Pharmacogenetics of tenofovir and emtricitabine penetration into cerebrospinal fluid

Background: Blood-cerebrospinal fluid (CSF) barrier transporters affect the influx and efflux of drugs. The antiretrovirals tenofovir and emtricitabine may be substrates of blood-brain barrier (BBB) and blood-CSF barrier transporters, but data are limited regarding the pharmacogenetics and pharmacokinetics of their central nervous system (CNS) penetration.

Objectives: We investigated genetic polymorphisms associated with CSF disposition of tenofovir and emtricitabine.

Method: We collected paired plasma and CSF samples from 47 HIV-positive black South African adults who were virologically suppressed on efavirenz, tenofovir and emtricitabine. We considered 1846 single-nucleotide polymorphisms from seven relevant transporter genes (ABCC5, ABCG2, ABCB1, SLCO2B1, SCLO1A2, SLCO1B1 and ABCC4) and 782 met a linkage disequilibrium (LD)-pruning threshold.

Results: The geometric mean (95% confidence interval [CI]) values for tenofovir and emtricitabine CSF-to-plasma concentration ratios were 0.023 (0.021–0.026) and 0.528 (0.460–0.605), respectively. In linear regression models, the lowest p-value for association with the tenofovir CSF-to-plasma ratio was ABCB1 rs1989830 (p = 1.2 × 10^-8) and for emtricitabine, it was ABCC5 rs11921035 (p = 1.4 × 10^-9). None withstood correction for multiple testing.

Conclusion: No genetic polymorphisms were associated with plasma, CSF concentrations or CSF-to-plasma ratios for either tenofovir or emtricitabine.

Keywords: pharmacokinetics; pharmacogenetics; tenofovir; emtricitabine; cerebrospinal fluid.

Introduction

Tenofovir and emtricitabine are part of the current first-line antiretroviral therapy (ART) regimens for HIV-positive adults in resource-limited settings and both are widely used in high-income countries.\(^1\) Infection of the central nervous system (CNS) by HIV-1 occurs early in infection and its clearance is reliant on adequate CNS antiretroviral concentrations.\(^2\) However, there are limited data regarding determinants of cerebrospinal fluid (CSF) penetration by tenofovir and emtricitabine. Data from small cohorts indicate that CSF concentrations of tenofovir and emtricitabine are 5% and 50% of plasma concentrations, respectively.\(^3,5\)

However, higher CSF tenofovir concentrations and lower emtricitabine concentrations have been reported, which may be explained by polymorphisms in drug transporters or altered blood–brain barrier (BBB) permeability.\(^4,6\) Transporters in the BBB and blood–CSF barrier (BCB) affect the influx and efflux of drugs, including tenofovir and emtricitabine.\(^3,6,7\) Multidrug resistance protein-5 (MRP-5, encoded by ABCC5) is ubiquitous and mediates the efflux of nucleoside reverse transcriptase inhibitors.\(^8\) Lower CSF emtricitabine exposure in females compared to males is hypothesised to reflect differential expression of MRP transporters at the BBB and BCB.\(^7\) In vitro, tenofovir is a substrate of the breast cancer resistance protein (BCRP, encoded by ABCG2), MRP-4 (encoded by ABCC4) and P-glycoprotein (encoded by ABCB1).\(^3,9,10\) A polymorphism in ABCG2 rs2231142 has been associated with 1.5-fold increased plasma tenofovir exposure and Thai patients carrying ABCC4 3463 AG or GG (rs1751034) had an 11% greater tenofovir clearance compared with AA.\(^12,13\)

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Loss-of-function ABCC4 polymorphisms have been associated with reduced clearance of tenofovir. In genome-wide analyses, SLC17A1 rs12662869 was associated with an increase in tenofovir clearance. It is possible that genetic polymorphisms that affect transporter function will affect tenofovir or emtricitabine CSF penetration. The pharmacogenetics of CSF penetration of tenofovir and emtricitabine have not been described.

Africans are the most genetically diverse population worldwide. South Africa has the world’s largest ART programme, with most patients currently receiving efavirenz-based regimens that include the nucleos(t)ides tenofovir and emtricitabine. We previously reported on the pharmacogenetics of CSF penetration of efavirenz in black South Africans. Here, we characterise the associations between transporter gene polymorphisms and CSF penetration of tenofovir and emtricitabine in the same cohort.

**Patients and methods**

**Participants**

Adults (≥ 18 and ≤ 70 years of age) from a randomised control trial (PACTR201310000635418) that investigated lithium for HIV-associated neurocognitive impairment were invited to participate in the present study. We also invited participants who were screened for that trial but were excluded based on cognitive impairment criteria. All participants provided written informed consent. This study was approved by the University of Cape Town Human Research Ethics Committee (HREC 071/2013).

**Pharmacokinetic sampling**

We collected paired plasma and CSF samples for tenofovir and emtricitabine assays. Participants recorded the dosing time the night before and were admitted in the morning for pharmacokinetic sampling. Whole blood was collected within 45 min of CSF sampling and centrifuged within 1 h of collection. Plasma and CSF aliquots were stored at −80 °C until analysis.

**Tenofovir and emtricitabine measurement**

The analytical laboratory in the Division of Clinical Pharmacology at the University of Cape Town quantified total tenofovir and emtricitabine in plasma and CSF using validated liquid chromatography tandem mass spectrometry assays.

The lower limits of quantification (LLQs) for plasma tenofovir and emtricitabine were 10.0 ng/mL and 37.5 ng/mL, respectively. For CSF, the LLQs for total tenofovir and emtricitabine were 0.5 ng/mL. Concentrations below the limits of quantification were treated as missing data.

**Characterisation of genetic polymorphisms**

We extracted DNA from the buffy coat using the QIAsymphony kit. Genotyping was performed using the Infinium® Expanded Multi-Ethnic Genotyping Array (MEGA), Illumina, San Diego, CA, USA).

Polymorphisms that were not genotyped were imputed. Polymorphisms were extracted from seven genes ±50 kbp: ABCB1 (301 polymorphisms), ABCC4 (630 polymorphisms), ABCC5 (225 polymorphisms), ABCG2 (164 polymorphisms), SLC01A2 (406 polymorphisms) and SLC02B1 (118 polymorphisms). Polymorphisms were excluded for genotyping efficiency less than 99%, minor allele frequency less than 5% and Hardy-Weinberg equilibrium p-values less than 0.00001. We also genotyped SLC01B1 521T→C (rs4149056) and SLC01B1 (rs4149032) using the MassARRAY iPLEX® Gold system (Sequenom, Inc., San Diego, CA, USA).

All genotyping was performed at Vanderbilt Technologies for Advanced Genomics (VANTAGE), by laboratory personnel with no knowledge of clinical data. All samples were genotyped in duplicate. The final dataset included 1846 polymorphisms from 47 participants.

**Pharmacokinetic statistical analysis**

Pharmacokinetic data were not normally distributed so were expressed as median and interquartile ranges (IQRs) and geometric means (95% confidence interval [CI]). Pearson’s r correlation was used to assess the correlations between plasma and CSF concentrations. We performed statistical analysis using STATA version 15.0 (StataCorp, College Station, TX, USA). Graphs were created using GraphPad Prism version 7.03 for Windows (GraphPad Software, La Jolla, CA, USA).

**Genetic associations**

Associations with pharmacokinetic parameters were assessed by univariable analysis. Pharmacokinetic data were log_{10} transformed for association analyses. We used ratios of total concentrations without correcting for protein binding. Cerebrospinal fluid-to-plasma concentration ratios were calculated using raw concentrations and then log_{10} transformed. We performed genetic association analyses using PLINK version 1.9.

For primary analyses, we conducted linkage disequilibrium (LD) pruning with an R^2 threshold of 0.95 within a 50-kb window at 5-kb increments.

The final analysis included 782 polymorphisms that met the LD-pruning threshold. We used Bonferroni correction to adjust for multiple testing (p = 0.05 divided by 782 polymorphisms). We generated an LD plot using Haploview (https://www.broadinstitute.org/haploview/haploview). We previously reported LD plots for these polymorphisms.

**Ethical considerations**

All participants provided written informed consent. This study was approved by the University of Cape Town Human Research Ethics Committee (HREC 071/2013).
Results

We studied 47 participants who self-identified as black South Africans (isiXhosa speaking), of whom 41 were female. All were virologically suppressed and were receiving efavirenz, tenofovir and emtricitabine (n = 43) or efavirenz, tenofovir and lamivudine (n = 4). The median (IQR) values of the baseline characteristics were age 36 (IQR = 32–43) years, a CD4 T-cell count of 470 (IQR = 384–586) cells/μL, a time on ART of 38 (IQR = 18–54) months and a body mass index (BMI) of 25.6 (IQR = 22.7–29.3) kg/m². The concentrations of tenofovir (plasma and CSF) and emtricitabine (plasma and CSF) are presented in Table 1. The plasma and CSF concentrations of tenofovir and emtricitabine were each correlated (p < 0.0001, R² = 0.53 and p < 0.0001, R² = 0.45; respectively) (Appendix Figure 1a and 1b). There was no statistically significant association of CSF-to-plasma ratios versus time after dosing (Appendix Figure 2).

Genetic polymorphisms

Amongst the 47 participants, 1846 polymorphisms were successfully genotyped. Only SLCO1B1 rs4149056 was monomorphic (i.e. no minor alleles). The remaining 1845 polymorphisms were in Hardy–Weinberg equilibrium based on a Bonferroni-adjusted p-value threshold of 6.4 × 10⁻³; 56 had unadjusted Bonferroni p-values of <0.05. Minor allele frequencies for all polymorphisms are provided in Appendix Table 1.

Genetic associations with detectable log10-transformed cerebrospinal fluid-to-plasma tenofovir concentrations in 43 black South African adults.

In univariable linear regression analyses (Table 2), the tenofovir CSF-to-plasma ratio was best predicted by a model that included ABCB1 rs1989830 (β = −0.12; 95% CI = −0.19 − −0.05; p = 1.2 × 10⁻³). The emtricitabine CSF-to-plasma ratio was best predicted by a model that included ABCC5 rs11921035 (β = −0.32; 95% CI = −0.50 − −0.14; p = 1.4 × 10⁻³), as shown in Table 3. No association achieved significance after correcting for multiple testing. Univariable linear regression analyses and polymorphisms with p-values below 0.01 for tenofovir and emtricitabine CSF-to-plasma ratios are shown in Tables 2 and 3, respectively. For absolute plasma and CSF tenofovir concentrations, 10 polymorphisms in ABCG2, ABC5, SLCO1A2 and ABCC4 for plasma and six in ABCB1, ABCG2, ABCC5, SLCO1A2 and ABCC4 for CSF had p-values less than 0.01 (data not shown). For absolute plasma and CSF emtricitabine concentrations, six polymorphisms in ABC5, SLCO1A2, ABCC4 and SLCO2B1 for plasma and 12 in ABCB1, ABCG2, ABCC5, SLCO1A2 and ABCC4 had p-values less than 0.01 (data not shown). No associations with SLCO1B1 rs4149032 were found.

Discussion

We characterised the associations between 782 genetic polymorphisms and CSF disposition of tenofovir and emtricitabine in black South African adults. The lowest
 Associations with tenofovir pharmacokinetics and genetic polymorphisms were found in other populations. An increase in tenofovir plasma concentrations were independently associated with ABC4 rs11921035 (p = 1.2 × 10⁻⁵), and for emtricitabine was ABC5 rs11928606 (p = 1.4 × 10⁻⁴). None were significant after correcting for multiple testing. In addition, we found no significant associations with absolute CSF or plasma concentration after correcting for multiple testing.

Our study has limitations. With our sample size, we were underpowered to detect associations with small effect sizes. We could only detect associations with relatively frequent polymorphisms and with large effect sizes. Therefore, these data should be regarded as exploratory. Polymorphisms not genotyped in our study may be associated with tenofovir or emtricitabine disposition into CSF. Whilst we did not adjust for creatinine clearance, this should not be a confounder that affects drug disposition into CSF. We included 33 (70%) participants with mild to moderate neurocognitive impairment, as previously reported. We may therefore have introduced a selection bias.

**Conclusion**

In conclusion, we found no significant associations between any of the 782 polymorphisms and plasma concentrations, CSF concentrations or CSF-to-plasma ratios for either tenofovir or emtricitabine in univariate linear regression models after correcting for multiple testing.

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Appendix

**Figure 1-A1:** Pearson correlation plots for log$_{10}$-transformed plasma and cerebrospinal fluid (CSF) concentrations emtricitabine and tenofovir. **Panel A:** Relationship between CSF and plasma tenofovir concentrations. **Panel B:** Relationship between CSF and plasma emtricitabine concentrations. All concentrations are log$_{10}$ transformed.

**Figure 2-A1:** Cerebrospinal fluid (CSF)-to-plasma concentration ratios of detectable pairs of plasma and CSF samples versus time after dosing. The lines are linear regression lines and were not statistically significant.
| Chromosome | Polymorphism | Minor allele frequency | Major allele frequency |
|------------|--------------|------------------------|------------------------|
| 1          | rs2292998    | 0.2442                 | 0.2093                 |
| 1          | rs111248225  | 0.3488                 | 0.2209                 |
| 1          | rs1879256    | 0.2209                 | 0.0581                 |
| 1          | rs562        | 0.4884                 | 0.2209                 |
| 1          | rs3792583    | 0.3488                 | 0.0697                 |
| 1          | rs4148579    | 0.186                   | 0.3605                 |
| 1          | rs35494670   | 0.2442                 | 0.0581                 |
| 1          | rs2139562    | 0.4884                 | 0.2209                 |
| 1          | rs1879255    | 0.2209                 | 0.3372                 |
| 1          | rs1401999    | 0.0930                 | 0.0930                 |
| 1          | rs6443917    | 0.3488                 | 0.0581                 |
| 1          | rs11928606   | 0.0581                 | 0.0814                 |
| 1          | rs6790814    | 0.2209                 | 0.2558                 |
| 1          | rs11926985   | 0.2209                 | 0.3023                 |
| 1          | rs73044690   | 0.2209                 | 0.2209                 |
| 1          | rs113227666  | 0.3721                 | 0.3023                 |
| 1          | rs115851049  | 0.3605                 | 0.2093                 |
| 1          | rs73044605   | 0.2209                 | 0.0581                 |
| 1          | rs11914437   | 0.2209                 | 0.2209                 |
| 1          | rs116312201  | 0.0581                 | 0.0581                 |
| 1          | rs1012989    | 0.3721                 | 0.3023                 |
| 1          | rs1742623    | 0.2209                 | 0.2209                 |
| 1          | rs1533684    | 0.3721                 | 0.3023                 |
| 1          | rs10575785   | 0.2209                 | 0.0581                 |
| 1          | rs11714326   | 0.3721                 | 0.3023                 |
| 1          | rs112357546  | 0.2209                 | 0.0581                 |
| 1          | rs112840402  | 0.3721                 | 0.3023                 |
| 1          | rs75822913   | 0.2209                 | 0.0581                 |
| 1          | rs11928606   | 0.0581                 | 0.0814                 |
| 1          | rs115851049  | 0.3605                 | 0.2093                 |
| 1          | rs116312201  | 0.0581                 | 0.0581                 |
| 1          | rs1012989    | 0.3721                 | 0.3023                 |
| 1          | rs1742623    | 0.2209                 | 0.2209                 |
| 1          | rs1533684    | 0.3721                 | 0.3023                 |
| 1          | rs10575785   | 0.2209                 | 0.0581                 |
| 1          | rs11714326   | 0.3721                 | 0.3023                 |
| 1          | rs112357546  | 0.2209                 | 0.0581                 |
| 1          | rs112840402  | 0.3721                 | 0.3023                 |
| 1          | rs75822913   | 0.2209                 | 0.0581                 |
### Table 1-A1 (Continues...): Minor allele frequencies for 1846 polymorphisms in 43 black South Africans.

| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|------------------------|
| 3          | rs6800217    | T            | C            | 0.2442                 |
| 3          | rs35240483   | A            | C            | 0.2209                 |
| 3          | rs112737137  | T            | C            | 0.2209                 |
| 3          | rs7636305    | A            | G            | 0.2209                 |
| 3          | rs9861983    | T            | C            | 0.2209                 |
| 3          | rs869417     | T            | C            | 0.2209                 |
| 3          | rs28365012   | A            | G            | 0.0581                 |
| 3          | rs3828469    | G            | A            | 0.2209                 |
| 3          | rs3805108    | T            | C            | 0.3372                 |
| 3          | rs7319688    | T            | C            | 0.4419                 |
| 3          | rs344552121  | C            | T            | 0.0581                 |
| 3          | rs11468175   | C            | G            | 0.0581                 |
| 3          | rs144412198  | A            | G            | 0.0581                 |
| 3          | rs3792581    | A            | C            | 0.2209                 |
| 3          | rs114398776  | C            | T            | 0.2209                 |
| 3          | rs4148578    | A            | C            | 0.2209                 |
| 3          | rs4148577    | C            | T            | 0.2209                 |
| 3          | rs1132776    | A            | G            | 0.3372                 |
| 3          | rs6775518    | A            | G            | 0.2209                 |
| 3          | rs6791345    | T            | C            | 0.3372                 |
| 3          | rs6802849    | A            | C            | 0.2209                 |
| 3          | rs55695073   | T            | C            | 0.2093                 |
| 3          | rs7636910    | C            | T            | 0.186                  |
| 3          | rs2293001    | T            | C            | 0.4419                 |
| 3          | rs2313212    | A            | G            | 0.2442                 |
| 3          | rs939337     | G            | C            | 0.2209                 |
| 3          | rs75617395   | T            | C            | 0.0930                 |
| 3          | rs3749440    | G            | A            | 0.4419                 |
| 3          | rs4148575    | A            | G            | 0.3372                 |
| 3          | rs6795595    | T            | C            | 0.2558                 |
| 3          | rs7777233    | T            | C            | 0.2558                 |
| 3          | rs3749438    | A            | G            | 0.186                  |
| 3          | rs114003322  | G            | C            | 0.0581                 |
| 3          | rs6443926    | A            | C            | 0.3372                 |
| 3          | rs73884816   | G            | A            | 0.2558                 |
| 3          | rs7635548    | A            | G            | 0.3372                 |
| 3          | rs10937157   | A            | G            | 0.2791                 |
| 3          | rs12634398   | G            | A            | 0.4419                 |
| 3          | rs10937158   | T            | C            | 0.2791                 |
| 3          | rs113691647  | A            | ACAAAAGTGCACTG | 0.2096 |
| 3          | rs11404217   | GA           | G            | 0.3953                 |
| 3          | rs75393197   | G            | T            | 0.0581                 |
| 3          | rs28680881   | G            | T            | 0.1628                 |
| 3          | rs7620350    | A            | T            | 0.2791                 |
| 3          | rs7620781    | A            | G            | 0.2907                 |
| 3          | rs138640574  | A            | C            | 0.2558                 |
| 3          | rs35740940   | G            | C            | 0.0697                 |
| 3          | rs7705190    | T            | C            | 0.2558                 |
| 3          | rs75448974   | A            | G            | 0.2442                 |
| 3          | rs3888419    | T            | G            | 0.2442                 |
| 3          | rs9290779    | A            | C            | 0.1628                 |
| 3          | rs145536424  | T            | A            | 0.0581                 |
| 3          | rs55831983   | C            | T            | 0.1047                 |
| 3          | rs1879259    | A            | G            | 0.2209                 |
| 3          | rs4148557    | A            | G            | 0.2558                 |
| 3          | rs6710724    | G            | T            | 0.0697                 |
| 3          | rs7612327    | C            | T            | 0.407                  |
| 3          | rs939335     | A            | G            | 0.2791                 |
| 3          | rs11917442   | T            | C            | 0.0581                 |
| 3          | rs201188880  | CT           | C            | 0.2442                 |

Table 1-A1 continues on the next page →
Table 1-A1 (Continues...): Minor allele frequencies for 1846 polymorphisms in 43 black South Africans.

| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|------------------------|
| 4          | rs45442445   | A            | T            | 0.0581                 |
| 4          | rs115770495  | T            | C            | 0.0581                 |
| 4          | rs1448784    | G            | A            | 0.0465                 |
| 4          | rs4148159    | T            | A            | 0.1744                 |
| 4          | rs2231164    | A            | G            | 0.3023                 |
| 4          | rs2725267    | T            | C            | 0.2907                 |
| 4          | rs2231162    | A            | G            | 0.141                  |
| 4          | rs2231159    | C            | A            | 0.2093                 |
| 4          | rs2231158    | T            | C            | 0.2093                 |
| 4          | rs45621036   | T            | C            | 0.1628                 |
| 4          | rs45566834   | G            | A            | 0.2093                 |
| 4          | rs4569894    | C            | T            | 0.1628                 |
| 4          | rs1383586    | G            | A            | 0.3023                 |
| 4          | rs1383584    | A            | G            | 0.3023                 |
| 4          | rs45592333   | C            | T            | 0.1628                 |
| 4          | rs1043946    | C            | T            | 0.0581                 |
| 4          | rs2231155    | T            | C            | 0.1744                 |
| 4          | rs45566934   | C            | T            | 0.1628                 |
| 4          | rs140107556  | C            | G            | 0.1628                 |
| 4          | rs2626214    | A            | G            | 0.314                  |
| 4          | rs2626213    | A            | G            | 0.314                  |
| 4          | rs45443998   | T            | C            | 0.1163                 |
| 4          | rs2231153    | T            | C            | 0.3023                 |
| 4          | rs141518597  | T            | G            | 0.0814                 |
| 4          | rs201742138  | AG           | A            | 0.1163                 |
| 4          | rs28665233   | A            | G            | 0.1395                 |
| 4          | rs2725264    | T            | C            | 0.1395                 |
| 4          | rs2725263    | C            | A            | 0.1512                 |
| 4          | rs262628     | A            | C            | 0.3256                 |
| 4          | rs12505410   | G            | T            | 0.0814                 |
| 4          | rs2626261    | G            | C            | 0.0581                 |
| 4          | rs13120400   | C            | T            | 0.0697                 |
| 4          | rs201460174  | G            | T            | 0.0697                 |
| 4          | rs199994188  | C            | T            | 0.0697                 |
| 4          | rs13789286   | C            | T            | 0.0697                 |
| 4          | rs302048     | G            | A            | 0.0814                 |
| 4          | rs2231147    | C            | T            | 0.1395                 |
| 4          | rs1871744    | C            | T            | 0.0814                 |
| 4          | rs2626218    | A            | G            | 0.0665                 |
| 4          | rs2231144    | C            | T            | 0.3372                 |
| 4          | rs113752350  | C            | T            | 0.3372                 |
| 4          | rs185151667  | T            | C            | 0.3372                 |
| 4          | rs2725259    | T            | C            | 0.0465                 |
| 4          | rs6832558    | T            | C            | 0.0465                 |
| 4          | rs2725258    | T            | C            | 0.0466                 |
| 4          | rs2725256    | G            | A            | 0.3372                 |
| 4          | rs4548400    | C            | T            | 0.3372                 |
| 4          | rs17013859   | T            | C            | 0.3372                 |
| 4          | rs200576598  | AG           | A            | 0.0581                 |
| 4          | rs2725255    | A            | G            | 0.0581                 |
| 4          | rs2626219    | G            | C            | 0.0655                 |
| 4          | rs17013870   | C            | T            | 0.3372                 |
| 4          | rs72875335   | A            | G            | 0.3372                 |
| 4          | rs113737999  | A            | G            | 0.3372                 |
| 4          | rs2626231    | G            | A            | 0.0655                 |
| 4          | rs2626232    | G            | A            | 0.0655                 |
| 4          | rs12641369   | A            | G            | 0.4655                 |
| 4          | rs2725253    | C            | T            | 0.0581                 |
| 4          | rs2626217    | G            | A            | 0.0581                 |
| 4          | rs1564481    | T            | C            | 0.1628                 |

Table 1-A1 continues in the next column →
| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|------------------------|
| 4          | rs13128241   | T            | C            | 0.3488                 |
| 4          | rs13128083   | G            | A            | 0.3488                 |
| 4          | rs55987521   | T            | A            | 0.3721                 |
| 4          | rs60816576   | T            | G            | 0.3953                 |
| 4          | rs57545797   | C            | T            | 0.3953                 |
| 4          | rs1481014    | A            | C            | 0.3721                 |
| 4          | rs13135956   | A            | G            | 0.3721                 |
| 4          | rs7642678    | T            | A            | 0.0814                 |
| 4          | rs6821227    | C            | T            | 0.2442                 |
| 4          | rs6821239    | A            | G            | 0.2442                 |
| 4          | rs7864545    | C            | T            | 0.2442                 |
| 4          | rs6532055    | A            | G            | 0.1442                 |
| 4          | rs6837313    | G            | A            | 0.2442                 |
| 4          | rs683950     | G            | A            | 0.2442                 |
| 4          | rs2127861    | C            | G            | 0.2442                 |
| 4          | rs2127863    | T            | C            | 0.2442                 |
| 4          | rs70959608   | C            | CA           | 0.2442                 |
| 4          | rs6854688    | G            | A            | 0.314                  |
| 4          | rs11097182   | T            | C            | 0.3837                 |
| 4          | rs113611770  | G            | A            | 0.0465                 |
| 4          | rs112710034  | G            | C            | 0.0465                 |
| 4          | rs6532055    | C            | T            | 0.1628                 |
| 4          | rs10856870   | C            | T            | 0.4651                 |
| 4          | rs150614746  | G            | A            | 0.0465                 |
| 4          | rs140027200  | T            | C            | 0.0465                 |
| 4          | rs75048878   | T            | G            | 0.1279                 |
| 4          | rs4693930    | A            | G            | 0.1047                 |
| 4          | rs139884402  | G            | C            | 0.0465                 |
| 4          | rs1172364    | A            | G            | 0.3953                 |
| 7          | rs67721532   | G            | A            | 0.1512                 |
| 7          | rs45505929   | C            | T            | 0.0930                 |
| 7          | rs112113287  | G            | GTGTTGTTT   | 0.407                  |
| 7          | rs60213540   | C            | T            | 0.407                  |
| 7          | rs17149637   | A            | G            | 0.407                  |
| 7          | rs17149640   | C            | A            | 0.407                  |
| 7          | rs17149641   | C            | T            | 0.407                  |
| 7          | rs45580239   | A            | G            | 0.2093                 |
| 7          | rs45564612   | T            | C            | 0.407                  |
| 7          | rs45447097   | A            | G            | 0.407                  |
| 7          | rs17149647   | C            | T            | 0.3837                 |
| 7          | rs45607141   | G            | A            | 0.407                  |
| 7          | rs17149652   | T            | G            | 0.407                  |
| 7          | rs4148817    | G            | C            | 0.407                  |
| 7          | rs4148815    | T            | A            | 0.407                  |
| 7          | rs66463970   | GT            | G            | 0.407                  |
| 7          | rs45593435   | G            | A            | 0.407                  |
| 7          | rs17149660   | C            | T            | 0.407                  |
| 7          | rs45502492   | T            | C            | 0.3605                 |
| 7          | rs45526438   | A            | G            | 0.3605                 |
| 7          | rs45605032   | T            | C            | 0.407                  |
| 7          | rs45590633   | T            | C            | 0.1512                 |
| 7          | rs45447073   | A            | G            | 0.0930                 |
| 7          | rs4148814    | C            | T            | 0.3605                 |
| 7          | rs2302385    | C            | T            | 0.3605                 |
| 7          | rs2302386    | G            | A            | 0.3605                 |
| 7          | rs2302387    | A            | G            | 0.407                  |
| 7          | rs7782643    | A            | G            | 0.1512                 |
| 7          | rs45564638   | G            | A            | 0.0465                 |
| 7          | rs2888611    | G            | C            | 0.407                  |
| 7          | rs4148808    | C            | T            | 0.2674                 |

Table 1-A1 continues on the next page →
### Table 1-A1 (Continues...): Minor allele frequencies for 1846 polymorphisms in 43 black South Africans.

| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|------------------------|
| 7          | rs28041781   | T            | C            | 0.2442                 |
| 7          | rs147600670  | A            | AC           | 0.1744                 |
| 7          | rs2235067    | T            | C            | 0.1279                 |
| 7          | rs4148743    | T            | C            | 0.314                  |
| 7          | rs1882477    | C            | G            | 0.2326                 |
| 7          | rs2373589    | T            | C            | 0.3488                 |
| 7          | rs113822506  | A            | G            | 0.1047                 |
| 7          | rs4148740    | G            | A            | 0.186                  |
| 7          | rs147898841  | C            | T            | 0.0697                 |
| 7          | rs113521552  | C            | T            | 0.0697                 |
| 7          | rs10246606   | A            | G            | 0.186                  |
| 7          | rs1197902    | A            | T            | 0.1279                 |
| 7          | rs2141849    | A            | C            | 0.1628                 |
| 7          | rs112216837  | G            | C            | 0.0697                 |
| 7          | rs55912869   | A            | G            | 0.1628                 |
| 7          | rs2373587    | A            | G            | 0.186                  |
| 7          | rs10280101   | C            | A            | 0.186                  |
| 7          | rs35572998   | A            | AG           | 0.0814                 |
| 7          | rs150867018  | G            | A            | 0.0697                 |
| 7          | rs16885829   | C            | T            | 0.1395                 |
| 7          | rs67151359   | G            | GT           | 0.1628                 |
| 7          | rs10225473   | G            | A            | 0.1279                 |
| 7          | rs6971264    | A            | G            | 0.1395                 |
| 7          | rs35280822   | A            | G            | 0.0814                 |
| 7          | rs10240953   | T            | G            | 0.0697                 |
| 7          | rs7787082    | G            | A            | 0.2442                 |
| 7          | rs2373587    | G            | C            | 0.1628                 |
| 7          | rs113158842  | G            | T            | 0.0697                 |
| 7          | rs28681479   | C            | T            | 0.2093                 |
| 7          | rs2373585    | T            | C            | 0.1628                 |
| 7          | rs2032583    | G            | A            | 0.186                  |
| 7          | rs4148739    | T            | C            | 0.186                  |
| 7          | rs11983225   | C            | T            | 0.186                  |
| 7          | rs113106026  | G            | A            | 0.0697                 |
| 7          | rs10362747   | G            | A            | 0.2442                 |
| 7          | rs183410324  | G            | A            | 0.0697                 |
| 7          | rs11760837   | C            | T            | 0.186                  |
| 7          | rs139774375  | A            | G            | 0.0697                 |
| 7          | rs11972405   | C            | T            | 0.186                  |
| 7          | rs10274587   | A            | G            | 0.1512                 |
| 7          | rs28381959   | A            | G            | 0.1047                 |
| 7          | rs28381958   | G            | GA           | 0.3721                 |
| 7          | rs10248420   | A            | G            | 0.3721                 |
| 7          | rs149043325  | A            | G            | 0.0581                 |
| 7          | rs113764224  | G            | A            | 0.0814                 |
| 7          | rs2235040    | T            | C            | 0.1512                 |
| 7          | rs111992902  | T            | C            | 0.0697                 |
| 7          | rs7989058    | A            | G            | 0.0348                 |
| 7          | rs28381951   | T            | G            | 0.0348                 |
| 7          | rs12668877   | T            | C            | 0.2326                 |
| 7          | rs111538144  | G            | A            | 0.0697                 |
| 7          | rs3789246    | T            | C            | 0.2326                 |
| 7          | rs2235064    | G            | T            | 0.0697                 |
| 7          | rs7795817    | T            | C            | 0.2326                 |
| 7          | rs12154941   | T            | C            | 0.0814                 |
| 7          | rs28381940   | G            | A            | 0.1744                 |
| 7          | rs4148737    | C            | T            | 0.4651                 |
| 7          | rs4148736    | A            | G            | 0.4651                 |
| 7          | rs4728700    | T            | C            | 0.1977                 |
| 7          | rs28381933   | G            | A            | 0.0465                 |

Table 1-A1 continues in the next column.
Table 1-A1 (Continues...): Minority allele frequencies for 1846 polymorphisms in 43 black South Africans.

| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|------------------------|
| 7          | rs3789243    | G            | A            | 0.4651                 |
| 7          | rs1858923    | G            | A            | 0.0645                 |
| 7          | rs3214119    | T            | TC           | 0.0697                 |
| 7          | rs3213619    | G            | A            | 0.1395                 |
| 7          | rs28381800   | A            | T            | 0.0697                 |
| 7          | rs11395081   | AT           | A            | 0.0697                 |
| 7          | rs4148731    | A            | G            | 0.0697                 |
| 7          | rs4148730    | G            | A            | 0.0697                 |
| 7          | rs28381775   | C            | T            | 0.0697                 |
| 7          | rs28381772   | T            | G            | 0.0697                 |
| 7          | rs11954093   | A            | G            | 0.0581                 |
| 7          | rs10231033   | G            | A            | 0.0697                 |
| 7          | rs4148729    | G            | T            | 0.0697                 |
| 7          | rs17149840   | A            | G            | 0.0697                 |
| 7          | rs75974753   | C            | T            | 0.0697                 |
| 7          | rs10280686   | T            | A            | 0.0697                 |
| 7          | rs10233247   | G            | A            | 0.0814                 |
| 7          | rs10224594   | C            | T            | 0.0697                 |
| 7          | rs10275831   | T            | C            | 0.0697                 |
| 7          | rs10246878   | A            | G            | 0.0581                 |
| 7          | rs200339290  | C            | CT           | 0.0930                 |
| 7          | rs10267099   | G            | A            | 0.1163                 |
| 7          | rs7648194    | A            | G            | 0.0930                 |
| 7          | rs11973812   | G            | C            | 0.0697                 |
| 7          | rs11977492   | A            | T            | 0.0697                 |
| 7          | rs28483333   | T            | C            | 0.0697                 |
| 7          | rs7810499    | C            | T            | 0.0697                 |
| 7          | rs28746495   | T            | C            | 0.1047                 |
| 7          | rs28746492   | G            | A            | 0.0697                 |
| 7          | rs6951067    | T            | C            | 0.4884                 |
| 7          | rs142999199  | A            | AG           | 0.0697                 |
| 7          | rs78413330   | A            | G            | 0.0697                 |
| 7          | rs76190983   | A            | G            | 0.0697                 |
| 7          | rs6465117    | A            | G            | 0.1977                 |
| 7          | rs10254392   | C            | T            | 0.0697                 |
| 7          | rs2106522    | G            | T            | 0.1047                 |
| 7          | rs2157930    | A            | G            | 0.1163                 |
| 7          | rs58101885   | A            | G            | 0.0930                 |
| 7          | rs75910150   | T            | C            | 0.0697                 |
| 7          | rs73705296   | A            | G            | 0.0930                 |
| 7          | rs1254931    | C            | T            | 0.1977                 |
| 7          | rs73705298   | A            | G            | 0.0930                 |
| 7          | rs145424538  | A            | AAAC         | 0.0697                 |
| 7          | rs77394523   | T            | C            | 0.0930                 |
| 7          | rs6957599    | A            | G            | 0.0697                 |
| 7          | rs11983274   | G            | A            | 0.0697                 |
| 7          | rs7796247    | A            | G            | 0.0697                 |
| 7          | rs1015415    | T            | A            | 0.2093                 |
| 7          | rs6465118    | A            | G            | 0.1977                 |
| 7          | rs10278483   | C            | T            | 0.0697                 |
| 7          | rs2188530    | G            | A            | 0.0697                 |
| 7          | rs2188529    | A            | T            | 0.0697                 |
| 7          | rs20176076   | A            | AT           | 0.0930                 |
| 7          | rs17149864   | G            | A            | 0.2209                 |
| 7          | rs78854352   | T            | C            | 0.0697                 |
| 7          | rs7474276    | T            | C            | 0.0697                 |
| 7          | rs11972683   | T            | C            | 0.0697                 |
| 7          | rs10232449   | A            | G            | 0.0697                 |
| 7          | rs10261685   | C            | A            | 0.0697                 |
| 7          | rs10243845   | G            | T            | 0.0697                 |

Table 1-A1 continues on the next column  
Table 1-A1 continues on the next page
Table 1-A1 (Continues…): Minor allele frequencies for 1846 polymorphisms in 43 black South Africans.

| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|------------------------|
| 11         | rs2513656    | T            | C            | 0.2442                 |
| 11         | rs2712812    | T            | C            | 0.2442                 |
| 11         | rs2851091    | A            | G            | 0.3953                 |
| 11         | rs2712803    | T            | C            | 0.2442                 |
| 11         | rs2712791    | A            | G            | 0.2442                 |
| 11         | rs2712794    | A            | G            | 0.4535                 |
| 11         | rs12279394   | G            | A            | 0.4186                 |
| 11         | rs14463665   | T            | C            | 0.0930                 |
| 11         | rs2712799    | A            | G            | 0.1977                 |
| 11         | rs114000664  | T            | C            | 0.0930                 |
| 11         | rs79297525   | T            | C            | 0.1395                 |
| 11         | rs11236348   | A            | C            | 0.407                  |
| 11         | rs11236349   | G            | T            | 0.407                  |
| 11         | rs11236351   | G            | A            | 0.407                  |
| 11         | rs4100076    | C            | A            | 0.1628                 |
| 11         | rs2712807    | G            | A            | 0.3023                 |
| 11         | rs2851069    | C            | T            | 0.1744                 |
| 11         | rs2712810    | T            | A            | 0.3023                 |
| 11         | rs2712819    | G            | A            | 0.3023                 |
| 11         | rs2712820    | T            | C            | 0.3023                 |
| 11         | rs11236359   | A            | G            | 0.4767                 |
| 11         | rs1109407    | A            | G            | 0.1279                 |
| 11         | rs1789694    | T            | C            | 0.3256                 |
| 11         | rs12422149   | A            | G            | 0.0697                 |
| 11         | rs61741839   | T            | C            | 0.0465                 |
| 11         | rs1612859    | C            | T            | 0.3837                 |
| 11         | rs115881705  | C            | T            | 0.0814                 |
| 11         | rs142877598  | A            | G            | 0.1047                 |
| 11         | rs3824903    | C            | A            | 0.4535                 |
| 11         | rs114169536  | T            | A            | 0.1977                 |
| 11         | rs116456559  | A            | G            | 0.1047                 |
| 11         | rs112455521  | A            | G            | 0.0697                 |
| 11         | rs139480360  | A            | G            | 0.0581                 |
| 11         | rs145026251  | C            | T            | 0.1047                 |
| 11         | rs149636191  | C            | G            | 0.1395                 |
| 11         | rs2066168    | C            | T            | 0.05                   |
| 11         | rs139408570  | G            | T            | 0.1395                 |
| 11         | rs200583779  | G            | GT           | 0.1395                 |
| 11         | rs190362624  | A            | G            | 0.1395                 |
| 11         | rs116211275  | G            | A            | 0.1395                 |
| 11         | rs114730634  | T            | C            | 0.1395                 |
| 11         | rs57141326   | A            | G            | 0.0814                 |
| 11         | rs3781727    | C            | T            | 0.1744                 |
| 11         | rs41298117   | G            | C            | 0.2442                 |
| 11         | rs1801906    | C            | T            | 0.4419                 |
| 11         | rs41298121   | C            | T            | 0.4419                 |
| 11         | rs17133818   | T            | C            | 0.1279                 |
| 11         | rs7951787    | G            | A            | 0.4302                 |
| 11         | rs143590827  | C            | CA           | 0.1395                 |
| 11         | rs74328774   | A            | G            | 0.1395                 |
| 11         | rs57279023   | G            | A            | 0.4419                 |
| 11         | rs10793116   | G            | A            | 0.0581                 |
| 11         | rs115385770  | T            | C            | 0.1395                 |
| 11         | rs14872627   | A            | G            | 0.1395                 |
| 11         | rs7924924    | C            | T            | 0.2558                 |
| 11         | rs137940642  | A            | G            | 0.0581                 |
| 11         | rs7738883    | T            | A            | 0.1395                 |
| 11         | rs78028968   | C            | T            | 0.1395                 |
| 11         | rs10793117   | T            | A            | 0.0465                 |
| 11         | rs147451830  | G            | A            | 0.1395                 |

Table 1-A1 continues on the next column →
Table 1-A1 (Continues...): Minor allele frequencies for 1846 polymorphisms in 42 black South Africans

| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|------------------------|
| 12         | rs753829     | G            | T            | 0.0581                 |
| 12         | rs18389222   | T            | G            | 0.0581                 |
| 12         | rs414908     | G            | C            | 0.0930                 |
| 12         | rs5896144    | G            | T            | 0.0581                 |
| 12         | rs115108625  | A            | T            | 0.0581                 |
| 12         | rs11045877   | G            | T            | 0.0930                 |
| 12         | rs12369359   | G            | T            | 0.0930                 |
| 12         | rs71444108   | GAGT          | CCACG        | 0.2                    |
| 12         | rs78695636   | A            | C            | 0.1047                 |
| 12         | rs20087545   | C            | CAT          | 0.0814                 |
| 12         | rs10841763   | C            | T            | 0.0930                 |
| 12         | rs717959     | C            | T            | 0.0930                 |
| 12         | rs11591330   | C            | T            | 0.0697                 |
| 12         | rs116180575  | A            | G            | 0.0697                 |
| 12         | rs115108635  | T            | C            | 0.0697                 |
| 12         | rs3962562    | T            | G            | 0.1628                 |
| 12         | rs11045881   | C            | T            | 0.1628                 |
| 12         | rs138156422  | C            | G            | 0.0814                 |
| 12         | rs11045882   | T            | C            | 0.2674                 |
| 12         | rs11045883   | G            | A            | 0.0930                 |
| 12         | rs10841764   | G            | C            | 0.1628                 |
| 12         | rs10841765   | T            | C            | 0.0930                 |
| 12         | rs111359254  | C            | T            | 0.0697                 |
| 12         | rs77853537   | A            | G            | 0.0697                 |
| 12         | rs78545516   | T            | C            | 0.1047                 |
| 12         | rs10841767   | G            | A            | 0.0465                 |
| 12         | rs10841768   | C            | A            | 0.0465                 |
| 12         | rs11513225   | C            | T            | 0.0697                 |
| 12         | rs11647641   | G            | C            | 0.1047                 |
| 12         | rs14605982   | T            | A            | 0.0697                 |
| 12         | rs201304263  | AG           | A            | 0.0465                 |
| 12         | rs12829704   | A            | G            | 0.0465                 |
| 12         | rs143654242  | G            | T            | 0.0695                 |
| 12         | rs116166170  | G            | A            | 0.1047                 |
| 12         | rs11045890   | T            | C            | 0.0697                 |
| 12         | rs56164184   | C            | T            | 0.0697                 |
| 12         | rs200739289  | CT           | C            | 0.1395                 |
| 12         | rs56370646   | TA           | T            | 0.1395                 |
| 12         | rs12578392   | C            | T            | 0.1395                 |
| 12         | rs57130116   | A            | G            | 0.1395                 |
| 12         | rs34111581   | C            | T            | 0.0695                 |
| 12         | rs11284985   | T            | A            | 0.0695                 |
| 12         | rs11615107   | T            | C            | 0.1047                 |
| 12         | rs12371604   | C            | T            | 0.0930                 |
| 12         | rs12815795   | C            | T            | 0.0695                 |
| 12         | rs34671512   | C            | A            | 0.1047                 |
| 12         | rs72653563   | T            | C            | 0.1047                 |
| 12         | rs4149087    | G            | T            | 0.1395                 |
| 12         | rs4149088    | G            | A            | 0.1395                 |
| 12         | rs11045892   | G            | A            | 0.0465                 |
| 12         | rs11045893   | C            | T            | 0.0465                 |
| 12         | rs12372157   | G            | T            | 0.1395                 |
| 12         | rs11045895   | C            | T            | 0.0814                 |
| 12         | rs77757956   | T            | C            | 0.0697                 |
| 12         | rs12370842   | A            | G            | 0.0465                 |
| 12         | rs11045896   | C            | A            | 0.0930                 |
| 12         | rs111237303  | G            | A            | 0.1047                 |
| 12         | rs11543117   | C            | A            | 0.0697                 |
| 12         | rs114436442  | G            | A            | 0.1047                 |
| 12         | rs200689244  | G            | GT           | 0.0465                 |

Table 1-A1 continues in the next column →
| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency | Minor allele frequency |
|------------|--------------|--------------|--------------|-----------------------|-----------------------|
| 12         | rs12230401   | C            | G            | 0.1512                |                       |
| 12         | rs57899519   | A            | T            | 0.4186                |                       |
| 12         | rs16923597   | A            | G            | 0.4186                |                       |
| 12         | rs7980842    | T            | G            | 0.2093                |                       |
| 12         | rs7967354    | T            | C            | 0.3837                |                       |
| 12         | rs10841782   | T            | C            | 0.2093                |                       |
| 12         | rs190500283  | A            | G            | 0.0697                |                       |
| 12         | rs7955581    | C            | G            | 0.3721                |                       |
| 12         | rs150018731  | GAGAT        | G            | 0.4186                |                       |
| 12         | rs2417971    | G            | A            | 0.3256                |                       |
| 12         | rs11045922   | C            | G            | 0.3837                |                       |
| 12         | rs11045923   | C            | G            | 0.3605                |                       |
| 12         | rs16923608   | G            | T            | 0.3837                |                       |
| 12         | rs183479283  | A            | G            | 0.0697                |                       |
| 12         | rs12298817   | C            | T            | 0.4186                |                       |
| 12         | rs143783884  | C            | A            | 0.0697                |                       |
| 12         | rs58923303   | T            | TGA          | 0.1395                |                       |
| 12         | rs12300594   | C            | T            | 0.4186                |                       |
| 12         | rs7503786    | T            | G            | 0.2093                |                       |
| 12         | rs201191507  | AAGT         | G            | 0.0581                |                       |
| 12         | rs4194005    | G            | T            | 0.3721                |                       |
| 12         | rs4194004    | C            | T            | 0.0581                |                       |
| 12         | rs3736081    | C            | T            | 0.0581                |                       |
| 12         | rs12303996   | C            | T            | 0.1977                |                       |
| 12         | rs12297072   | A            | G            | 0.0930                |                       |
| 12         | rs2199688    | G            | T            | 0.3837                |                       |
| 12         | rs11568565   | A            | G            | 0.0581                |                       |
| 12         | rs3764044    | C            | T            | 0.1395                |                       |
| 12         | rs11829484   | T            | C            | 0.2093                |                       |
| 12         | rs11203446   | A            | G            | 0.0581                |                       |
| 12         | rs10431251   | T            | C            | 0.4186                |                       |
| 12         | rs11045926   | C            | T            | 0.4186                |                       |
| 12         | rs11045927   | G            | T            | 0.4186                |                       |
| 12         | rs184309917  | C            | T            | 0.0697                |                       |
| 12         | rs112546011  | C            | G            | 0.0581                |                       |
| 12         | rs113601942  | T            | C            | 0.0581                |                       |
| 12         | rs11676958   | C            | T            | 0.0697                |                       |
| 12         | rs4543284    | C            | G            | 0.0581                |                       |
| 12         | rs61926248   | G            | C            | 0.2442                |                       |
| 12         | rs143498446  | A            | G            | 0.0697                |                       |
| 12         | rs112699138  | A            | C            | 0.0581                |                       |
| 12         | rs7316412    | G            | C            | 0.2209                |                       |
| 12         | rs73250866   | C            | G            | 0.1628                |                       |
| 12         | rs2199687    | A            | T            | 0.3837                |                       |
| 12         | rs11225684   | A            | G            | 0.2209                |                       |
| 12         | rs11045930   | T            | C            | 0.407                 |                       |
| 12         | rs7720986    | C            | T            | 0.0697                |                       |
| 12         | rs60594228   | C            | T            | 0.1395                |                       |
| 12         | rs15135999   | A            | C            | 0.3256                |                       |
| 12         | rs116452856  | C            | T            | 0.1744                |                       |
| 12         | rs2417972    | C            | T            | 0.407                 |                       |
| 12         | rs113662450  | C            | T            | 0.0581                |                       |
| 12         | rs11833627   | C            | T            | 0.314                 |                       |
| 12         | rs11226153   | G            | T            | 0.0581                |                       |
| 12         | rs11533477   | A            | G            | 0.0581                |                       |
| 12         | rs60098288   | C            | G            | 0.0814                |                       |
| 12         | rs184036934  | T            | C            | 0.0581                |                       |
| 12         | rs61552073   | A            | G            | 0.1395                |                       |
| 12         | rs11045941   | G            | A            | 0.1279                |                       |
| 12         | rs79349376   | T            | A            | 0.0581                |                       |
Table 1-A1 (Continues...): Minor allele frequencies for 1846 polymorphisms in 43 black South Africans.

| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|-----------------------|
| 12         | rs14836950    | T            | TAATA        | 0.0581                |
| 12         | rs80225829    | C            | T            | 0.0697                |
| 12         | rs111254386   | G            | A            | 0.1744                |
| 12         | rs11568567    | A            | T            | 0.0697                |
| 12         | rs4148994     | T            | C            | 0.0581                |
| 12         | rs11045960    | G            | A            | 0.1744                |
| 12         | rs4148993     | G            | A            | 0.3256                |
| 12         | rs11836396    | C            | T            | 0.2674                |
| 12         | rs113494988   | T            | C            | 0.1744                |
| 12         | rs34211424    | G            | A            | 0.1744                |
| 12         | rs112130054   | G            | C            | 0.1744                |
| 12         | rs148678212   | A            | AAC          | 0.1744                |
| 12         | rs12314183    | A            | G            | 0.2791                |
| 12         | rs2417974     | C            | T            | 0.0581                |
| 12         | rs2127117     | T            | C            | 0.1163                |
| 12         | rs2169883     | G            | A            | 0.1163                |
| 12         | rs7304940     | C            | T            | 0.1744                |
| 12         | rs112297403   | A            | G            | 0.1977                |
| 12         | rs199881908   | A            | AGAG         | 0.0581                |
| 12         | rs142521520   | CA           | C            | 0.1163                |
| 12         | rs142749463   | T            | C            | 0.0697                |
| 12         | rs12231484    | A            | C            | 0.0581                |
| 12         | rs2306226     | C            | T            | 0.0581                |
| 12         | rs10841789    | C            | A            | 0.1047                |
| 12         | rs58587133    | C            | T            | 0.0814                |
| 12         | rs61927778    | T            | C            | 0.0697                |
| 12         | rs7137014     | C            | T            | 0.1744                |
| 12         | rs61537911    | C            | T            | 0.1512                |
| 12         | rs77315871    | C            | T            | 0.0581                |
| 12         | rs7974575     | A            | G            | 0.1047                |
| 12         | rs12228765    | C            | T            | 0.0581                |
| 12         | rs12227319    | C            | G            | 0.2907                |
| 12         | rs34249976    | C            | T            | 0.1744                |
| 12         | rs11224775    | A            | C            | 0.1977                |
| 12         | rs59950654    | A            | T            | 0.1512                |
| 12         | rs199577219   | GA           | G            | 0.1628                |
| 12         | rs7237221     | T            | A            | 0.0814                |
| 12         | rs11045966    | T            | C            | 0.1163                |
| 12         | rs58406283    | A            | G            | 0.0930                |
| 12         | rs2219793     | G            | T            | 0.2907                |
| 12         | rs11568570    | A            | T            | 0.0581                |
| 12         | rs2219792     | C            | G            | 0.0697                |
| 12         | rs10505872    | A            | G            | 0.0930                |
| 12         | rs76669231    | A            | G            | 0.0581                |
| 12         | rs11045969    | A            | C            | 0.0581                |
| 12         | rs11833771    | G            | A            | 0.1512                |
| 12         | rs11049571    | C            | G            | 0.0581                |
| 12         | rs10082739    | T            | C            | 0.0465                |
| 12         | rs12298237    | T            | C            | 0.1977                |
| 12         | rs7312628     | T            | C            | 0.1512                |
| 12         | rs61927780    | A            | G            | 0.0930                |
| 12         | rs61927781    | C            | T            | 0.0697                |
| 12         | rs139621920   | TA           | T            | 0.0697                |
| 12         | rs11830993    | T            | C            | 0.1395                |
| 12         | rs4078        | G            | A            | 0.0930                |
| 12         | rs77207093    | T            | A            | 0.0930                |
| 12         | rs113307426   | G            | A            | 0.0581                |
| 12         | rs61927782    | A            | G            | 0.0930                |
| 12         | rs11836945    | C            | A            | 0.1512                |
| 12         | rs61927783    | T            | C            | 0.0930                |

Table 1-A1 continues in the next column.
| Chromosome | Polymorphism   | Minor allele | Major allele | Minor allele frequency |
|----------------|----------------|--------------|--------------|------------------------|
| 12             | rs77399780     | C            | T            | 0.0581                 |
|                | rs114958964    | C            | T            | 0.1512                 |
|                | rs114486873    | G            | A            | 0.1512                 |
|                | rs63378611     | G            | A            | 0.1512                 |
|                | rs140377659    | C            | T            | 0.1744                 |
|                | rs7831403      | A            | G            | 0.1163                 |
|                | rs5484         | T            | C            | 0.1744                 |
|                | rs5486         | G            | A            | 0.0581                 |
|                | rs1056007      | T            | G            | 0.1744                 |
|                | rs5488         | A            | T            | 0.1744                 |
|                | rs3213208      | G            | T            | 0.1163                 |
|                | rs12826421     | C            | G            | 0.1744                 |
|                | rs12833409     | T            | C            | 0.1163                 |
|                | rs4762700      | C            | T            | 0.4767                 |
|                | rs55785938     | A            | G            | 0.0581                 |
|                | rs12317073     | A            | G            | 0.4767                 |
|                | rs73551639     | A            | T            | 0.2442                 |
|                | rs73551640     | G            | T            | 0.2442                 |
|                | rs73551643     | A            | G            | 0.2442                 |
|                | rs73551645     | A            | G            | 0.2442                 |
|                | rs11574968     | G            | C            | 0.1628                 |
|                | rs9516500      | A            | G            | 0.1279                 |
|                | rs73551647     | A            | C            | 0.2442                 |
|                | rs60329452     | T            | C            | 0.1628                 |
|                | rs9524719      | A            | G            | 0.1279                 |
|                | rs11841559     | G            | C            | 0.2442                 |
|                | rs11841597     | G            | C            | 0.2442                 |
|                | rs10508010     | C            | A            | 0.1279                 |
|                | rs113234367    | A            | C            | 0.1628                 |
|                | rs113546805    | T            | C            | 0.1628                 |
|                | rs112160020    | A            | T            | 0.1628                 |
|                | rs7996263      | T            | G            | 0.2442                 |
|                | rs7998670      | G            | A            | 0.2442                 |
|                | rs113814775    | A            | G            | 0.407                  |
|                | rs73551665     | C            | G            | 0.2442                 |
|                | rs111880403    | A            | G            | 0.1628                 |
|                | rs8002563      | A            | G            | 0.407                  |
|                | rs7981159      | A            | G            | 0.2442                 |
|                | rs95901019     | G            | C            | 0.4302                 |
|                | rs95901050     | T            | A            | 0.3372                 |
|                | rs6492760      | T            | C            | 0.2442                 |
|                | rs1925878      | C            | G            | 0.4302                 |
|                | rs1925879      | C            | T            | 0.4302                 |
|                | rs1925877      | A            | G            | 0.2674                 |
|                | rs200517290    | A            | AT           | 0.1512                 |
|                | rs9302029      | C            | T            | 0.4302                 |
|                | rs14995938     | A            | G            | 0.1628                 |
|                | rs9302030      | C            | T            | 0.4302                 |
|                | rs9302031      | C            | T            | 0.4302                 |
|                | rs116317258    | T            | C            | 0.1628                 |
|                | rs1925876      | C            | T            | 0.4302                 |
|                | rs1925875      | G            | A            | 0.2674                 |
|                | rs112661898    | T            | A            | 0.1628                 |
|                | rs16950404     | C            | T            | 0.1628                 |
|                | rs2148066      | G            | A            | 0.4302                 |
|                | rs2148065      | T            | C            | 0.4302                 |
|                | rs1952108      | G            | A            | 0.4302                 |
|                | rs2148064      | G            | A            | 0.4302                 |
|                | rs113589545    | T            | C            | 0.2442                 |
|                | rs141106024    | T            | C            | 0.2442                 |

Table 1-A1 (Continues...): Minor allele frequencies for 1846 polymorphisms in 43 black South Africans.
### Table 1-A1 (Continues...): Minor allele frequencies for 1846 polymorphisms in 43 black South Africans.

| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|------------------------|
| 13         | rs9516518    | C            | T            | 0.1163                 |
| 13         | rs61530740   | G            | A            | 0.3372                 |
| 13         | rs9590161    | G            | A            | 0.1047                 |
| 13         | rs3770       | A            | G            | 0.4302                 |
| 13         | rs16950472   | G            | A            | 0.1047                 |
| 13         | rs9584273    | T            | C            | 0.0697                 |
| 13         | rs1059751    | G            | A            | 0.2442                 |
| 13         | rs4148553    | T            | C            | 0.2442                 |
| 13         | rs74107819   | A            | C            | 0.1047                 |
| 13         | rs115266179  | T            | C            | 0.0581                 |
| 13         | rs4148551    | T            | C            | 0.3605                 |
| 13         | rs3742106    | C            | A            | 0.3272                 |
| 13         | rs4148549    | C            | T            | 0.3605                 |
| 13         | rs113454973  | T            | C            | 0.0581                 |
| 13         | rs96600142   | A            | G            | 0.2791                 |
| 13         | rs61667065   | T            | C            | 0.2326                 |
| 13         | rs7331508    | G            | A            | 0.186                  |
| 13         | rs112975730  | C            | G            | 0.1977                 |
| 13         | rs200689258  | AC           | A            | 0.0930                 |
| 13         | rs4773838    | C            | A            | 0.4651                 |
| 13         | rs4771904    | T            | G            | 0.2674                 |
| 13         | rs9805226    | T            | A            | 0.1047                 |
| 13         | rs9302039    | T            | A            | 0.4884                 |
| 13         | rs114719300  | C            | T            | 0.0581                 |
| 13         | rs75080423   | C            | A            | 0.2907                 |
| 13         | rs202160354  | CCA           | C            | 0.1047                 |
| 13         | rs4148547    | T            | C            | 0.2907                 |
| 13         | rs4148546    | G            | A            | 0.3605                 |
| 13         | rs4274307    | C            | T            | 0.0697                 |
| 13         | rs4148544    | T            | C            | 0.2907                 |
| 13         | rs4148543    | G            | A            | 0.314                  |
| 13         | rs61967636   | G            | A            | 0.3372                 |
| 13         | rs67308757   | G            | GA           | 0.3372                 |
| 13         | rs191458655  | A            | G            | 0.0581                 |
| 13         | rs9561765    | A            | G            | 0.0814                 |
| 13         | rs11633602   | A            | G            | 0.0697                 |
| 13         | rs150571031  | CAT           | C            | 0.0697                 |
| 13         | rs7323148    | C            | T            | 0.0581                 |
| 13         | rs9302040    | A            | C            | 0.2558                 |
| 13         | rs58286099   | C            | T            | 0.0814                 |
| 13         | rs112792420  | T            | A            | 0.2558                 |
| 13         | rs11568695   | T            | C            | 0.1512                 |
| 13         | rs9556455    | A            | G            | 0.2558                 |
| 13         | rs9561768    | C            | T            | 0.2558                 |
| 13         | rs115100521  | G            | T            | 0.0581                 |
| 13         | rs9590168    | G            | C            | 0.2558                 |
| 13         | rs9590169    | G            | A            | 0.2558                 |
| 13         | rs115850104  | G            | T            | 0.0814                 |
| 13         | rs9561769    | A            | G            | 0.2558                 |
| 13         | rs20091629   | CT           | C            | 0.2558                 |
| 13         | rs139228772  | AT           | A            | 0.2558                 |
| 13         | rs113574255  | C            | G            | 0.0814                 |
| 13         | rs61967172   | T            | C            | 0.2558                 |
| 13         | rs61967173   | T            | C            | 0.2558                 |
| 13         | rs114400105  | G            | T            | 0.0814                 |
| 13         | rs10219913   | C            | T            | 0.2558                 |
| 13         | rs9302043    | G            | A            | 0.2558                 |
| 13         | rs61178570   | AT           | A            | 0.2558                 |
| 13         | rs7324971    | A            | G            | 0.0814                 |
| 13         | rs199553697  | CAAAT          | C            | 0.2442                 |

Table 1-A1 continues in the next column...
| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency | Minor allele frequency |
|------------|--------------|--------------|--------------|------------------------|------------------------|
| 13         | rs1617888    | T            | G            | 0.3488                 |                        |
| 13         | rs943289     | A            | G            | 0.1047                 |                        |
| 13         | rs73557775   | A            | G            | 0.0814                 |                        |
| 13         | rs1751011    | T            | A            | 0.2791                 |                        |
| 13         | rs2766478    | A            | T            | 0.2791                 |                        |
| 13         | rs12487686   | A            | C            | 0.0697                 |                        |
| 13         | rs7987838    | T            | C            | 0.3721                 |                        |
| 13         | rs1751052    | G            | A            | 0.3721                 |                        |
| 13         | rs1189440    | G            | A            | 0.1047                 |                        |
| 13         | rs189439     | C            | T            | 0.3721                 |                        |
| 13         | rs1189432    | G            | A            | 0.3721                 |                        |
| 13         | rs9590117    | T            | C            | 0.1744                 |                        |
| 13         | rs1189436    | A            | G            | 0.1047                 |                        |
| 13         | rs1189435    | C            | T            | 0.1047                 |                        |
| 13         | rs4148350    | T            | C            | 0.0814                 |                        |
| 13         | rs1189434    | A            | G            | 0.1047                 |                        |
| 13         | rs34857509   | A            | G            | 0.0814                 |                        |
| 13         | rs35904677   | A            | AT           | 0.1047                 |                        |
| 13         | rs1189433    | C            | T            | 0.1047                 |                        |
| 13         | rs60205363   | CA           | C            | 0.0697                 |                        |
| 13         | rs149521078  | A            | C            | 0.0697                 |                        |
| 13         | rs145337567  | T            | C            | 0.0697                 |                        |
| 13         | rs1617785    | G            | A            | 0.2907                 |                        |
| 13         | rs1729760    | A            | G            | 0.2907                 |                        |
| 13         | rs4148527    | A            | G            | 0.0814                 |                        |
| 13         | rs12584534   | T            | C            | 0.0697                 |                        |
| 13         | rs9590184    | C            | T            | 0.1744                 |                        |
| 13         | rs145277775  | A            | G            | 0.0697                 |                        |
| 13         | rs11232943   | A            | C            | 0.0697                 |                        |
| 13         | rs147385814  | C            | T            | 0.0697                 |                        |
| 13         | rs4773840    | G            | A            | 0.2442                 |                        |
| 13         | rs74105436   | G            | A            | 0.2558                 |                        |
| 13         | rs16950650   | T            | C            | 0.1395                 |                        |
| 13         | rs1564355    | G            | A            | 0.314                  |                        |
| 13         | rs1564354    | A            | C            | 0.314                  |                        |
| 13         | rs1564353    | C            | A            | 0.314                  |                        |
| 13         | rs143551018  | T            | C            | 0.0697                 |                        |
| 13         | rs1751069    | A            | G            | 0.0930                 |                        |
| 13         | rs4148515    | T            | G            | 0.2907                 |                        |
| 13         | rs4148512    | A            | G            | 0.3256                 |                        |
| 13         | rs4148509    | T            | C            | 0.3023                 |                        |
| 13         | rs16950656   | G            | T            | 0.0465                 |                        |
| 13         | rs57927922   | A            | G            | 0.0581                 |                        |
| 13         | rs3782958    | C            | G            | 0.3023                 |                        |
| 13         | rs61966885   | A            | G            | 0.3023                 |                        |
| 13         | rs114479588  | T            | C            | 0.0581                 |                        |
| 13         | rs72643607   | A            | G            | 0.0581                 |                        |
| 13         | rs4148506    | T            | C            | 0.4884                 |                        |
| 13         | rs1471481    | G            | A            | 0.1163                 |                        |
| 13         | rs114964035  | A            | G            | 0.0697                 |                        |
| 13         | rs79341676   | C            | T            | 0.0814                 |                        |
| 13         | rs1678936    | A            | G            | 0.1628                 |                        |
| 13         | rs1750996    | A            | G            | 0.4186                 |                        |
| 13         | rs1729764    | A            | G            | 0.4186                 |                        |
| 13         | rs1038138    | C            | T            | 0.3488                 |                        |
| 13         | rs56261894   | C            | T            | 0.1163                 |                        |
| 13         | rs1750999    | T            | C            | 0.1512                 |                        |
| 13         | rs7982526    | T            | G            | 0.0465                 |                        |
| 13         | rs2646363    | T            | C            | 0.0697                 |                        |
| 13         | rs1189458    | G            | A            | 0.407                  |                        |
| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|------------------------|
| 13         | rs7332836    | G            | A            | 0.4535                 |
| 13         | rs7333281    | G            | T            | 0.2674                 |
| 13         | rs7335147    | T            | C            | 0.5                     |
| 13         | rs9516539    | A            | G            | 0.5                     |
| 13         | rs9524830    | A            | T            | 0.5                     |
| 13         | rs7322825    | C            | T            | 0.5                     |
| 13         | rs719533     | A            | G            | 0.5                     |
| 13         | rs3457476    | T            | TG           | 0.1163                 |
| 13         | rs9524831    | A            | C            | 0.5                     |
| 13         | rs7983336    | G            | A            | 0.5                     |
| 13         | rs7987533    | T            | C            | 0.5                     |
| 13         | rs9524832    | A            | G            | 0.5                     |
| 13         | rs3434136    | C            | A            | 0.5                     |
| 13         | rs58725124   | A            | C            | 0.0465                 |
| 13         | rs1824913    | G            | A            | 0.5                     |
| 13         | rs1824912    | A            | G            | 0.5                     |
| 13         | rs1824911    | T            | A            | 0.5                     |
| 13         | rs7999175    | C            | T            | 0.5                     |
| 13         | rs143604864  | C            | T            | 0.186                  |
| 13         | rs9524835    | A            | G            | 0.5                     |
| 13         | rs9524836    | A            | G            | 0.5                     |
| 13         | rs4773847    | T            | C            | 0.5                     |
| 13         | rs201259935  | C            | CA           | 0.186                  |
| 13         | rs4148467    | T            | C            | 0.5                     |
| 13         | rs34429583   | AC           | A            | 0.4535                 |
| 13         | rs34429583_t3| C            | A            | 0.4535                 |
| 13         | rs4771907    | C            | G            | 0.5                     |
| 13         | rs4148465    | A            | G            | 0.5                     |
| 13         | rs11579275   | G            | C            | 0.186                  |
| 13         | rs4148464    | G            | A            | 0.5                     |
| 13         | rs4148463    | C            | G            | 0.5                     |
| 13         | rs7321744    | G            | A            | 0.5                     |
| 13         | rs113500636  | CCACCTG      | C            | 0.5                     |
| 13         | rs6492769    | T            | C            | 0.5                     |
| 13         | rs75567542   | G            | A            | 0.5                     |
| 13         | rs114512462  | T            | C            | 0.0814                 |
| 13         | rs9524840    | A            | G            | 0.5                     |
| 13         | rs115690139  | G            | A            | 0.186                  |
| 13         | rs9590203    | C            | T            | 0.0697                 |
| 13         | rs4111022    | T            | C            | 0.4535                 |
| 13         | rs7321623    | A            | G            | 0.5                     |
| 13         | rs11431283   | CT           | C            | 0.5                     |
| 13         | rs4771908    | C            | T            | 0.5                     |
| 13         | rs67413584   | A            | AATATT       | 0.5                    |
| 13         | rs2766476    | A            | C            | 0.1163                 |
| 13         | rs9302048    | G            | C            | 0.2674                 |
| 13         | rs4773848    | A            | G            | 0.3721                 |
| 13         | rs9590204    | T            | G            | 0.2674                 |
| 13         | rs9590205    | T            | A            | 0.2674                 |
| 13         | rs9302049    | C            | T            | 0.2674                 |
| 13         | rs79083026   | G            | C            | 0.0697                 |
| 13         | rs114579713  | T            | C            | 0.186                  |
| 13         | rs4773849    | G            | A            | 0.3721                 |
| 13         | rs1926656    | G            | A            | 0.3953                 |
| 13         | rs1926657    | T            | C            | 0.3372                 |
| 13         | rs7330519    | C            | T            | 0.3837                 |
| 13         | rs7325019    | C            | T            | 0.3488                 |
| 13         | rs4612933    | T            | C            | 0.3488                 |
| 13         | rs200179424  | A            | ACT          | 0.3488                 |
| 13         | rs4371040    | T            | G            | 0.3488                 |
| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|-----------------------|
| 13         | rs4148442    | T            | C            | 0.2558                |
| 13         | rs36077567   | GA           | G            | 0.2093                |
| 13         | rs4148441    | A            | G            | 0.0697                |
| 13         | rs4148440    | T            | C            | 0.0814                |
| 13         | rs7335257    | C            | T            | 0.1163                |
| 13         | rs7336202    | A            | T            | 0.1163                |
| 13         | rs8000333    | A            | G            | 0.1163                |
| 13         | rs9524864    | T            | C            | 0.0814                |
| 13         | rs7982955    | A            | G            | 0.1163                |
| 13         | rs4773861    | T            | C            | 0.1163                |
| 13         | rs60115298   | C            | CT           | 0.1163                |
| 13         | rs12548649   | C            | T            | 0.3837                |
| 13         | rs9524866    | G            | A            | 0.1163                |
| 13         | rs60769646   | A            | C            | 0.0465                |
| 13         | rs7320383    | G            | A            | 0.1163                |
| 13         | rs9516550    | G            | C            | 0.152                 |
| 13         | rs73546891   | A            | G            | 0.0465                |
| 13         | rs9556467    | C            | T            | 0.1163                |
| 13         | rs2389227    | T            | C            | 0.1163                |
| 13         | rs2389228    | G            | A            | 0.1279                |
| 13         | rs7319126    | A            | C            | 0.2558                |
| 13         | rs74893509   | T            | C            | 0.2209                |
| 13         | rs7665052    | T            | G            | 0.2209                |
| 13         | rs7320375    | G            | A            | 0.2674                |
| 13         | rs7325256    | C            | T            | 0.2674                |
| 13         | rs7325861    | G            | T            | 0.2674                |
| 13         | rs4148433    | C            | T            | 0.2093                |
| 13         | rs4148432    | T            | C            | 0.2674                |
| 13         | rs4148430    | A            | T            | 0.2674                |
| 13         | rs16950847   | T            | A            | 0.2093                |
| 13         | rs79474277   | A            | G            | 0.2093                |
| 13         | rs9524869    | C            | G            | 0.3605                |
| 13         | rs11842634   | C            | T            | 0.2674                |
| 13         | rs201251479  | AC           | A            | 0.1163                |
| 13         | rs95689275   | C            | A            | 0.1163                |
| 13         | rs11842091   | C            | T            | 0.2558                |
| 13         | rs7338004    | A            | G            | 0.0581                |
| 13         | rs7338429    | A            | G            | 0.0581                |
| 13         | rs7321532    | T            | C            | 0.0581                |
| 13         | rs11843102   | G            | A            | 0.0581                |
| 13         | rs7986087    | T            | C            | 0.2558                |
| 13         | rs797353     | G            | A            | 0.2558                |
| 13         | rs60223044   | C            | T            | 0.0581                |
| 13         | rs9516552    | C            | T            | 0.0814                |
| 13         | rs79921462   | C            | T            | 0.0930                |
| 13         | rs870004     | A            | G            | 0.3721                |
| 13         | rs7333118    | T            | G            | 0.0465                |
| 13         | rs9590228    | C            | T            | 0.3837                |
| 13         | rs9590229    | C            | T            | 0.3837                |
| 13         | rs7317112    | A            | G            | 0.3837                |
| 13         | rs7322318    | T            | C            | 0.3372                |
| 13         | rs73548830   | T            | C            | 0.0465                |
| 13         | rs150988051  | ACATTGC      | A            | 0.1163                |
| 13         | rs73548833   | C            | A            | 0.0465                |
| 13         | rs7324503    | C            | A            | 0.1163                |
| 13         | rs201187127  | AAAAT         | A            | 0.0465                |
| 13         | rs112859374  | T            | C            | 0.0465                |
| 13         | rs56891151   | G            | A            | 0.0465                |
| 13         | rs59514866   | G            | C            | 0.0465                |
| 13         | rs4148428    | C            | T            | 0.2093                |

Table 1-A1 continues in the next column...
Table 1-A1 (Continues...): Minor allele frequencies for 1846 polymorphisms in 43 black South Africans.

| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|------------------------|
| 19         | rs2843845    | T            | C            | 0.4767                 |
| 19         | rs112673025  | A            | G            | 0.0465                 |
| 19         | rs79366653   | G            | A            | 0.0581                 |
| 19         | rs11878604   | C            | T            | 0.2907                 |
| 19         | rs55978439   | A            | T            | 0.0465                 |
| 19         | rs2258314    | T            | C            | 0.0697                 |
| 19         | rs10853742   | G            | C            | 0.1977                 |
| 19         | rs12327581   | T            | C            | 0.4419                 |
| 19         | rs11667314   | T            | C            | 0.1977                 |
| 19         | rs7251418    | A            | G            | 0.1047                 |
| 19         | rs76112798   | T            | C            | 0.0697                 |
| 19         | rs7248240    | G            | C            | 0.1163                 |
| 19         | rs56164728   | C            | T            | 0.0697                 |
| 19         | rs28399462   | A            | G            | 0.0697                 |
| 19         | rs4803380    | T            | C            | 0.0697                 |
| 19         | rs28399454   | T            | C            | 0.0697                 |
| 19         | rs144437384  | A            | G            | 0.0697                 |
| 19         | rs72549444   | G            | A            | 0.0697                 |
| 19         | rs56113850   | C            | T            | 0.2791                 |
| 19         | rs28399433   | C            | A            | 0.0697                 |
| 19         | rs61663607   | C            | T            | 0.1512                 |
| 19         | rs111822043  | A            | T            | 0.0465                 |
| 19         | rs8102683    | T            | C            | 0.2209                 |
| 19         | rs8105704    | T            | C            | 0.2093                 |
| 19         | rs12610432   | T            | C            | 0.2093                 |
| 19         | rs186830274  | C            | T            | 0.0581                 |
| 19         | rs111867898  | C            | T            | 0.0465                 |
| 19         | rs4570983    | T            | C            | 0.1279                 |
| 19         | rs75152309   | A            | T            | 0.0697                 |
| 19         | rs74493998   | T            | C            | 0.0697                 |
| 19         | rs28575771   | A            | G            | 0.2209                 |
| 19         | rs2261144    | G            | A            | 0.1512                 |
| 19         | rs12975382   | T            | G            | 0.4535                 |
| 19         | rs73032311   | C            | T            | 0.0697                 |
| 19         | rs73032316   | C            | G            | 0.0697                 |
| 19         | rs2815706    | G            | T            | 0.0697                 |
| 19         | rs56081734   | A            | C            | 0.4535                 |
| 19         | rs6682672    | G            | A            | 0.0814                 |
| 19         | rs6780403    | G            | A            | 0.0814                 |
| 19         | rs149560129  | G            | A            | 0.0465                 |
| 19         | rs4803393    | C            | T            | 0.1163                 |
| 19         | rs79809963   | C            | A            | 0.0814                 |
| 19         | rs76734307   | C            | T            | 0.0814                 |
| 19         | rs10853743   | T            | C            | 0.0697                 |
| 19         | rs3875155    | C            | T            | 0.0814                 |
| 19         | rs4105141    | A            | T            | 0.2236                 |
| 19         | rs5007415    | A            | C            | 0.2236                 |
| 19         | rs10411264   | T            | C            | 0.2236                 |
| 19         | rs115564457  | T            | C            | 0.1279                 |
| 19         | rs28472879   | A            | G            | 0.2236                 |
| 19         | rs28463685   | A            | G            | 0.1395                 |
| 19         | rs10406188   | G            | A            | 0.2236                 |
| 19         | rs8103288    | G            | C            | 0.2236                 |
| 19         | rs8103444    | C            | A            | 0.0697                 |
| 19         | rs10414481   | T            | C            | 0.2236                 |
| 19         | rs78374326   | G            | T            | 0.2236                 |
| 19         | rs8865457    | T            | C            | 0.2236                 |
| 19         | rs12611183   | A            | T            | 0.0814                 |
| 19         | rs199970591  | T            | TATCA        | 0.0814                 |
| 19         | rs76297159   | G            | A            | 0.0814                 |

Table 1-A1 continues on the next page →
| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|------------------------|
| 19         | rs12609982   | G            | A            | 0.0814                 |
| 19         | rs12608615   | C            | T            | 0.0814                 |
| 19         | rs34127861   | TA           | T            | 0.0814                 |
| 19         | rs73931385   | C            | A            | 0.0697                 |
| 19         | rs142357867  | T            | G            | 0.0348                 |
| 19         | rs73931386   | A            | G            | 0.0697                 |
| 19         | rs9630870    | A            | G            | 0.0581                 |
| 19         | rs6508953    | A            | G            | 0.0814                 |
| 19         | rs150311873  | T            | C            | 0.0465                 |
| 19         | rs7252825    | T            | C            | 0.3372                 |
| 19         | rs66657317   | G            | GT           | 0.0814                 |
| 19         | rs3852871    | C            | A            | 0.0697                 |
| 19         | rs201010762  | G            | GA           | 0.0697                 |
| 19         | rs17726493   | T            | C            | 0.0914                 |
| 19         | rs55790533   | A            | G            | 0.0814                 |
| 19         | rs119921300  | A            | G            | 0.0465                 |
| 19         | rs34724660   | A            | G            | 0.0697                 |
| 19         | rs3892666    | C            | G            | 0.1628                 |
| 19         | rs78367667   | G            | A            | 0.0697                 |
| 19         | rs73034462   | A            | G            | 0.3023                 |
| 19         | rs73034465   | G            | A            | 0.3023                 |
| 19         | rs7252501    | T            | C            | 0.1628                 |
| 19         | rs4358050    | A            | G            | 0.1628                 |
| 19         | rs4359558    | A            | G            | 0.3023                 |
| 19         | rs112531545  | G            | C            | 0.1628                 |
| 19         | rs4803404    | A            | C            | 0.1628                 |
| 19         | rs4468739    | C            | T            | 0.3023                 |
| 19         | rs4001944    | A            | C            | 0.3023                 |
| 19         | rs55779134   | GT           | G            | 0.3023                 |
| 19         | rs4001941    | G            | A            | 0.4767                 |
| 19         | rs34418474   | T            | G            | 0.0697                 |
| 19         | rs12459860   | C            | T            | 0.0697                 |
| 19         | rs57244441   | T            | G            | 0.3023                 |
| 19         | rs4609955    | C            | T            | 0.3023                 |
| 19         | rs12150973   | C            | T            | 0.3023                 |
| 19         | rs2155901    | C            | T            | 0.3023                 |
| 19         | rs12459233   | G            | C            | 0.0697                 |
| 19         | rs35781447   | A            | G            | 0.0697                 |
| 19         | rs12985721   | G            | A            | 0.0697                 |
| 19         | rs28687008   | T            | C            | 0.1512                 |
| 19         | rs145709497  | C            | T            | 0.0930                 |
| 19         | rs34151237   | G            | T            | 0.4186                 |
| 19         | rs34013487   | G            | C            | 0.2093                 |
| 19         | rs8107329    | T            | C            | 0.3023                 |
| 19         | rs74723889   | T            | C            | 0.0930                 |
| 19         | rs8100958    | C            | T            | 0.314                  |
| 19         | rs4124633    | C            | T            | 0.186                  |
| 19         | rs7245500    | C            | A            | 0.3837                 |
| 19         | rs11667592   | C            | T            | 0.0814                 |
| 19         | rs8109818    | G            | A            | 0.3837                 |
| 19         | rs73557157   | A            | C            | 0.2442                 |
| 19         | rs61586981   | G            | A            | 0.2442                 |
| 19         | rs60618302   | T            | A            | 0.2558                 |
| 19         | rs111589961  | T            | C            | 0.2442                 |
| 19         | rs73933714   | T            | G            | 0.4651                 |
| 19         | rs35906311   | C            | A            | 0.3953                 |
| 19         | rs16974790   | A            | G            | 0.3953                 |
| 19         | rs73933721   | A            | G            | 0.3953                 |
| 19         | rs16974794   | G            | A            | 0.3953                 |
| 19         | rs73559241   | G            | A            | 0.3953                 |
| Chromosome | Polymorphism | Minor allele | Major allele | Minor allele frequency |
|------------|--------------|--------------|--------------|------------------------|
| 19         | rs28502605   | C            | T            | 0.2558                 |
| 19         | rs7255149    | C            | A            | 0.4535                 |
| 19         | rs12459147   | G            | A            | 0.4651                 |
| 19         | rs34150638   | A            | G            | 0.4535                 |
| 19         | rs202055073  | AT           | A            | 0.0697                 |
| 19         | rs11672085   | T            | C            | 0.2791                 |