**Supplement table 1. List of the 96 selected SNPs and their frequencies in the subjects**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene** | **rs NCBI** | **Nucleotide change** | **Amino-acid change** | **Minor allele frequency** |
| **Tobacco smoking-response genes1)** | |  |  |  |
| *ACTG1* | rs1139405 | C>T |  | 0.22 |
|  | rs11657440 | T>C |  | 0.30 |
| *ARTN* | rs2853224 | A>C |  | 0.43 |
|  | rs3848809 | A>G |  | 0.22 |
| *CXCR4* | rs882300 | A>G |  | 0.28 |
| *DEFA1B* | rs2979392 | G>A |  |  |
| *DEFA4* | rs10103091 | T>A |  | 0.18 |
|  | rs2738102 | C>T |  | 0.34 |
| *ELANE* | rs3761007 | C>T |  | 0.09 |
| *FCGR3A* | rs396991 | T>G | Phe158Val | 0.25 |
| *MARCH6* | rs7720490 | T>G |  | 0.31 |
| *TGM2* | rs4811528 | G>A |  | 0.31 |
|  | rs7270785 | G>T |  | 0.44 |
| *VAV3* | rs1410403 | G>A |  | 0.26 |
|  | rs7528153 | A>T | Thr298Ser | 0.45 |
| *ACTG1* | rs1139405 | C>T |  | 0.22 |
|  | rs11657440 | T>C |  | 0.30 |
| *ARTN* | rs2853224 | A>C |  | 0.43 |
| **Metabolism** |  |  |  |  |
| *ADH1B* | rs1229984 | A>G | His48Arg | 0.21 |
| *ALDH2* | rs671 | G>A | Glu504Lys | 0.06 |
| *CYP1A2* | rs2472304 | G>A |  | 0.32 |
| *CYP1B1* | rs1056836 | C>G | Leu432Val | 0.39 |
| *CYP2A13* | rs8192789 | C>T | Arg257Cys | 0.07 |
| *CYP2A6* | rs1137115 | A>G |  | 0.21 |
|  | rs11878604 | T>C |  | 0.22 |
|  | rs28399433 | T>G |  | 0.13 |
| *CYP2B6* | rs3745274 | G>T | Gln172His | 0.27 |
| *CYP2C19* | rs12777823 | G>A |  | 0.22 |
| *CYP2D6* | rs35028622 | C>A |  | 0.40 |
| *CYP2E1* | rs1329149 | T>C |  | 0.27 |
|  | rs3813867 | G>C |  | 0.10 |
| *CYP3A4* | rs2242480 | C>T |  | 0.33 |
| *EPHX1* | rs1051740 | T>C | Tyr113His | 0.32 |
|  | rs2234922 | A>G | His139Arg | 0.19 |
| *FMO3* | rs1736557 | G>A | Val257Met | 0.09 |
|  | rs2266782 | G>A | Glu158Lys | 0.35 |
| *GSTM2* | rs638820 | T>C |  | 0.43 |
|  | rs655315 | T>C |  | 0.48 |
| *GSTP1* | rs1695 | A>G | Ile105Val | 0.33 |
| *NQO1* | rs1800566 | C>T | Pro187Ser | 0.28 |
| *MPO* | rs2333227 | C>T |  | 0.23 |
| *SULT1A1* | rs9282861 | G>A | Arg213His | 0.23 |
| *UGT1A4* | rs2011425 | T>G | Leu48Val | 0.11 |
| *UGT1A6* | rs2070959 | A>G | Thr181Ala | 0.27 |
| *UGT2B15* | rs1902023 | T>G | Tyr85Asp | 0.44 |
| *UGT2B7* | rs7439366 | T>C | Tyr268His | 0.47 |
| **Tobacco addiction** | | | | |
| *5-HT2A* | rs6313 | C>T |  | 0.43 |
| *CHRNA3* | rs12914385 | C>T |  | 0.31 |
|  | rs578776 | C>T |  | 0.46 |
|  | rs6495308 | T>C |  | 0.44 |
|  | rs6495309 | C>T |  | 0.34 |
| *CHRNB4* | rs11072768 | T>G |  | 0.50 |
| *COMT* | rs4680 | G>A | Val158Met | 0.39 |
|  | rs174699 | C>T |  | 0.16 |
| *DBH* | rs5320 | G>A | Ala211Thr | 0.11 |
| *DRD2* | rs1800497 | C>T | Glu713Lys | 0.30 |
| *HTR3A* | rs10160548 | G>T |  | 0.45 |
| *LAMB4/NRCAM* | rs382140 | A>G |  | 0.25 |
| *NCALD* | rs16868941 | G>A |  | 0.14 |
| *NET-8* | rs5569 | C>T |  | 0.27 |
| *OPRM1* | rs1799971 | A>G | Asn40Asp | 0.19 |
| *SLC6A3* | rs27072 | C>T |  | 0.19 |
| *SLC6A4* | rs2020936 | C>T |  | 0.23 |
| *TPH1* | rs1799913 | C>A |  | 0.36 |
|  | rs1800532 | C>A |  | 0.36 |
| *TPH2* | rs4570625 | G>T |  | 0.36 |
| **Tobacco smoke induced diseases** | | | | |
| *AHR* | rs2066853 | G>A | Arg554Lys | 0.27 |
| *AHRR* | rs2292596 | C>G | Pro189Ala | 0.31 |
| *ALOX5* | rs4948671 | C>T |  | 0.25 |
|  | rs7099684 | A>T |  | 0.16 |
| *AOX1* | rs17593621 | T>C |  | 0.23 |
|  | rs12621063 | C>A |  | 0.29 |
| *ARNT* | rs12410394 | G>A |  | 0.39 |
| *CSK* | rs1378942 | G>T |  | 0.33 |
| *DNER* | rs7594321 | T>C |  | 0.23 |
| *HPRT1* | rs6634990 | T>G |  | 0.45 |
| *IKBKE* | rs10863430 | T>G |  | 0.14 |
| *IL17A* | rs4711998 | A>G |  | 0.46 |
| *KCNJ2/SOX9* | rs11654749 | G>T |  | 0.34 |
| *PPARG* | rs3856806 | C>T |  | 0.12 |
| *TP53* | rs1042522 | C>G | Pro72Arg | 0.40 |
|  | rs12951053 | A>C |  | 0.16 |
| *WRN* | rs1801195 | G>T | Leu1074Phe | 0.47 |
| **Epigenetic modulation** | | | | |
| *HDAC1* | rs1741981 | T>C |  | 0.49 |
| *MTHFR* | rs1801133 | C>T | Ala222Val | 0.32 |
| **DNA repair** |  |  |  |  |
| *ERCC1* | rs4253211 | G>C | Arg1230Pro | 0.06 |
|  | rs11615 | T>C |  | 0.36 |
|  | rs2298881 | C>A |  | 0.19 |
|  | rs3212961 | C>A |  | 0.26 |
|  | rs3212986 | G>T | Gln504Lys | 0.29 |
| *MGMT* | rs12917 | C>T | Leu84Phe | 0.15 |
| *MSH3* | rs1042821 | C>T | Gly39Glu | 0.19 |
|  | rs26279 | G>A | Ala1045Thr | 0.31 |
| *OGG1* | rs1052133 | C>G | Ser326Cys | 0.30 |
| *XPC* | rs2228001 | C>A | Lys939Gln | 0.34 |
|  | rs2228000 | C>T | Ala462Val | 0.25 |
| *XRCC1* | rs1799782 | C>T | Arg194Trp | 0.13 |
|  | rs25487 | A>G | Gln399Arg | 0.26 |
| *XRCC3* | rs861539 | C>T | Thr241Met | 0.25 |

1) based on Na et al. 2015

Suppement Table 2. Associated SNPs with urinary cotinine levels

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene name**  **(rs number)** | **Genotype** | **N** | **Cotinine (mg/L)** | **P value** |
| SULT1A1  (rs9282861) | AA | 13 | 0.81±0.20 | **<0.01** |
| AG | 65 | 0.95±0.09 |
| GG | 335 | 0.25±0.04 |
| SLC6A3  (rs27072) | CC | 39 | 0.27±0.11 | **<0.01** |
| CT | 28 | 0.02±0.13 |
| TT | 156 | 0.48±0.06 |
| MTHFR  (rs1801133) | CC | 154 | 0.58±0.06 | **<0.01** |
| CT | 276 | 0.27±0.05 |
| TT | 107 | 0.39±0.07 |
| ARTN  (rs2853224) | AA | 64 | 0.63±0.09 | **<0.01** |
| AC | 193 | 0.34±0.05 |
| CC | 213 | 0.22±0.05 |
| FCGR3A  (rs396991) | GG | 13 | 0.45±0.21 | **0.02** |
| GT | 209 | 0.27±0.05 |
| TT | 295 | 0.45±0.04 |
| DRD2  (rs1800497) | CC | 223 | 0.44±0.05 | **0.01** |
| CT | 196 | 0.29±0.05 |
| TT | 69 | 0.17±0.09 |

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|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| ALOX5  (rs7099684) | AA | 7 | 0.86±0.29 | **0.01** |
| AT | 114 | 0.53±0.07 |
| TT | 416 | 0.34±0.04 |
| CHRNA3  (rs578776) | CC | 14 | 0.23±0.20 | **0.04** |
| CT | 182 | 0.50±0.06 |
| TT | 341 | 0.33±0.04 |
| CYP2E1  (rs3813867) | CC | 58 | 0.83±0.10 | **<0.01** |
| CG | 125 | 0.25±0.07 |
| GG | 295 | 0.29±0.04 |
| DEFA4  (rs2738102) | CC | 85 | 0.66±0.08 | **<0.01** |
| CT | 241 | 0.32±0.05 |
| TT | 206 | 0.36±0.05 |
| HPRT1  (rs6634990) | GG | 291 | 0.44±0.04 | **<0.01** |
| GT | 85 | 0.03±0.08 |
| TT | 155 | 0.48±0.06 |
| TP53  (rs1295105) | AA | 277 | 0.44±0.04 | **0.04** |
| AC | 225 | 0.36±0.05 |
| CC | 34 | 0.10±0.13 |
| CYP3A4  (rs2242480) | CC | 279 | 0.47±0.05 | **0.03** |
| CT | 144 | 0.42±0.07 |
| TT | 57 | 0.16±0.11 |

Suppement Table 3. Associated SNPs with urinary TTMA levels

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene name**  **(rs number)** | **Genotype** | **N** | **Cotinine (mg/L)** | **P value** |
| SULT1A1  (rs9282861) | AA | 13 | 203.46±43.40 | **<0.01** |
| AG | 65 | 165.60±19.40 |
| GG | 335 | 64.29±8.55 |
| ADH1B  (rs1229984) | AA | 67 | 81.09±17.85 | **<0.01** |
| AG | 111 | 59.11±13.87 |
| GG | 26 | 267.63±28.66 |
| CYP2D6  (rs3502862) | AA | 92 | 65.54±15.96 | **0.02** |
| AC | 206 | 68.63±10.67 |
| CC | 240 | 104.85±9.88 |
| AOX1  (rs1759362) | CC | 40 | 133.99±17.65 | **<0.01** |
| CT | 139 | 67.70±9.47 |
| TT | 209 | 52.38±7.72 |
| GSTM2  (rs638820) | CC | 70 | 50.49±18.25 | **0.04** |
| CT | 184 | 74.41±11.26 |
| TT | 283 | 97.79±9.08 |
| IL17A  (rs4711998) | AA | 183 | 59.74±9.35 | **0.02** |
| AG | 99 | 62.96±12.71 |
| GG | 132 | 98.82±11.00 |
| ERCC1  (rs3212986) | GG | 271 | 94.22±9.29 | **<0.01** |
| GT | 195 | 53.47±10.95 |
| TT | 62 | 136.74±19.41 |

Suppement Table 4.. Associated SNPs with urinary MDA levels

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Gene name**  **(rs number)** | **Genotype** | **N** | **Cotinine (mg/L)** | **P value** |
| ALDH2  (rs671) | AA | 12 | 2.55±0.39 | **<0.01** |
| AG | 145 | 2.91±0.11 |
| GG | 379 | 2.47±0.07 |
| VAV3  (rs1410403) | AA | 225 | 2.66±0.09 | **<0.01** |
| AG | 177 | 2.40±0.10 |
| GG | 75 | 3.02±0.16 |
| MGMT  (rs12917) | CC | 70 | 2.68±0.14 | **<0.01** |
| CT | 16 | 1.60±0.30 |
| TT | 7 | 2.17±0.45 |
| CYP3A4  (rs2242480) | CC | 279 | 2.45±0.08 | **<0.01** |
| CT | 144 | 2.52±0.11 |
| TT | 57 | 3.12±0.18 |
| ADH1B  (rs1229984) | AA | 67 | 2.15±0.17 | **0.01** |
| AG | 111 | 2.67±0.13 |
| GG | 26 | 3.01±0.27 |
| XRCC3  (rs861539) | CC | 55 | 2.47±0.19 | **0.02** |
| CT | 350 | 2.71±0.07 |
| TT | 105 | 2.29±0.14 |
| MPO  (rs2333227) | CC | 5 | 3.36±0.62 | **0.02** |
| CT | 283 | 2.42±0.08 |
| TT | 98 | 2.82±0.14 |
| DEFA4  (rs10103091) | AA | 428 | 2.55±0.07 | **0.02** |
| AT | 95 | 2.86±0.14 |
| TT | 7 | 1.59±0.52 |
| DRD2  (rs1800497) | CC | 223 | 2.76±0.09 | **0.04** |
| CT | 196 | 2.43±0.10 |
| TT | 69 | 2.54±0.17 |
| TP53  (rs1295105) | AA | 277 | 2.62±0.08 | **0.05** |
| AC | 225 | 2.48±0.09 |
| CC | 34 | 3.10±0.24 |