E-01 |  | 4.02E-05 |
| rs10505743 | rs4764187 | 0.873 | 4.19E-05 |  | NA | NA |  | 4.19E-05 |
| rs4833421 | rs29319 | 0.914 | 4.14E-05 |  | 0.965 | 4.84E-01 |  | 4.19E-05 |
| rs2815122 | rs11961538 | 1.068 | 4.59E-06 |  | 0.972 | 4.04E-01 |  | 5.42E-05 |
| rs17610159 | rs997264 | 0.837 | 3.07E-05 |  | 0.964 | 7.90E-01 |  | 5.91E-05 |
| rs17813455 | rs10879039 | 1.085 | 4.29E-05 |  | 1.019 | 6.57E-01 |  | 6.25E-05 |
| rs1528198 | rs13325751 | 0.909 | 3.64E-05 |  | 0.986 | 8.01E-01 |  | 7.05E-05 |
| rs41377246 | rs4951095 | 0.907 | 1.93E-05 |  | 1.009 | 8.56E-01 |  | 7.37E-05 |
| rs10869704 | rs927632 | 1.079 | 1.98E-05 |  | 0.993 | 8.54E-01 |  | 7.57E-05 |
| rs251412 | rs875214 | 1.167 | 3.55E-05 |  | 1.013 | 8.57E-01 |  | 7.63E-05 |
| rs17698379 | rs4234669 | 0.902 | 2.68E-06 |  | 1.069 | 1.55E-01 |  | 7.99E-05 |
| rs17825727 | rs2929576 | 0.879 | 1.99E-05 |  | 1.018 | 8.19E-01 |  | 8.10E-05 |
| rs11914507 | rs10490792 | 0.840 | 3.39E-06 |  | 1.122 | 1.75E-01 |  | 8.80E-05 |
| rs12595780 | rs10520750 | 0.918 | 1.30E-05 |  | 1.025 | 5.71E-01 |  | 8.93E-05 |
| rs12149938 | rs12446064 | 0.909 | 3.79E-05 |  | 0.997 | 9.53E-01 |  | 9.59E-05 |
| rs9844784 | rs4234669 | 0.909 | 5.88E-06 |  | 1.054 | 2.46E-01 |  | 1.05E-04 |
| rs10977624 | rs7049205 | 1.107 | 2.41E-05 |  | 0.979 | 6.92E-01 |  | 1.21E-04 |
| rs2035546 | rs7973136 | 0.924 | 2.57E-05 |  | 1.015 | 7.09E-01 |  | 1.23E-04 |
| rs6112589 | rs200184 | 0.928 | 2.92E-05 |  | 1.012 | 7.54E-01 |  | 1.27E-04 |
| rs9881055 | rs4858379 | 1.099 | 2.11E-05 |  | 0.975 | 5.75E-01 |  | 1.35E-04 |
| rs12128325 | rs1002480 | 1.076 | 2.90E-05 |  | 0.985 | 6.88E-01 |  | 1.42E-04 |
| rs11087123 | rs1233744 | 0.928 | 5.64E-05 |  | 1.001 | 9.89E-01 |  | 1.51E-04 |
| rs221293 | rs9654709 | 1.073 | 2.54E-05 |  | 0.981 | 5.95E-01 |  | 1.51E-04 |
| rs12360734 | rs11234251 | 0.889 | 4.95E-05 |  | 1.006 | 9.18E-01 |  | 1.52E-04 |
| rs1316257 | rs10803338 | 1.083 | 2.10E-05 |  | 0.973 | 4.74E-01 |  | 1.65E-04 |
| rs10452272 | rs17054576 | 0.915 | 4.22E-05 |  | 1.038 | 4.63E-01 |  | 3.05E-04 |
| rs7973972 | rs2082529 | 0.880 | 3.11E-05 |  | 1.075 | 1.94E-01 |  | 4.86E-04 |
| rs4904516 | rs10132162 | 0.928 | 4.12E-05 |  | 1.051 | 1.64E-01 |  | 6.84E-04 |
| rs7973972 | rs12823670 | 0.880 | 4.10E-05 |  | 1.086 | 1.44E-01 |  | 7.44E-04 |
| rs10508964 | rs11815205 | 0.906 | 1.28E-05 |  | 1.110 | 2.28E-02 |  | 8.19E-04 |
| rs428321 | rs7652606 | 1.171 | 4.15E-05 |  | 0.866 | 1.12E-01 |  | 8.74E-04 |

Note: OR, odds ratio; GENEVA, Gene Environment Association Studies initiative in Type 2 Diabetes; IPM, Biobank Program of the Institute of Personalized Medicine. aMeta-analyses results by using two GWAS samples.

Supplemental Table 2. The association between all EGFR polymorphisms and T2D.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| SNP | GENEVA |  | IPM | Combined *P*a |
| OR | *P* |  | OR | *P* |
| rs10244108 | 0.976 | 0.016 |  | 0.959 | 0.063 | 0.004 |
| rs2110290 | 1.022 | 0.026 |  | 1.027 | 0.235 | 0.013 |
| rs11487218 | 0.980 | 0.040 |  | 0.969 | 0.157 | 0.016 |
| rs12671550 | 1.020 | 0.043 |  | 1.035 | 0.135 | 0.016 |
| rs845558 | 1.021 | 0.032 |  | 1.015 | 0.463 | 0.024 |
| rs6978771 | 1.023 | 0.038 |  | 1.015 | 0.526 | 0.030 |
| rs12668421 | 1.021 | 0.051 |  | 1.018 | 0.448 | 0.036 |
| rs6947594 | 1.028 | 0.049 |  | 1.018 | 0.563 | 0.040 |
| rs7796139 | 0.983 | 0.117 |  | 0.968 | 0.155 | 0.051 |
| rs17172446 | 0.977 | 0.043 |  | 1.003 | 0.899 | 0.063 |
| rs883117 | 0.963 | 0.054 |  | 0.995 | 0.904 | 0.064 |
| rs12666347 | 1.014 | 0.171 |  | 1.036 | 0.113 | 0.069 |
| rs10234806 | 0.988 | 0.286 |  | 0.948 | 0.019 | 0.073 |
| rs13234622 | 1.014 | 0.154 |  | 1.027 | 0.207 | 0.078 |
| rs17746476 | 0.966 | 0.071 |  | 0.995 | 0.904 | 0.082 |
| rs11975042 | 0.966 | 0.070 |  | 0.997 | 0.943 | 0.083 |
| rs4947986 | 1.018 | 0.093 |  | 1.010 | 0.673 | 0.084 |
| rs845552 | 1.012 | 0.188 |  | 1.028 | 0.168 | 0.088 |
| rs2877260 | 0.986 | 0.184 |  | 0.973 | 0.233 | 0.099 |
| rs845559 | 1.021 | 0.117 |  | NA | NA | 0.117 |
| rs9642391 | NA | NA |  | 0.966 | 0.119 | 0.119 |
| rs1107617 | 0.972 | 0.081 |  | 1.010 | 0.772 | 0.122 |
| rs6593210 | NA | NA |  | 0.967 | 0.150 | 0.150 |
| rs11238349 | NA | NA |  | 1.031 | 0.159 | 0.159 |
| rs10488143 | 0.984 | 0.440 |  | 0.921 | 0.048 | 0.165 |
| rs6954351 | 0.989 | 0.396 |  | 0.954 | 0.084 | 0.168 |
| rs4947984 | 0.987 | 0.487 |  | 0.934 | 0.056 | 0.194 |
| rs1107616 | NA | NA |  | 1.034 | 0.201 | 0.201 |
| rs7801956 | 0.980 | 0.221 |  | NA | NA | 0.221 |
| rs17518446 | 0.989 | 0.450 |  | 0.958 | 0.195 | 0.251 |
| rs11976696 | 0.979 | 0.063 |  | 1.046 | 0.070 | 0.252 |
| rs6593211 | NA | NA |  | 1.028 | 0.261 | 0.261 |
| rs7786831 | 0.992 | 0.609 |  | 0.943 | 0.075 | 0.280 |
| rs35891645 | 0.982 | 0.137 |  | 1.025 | 0.326 | 0.283 |
| rs10280515 | 1.028 | 0.130 |  | 0.959 | 0.276 | 0.289 |
| rs11977660 | 1.010 | 0.294 |  | NA | NA | 0.294 |
| rs763317 | 0.991 | 0.363 |  | 0.989 | 0.581 | 0.297 |
| rs17172432 | 1.014 | 0.247 |  | 0.992 | 0.747 | 0.326 |
| rs917880 | 0.991 | 0.342 |  | 0.961 | 0.124 | 0.342 |
| rs7809332 | 0.986 | 0.219 |  | 1.016 | 0.523 | 0.346 |
| rs11760524 | 1.011 | 0.420 |  | 1.015 | 0.590 | 0.347 |
| rs6948867 | NA | NA |  | 1.023 | 0.367 | 0.367 |
| rs10488140 | 1.013 | 0.312 |  | 0.995 | 0.853 | 0.373 |
| rs7804688 | 1.013 | 0.403 |  | 1.009 | 0.768 | 0.375 |
| rs12534147 | 1.010 | 0.285 |  | 0.992 | 0.695 | 0.381 |
| rs4947963 | 1.008 | 0.453 |  | 1.010 | 0.639 | 0.387 |
| rs1997083 | 0.980 | 0.143 |  | 1.054 | 0.124 | 0.388 |
| rs11770506 | 1.008 | 0.455 |  | 1.010 | 0.647 | 0.392 |
| rs7783970 | 0.995 | 0.570 |  | 0.983 | 0.400 | 0.413 |
| rs759169 | 0.989 | 0.416 |  | NA | NA | 0.416 |
| rs12535328 | 1.010 | 0.316 |  | 0.991 | 0.657 | 0.426 |
| rs2241055 | 0.998 | 0.856 |  | 0.963 | 0.066 | 0.431 |
| rs13244925 | 0.994 | 0.519 |  | 0.991 | 0.664 | 0.451 |
| rs35699152 | 0.987 | 0.278 |  | 1.021 | 0.406 | 0.457 |
| rs12718947 | 1.008 | 0.466 |  | NA | NA | 0.466 |
| rs759166 | 0.986 | 0.230 |  | 1.032 | 0.218 | 0.474 |
| rs12718939 | 0.983 | 0.083 |  | 1.065 | 0.005 | 0.485 |
| rs883118 | 1.007 | 0.495 |  | NA | NA | 0.495 |
| rs17746482 | 0.989 | 0.460 |  | 1.004 | 0.891 | 0.516 |
| rs10229932 | 0.992 | 0.617 |  | 0.986 | 0.672 | 0.539 |
| rs759162 | 1.006 | 0.563 |  | 1.004 | 0.869 | 0.548 |
| rs3823585 | 1.005 | 0.625 |  | 1.009 | 0.685 | 0.550 |
| rs1558544 | 1.007 | 0.540 |  | 1.001 | 0.972 | 0.555 |
| rs17586344 | 0.987 | 0.299 |  | 1.039 | 0.235 | 0.562 |
| rs41324647 | 0.985 | 0.315 |  | 1.050 | 0.199 | 0.607 |
| rs6960438 | 0.988 | 0.295 |  | 1.037 | 0.157 | 0.610 |
| rs980653 | 0.996 | 0.758 |  | 0.983 | 0.538 | 0.619 |
| rs2072454 | 1.000 | 0.992 |  | 0.972 | 0.175 | 0.642 |
| rs2740764 | 1.005 | 0.642 |  | NA | NA | 0.642 |
| rs12538489 | 1.014 | 0.306 |  | 0.955 | 0.123 | 0.654 |
| rs17586365 | 1.006 | 0.658 |  | NA | NA | 0.658 |
| rs10488142 | 1.009 | 0.552 |  | 0.990 | 0.727 | 0.658 |
| rs2075109 | 1.000 | 0.964 |  | 0.972 | 0.163 | 0.670 |
| rs11771471 | 1.001 | 0.934 |  | 1.018 | 0.397 | 0.717 |
| rs11536635 | 1.004 | 0.719 |  | NA | NA | 0.719 |
| rs2075110 | 1.001 | 0.930 |  | 0.973 | 0.190 | 0.721 |
| rs12535226 | 1.007 | 0.461 |  | 0.978 | 0.270 | 0.746 |
| rs11982525 | 0.993 | 0.568 |  | 1.018 | 0.520 | 0.747 |
| rs10277413 | 1.003 | 0.730 |  | 0.962 | 0.057 | 0.754 |
| rs759167 | 0.992 | 0.465 |  | 1.029 | 0.255 | 0.760 |
| rs7809028 | 0.991 | 0.546 |  | 1.031 | 0.407 | 0.772 |
| rs729969 | 1.010 | 0.463 |  | 0.962 | 0.218 | 0.781 |
| rs11506105 | 1.004 | 0.665 |  | 0.991 | 0.662 | 0.794 |
| rs2877261 | 1.000 | 0.999 |  | 1.016 | 0.450 | 0.799 |
| rs11767730 | 1.006 | 0.588 |  | 0.983 | 0.436 | 0.804 |
| rs1525643 | 1.007 | 0.504 |  | 0.975 | 0.250 | 0.808 |
| rs4140770 | 0.995 | 0.585 |  | 1.019 | 0.368 | 0.832 |
| rs7795743 | 0.999 | 0.912 |  | 1.020 | 0.370 | 0.845 |
| rs17172438 | 1.006 | 0.623 |  | 0.974 | 0.356 | 0.878 |
| rs7795728 | 0.999 | 0.889 |  | NA | NA | 0.889 |
| rs1534130 | 1.002 | 0.894 |  | NA | NA | 0.894 |
| rs7781264 | 1.002 | 0.826 |  | 0.980 | 0.370 | 0.926 |
| rs2293347 | 0.994 | 0.692 |  | 1.034 | 0.401 | 0.927 |
| rs759170 | 1.004 | 0.761 |  | 0.982 | 0.544 | 0.933 |
| rs940806 | 1.004 | 0.680 |  | 0.981 | 0.354 | 0.938 |
| rs868254 | 1.003 | 0.773 |  | 0.988 | 0.555 | 0.941 |
| rs6970262 | 1.003 | 0.769 |  | 0.980 | 0.331 | 0.960 |
| rs11768038 | 1.004 | 0.726 |  | 0.978 | 0.287 | 0.978 |
| rs7785013 | 1.003 | 0.830 |  | 0.982 | 0.541 | 0.998 |

Note: OR, odds ratio; GENEVA, Gene Environment Association Studies initiative in Type 2 Diabetes; IPM, Biobank Program of the Institute of Personalized Medicine. aMeta-analyses results by using two GWAS samples.

Supplemental Table 3. The interaction effects of the previously identified SNP pairs.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| SNP1 | SNP2 | D' | GENEVA |  | IPM | Combined *Pa* |
| OR (95% CI) | *P* |  | OR (95% CI) | *P* |
| rs7991210 | rs4772265 | 0.96 | 0.95 (0.92-0.98) | 0.0018 |  | 0.97 (0.90-1.04) | 0.41 | 0.0013 |
| rs4772268 | 0.76 | 1.05 (1.02-1.08) | 0.0038 |  | 0.95 (0.89-1.02) | 0.12 | 0.0264 |

Note: SNP2, SNPs that in linkage disequilibrium (LD) with previously identified promoter SNP (rs3742250); D’, coefficient of LD between SNP2 and rs3742250 in 1000 Genomes Phase 3. aMeta-analyses results by using two GWAS samples.