|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Supplemental Table 1. Summary of MAPK genes evaluated | | | | |  |  |  |  |  |  |
|  |  |  | Chromosome Location |  |  | Major/Minor Allele | MAF | | FDR HWE *p* | |
| Pathway | Gene | Alias | tagSNP | Coordinate | NHW | HISP/NA | NHW | HISP/NA |
| DUSP | *DUSP4* | *HVH2* | 8p12-p11 | rs12540995 | 29197529 | C/T | 0.25 | 0.47 | 0.86 | **0.01** |
|  |  | *MKP-2* |  | rs2341674 | 29198256 | C/T | 0.16 | 0.17 | 0.96 | 1.00 |
|  |  | *MKP2* |  | rs3824133 | 29199062 | A/G | 0.22 | 0.46 | 0.78 | **0.001** |
|  |  | *TYP* |  | rs2056025 | 29199556 | T/G | 0.12 | 0.16 | 0.94 | 0.87 |
|  |  |  |  | rs567436 | 29202050 | A/T | 0.23 | 0.48 | 0.96 | **0.004** |
|  |  |  |  | rs474824 | 29206790 | C/T | 0.64 | 0.35 | 0.99 | **0.0002** |
|  | *DUSP6* | *MKP3, PYST1* | 12q22-q23 | rs10744 | 89741904 | A/T | 0.20 | 0.23 | 0.96 | 0.82 |
|  |  |  |  |  |  |  |  |  |  |  |
| ERK | *MAPK1* | *ERK, ERK2* | 22q11.21 | rs17759598 | 22122149 | T/C | 0.14 | 0.09 | 0.96 | 0.25 |
|  |  | *ERT1, MAPK2* |  | rs2298432 | 22123189 | C/A | 0.37 | 0.25 | 0.96 | 0.73 |
|  |  | *P42MAPK, PRKM1* |  | rs743409 | 22129215 | C/T | 0.48 | 0.34 | 0.96 | 1.00 |
|  |  | *PRKM2, p38p40,* |  | rs9610375 | 22187093 | G/T | 0.48 | 0.37 | 0.89 | 0.53 |
|  |  | *p41, p41mapk* |  | rs8136867 | 22204793 | A/G | 0.46 | 0.40 | 0.93 | 0.68 |
|  |  |  |  | rs9610470 | 22209139 | T/C | 0.25 | 0.15 | 0.96 | 0.98 |
|  | *MAPK3* | *ERK1, HS44KDAP* | 16p11.2 | rs7698 | 30125800 | C/T | 0.08 | 0.07 | 0.96 | 0.83 |
|  |  | *HUMKER1A, MGC20180, P44ERK1, P44MAPK, PRKM3* | | | |  |  |  |  |  |
|  | *MAP2K1* | *MAPKK1* | 15q22.1-q22.33 | rs1549854 | 66696735 | G/T | 0.50 | 0.41 | 1.00 | 0.68 |
|  |  | *MEK1* |  | rs891848 | 66698172 | C/T | 0.15 | 0.14 | 0.96 | 0.95 |
|  |  | *MKK1* |  | rs1432442 | 66719269 | G/A | 0.08 | 0.16 | 0.97 | 0.65 |
|  |  | *PRKMK1* |  | rs11637556 | 66728951 | A/C | 0.26 | 0.14 | 0.98 | 0.98 |
|  |  |  |  | rs7181936 | 66747909 | G/T | 0.35 | 0.44 | 0.96 | 0.70 |
|  |  |  |  | rs8039880 | 66760342 | A/G | 0.17 | 0.22 | 0.62 | 0.74 |
|  | *MAP3K2* | *MEKK2* | 2q14.3 | rs3732209 | 128079806 | T/C | 0.31 | 0.17 | 0.96 | 0.96 |
|  |  | *MEKK2B* |  | rs12613413 | 128086354 | T/C | 0.21 | 0.13 | 0.99 | 0.68 |
|  |  |  |  | rs6732279 | 128089540 | T/G | 0.62 | 0.37 | 0.96 | 0.24 |
|  |  |  |  |  |  |  |  |  |  |  |
| **JNK** | *MAPK8* | *JNK, JNK1* | 10q11.22 | rs10857565 | 49619793 | G/A | 0.24 | 0.14 | 0.96 | 0.07 |
|  |  | *JNK1A2, JNK21B1/2* |  | rs10508901 | 49627398 | C/A | 0.35 | 0.19 | 1.00 | 0.14 |
|  |  | *PRKM8, SAPK1* |  | rs11101320 | 49642146 | G/A | 0.43 | 0.47 | 0.96 | 0.71 |
|  |  |  |  | rs4838590 | 49642591 | C/A | 0.44 | 0.47 | 0.96 | 0.77 |
|  | *MAP3K1 \** | *MAPKKK1* | 5q11.2 | rs889312 | 56031884 | A/C | 0.29 | 0.43 | 0.86 | 0.30 |
|  |  | *MEKK* |  | rs16886403 | 56139246 | T/C | 0.12 | 0.16 | 0.96 | 0.51 |
|  |  | *MEKK1* |  | rs43184 | 56141777 | C/G | 0.17 | 0.38 | 0.93 | 0.73 |
|  |  |  |  | rs33330 | 56145997 | G/A | 0.35 | 0.18 | 1.00 | 0.85 |
|  |  |  |  | rs832575 | 56161787 | A/G | 0.12 | 0.28 | 0.49 | 0.71 |
|  |  |  |  | rs2548663 | 56172778 | A/G | 0.29 | 0.55 | 0.84 | 0.21 |
|  |  |  |  | rs33323 | 56175566 | C/G | 0.64 | 0.36 | 0.68 | 0.15 |
|  | *MAP3K3 \** | *MAPKKK3* | 17q23.3 | rs11658329 | 61763031 | G/C | 0.28 | 0.23 | 0.96 | 0.93 |
|  |  | *MEKK3* |  | rs3785574 | 61763185 | A/G | 0.30 | 0.36 | 0.96 | 0.81 |
|  | *MAP3K7 \** | *TAK1* | 6q16.1-q16.3 | rs205342 | 91229445 | A/G | 0.29 | 0.44 | 0.99 | 0.02 |
|  |  | *TGF1a* |  | rs711267 | 91235728 | A/G | 0.28 | 0.15 | 0.97 | 0.09 |
|  |  |  |  | rs13208824 | 91244729 | C/A | 0.14 | 0.05 | 0.96 | 0.65 |
|  |  |  |  | rs1144159 | 91247700 | T/C | 0.15 | 0.08 | 0.96 | 0.03 |
|  |  |  |  | rs3799912 | 91248743 | A/G | 0.12 | 0.06 | 0.96 | 0.27 |
|  |  |  |  | rs150117 | 91268349 | A/T | 0.32 | 0.30 | 0.96 | 0.75 |
|  | *MAP3K9* | *MLK1* | 14q24.3-q31 | rs11625206 | 71194153 | C/T | 0.35 | 0.34 | 0.96 | 0.41 |
|  |  | *PRKE1* |  | rs11844774 | 71198551 | T/C | 0.41 | 0.46 | 0.97 | 0.42 |
|  |  |  |  | rs8010714 | 71204165 | C/G | 0.41 | 0.48 | 0.96 | 0.28 |
|  |  |  |  | rs11628333 | 71205727 | T/C | 0.37 | 0.40 | 0.98 | 0.41 |
|  |  |  |  | rs10483834 | 71212158 | A/G | 0.23 | 0.13 | 0.98 | 0.28 |
|  |  |  |  | rs8011507 | 71213086 | A/G | 0.14 | 0.13 | 0.96 | 0.61 |
|  |  |  |  | rs11622989 | 71217013 | C/T | 0.49 | 0.45 | 0.93 | 0.80 |
|  |  |  |  | rs17176971 | 71234395 | G/A | 0.20 | 0.20 | 0.96 | 0.74 |
|  |  |  |  | rs12883244 | 71246386 | C/T | 0.52 | 0.47 | 0.96 | 0.95 |
|  |  |  |  | rs11158881 | 71248229 | T/C | 0.24 | 0.30 | 0.98 | 0.68 |
|  |  |  |  | rs4902854 | 71248391 | C/T | 0.40 | 0.29 | 0.96 | **0.01** |
|  |  |  |  | rs1034769 | 71254698 | T/G | 0.11 | 0.12 | 0.98 | 0.45 |
|  |  |  |  | rs4902855 | 71254954 | C/T | 0.44 | 0.42 | 0.96 | 0.93 |
|  |  |  |  | rs12590049 | 71256367 | G/A | 0.28 | 0.17 | 0.96 | 0.13 |
|  |  |  |  | rs10143031 | 71260091 | C/T | 0.48 | 0.48 | 0.97 | 0.85 |
|  |  |  |  | rs17108548 | 71260307 | T/C | 0.17 | 0.26 | 0.96 | 0.17 |
|  |  |  |  | rs17766621 | 71262932 | T/C | 0.35 | 0.26 | 0.86 | 0.12 |
|  |  |  |  | rs8022269 | 71266779 | G/A | 0.41 | 0.44 | 0.96 | 1.00 |
|  |  |  |  | rs11624934 | 71266922 | A/G | 0.33 | 0.38 | 0.96 | 0.62 |
|  |  |  |  |  |  |  |  |  |  |  |
| p38 | *MAPK12* | *ERK3, ERK6, P38GAMMA* | 22q13.33 | rs742184 | 50697119 | C/T | 0.30 | 0.40 | 0.96 | 0.95 |
|  |  | *PRKM12, SAPK-3, SAPK3* |  | rs2272857 | 50699668 | G/A | 0.22 | 0.26 | 0.96 | 0.66 |
|  | *MAPK14* | *RP1-179N16.5* | 6p21.3-p21.2 | rs13196204 | 35998776 | T/G | 0.17 | 0.09 | 1.00 | 0.02 |
|  |  | *CSBP1, CSBP2, CSPB1* |  | rs10807156 | 36004859 | T/A | 0.20 | 0.44 | 0.96 | 0.02 |
|  |  | *EXIP, Mxi2* |  | rs3804454 | 36006998 | A/C | 0.20 | 0.15 | 0.90 | 0.43 |
|  |  | *PRKM14, PRKM15RK* |  | rs17714205 | 36019336 | C/T | 0.10 | 0.09 | 0.96 | 0.24 |
|  |  | *SAPK2A* |  | rs3730327 | 36027142 | A/G | 0.10 | 0.06 | 0.89 | 1.00 |
|  |  | *p38, p38ALPHA* |  | rs851011 | 36037983 | T/C | 0.15 | 0.07 | 0.96 | 0.99 |
|  |  |  |  | rs851010 | 36041431 | T/C | 0.53 | 0.40 | 0.96 | 0.53 |
|  |  |  |  | rs851006 | 36065185 | G/A | 0.26 | 0.16 | 0.99 | 0.40 |
|  |  |  |  | rs7761118 | 36068303 | G/A | 0.10 | 0.06 | 0.93 | 0.94 |
|  |  |  |  |  |  |  |  |  |  |  |
| \* operates in both JNK and ERK pathways | | | |  |  |  |  |  |  |  |
| Minor Allele Frequency (MAF) and FDR-adjusted Hardy-Weinberg Equilibrium (FDR HWE) based on control population. | | | | | | | | | |  |

Supplemental Table 2. LD between SNPs

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  |  | R-Square | | |
| Gene | SNP1 | SNP2 | 0-28% NA | 29-70% NA | 71-100% NA |
| DUSP4 | rs3824133 | rs12540995 | 0.79 | 0.85 | 0.88 |
|  | rs567436 | rs12540995 | 0.69 | 0.77 | 0.83 |
|  | rs567436 | rs3824133 | 0.87 | 0.89 | 0.92 |
|  | rs2056025 | rs2341674 | 0.76 |  |  |
| MAP2K1 | rs8039880 | rs1432442 |  |  | 0.77 |
| MAP3K1 | rs832575 | rs43184 | 0.66 | 0.60 |  |
|  | rs33323 | rs889312 | 0.64 |  |  |
|  | rs33323 | rs2548663 | 0.71 | 0.67 | 0.61 |
| MAP3K9 | rs8010714 | rs11844774 | 0.98 | 0.94 | 0.97 |
|  | rs11628333 | rs11625206 | 0.64 | 0.61 | 0.62 |
|  |  | rs11844774 |  |  | 0.68 |
|  |  | rs8010714 |  |  | 0.68 |
|  | rs12883244 | rs11622989 | 0.79 | 0.80 | 0.92 |
|  | rs11158881 | rs11622989 |  |  | 0.76 |
|  |  | rs12883244 |  |  | 0.73 |
|  | rs1034769 | rs8011507 | 0.74 | 0.77 | 0.84 |
|  | rs4902855 | rs11622989 |  | 0.64 | 0.79 |
|  |  | rs12883244 | 0.73 | 0.81 | 0.86 |
|  |  | rs11158881 |  |  | 0.61 |
|  | rs12590049 | rs10483834 | 0.79 | 0.74 | 0.78 |
|  | rs10143031 | rs11628333 |  | 0.66 | 0.77 |
|  | rs17108548 | rs11622989 |  |  | 0.65 |
|  |  | rs12883244 |  |  | 0.62 |
|  |  | rs11158881 | 0.62 | 0.78 | 0.85 |
|  |  | rs4902855 |  |  | 0.72 |
|  | rs17766621 | rs4902854 |  | 0.65 | 0.79 |
|  |  | rs12590049 | 0.71 |  |  |
|  | rs8022269 | rs11844774 |  |  | 0.64 |
|  |  | rs8010714 |  |  | 0.62 |
|  |  | rs11628333 |  | 0.68 | 0.84 |
|  |  | rs11622989 |  |  | 0.63 |
|  |  | rs12883244 | 0.74 | 0.70 | 0.68 |
|  |  | rs10143031 |  |  | 0.70 |
|  | rs11624934 | rs11625206 | 0.76 | 0.66 | 0.63 |
|  |  | rs11844774 |  |  | 0.71 |
|  |  | rs8010714 |  |  | 0.68 |
|  |  | rs11628333 | 0.78 | 0.86 | 0.91 |
|  |  | rs12883244 |  |  | 0.62 |
|  |  | rs10143031 |  | 0.65 | 0.79 |
|  |  | rs8022269 | 0.71 | 0.77 | 0.92 |
| MAPK1 | rs743409 | rs2298432 | 0.64 | 0.65 | 0.71 |
|  | rs9610375 | rs743409 | 0.80 |  |  |
|  | rs8136867 | rs743409 | 0.91 | 0.73 |  |
|  | rs8136867 | rs9610375 | 0.78 |  |  |
| MAPK8 | rs11101320 | rs10508901 | 0.66 |  |  |
|  | rs4838590 | rs10508901 | 0.64 |  |  |
|  | rs10508901 | rs10857565 |  | 0.68 | 0.85 |
|  | rs4838590 | rs11101320 | 0.97 | 0.97 | 0.98 |
| MAPK14 | rs7761118 | rs3730327 | 0.93 | 0.89 | 0.96 |
|  | rs851010 | rs10807156 |  |  | **0.63** |