GMR
The Original

Ethnic categorization of the Brazilian population samples — Native Americans, European descendants, Mulattoes, and African descendants — using allelic frequencies distribution of gene variants associated with neurodegenerative diseases

Ana Paula Maette Passos[1], Tatiana Lucia Santos Nogueira[2], Rosane Silva[1] and Rodrigo Soares de Moura-Neto[3]

[1]Instituto de Biofísica Carlos Chagas Filho, Universidade Federal do Rio de Janeiro, Av. Carlos Chagas Filho 373, Sala G1-50, Rio de Janeiro, RJ, 21941-902, Brazil.
[2]Laboratório de Biodefesa, Instituto de Biologia do Exército, Rio de Janeiro, RJ 20911-270 Brazil.
[3]Instituto de Biologia, Universidade Federal do Rio de Janeiro, Av. Carlos Chagas Filho 373, Sala A1-88, Rio de Janeiro, RJ, 21941-902, Brazil.

Corresponding Author: Rodrigo Soares de Moura-Neto
Email: rodrigomouraneto@ufrj.br

Genet. Mol. Res. 24 (1): gmr24112
Received January 09, 2025
Accepted February 19, 2025
Published February 24, 2025
DOI http://dx.doi.org/10.4238/gmr24112

ABSTRACT. Three ancestral components — Native American, European, and African — comprise the Brazilian population, resulting in a high genetic diversity and distribution of polymorphism frequency. Therefore, a population study is necessary before analyzing disease-associated variants. Several genes previously described are associated with neurodegenerative diseases and their respective variants. However, the distribution of these gene variants has not been established in the heterogeneous Brazilian population. In this work, we analyzed polymorphic variants in samples of a stratified Brazilian population to observe if there is any correlation between such heterogeneity and their respective ethnic and geographical origins. We selected individuals from Brazilian ethnic groups according to racial self-declaration: European descendants (N = 30), African descendants (N

= 30), Mulattoes Brazilians (N = 30), as well as Native Americans (N = 20), and individuals of Japanese descent (N = 30). The study of PCA and other population parameters allowed the characterization of populations and population groups. European descendant individuals were indistinguishable from Mulattoes (Fst = 0.001); on the other hand, the group of European descendant and Mulatto individuals indicated a moderate genetic differentiation from the European population (Fst = 0.102). The analyses showed that Native Americans (NAT) are a distinct group with moderate to significant differentiation from other population groups. We showed that the genotypic distributions of markers associated with neurodegenerative diseases vary in our populations. Thus, the interpretation of the associated genotypes should consider the genetic composition of this population.

Key words: Population Genetics; Brazil; Admixed Populations; SNPs.

INTRODUCTION

The advances in diagnostic techniques, treatments, medications, and control strategies, promoted remarkable progress in the medical and biomedical fields and caused an increase in human life expectancy from approximately 49 to more than 75 years old (Havranek, 2019). Due to the increased aging population, neurodegenerative diseases are more frequent. Neurodegenerative diseases refer to a series of neuronal disorders accompanied by massive neuronal loss in the later stages of the disease. These include Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis. Alzheimer's disease (Querfurth, 2010), the leading cause of dementia in the elderly around 60 years old, is estimated to affect 36 million people (Querfurth, 2010), accounting for 10.8% of the population aged 80 to 90 years (Burns, et al., 2002).

In Brazil, the number of older adults grew by 23% in 10 years, exceeding 31 million in 2022, thus calling for a review of public policies aimed at this population segment (Paradella, 2018). Several genes were previously described in the literature as being associated with samples from patients with neurodegenerative diseases and their respective variants (Supplementary Table 1). However, the distribution of these gene variants has not been established in a heterogeneous population such as Rio de Janeiro, considering that the exponential increase of people meant an abundance of rare variants, where their sharing depends on geographic distances (Tennessen, et al., 2012).

Since world populations vary considerably in their predisposition to certain diseases concerning the frequency of alleles (Pena, et al., 2011; Asiimwe, 2022; Harerimana, et al., 2022; Mishra, et al., 2022, Paradela, et al., 2023), the Brazilian people, which carry the three ancestral components, promote a model of study of high impact in the concepts of development, interpretation, and clinical implementation (Suarez-Kurtz, 2010; Pena, et al., 2011; Deng, et al., 2016). Because the high level of genetic diversity, implying the frequency of polymorphisms distribution, it is vital to study the precedent population so that the best ordering can be followed (Lillo, et al., 2021; Rajabli, et al., 2022; Ali, et al., 2023). Therefore, each person is required to be treated individually, considering the approach based on their ancestry. This new genetic information regarding the Brazilian population needs to be placed in a historical and phylogeographic context (Pena, et al., 2011).

Many studies have been conducted on the relationship between target genes related to neurodegenerative diseases and their variants. Studies in a mixed population, as in the case of Rio de Janeiro, are still scarce for observing population variability (Benedet, et al., 2012; Horimoto, et al., 2021). We sought to follow how the polymorphisms related to neurodegenerative diseases behaved in the population of Rio de Janeiro, given the unique ethnic mix that Brazil suffered with its colonization and the abundance of immigrants. Is there any correlation between such heterogeneity and their ethnic and geographical origins? In this way, we propose to evaluate the distribution of these variants in a sample of the mixed population of Rio de Janeiro, its percentage of admixture and population substructures, and to carry out a comparative analysis to reference populations from the 1KG Project database (Europeans, Africans, and Asians).

METHODS

Reference populations

Genotyping data were obtained from a total of 319 individuals. Three reference populations from the 1000 Genomes Project Consortium (Auton, et al., 2015) were selected: 108 Africans from Yoruba (YRI), 107 Spaniards from the Iberian Peninsula (IBS), and 104 Japanese from Tokyo (JPT).

Samples of the Brazilian population

Ninety samples of anonymized individuals from populations previously studied by the group were selected (Silva and Moura-Neto, 1998, 2004; Sucharov, et al., 1999; Costa, et al., 2002; Aranda, et al., 2011; Moura-Neto, et al., 2018, 2021; Woerner, et al., 2018; Strobl, et al., 2019). Through ethnic-racial self-declaration, 30 individuals were classified as African descendants of Brazil - ABR (Silva and Moura-Neto, 1998), 30 as European descendants of Brazil - EBR (Silva and Moura-Neto, 1998), and 30 as the admixed population of Mulattoes - MUL (Aranda, et al., 2011). In addition, 34 samples of individuals classified as JPBR (Japanese from Brazil) and descendants of Japanese residing in São Paulo, Brazil, were used. The study was approved by the Research Ethics Committee of the UFRJ (Process No. 214/03). In addition, 20 samples of Native American individuals (NAT) were collected from São Gabriel da Cachoeira, a municipality in the State of Amazonas in the extreme northwest of Brazil (-0.13, - 67.088889). The Brazilian National Survey Office estimates a population of 47,000 in São Gabriel da Cachoeira. Eight out of ten inhabitants are Native Americans, the highest predominance of autochthonous people in Brazil. (https://cidades.ibge.gov.br/brasil/am/sao-gabriel-da-cachoeira/pesquisa/23/22107?detalhes=true, accessed 02/03/2023). The criteria for samples selected of native individuals were the ones of mitochondrial haplogroup A, B, C, or D (EMPOP, https://empop.online), and prediction of haplogroup Q based on Y-STR NEVGEN (https://nevgen.org) (data not shown), also other evidence for Native American ancestry maternal and paternal, respectively (Moura-Neto, et al., 2015; Strobl, et al., 2019). Biological samples from those individuals, kept on paper cards, were anonymized, and the DNA was extracted using the QIAamp DNA Investigator Kit (QiagenTM), according to the manufacturer's instructions. DNA was subsequently quantified using the QubitTM (Thermo Fisher Scientific).

Genotyping

Twenty-five SNPs of genetic markers associated with neurodegenerative pathologies were selected according to reports in the literature (Supplementary Table 1). Genotyping was performed with a TaqMan^{TM} probe system supplied by Thermo Fisher Scientific, Carlsbad, USA. The reactions were prepared according to the manufacturer's instructions, with a DNA input of 10 ng for all samples drawn from blood or swabs except for Native American samples (1 ng) from DNA cards. Genotyping was performed using ViiA 7 Real-Time PCR (Applied Biosystems, Carlsbad, USA) in duplicates to confirm the generated data. Genotyping was interpreted when the fluorophore was equivalent to a specific probe for a given allele and was detected in both reactions.

Population analysis

The genotypes were coded in numerals, with the number 1 corresponding to the ancestral allele and 2 to the variant allele to assign weight to the variants. Population parameters, such as allelic frequencies, Hardy-Weinberg equilibrium, linkage disequilibrium, and co-ancestry coefficient data (Fst), were generated by the Fstat v.2.9.4 package (https://www2.unil.ch). Principal Component Analysis (PCA) was performed by PCA-Gen v. 1.2.0 (https://www2.unil.ch). The neighbor-joining tree was obtained in FST format, generated by Fstat, and built using Genetic Data Analysis version 1.1 (http://lewis. eeb. uconn. edu/lewishome/software. html) and TreeView version 1.6.6 (Page 1996). The population stratification values were evaluated using the Structure v. 2.3.4 program (Pritchard, et al., 2000; Falush, et al., 2003; Hubisz, et al., 2009). The WEKA software (Smith and Frank, 2016), which used the Random Forest algorithm to construct a decision tree and 10-fold cross-validation, was used to determine the possible associations between the variants and the geographic and ethnic origin. This approach has been described as an aid in diagnosing neurodegenerative diseases (Briones and Dinu, 2012; Kumar and Singh, 2017; Geeitha and Thangamani, 2018; Brasil, et al., 2019).

RESULTS

Distribution of allele frequencies in the reference and Brazilian populations

The allele frequencies of the 25 SNPs for the reference populations (319 individuals) and the Brazilian population samples (140 individuals) are described in Supplementary Table 2. The test for deviation from the Hardy-Weinberg equilibrium (HWE) was applied to the groups of populations of ABR, EBR, MUL, JPBR, and NAT individuals (Supplementary Table 3). All loci in the Native American population were in equilibrium except for the monomorphic SNPs rs11121679, rs7412, and rs3818361. All genotyped SNPs were balanced for the ABR sample population. In the mulatto group, the SNP rs2435207 showed a deviation in balance ($p<0.001$). Population parameters of the white population, the SNPs rs5848 and rs3764650, both showed $p<0.002$. In the JPBR population, all SNPs were in equilibrium, except for rs3764650 ($p<0.001$), where a monomorphic locus rs11121679 was also observed (Supplementary Table 3). Despite the deviations observed in the loci, population equilibrium is assumed because they are within the expected random deviation value of 1 to 2 loci (5%).

Linkage disequilibrium (LD) analysis provides population information regarding neighboring alleles, as it expresses the absence of dependence between two alleles. For the study, 300 pairwise matches were made on the 25 SNPs. At a nominal level of 5%, SNPs in linkage disequilibrium was observed with an adjusted *p*-value of 0.000021 (Supplementary Table 4). The monomorphic SNPs were removed from the analysis since the analysis takes place to the difference of alleles. They would present deviations due to artifacts resulting from the algorithm and not biological causes. Of the 300 pairwise combinations tested, only seven showed deviations ($p<0.00001$), with all pairs located close to each other. Markers rs2435207 and rs2471738 are separated on chromosome 17 by 17 kb; on chromosome 1, markers rs8231244 and rs823118 are separated by 21 kb. And markers rs7982 and rs4236673 are separated, on chromosome 19, by 2.5 kb.

Genetic distance between populations

We initially evaluated the distances from the genotypes by principal component analysis (PCA) (Figure 1). The overall genetic relationships were confirmed as expected groups of Asian origin clustered in a single quadrant, just as the African population clustered in another. The European population grouped the EBR and MUL sample populations from Brazil, indicating that this reference population contributed more to these two groups. As might be expected, the ABR

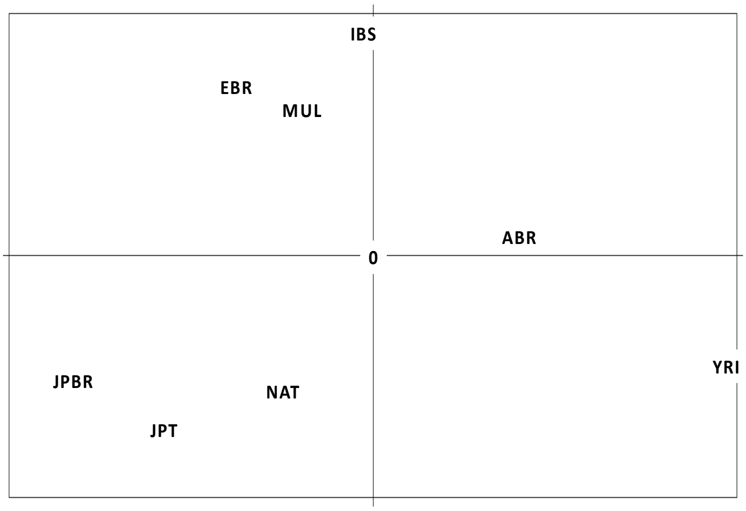

Figure 1. Principal Component Analysis (PCA) based on the genotypes of the 25 SNPs genotyped in population samples of individuals. YRI (Yoruba, N = 106), IBS (Iberian Peninsula, N = 94), and JPT (Japan, N = 104), NAT (Native Americans, N = 20), JPBR (Japanese descendants, N = 30), EBR (Europeans descendants, N = 30), MUL (Mulattoes, N = 30); ABR (Africans descendants, N = 30).

Table 1. Genetic diversity measured by the Fst distance. YRI (Yoruba, N = 106), IBS (Iberian Peninsula, N = 94), and JPT (Japan, N = 104), NAT (Native Americans, N = 20), JPBR (Japanese descendants, N = 30), EBR (Europeans descendants, N = 30), MUL (Mulattoes, N = 30); ABR (Africans descendants, N = 30).

	YRI	IBS	JPT	NAT	JPBR	EBR	MUL	ABR
YRI	-							
IBS	0.1790	-						
JPT	0.2276	0.1320	-					
NAT	0.2377	0.1533	0.0887	-				
JPBR	0.2953	0.1728	0.0381	0.1896	-			
EBR	0.2430	0.1069	0.1414	0.1885	0.1031	-		
MUL	0.2130	0.1084	0.1441	0.1879	0.1048	0.0013	-	
ABR	0.0580	0.0610	0.1142	0.1237	0.1532	0.0967	0.0796	-

group was intermediate between Africans and Europeans. Another statistical algorithm was used to estimate the population substructure using Fst to the variation of the genotypes among the five population groups (Table 1). The genetic distance between EBR and MUL was unexpectedly low (Fst = 0.0013), and the distance between JPT and JPBR was higher than expected (Fst = 0.0381).

Nonetheless, we prepare a more detailed tree of neighbor-joining based on the co-ancestry values to evaluate the overall geographic relationship among those sample populations (Figure 2). As we can see, the genetic proximity between the JPT and JBBR groups is highest with the most distant NATs. The EBR and MUL groups are very close. And finally, the YRI and ABR groups follow the same clustering, with values at the limit of significant differences (Fst = 0.058). When comparing Native Americans (NAT) to all other sample populations, the Yoruba (YRI) had the most considerable distance, with Fst = 0.2430. Japan (JPT) came in second, with Fst = 0.0887. In general, our Brazilian group is characterized by a degree of miscegenation that can vary among these groups.

Individual population group substructure

Genotypes were analyzed to quantify the levels of miscegenation in samples from Brazilian sample populations. For the test, ten independent runs were used as parameters for each value of k, which measures the number of parental populations ranging from 2 to 7. Using the default admixture model, a long burn-in period of 1,000,000 steps of the MCMC procedure was also applied. The maximum likelihood value (L) was obtained at k=3 (data not shown). Figure 3 shows the distribution of parental populations among samples of Brazilian populations individually. The

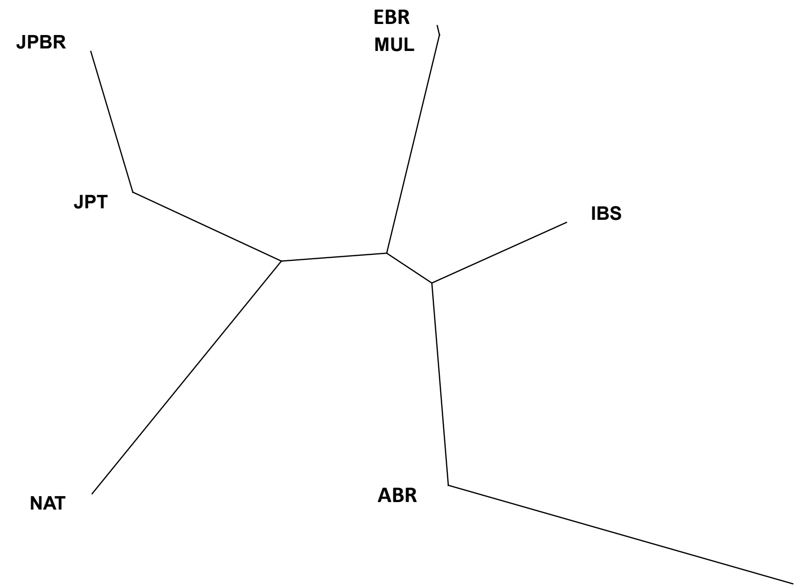

Figure 2. Neighbor-joining tree of five Brazilian population groups and three reference populations, using Fst as a measure of genetic distance: YRI (Yoruba, N = 106), IBS (Iberian Peninsula, N = 94), and JPT (Japan, N = 104), NAT (Native Americans, N = 20), JPBR (Japanese descendants, N = 30), EBR (Europeans descendants, N = 30), MUL (Mulattoes, N = 30); ABR (Africans descendants, N = 30).

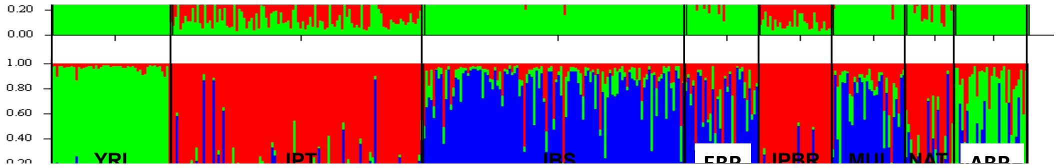

Figure 3. Individual substructure estimated from the genotype of individuals in the following populations. YRI (Yoruba, N = 106), IBS (Iberian Peninsula, N = 94), and JPT (Japan, N = 104), NAT (Native Americans, N = 20), JPBR (Japanese descendants, N = 30), EBR (Europeans descendants, N = 30), MUL (Mulattoes, N = 30); ABR (Africans descendants, N = 30). The bars represent estimated individual substructures, considering three parental populations.

African population (YRI) is the most homogeneous of the three parental populations, followed by the Asian population (JPT) and the population of the Iberian Peninsula (IBS). The Brazilian samples reflect what was observed with the previous algorithms. The EBR and MUL groups resemble IBS, as are the JPBR and NAT groups in Japan (JPT). The ABR group is the most miscegenated of all, with contributions from the three parental populations.

Ancestral composition of samples from the Brazilian population

The mixture values in each group (**Table** 2) indicate that in the YRI group, a value of 0.05 of genetic background composition is due to algorithmic background. Thus, the IBS and JPT parent populations do not have the same degree of homogeneity as the YRI population. Our Brazilian groups are mixed, with the proportion of Europeans (IBS) in the EBR and MUL groups being 67–68% and of Africans (YRI) 10–14%. On the other hand, the MUL group contains 53% African contributions (YRI) and 32% European contributions (IBS). The JPBR group resembles JPT. However, our NAT group has a distinguished European contribution (IBS, 0.281).

Table 2. Ancestral composition of the stratified Brazilian population sample Values represent the mean and standard deviation of 10 independent analyses by the Structure package. YRI (Yoruba, N = 106), IBS (Iberian Peninsula, N = 94), and JPT (Japan, N = 104), NAT (Native Americans, N = 20), JPBR (Japanese descendants, N = 30), EBR (Europeans descendants, N = 30), MUL (Mulattoes, N = 30); ABR (Africans descendants, N = 30).

POPULATIONS	**IBS**	**JPT**	**YRI**
YRI	0.041 ± 0.002	0.049 ± 0.002	**0.911 ± 0.003**
IBS	**0.791 ± 0.007**	0.110 ± 0.003	0.099 ± 0.004
JPT	0.116 ± 0.001	**0.829 ± 0.004**	0.055 ± 0.003
NAT	0.251 ± 0.003	0.617 ± 0.004	0.132 ± 0.006
JPBR	0.098 ± 0.002	0.873 ± 0.004	0.029 ± 0.002
EBR	0.668 ± 0.012	0.231 ± 0.007	0.101 ± 0.002
MUL	0.680 ± 0.013	0.180 ± 0.007	0.139 ± 0.007
ABR	0.319 ± 0.007	0.153 ± 0.004	0.528 ± 0.003

Table 3. Confusion matrix generated by the WEKA software, using Random Forest as a classifier model, with 81% accuracy. YRI (Yoruba, N = 106), IBS (Iberian Peninsula, N = 94), and JPT (Japan, N = 104), NAT (Native Americans, N = 20), JPBR (Japanese descendants, N = 30), EBR (Europeans descendants, N = 30), MUL (Mulattoes, N = 30); ABR (Africans descendants, N = 30).

YRI	**IBS**	**JPT**	**NAT**	**JPBR**	**EBR**	**MUL**	**ABR**	
105	3	0	0	0	0	0	0	**YRI (N=108)**
0	**101**	5	0	1	0	0	0	**IBS (N=107)**
1	6	**93**	1	3	0	0	0	**JPT (N=104)**
0	3	6	**10**	0	0	1	0	**NAT (N=20)**
0	1	10	0	**19**	0	0	0	**JPBR (N=30)**
1	2	0	0	1	**18**	8	0	**EBR (N=30)**
0	0	0	0	1	9	**19**	1	**MUL (N=30)**
11	6	0	1	1	1	3	**7**	**ABR (N=30)**

Modern approaches have been used to obtain a logical correlation between the distribution of alleles in different populations (Huang, et al., 2009). One approach is machine learning, which can determine the association of SNPs with neurodegenerative diseases. Here we tested the association of SNPs and the ethnic, and geographic origin of the reference population individuals (YRI, N = 108; IBS, N = 107; and JPT, N = 104) and samples from genotyped Brazilian populations (EBR, N = 30, MUL, N = 30, ABR, N = 30, JPBR, N = 30, and NAT, N = 20). The Random Forrest classification algorithm and cross-validation tests (Table 3) were applied, generating the confusion matrix through this algorithm. The reference populations demonstrated a strong relationship between genotype and ethnogeography of origin. The YRI was classified with 97% accuracy (105/108); for the Europeans (IBS), the result was 94% accuracy (101/107), while for the JPT group, which resembled the JPBR and NAT groups, was 89% (93/104). Considering the miscegenation data presented above, the Brazilian groups were classified as JPBR with 97% accuracy (19 JPBR + 10 JPT/30). The EBR groups, whose miscegenation includes populations from Europe and Africa, showed 66% accuracy (18/30). Likewise, the MUL group had 63% accuracy (19/30). The NAT group had an accuracy of 50% (10/20), and 15% were classified as Europeans (6/20). Only the ABR group, which presented the most complex mixed-race profile, had results below the other groups. In this case, it was 23% (07/30). Among the ABR group, the contribution value of 20% of Europeans was found (06/30). As a general result, a percentage of 81% correctness was found.

DISCUSSION

In this work, a population study was carried out in five Brazilian groups using 25 markers previously associated with neurodegenerative diseases, selected through a bibliographic survey, to observe the distribution of the genotypes of these SNPs in this sample of the Brazilian population. So far, there is no description in the literature of this type of work, neither among Brazilian individuals nor Native Americans.

Among the population groups used were individuals from Rio de Janeiro called European descendants (EBR, N = 30), Mulatto descendants (MUL, N = 30), and African descendants (ABR, N = 30); individuals of Japanese descent from São Paulo, Brazil (JPBR, N = 30); and Native Americans from São Gabriel da Cachoeira (NAT, N = 20), where we used genotypic data along with data from the reference population from the 1000 Genomes Project data bank Phase 3 (Auton, et al., 2015; Sudmant, et al., 2015).

For the analysis of the Brazilian population, we used 140, in which we tested the linkage disequilibrium between the markers. When these alleles are linked, divergences occur to expected and observed heterozygosity. This result may be due to the physical proximity between the alleles. In addition, inbreeding can also favor this event, as can a reduced population number, genetic isolation between populations, selection, and mutation (Farnir, et al., 2000). The Linkage Disequilibrium impacts population studies due to the non-independent segregation effect of specific alleles, leading to an association between them and impacting the accuracy of genetic predictability (Borges, et al., 2020). Here, only seven of the 300 pairwise combinations tested showed deviation ($p<0.00001$), suggesting that linkage disequilibrium due to stochastic effects with no impact on the results obtained, considering that the expected random products of the analysis are 5%, representing 15 pairs of markers (0.05 * 300 pairwise analyses).

The coancestry coefficient (Fst) of genetic differentiation was estimated among populations. The values between European descendants (EBR) and Mulattoes (MUL) were 0.0013, showing virtually no differentiation between these groups, which can be explained given the great miscegenation between individuals in the last 300 years. The same result was observed during the PCA and NJ tree analyses, in which the MUL and EBR groups were positioned close to each other, and in the population substructure analysis, in which they presented themselves as almost indistinguishable groups. The group of Japanese descendants (JPBR) showed little differentiation (Fst = 0.0381) from Asian individuals from Japan (JPT), which is consistent with the migration history that occurred in the 20th century, in which immigrants landed in the city of São Paulo to work in coffee cultivation (Nogueira 2000). The Fst values for African descendants (ABR) and Africans (YRI) also showed low genetic differentiation (Fst = 0.058), given the history of miscegenation of enslaved Africans in the period of Brazilian colonization (Pimenta et al. 2006). Regarding Native Americans (NAT) and Asians (JPT), the value of Fst = 0.0887 revealed a moderate difference between them. All the genetic diversity analyses (FST, NJ Tree, and PCA) agreed with one another and the stories of the reference population groups.

The analysis of the population substructure reveals the level of miscegenation in all groups. We observed that the YRI, IBS, and JPT populations are well defined through the representation of the bar plot, in which the substructure value considered most likely was three parental populations. From this, we see those individuals from the Americas, mainly Native Americans, are not well represented by the reference databases, making studies for the correlation and distribution of markers associated with neurodegenerative diseases more challenging. It is known that allele frequencies in genes associated with various conditions differ by racial and ethnic groups. Still, populations enrolled in disease risk studies often lack diversity in this dimension (Bustamante, et al., 2011; Lillo, et al., 2021; Torres-Valadez, et al., 2022). Evaluating the structure of Brazilian population groups individually, European descendants (EBR) and Mulattoes (MUL) were practically indistinguishable from each other. African descendants (ABR) showed miscegenation between the African component (YRI) and Europeans (EUR), with a negligible contribution from Native Americans. The dissimilarity between Native Americans and other groups was observed, especially among Japanese descendants (JPBR). Quantitatively, the EBR, MUL, and ABR groups have a high degree of miscegenation that varies between African (YRI, 0.101 to 0.528) and European (IBS, 0.319 to 0.680).

Each group has its particularity, making them models for unique studies in such estimates. was observed that even when using different algorithms for data analysis, including machine learning, our genotyped Brazilian population (EBR, MUL, ABR, and NAT) is complex in terms of its ethnic background. The group of Native Americans (NAT) resembles the Japanese (JPT) and Europeans (IBS) since we accept that this group is already mixed. The same fact appears with the genotypes of EBR and MUL, which are like each other. And finally, the ABR, with a high concentration of melanin, is mixed with Europeans (IBS) and Mulattoes (MUL), making it difficult to determine the ethnicity linked to the markers of interest for neurodegenerative diseases. Thus, the study then depends on the genomic and population context in which the individual is inserted, which can significantly alter the probability of developing the disease (Bustamante, et al., 2011; Horimoto, et al., 2021; Wang et al. 2023).

In summary, this study showed that the analysis of genotypic distributions of markers related to neurodegenerative diseases varies according to the investigated populations. Thus, the interpretation of the associated genotypes must consider the genetic composition of this population.

ACKNOWLEDGEMENTS

We are grateful to Laboratório de Metabolismo Macromolecular Firmino Torres de Castro group for the scientific support.

CONFLICT OF INTEREST STATEMENT

We declare no conflict of interest.

FUNDING

Rosane Silva: FAPERJ E-26/200.999/2022, SEI-260003/012994/2021, SEI-260003/001129/2020; CNPq 303.829/2019-2. **Rodrigo S Moura-Neto**: FAERJ E-26/202.532/2019, E-26/010.101033/2018; CNPq 311397/2022-0.

REFERENCES

Ali M, Archer DB, Gorijala P, Western D, et al. (2023). Large multi-ethnic genetic analyses of amyloid imaging identify new genes for Alzheimer disease. *Acta Neuropathol Commun.* 11: 68.

Aranda XG, Lage CAC, Planz JV. (2011). Genetic composition of six miniSTR in a Brazilian Mulatto sample population. *J Forensic Leg Med.* 18: 184–186.

Asiimwe IG, Pirmohamed M. (2022). Ethnic Diversity and Warfarin Pharmacogenomics. *Front Pharmacol.* 13: 866058.

Auton A, Abecasis GR, Altshuler DM. (2015). A global reference for human genetic variation. *Nature.* 526: 68–74.

Benedet AL, Moraes CF, Camargos EF. (2012). Amerindian Genetic Ancestry Protects against Alzheimer's Disease. *Dement Geriatr Cogn.* 33: 311–317.

Borges MG, Rocha CS, Carvalho BS, Lopes-Cendes I, et al. (2020). Methodological differences can affect sequencing depth with a possible impact on the accuracy of genetic diagnosis. *Genet Mol Biol.* 43: e20190270.

Brasil S, Pascoal C, Francisco R. (2019). Artificial Intelligence (AI) in Rare Diseases: Is the Future Brighter? *Genes-basel.* 10: 978.

Briones N, Dinu V. (2012). Data mining of high density genomic variant data for prediction of Alzheimer's disease risk. *Bmc Med Genet.* 13: 7.

Burns A, Byrne EJ, Maurer K. (2002). Alzheimer's disease. *Lancet.* 360: 163–165.

Bustamante CD, Vega FMDL, Burchard EG. (2011). Genomics for the world. *Nature.* 475: 163–165.

Costa AN da, Silva R, Moura-Neto RS. (2002). Y-chromosome variation. *Forensic Sci Int.* 126: 254–257.

Deng L, Ruiz-Linares A, Xu S, Wang S, et al. (2016). Ancestry variation and footprints of natural selection along the genome in Latin American populations. *Sci Rep.* 6: 21766.

Falush D, Stephens M, Pritchard JK. (2003). Inference of Population Structure Using Multilocus Genotype Data: Linked Loci and Correlated Allele Frequencies. *Genetics.* 164: 1567–1587.

Farnir F, Coppieters W, Arranz JJ. (2000). Extensive Genome-wide Linkage Disequilibrium in Cattle. *Genome Res.*10: 220–227.

Geeitha S, Thangamani M. (2018). Progress in Advanced Computing and Intelligent Engineering, Proceedings of ICACIE 2017, Volume 1. *Adv Intell Syst.* 139–148.

Harerimana NV, Goate AM, Bowles KR. (2022). The influence of 17q21.31 and APOE genetic ancestry on neurodegenerative disease risk. *Front Aging Neurosci.* 14: 1021918.

Havranek EP. (2019). The Influence of Social and Economic Factors on Heart Disease. *Jama Cardiol.* 4: 1212–1213.

Horimoto ARVR, Xue D, Thornton TA, Blue EE, et al. (2021). Admixture mapping reveals the association between Native American ancestry at 3q13.11 and reduced risk of Alzheimer's disease in Caribbean Hispanics. *Alzheimer's Res Ther.* 13: 122.

Huang LC, Hsu SY, Lin E. (2009). A comparison of classification methods for predicting Chronic Fatigue Syndrome based on genetic data. *J Transl Med.* 7: 81.

Hubisz MJ, Falush D, Stephens M, Pritchard JK, et al. (2009). Inferring weak population structure with the assistance of sample group information. *Mol Ecol Resour.* 9: 1322–1332.

Kumar A, Singh TR. (2017). A New Decision Tree to Solve the Puzzle of Alzheimer's Disease Pathogenesis Through Standard Diagnosis Scoring System. *Interdiscip Sci Comput Life Sci.* 9: 107–115.

Lillo AD, D'Antona S, Pathak GA. (2021). Cross-ancestry genome-wide association studies identified heterogeneous loci associated with differences of allele frequency and regulome tagging between participants of European descent and other ancestry groups from the UK Biobank. *Hum Mol Genet.* 30: 1457–1467.

Mishra A, Malik R, Hachiya T. (2022). Stroke genetics informs drug discovery and risk prediction across ancestries. *Nature.* 611: 115–123.

Moura-Neto R, King JL, Mello I. (2021). Evaluation of Promega PowerSeq™ Auto/Y systems prototype on an admixed sample of Rio de Janeiro, Brazil: Population data, sensitivity, stutter and mixture studies. *Forensic Sci Int Genetics.* 53: 102516.

Moura-Neto RS, Mello ICT, Silva R. (2018). Evaluation of InnoTyper® 21 in a sample of Rio de Janeiro population as an alternative forensic panel. *Int J Legal Med.* 132: 149–151.

Moura-Neto RS, Silva R, Mello IC. (2015). Evaluation of a 49 InDel Marker HID panel in two specific populations of South America and one population of Northern Africa. *Int J Legal Med.* 129: 245–249.

Nogueira AR. (2000). Japanese Immigration in Brazil. *Diogenes*. 48: 45–55.

Page RDM. (1996). Tree View: An application to display phylogenetic trees on personal computers. *Bioinformatics.* 12: 357–358.

Paradela RS, Justo AFO, Paes VR, Leite REP, et al. (2023). Association between APOE-ε4 allele and cognitive function is mediated by Alzheimer's disease pathology: a population-based autopsy study in an admixed sample. *Acta Neuropathol Commun.* 11: 205.

Paradella R. (2018). Elderly population increases 18% in 5 years and surpasses 30 million in 2017. IBGE.

Pena SDJ, Pietro GD, Fuchshuber-Moraes M. (2011). The Genomic Ancestry of Individuals from Different Geographical Regions of Brazil Is More Uniform Than Expected. *Plos One.* 6: e17063.

Pimenta JR, Zuccherato LW, Debes AA. (2006). Color and Genomic Ancestry in Brazilians: A Study with Forensic Microsatellites. *Hum Hered.* 62: 190–195.

Pritchard JK, Stephens M, Donnelly P. (2000). Inference of Population Structure Using Multilocus Genotype Data. *Genetics.* 155: 945–959.

Querfurth HW, LaFerla FM. (2010). Alzheimer's Disease. *New Engl J Medicine.* 362: 329–344.

Rajabli F, Beecham GW, Hendrie HC. (2022). A locus at 19q13.31 significantly reduces the ApoE ε4 risk for Alzheimer's Disease in African Ancestry. *PLoS Genet.* 18: e1009977.

Silva R, Moura-Neto RS. (1998). Allelic frequency distribution for three VNTR markers—D6S132, D7S467, D17S26—in Rio de Janeiro population, Brazil. *Forensic Sci Int.* 94: 33–38.

Silva R, Moura-Neto RS. (2004). Genetic diversity and admixture data on 11 STRs (F13B, TPOX, CSF1PO, F13A01, D7S820, LPL, TH01, vWA, D13S317, FESFPS, and D16S539) in a sample of Rio De Janeiro European-descendants population, Brazil. *Forensic Sci Int.* 142:51–53.

Smith TC, Frank E. (2016). Statistical Genomics, Methods and Protocols. *Methods Mol Biology.* 1418: 353–378.

Strobl C, Cihlar JC, Lagacé R. (2019). Evaluation of mitogenome sequence concordance, heteroplasmy detection, and haplogrouping in a worldwide lineage study using the Precision ID mtDNA Whole Genome Panel. *Forensic Sci Int Genetics.* 42: 244–251.

Suarez-Kurtz G. (2010). Pharmacogenetics in the Brazilian Population. *Front Pharmacol.* 1: 118.

Sucharov CC, Silva R, Rondinelli E, Moura-Neto RS, et al. (1999). Fragile X Trinucleotide Repeats from A Normal Population in Rio de Janeiro, Brazil. *Hereditas.* 130: 189–190.

Sudmant PH, Rausch T, Gardner EJ. (2015). An integrated map of structural variation in 2,504 human genomes. *Nature.* 526: 75–81.

Tennessen JA, Bigham AW, O'Connor TD. (2012). Evolution and Functional Impact of Rare Coding Variation from Deep Sequencing of Human Exomes. *Science.* 337: 64–69.

Torres-Valadez R, Roman S, Ojeda-Granados C. (2022). Differential distribution of gene polymorphisms associated with hypercholesterolemia, hypertriglyceridemia, and hypoalphalipoproteinemia among Native American and Mestizo Mexicans. *World J Hepatology.* 14: 1408–1420.

Wang J, Wei S, Zhang J, Wang H. (2023). Association between *RIT2* rs16976358 Polymorphism and Autism Spectrum Disorder in Asian Populations: A Meta-analysis. *Biomed Res Int.* 11: 2023:8886927.

Woerner AE, Ambers A, Wendt FR, et al. (2018). Evaluation of the precision ID mtDNA whole genome panel on two massively parallel sequencing systems. *Forensic Sci Int Genetics.* 36: 213–224.

Supplementary Table 1. List of genetic loci studied description, location, SNP number, polymorphism, and classification of SNPs.

Locus	Gene	Mapping (Hg19)	dbSNP	Classification	Polimorphism	Pathology	Reference
4GALT3/ ADAMTS4	a disintegrin-like and metalloproteinase with thrombospondin motifs-4	Chr 1:161185602	rs4575098	3'UTR	G > A	AD	(1,2)
ABCA7	ATP Binding Cassette Subfamily A Member 7	Chr 19:1046521	rs3764650	intron	T > G	AD	(3,4)
APOE	apolipoprotein E	Chr 19:44908684	rs429358	missense	C > T	AD	(5–8)
APOE	apolipoprotein E	Chr 19:44908822	rs7412	missense	C > T	AD	(9–11)
CLU	clusterin	Chr 8:27604964	rs7982	missense	G > A	AD	(12–14)
CLU	clusterin	Chr 8:27607412	rs4236673	intron	G > A	AD	(1,15)
CR1	Complement C3b/C4b Receptor 1	Chr 1:207611623	rs3818361	intron	G > A	AD	(3,16)
MS4A6A	Membrane Spanning 4-Domains A6A	Chr 11:60175342	rs7935829	intron	A > G	AD	(17)
TARDBP	TAR DNA Binding Protein	Chr 1:11012634	rs11121679	5'UTR	G > A	AD	(18,19)
MAPT	microtubule-associated protein tau	Chr 17:45998697	rs2471738	intron	C > T	PD/AD	(20,21)
BST1	Bone Marrow Stromal Cell Antigen 1	Chr 4:15736240	rs4273468	intron	G > A	PD	(22)
FAM47E1	Family With Sequence Similarity 47 Member E	Chr 4:76277833	rs6812193	intron	C > T	PD	(23–25)
GRN	Granulin Precursor	Chr 17:44352876	rs5848	3'UTR	C > T	PD	(26)
MAPT	microtubule-associated protein tau	Chr 17:45942346	rs242557	intron	G > A	PD	(27)
MAPT	microtubule-associated protein tau	Chr 17:45981562	rs2435207	intron	G > A	PD	(28,29)
RAB29/PARK16	Parkinson Disease 16	Chr 1:205775418	rs823144	5'UTR	C > A	PD	(30,31)
RAB7L1/NUCKS1	Nuclear Casein Kinase And Cyclin	Chr 1:205754444	rs823118	intergenic	C > T	PD	(24,32)

	Dependent Kinase Substrate 1						
SNCA	Synuclein Alpha	Chr 4:89716450	rs356219	intron	A > G	PD	(33,34)
ZNF646. KAT8	Zinc Finger Protein 646	Chr 16:31110472	rs14235	synonymous	G > A	PD	(35,36)
MOBP	Myelin Associated Oligodendrocyte Basic Protein	Chr 3:39492990	rs616147	intron	G > A	ALS	(37,38)
SCFD1	Sec1 Family Domain Containing 1	Chr 14:30678292	rs10139154	intron	T > C	ALS	(37,39)
DOCK1	–	Chr 10:127476239	rs4363506	intergenic	C > T	ALS	(22,40)
SNP1	–	Chr 2:18053180	rs16984239	intron	C > A	ALS	(22)
SNP3	–	Chr 5:77913837	rs5014235	intergenic	C > T	ALS	(22)
SNP4	–	Chr 12:51857488	rs7976059	intergenic	G > T	ALS	(22)

Chr. cromossomo; AD. Alzheimer's disease; PD. Parkinson's disease; ALS. Amyotrophic Lateral Sclerosis.

Supplementary Table 2. Allele frequency of reference and Brazilian populations selected in 25 SNPs YRI (Yoruba, Africa); JPT (Japanese); IBS (Iberian Peninsula); NAT (Native Americans); JPBR (Japanese descendants in Brazil); EBR (Europeans descendants in Brazil); MUL (mulattoes); and ABR (Africans descendants in Brazil). The underlined allele represents the most frequent ancestral allele in African populations, according to frequencies obtained from the Ensembl Genome Browser database.

Locus	dbSNP	Allele	YRI	IBS	JPT	NAT	JPBR	EBR	MUL	ABR
MAPT	rs242557	G	0.653	0.640	0.534	0.425	0.650	0.667	0.650	0.600
		A	0.347	0.360	0.466	0.575	0.350	0.333	0.350	0.400
	rs2435207	G	0.736	0.678	0.736	0.825	0.750	0.683	0.650	0.667
		A	0.264	0.322	0.264	0.175	0.250	0.317	0.350	0.333
	rs2471738	C	0.912	0.804	0.764	0.825	0.783	0.817	0.867	0.800
		T	0.088	0.196	0.236	0.175	0.217	0.183	0.133	0.200
SNCA	rs356219	A	0.259	0.650	0.409	0.425	0.500	0.550	0.533	0.483
		G	0.741	0.350	0.591	0.575	0.500	0.450	0.467	0.517
PARK16	rs823144	C	0.630	0.248	0.567	0.925	0.483	0.650	0.617	0.533
		A	0.370	0.752	0.433	0.075	0.517	0.350	0.383	0.467
FAM47E	rs6812193	C	0.593	0.626	0.918	0.900	0.900	0.750	0.583	0.617
		T	0.407	0.374	0.082	0.100	0.100	0.250	0.417	0.383

RAB7L1/NUCKS1	rs823118	C	0.838	0.453	0.553	0.925	0.500	0.533	0.483	0.683
		T	0.162	0.547	0.447	0.075	0.500	0.467	0.517	0.317
ZNF646. KAT8	rs14235	G	0.944	0.645	0.096	0.400	0.017	0.583	0.733	0.767
		A	0.056	0.355	0.904	0.600	0.983	0.417	0.267	0.233
BST1	rs4273468	G	0.653	0.827	0.404	0.600	0.400	0.767	0.500	0.643
		A	0.347	0.173	0.596	0.400	0.600	0.233	0.500	0.357
GRN	rs5848	C	0.218	0.664	0.745	0.975	0.683	0.567	0.583	0.500
		T	0.782	0.336	0.255	0.025	0.317	0.433	0.417	0.500
TARDBP	rs11121679	G	0.477	0.995	1.000	1.000	1.000	0.867	0.833	0.583
		A	0.523	0.005	0.000	0.000	0.000	0.133	0.167	0.417
APOE	rs429358	C	0.236	0.140	0.082	0.275	0.050	0.067	0.183	0.167
		T	0.764	0.860	0.918	0.725	0.950	0.933	0.817	0.833
	rs7412	C	0.894	0.944	0.952	1.000	0.967	0.967	0.950	0.917
		T	0.106	0.056	0.048	0.000	0.033	0.033	0.050	0.083
CLU	rs7982	G	0.514	0.654	0.779	0.600	0.800	0.633	0.633	0.450
		A	0.486	0.346	0.221	0.400	0.200	0.367	0.367	0.550
	rs4236673	G	0.968	0.654	0.779	0.600	0.633	0.300	0.350	0.683
		A	0.032	0.346	0.221	0.400	0.367	0.700	0.650	0.317
CR1	rs3818361	G	0.556	0.874	0.702	1.000	0.517	0.833	0.800	0.767
		A	0.444	0.126	0.298	0.000	0.483	0.167	0.200	0.233
ABCA7	rs3764650	T	0.736	0.893	0.582	0.975	0.500	0.804	0.786	0.733
		C	0.264	0.107	0.418	0.025	0.500	0.196	0.214	0.267
4GALT3/ ADAMTS4	rs4575098	G	0.991	0.771	0.601	0.775	0.467	0.233	0.367	0.800
		A	0.009	0.229	0.399	0.225	0.533	0.767	0.633	0.200
MS4A6A	rs7935829	A	0.838	0.603	0.798	0.900	0.800	0.683	0.683	0.783
		G	0.162	0.397	0.202	0.100	0.200	0.317	0.317	0.217
SNP1	rs16984239	C	0.926	0.860	0.755	0.950	0.217	0.183	0.117	0.833
		A	0.074	0.140	0.245	0.050	0.783	0.817	0.883	0.167
DOCK1	rs4363506	C	0.338	0.439	0.476	0.250	0.600	0.633	0.550	0.550
		T	0.662	0.561	0.524	0.750	0.400	0.367	0.450	0.450
SNP3	rs5014235	C	1.000	0.654	0.938	0.974	0.933	0.817	0.900	0.900
		T	0.000	0.346	0.063	0.026	0.067	0.183	0.100	0.100
SNP4	rs7976059	G	0.671	0.650	0.313	0.375	0.224	0.667	0.638	0.466
		T	0.329	0.350	0.688	0.625	0.776	0.333	0.362	0.534
MOBP	rs616147	G	0.995	0.720	0.404	0.325	0.467	0.717	0.750	0.828
		A	0.005	0.280	0.596	0.675	0.533	0.283	0.250	0.172
SCFD1	rs10139154	T	0.852	0.346	0.707	0.725	0.617	0.517	0.533	0.617
		C	0.148	0.654	0.293	0.275	0.383	0.483	0.467	0.383

Supplementary Table 3. Verification of the Hardy-Weinberg Equilibrium Deviation for Samples of the Brazilian Population NAT (Native Americans); JPBR (Japanese descendants in Brazil). EBR (Europeans descendants in Brazil); MUL (mulattos); and ABR (Africans descendants in Brazil). Highlighted in red are the loci that were outside the EHW. Loci rs11121679, rs7412, and rs3818361 are monomorphic in the JPBR and NAT samples (Supplementary Table 1).

	HWE (*P*-value)				
dbSNP	NAT	JPBR	EBR	MUL	ABR
rs242557	0.674	1.000	0.102	1.000	0.711
rs2435207	1.000	0.327	0.674	**0.001**	0.215
rs2471738	1.000	0.589	0.551	0.414	0.307
rs356219	1.000	0.141	1.000	0.723	1.000
rs823144	1.000	0.713	1.000	0.055	1.000
rs6812193	1.000	1.000	0.641	0.474	0.703
rs823118	1.000	0.465	0.462	0.032	0.411
rs14235	0.385	1.000	1.000	0.637	0.633
rs4273468	1.000	1.000	0.159	0.287	0.239
rs5848	1.000	0.100	**0.002**	0.706	1.000
rs11121679*	-	-	0.415	0.155	0.057
rs429358	0.592	1.000	1.000	0.551	0.155
rs7412*	-	1.000	1.000	1.000	1.000
rs7982	1.000	0.560	0.450	0.447	1.000
rs4236673	1.000	0.004	1.000	0.254	0.673
rs3818361*	-	1.000	0.155	0.308	0.295
rs3764650	1.000	**>0.001**	**>0.001**	1.000	1.000
rs4575098	1.000	1.000	1.000	0.021	0.060
rs7935829	1.000	1.000	1.000	0.028	0.292
rs16984239	1.000	0.589	0.551	1.000	0.015
rs4363506	1.000	0.264	1.000	0.481	0.482
rs5014235	1.000	1.000	0.551	1.000	1.000
rs7976059	0.648	0.287	0.681	1.000	0.710
rs616147	1.000	0.724	1.000	1.000	1.000
rs10139154	0.591	0.445	0.714	0.461	0.703

* Monomorphic marker for JPBR and NAT groups.

Supplementary Table 4. Pairs of loci exhibiting linkage disequilibrium (LD) for Brazilian population samples NAT (Native Americans); JPBR (Japanese descendants in Brazil); EBR (Europeans descendants in Brazil); MUL (mulattos); and ABR (Africans descendants in Brazil). The adjusted P-value for the 5% nominal level is 0.000021. The pairs of loci that were outside the LD are highlighted in red, as these markers are close by 2.5 kb (Table 1).

Pair of Loci	Sample Population				
	NAT	JPBR	EBR	MUL	ABR
rs242557 x rs2435207	0.002420	0.734230	0.368770	0.015670	0.545100
rs242557 x rs2471738	0.002060	0.794170	0.018190	0.139900	0.057080
rs242557 x rs356219	0.749670	0.125270	0.891290	0.045920	0.799290
rs242557 x rs823144	1.000000	0.348040	0.718080	0.539480	0.185730
rs242557 x rs6812193	0.148710	0.497650	0.065310	0.807710	0.678690
rs242557 x rs823118	1.000000	0.440190	0.240900	0.719520	0.256880
rs242557 x rs14235	0.488250	1.000000	0.801480	0.802270	0.910670
rs242557 x rs4273468	0.575480	0.783230	0.018130	0.421980	0.000560
rs242557 x rs5848	1.000000	0.359250	0.223270	0.922420	0.094500
rs242557 x rs11121679	NA	NA	0.833730	0.188400	0.838710
rs242557 x rs429358	0.629100	0.178630	0.366060	0.879730	0.621170
rs242557 x rs7412	NA	0.196440	1.000000	0.829500	0.511850
rs242557 x rs7982	0.425290	0.511350	0.078170	0.631500	0.489900
rs242557 x rs4236673	0.432100	0.563480	0.043940	0.234520	1.000000
rs242557 x rs3818361	NA	0.837730	0.482710	0.081190	0.881880
rs242557 x rs3764650	1.000000	0.725920	0.456480	0.806100	0.874650
rs242557 x rs4575098	0.540150	0.158380	0.290270	0.749190	0.181850
rs242557 x rs7935829	0.145130	0.503880	0.516650	0.393900	0.061020
rs242557 x rs16984239	0.671020	0.628400	0.165150	0.841920	1.000000
rs242557 x rs4363506	0.592460	0.818730	0.322210	0.117880	0.477000
rs242557 x rs5014235	0.211250	0.700900	0.407170	0.055480	0.246650
rs242557 x rs7976059	0.221380	0.178960	0.948630	0.369560	0.547380
rs242557 x rs616147	0.874190	0.871170	0.310580	0.635020	0.297500
rs242557 x rs10139154	0.287770	0.428380	0.765710	0.139810	0.691830
rs2435207 x rs2471738	**0.000020**	**0.000020**	0.000170	0.061920	0.000380
rs2435207 x rs356219	1.000000	0.870750	0.038830	0.934710	0.143980
rs2435207 x rs823144	1.000000	0.400810	0.238940	0.199600	0.505000
rs2435207 x rs6812193	0.588830	0.526500	0.161380	0.946710	0.103170
rs2435207 x rs823118	1.000000	0.353100	0.030080	0.425520	0.861400
rs2435207 x rs14235	0.810130	1.000000	0.756400	0.697520	0.520710
rs2435207 x rs4273468	0.381960	0.270750	0.016150	0.168880	0.587440
rs2435207 x rs5848	0.348650	0.740560	0.933170	0.324770	0.645310
rs2435207 x rs11121679	NA	NA	0.626730	0.020980	0.122810
rs2435207 x rs429358	0.671210	0.656940	0.702920	0.875520	0.501040
rs2435207 x rs7412	NA	1.000000	0.551020	0.565560	0.833150

rs2435207 x rs7982	0.565290	0.324980	0.812690	0.122940	0.093580
rs2435207 x rs4236673	0.566850	0.493810	0.337040	0.106770	0.058000
rs2435207 x rs3818361	NA	0.026830	0.642230	0.102290	0.889000
rs2435207 x rs3764650	0.350830	0.371170	0.895630	0.176380	0.362440
rs2435207 x rs4575098	0.423630	0.529690	0.737650	0.732980	0.439230
rs2435207 x rs7935829	0.006810	0.156190	0.901900	0.514730	0.691000
rs2435207 x rs16984239	0.109560	0.153690	0.639850	0.622730	0.632290
rs2435207 x rs4363506	0.329060	0.199900	0.162900	0.308770	0.023880
rs2435207 x rs5014235	0.590080	1.000000	1.000000	0.005690	0.719190
rs2435207 x rs7976059	0.263900	0.371770	0.456850	0.831060	0.736190
rs2435207 x rs616147	0.251830	0.513350	0.720080	0.069810	0.694730
rs2435207 x rs10139154	1.000000	0.214380	0.567880	0.358380	0.717000
rs2471738 x rs356219	1.000000	0.504290	0.148520	0.821170	0.340060
rs2471738 x rs823144	1.000000	0.247250	0.880460	0.873500	0.516690
rs2471738 x rs6812193	0.586790	0.170170	0.189100	0.311730	0.247730
rs2471738 x rs823118	1.000000	0.226440	0.757480	1.000000	0.401060
rs2471738 x rs14235	0.810500	1.000000	0.409250	0.625850	0.679150
rs2471738 x rs4273468	0.383060	0.454900	0.459900	0.940710	0.559500
rs2471738 x rs5848	0.345310	0.820440	0.696440	0.071460	0.645020
rs2471738 x rs11121679	NA	NA	0.246810	0.310500	0.964960
rs2471738 x rs429358	0.676880	0.617080	0.610730	0.776460	0.426460
rs2471738 x rs7412	NA	0.604920	1.000000	1.000000	1.000000
rs2471738 x rs7982	0.568960	0.443830	1.000000	0.705980	0.441380
rs2471738 x rs4236673	0.568350	0.112290	0.250100	0.471790	0.455310
rs2471738 x rs3818361	NA	0.253040	0.068920	0.231480	1.000000
rs2471738 x rs3764650	0.348600	0.522500	0.907630	0.183000	0.672730
rs2471738 x rs4575098	0.428330	0.958190	0.533500	0.126790	0.864710
rs2471738 x rs7935829	0.006790	0.675690	0.325810	0.596480	0.352960
rs2471738 x rs16984239	0.114000	0.545250	0.241040	0.452400	0.875730
rs2471738 x rs4363506	0.324920	0.046630	0.252630	0.143810	0.305100
rs2471738 x rs5014235	0.589670	0.458100	0.695750	0.659170	1.000000
rs2471738 x rs7976059	0.263580	0.745770	0.212960	0.703630	0.204880
rs2471738 x rs616147	0.250980	0.932520	0.104790	0.195980	0.465980
rs2471738 x rs10139154	1.000000	0.525500	0.172520	0.511600	0.427600
rs356219 x rs823144	0.064980	1.000000	0.049770	0.011770	0.813190
rs356219 x rs6812193	0.029420	0.800000	0.109920	0.971980	0.123920
rs356219 x rs823118	0.062440	1.000000	0.724290	0.307670	0.673520
rs356219 x rs14235	0.593540	1.000000	0.019350	0.135810	1.000000
rs356219 x rs4273468	0.650250	0.345920	0.152770	0.859330	0.078460
rs356219 x rs5848	1.000000	0.395690	0.888020	0.868270	0.061770
rs356219 x rs11121679	NA	NA	0.919130	0.147880	0.162040
rs356219 x rs429358	0.059380	0.528670	0.384350	0.497540	0.959520
rs356219 x rs7412	NA	1.000000	0.240560	0.784650	0.820000

rs356219 x rs7982	0.217920	1.000000	0.151230	0.097150	0.474850
rs356219 x rs4236673	0.216670	0.706980	0.428690	0.552650	0.259000
rs356219 x rs3818361	NA	0.236980	0.637750	1.000000	0.363670
rs356219 x rs3764650	1.000000	1.000000	0.365330	0.102630	0.049940
rs356219 x rs4575098	0.700440	0.102400	0.897980	0.718000	0.160330
rs356219 x rs7935829	1.000000	1.000000	0.335940	0.492830	0.570080
rs356219 x rs16984239	1.000000	0.753600	0.277580	0.544850	0.418600
rs356219 x rs4363506	0.651690	0.577940	0.219310	0.924230	0.888630
rs356219 x rs5014235	0.364080	1.000000	0.017710	1.000000	0.117630
rs356219 x rs7976059	0.030540	0.130170	0.760960	0.204150	0.831730
rs356219 x rs616147	0.801020	0.945310	0.242830	0.224520	0.841230
rs356219 x rs10139154	1.000000	0.551040	0.682270	0.041500	0.467270
rs823144 x rs6812193	1.000000	0.688500	0.465500	0.574250	0.498500
rs823144 x rs823118	0.001020	**0.000020**	0.010460	**0.000020**	0.002270
rs823144 x rs14235	0.650380	1.000000	0.194540	0.093710	0.318770
rs823144 x rs4273468	0.817920	0.396790	0.810540	0.723020	0.570210
rs823144 x rs5848	1.000000	0.259190	0.463100	0.304420	0.498350
rs823144 x rs11121679	NA	NA	0.735670	0.957250	0.533830
rs823144 x rs429358	0.662900	0.586670	0.171170	1.000000	0.108710
rs823144 x rs7412	NA	0.495670	1.000000	0.225170	0.311170
rs823144 x rs7982	0.075690	0.523690	0.551500	0.745960	0.004460
rs823144 x rs4236673	0.076580	0.571480	0.159480	0.398650	0.346000
rs823144 x rs3818361	NA	0.898810	0.312520	0.396790	1.000000
rs823144 x rs3764650	1.000000	0.105210	0.807600	0.222480	0.709170
rs823144 x rs4575098	1.000000	0.934270	1.000000	0.371940	0.308130
rs823144 x rs7935829	1.000000	0.725900	0.824190	0.443790	0.607170
rs823144 x rs16984239	1.000000	0.385060	0.676540	0.869500	0.008270
rs823144 x rs4363506	0.614060	0.390920	0.398980	0.309040	0.101980
rs823144 x rs5014235	0.281150	0.791330	0.283810	0.416670	0.310480
rs823144 x rs7976059	0.229810	0.495170	0.677730	0.889150	0.162150
rs823144 x rs616147	1.000000	0.926060	0.285580	0.840040	0.260750
rs823144 x rs10139154	0.525920	0.434940	0.973170	0.084480	1.000000
rs6812193 x rs823118	1.000000	0.814960	0.370020	0.957730	0.156330
rs6812193 x rs14235	0.195020	1.000000	0.891230	0.739580	0.851540
rs6812193 x rs4273468	1.000000	1.000000	1.000000	0.563480	1.000000
rs6812193 x rs5848	1.000000	0.069290	0.377380	0.339710	0.053350
rs6812193 x rs11121679	NA	NA	0.431170	0.571310	0.472940
rs6812193 x rs429358	0.600170	1.000000	0.165880	0.565270	0.486710
rs6812193 x rs7412	NA	0.363460	1.000000	0.060630	0.157940
rs6812193 x rs7982	1.000000	1.000000	1.000000	0.628290	0.177900
rs6812193 x rs4236673	1.000000	0.844230	0.772380	0.164250	0.959270
rs6812193 x rs3818361	NA	1.000000	0.090630	0.139310	0.393150
rs6812193 x rs3764650	1.000000	0.470100	0.016750	0.873020	0.415210

rs6812193 x rs4575098	0.218000	0.175100	0.017770	1.000000	0.623210
rs6812193 x rs7935829	0.163670	1.000000	1.000000	0.884080	0.701690
rs6812193 x rs16984239	1.000000	0.530270	0.191230	0.091380	0.088380
rs6812193 x rs4363506	0.683380	0.850810	0.505350	0.730580	0.239130
rs6812193 x rs5014235	0.365980	0.558560	0.039710	0.614020	0.069670
rs6812193 x rs7976059	0.121250	0.119480	0.895330	0.454170	0.532250
rs6812193 x rs616147	1.000000	0.610790	0.795080	0.428810	0.672310
rs6812193 x rs10139154	0.599170	0.845020	0.933630	0.922210	1.000000
rs823118 x rs14235	0.653350	1.000000	0.807540	0.203980	0.227310
rs823118 x rs4273468	0.814790	0.152020	1.000000	0.861810	0.381080
rs823118 x rs5848	1.000000	0.408210	0.454310	0.140000	0.534000
rs823118 x rs11121679	NA	NA	0.061940	0.764440	0.903100
rs823118 x rs429358	0.658980	0.840940	0.803940	0.407880	0.544380
rs823118 x rs7412	NA	0.505880	0.502060	0.379150	0.839630
rs823118 x rs7982	0.076190	0.361290	0.086540	0.180650	0.104400
rs823118 x rs4236673	0.077440	0.515560	0.145630	1.000000	0.107600
rs823118 x rs3818361	NA	0.764290	0.809040	0.227100	0.466460
rs823118 x rs3764650	1.000000	0.109020	0.835330	0.382650	0.369380
rs823118 x rs4575098	1.000000	0.789520	1.000000	0.053270	0.431060
rs823118 x rs7935829	1.000000	0.751210	0.737440	0.511830	0.184920
rs823118 x rs16984239	1.000000	0.543830	0.236400	1.000000	0.120230
rs823118 x rs4363506	0.613960	0.692960	0.220670	0.208210	0.432060
rs823118 x rs5014235	0.284100	0.802900	0.123380	0.064330	1.000000
rs823118 x rs7976059	0.224580	0.607790	0.567830	0.704730	0.679400
rs823118 x rs616147	1.000000	0.937690	0.101540	1.000000	0.714730
rs823118 x rs10139154	0.525790	0.537290	0.653600	0.208540	0.668710
rs14235 x rs4273468	0.168460	0.167580	0.202540	0.108210	0.824210
rs14235 x rs5848	0.400380	0.467210	0.789350	0.953170	0.451250
rs14235 x rs11121679	NA	NA	0.232380	0.685400	0.568310
rs14235 x rs429358	0.387560	1.000000	0.208210	1.000000	0.532060
rs14235 x rs7412	NA	1.000000	0.241880	0.635730	0.743000
rs14235 x rs7982	0.696130	1.000000	0.539630	0.531900	0.433420
rs14235 x rs4236673	0.700270	1.000000	0.826290	1.000000	0.004880
rs14235 x rs3818361	NA	0.229400	0.834670	0.798380	1.000000
rs14235 x rs3764650	0.405980	1.000000	0.803000	0.346420	0.932900
rs14235 x rs4575098	0.883330	1.000000	0.938940	0.030540	0.167400
rs14235 x rs7935829	0.560080	1.000000	0.487940	0.650350	0.616980
rs14235 x rs16984239	1.000000	0.066380	0.259350	1.000000	0.694270
rs14235 x rs4363506	0.286520	1.000000	0.953380	0.493690	0.032150
rs14235 x rs5014235	1.000000	1.000000	0.119170	0.264000	0.767380
rs14235 x rs7976059	0.701670	0.463540	0.239150	0.745980	0.681020
rs14235 x rs616147	0.320350	0.534130	0.256210	0.598080	0.950630
rs14235 x rs10139154	0.353880	0.433210	0.696960	0.677960	0.549100

rs4273468 x rs5848	1.000000	0.704500	0.587460	0.232500	0.612230
rs4273468 x rs11121679	NA	NA	0.905830	0.733020	0.531480
rs4273468 x rs429358	0.582650	0.566290	0.849190	1.000000	0.561600
rs4273468 x rs7412	NA	0.150940	0.649710	0.759830	0.364980
rs4273468 x rs7982	0.061810	0.887690	0.433020	0.604730	0.929770
rs4273468 x rs4236673	0.061380	0.827980	0.181310	0.722630	0.181900
rs4273468 x rs3818361	NA	0.805980	0.772290	0.723650	0.882210
rs4273468 x rs3764650	1.000000	0.956560	0.553440	0.801350	0.575560
rs4273468 x rs4575098	0.329230	0.743920	0.911600	0.636630	0.756810
rs4273468 x rs7935829	0.675900	0.655600	0.118900	0.145710	0.315690
rs4273468 x rs16984239	1.000000	0.816880	0.006560	0.856880	0.503540
rs4273468 x rs4363506	0.151170	0.949770	0.033040	0.437310	0.468380
rs4273468 x rs5014235	0.760940	1.000000	0.341500	0.735920	0.890020
rs4273468 x rs7976059	0.424650	0.161190	1.000000	0.678020	0.815710
rs4273468 x rs616147	0.224420	0.793380	0.751230	0.524810	0.657880
rs4273468 x rs10139154	0.833190	0.778210	0.610960	0.709250	0.729400
rs5848 x rs11121679	NA	NA	0.722600	0.417290	0.148770
rs5848 x rs429358	1.000000	0.269420	0.112580	0.795380	0.107440
rs5848 x rs7412	NA	0.208190	0.679460	0.286920	0.347460
rs5848 x rs7982	1.000000	1.000000	0.215540	0.466600	0.577060
rs5848 x rs4236673	1.000000	0.932330	0.005480	0.440000	0.493350
rs5848 x rs3818361	NA	0.218380	0.009350	0.170420	0.232060
rs5848 x rs3764650	0.049330	0.204310	0.867250	0.094880	0.027350
rs5848 x rs4575098	0.401250	0.548230	0.433520	0.464940	0.094560
rs5848 x rs7935829	0.199880	0.539480	0.525940	0.424790	0.040310
rs5848 x rs16984239	1.000000	0.922020	0.701190	0.859920	0.257380
rs5848 x rs4363506	0.448900	0.030960	0.761130	0.671690	1.000000
rs5848 x rs5014235	1.000000	0.699830	0.785040	1.000000	0.254100
rs5848 x rs7976059	0.449060	0.655730	0.397020	0.043380	0.779310
rs5848 x rs616147	1.000000	0.737100	0.130380	0.300150	0.716480
rs5848 x rs10139154	1.000000	0.007420	0.694020	0.450040	0.920480
rs11121679 x rs429358	NA	NA	1.000000	0.825980	0.772540
rs11121679 x rs7412	NA	NA	1.000000	0.216520	1.000000
rs11121679 x rs7982	NA	NA	0.703980	0.066830	0.818880
rs11121679 x rs4236673	NA	NA	0.598750	0.313850	0.972650
rs11121679 x rs3818361	NA	NA	0.043380	0.596730	0.306100
rs11121679 x rs3764650	NA	NA	0.208190	0.743190	0.870500
rs11121679 x rs4575098	NA	NA	0.709690	1.000000	0.654080
rs11121679 x rs7935829	NA	NA	1.000000	0.221770	0.576060
rs11121679 x rs16984239	NA	NA	0.089020	1.000000	0.861020
rs11121679 x rs4363506	NA	NA	0.496190	0.238630	0.548650
rs11121679 x rs5014235	NA	NA	0.465210	0.854690	0.519480
rs11121679 x rs7976059	NA	NA	0.608540	0.524150	0.847520

rs11121679 x rs616147	NA	NA	0.356230	0.032250	0.531170
rs11121679 x rs10139154	NA	NA	0.007540	0.943980	0.234170
rs429358 x rs7412	NA	1.000000	1.000000	0.540420	0.247400
rs429358 x rs7982	0.332630	1.000000	0.673670	0.885750	0.469190
rs429358 x rs4236673	0.333830	0.812940	1.000000	0.356770	0.802190
rs429358 x rs3818361	NA	0.404130	0.170440	0.386440	0.066690
rs429358 x rs3764650	1.000000	0.373060	0.242040	0.055230	0.255790
rs429358 x rs4575098	0.903960	0.809670	0.091270	0.179440	0.622790
rs429358 x rs7935829	0.603310	0.128830	0.743500	0.696060	0.064960
rs429358 x rs16984239	1.000000	0.129130	0.611880	1.000000	0.440250
rs429358 x rs4363506	0.173270	0.268710	0.705940	0.277560	0.005420
rs429358 x rs5014235	1.000000	0.677940	0.609960	1.000000	0.851380
rs429358 x rs7976059	0.717900	0.019020	0.706850	0.515500	0.257920
rs429358 x rs616147	0.210850	1.000000	1.000000	0.190630	0.842270
rs429358 x rs10139154	0.859940	1.000000	1.000000	0.657460	1.000000
rs7412 x rs7982	NA	1.000000	0.492810	0.806560	0.571940
rs7412 x rs4236673	NA	0.705100	1.000000	0.141520	0.346250
rs7412 x rs3818361	NA	0.239480	1.000000	0.485060	0.158750
rs7412 x rs3764650	NA	0.130710	0.468710	1.000000	0.628400
rs7412 x rs4575098	NA	0.482350	0.218130	0.792060	1.000000
rs7412 x rs7935829	NA	1.000000	0.581520	0.541750	0.356690
rs7412 x rs16984239	NA	1.000000	0.516770	1.000000	1.000000
rs7412 x rs4363506	NA	0.626080	0.166670	0.436500	0.827080
rs7412 x rs5014235	NA	1.000000	1.000000	0.592750	0.551810
rs7412 x rs7976059	NA	0.521190	1.000000	0.845560	0.289810
rs7412 x rs616147	NA	0.711810	1.000000	1.000000	0.727730
rs7412 x rs10139154	NA	0.609400	1.000000	0.190290	0.278040
rs7982 x rs4236673	**0.000020**	**0.000020**	**0.000020**	0.000650	0.079150
rs7982 x rs3818361	NA	0.097130	0.663520	0.870060	0.495580
rs7982 x rs3764650	1.000000	0.739830	0.113000	0.229080	0.965460
rs7982 x rs4575098	0.399690	0.481380	0.820060	0.957690	0.441900
rs7982 x rs7935829	0.191060	0.311210	0.329540	0.238330	0.897100
rs7982 x rs16984239	0.474540	0.078980	0.690710	0.729210	0.135330
rs7982 x rs4363506	0.233830	0.238080	0.976560	0.978190	0.448210
rs7982 x rs5014235	0.123040	1.000000	0.543560	0.001380	0.834630
rs7982 x rs7976059	1.000000	1.000000	1.000000	0.799790	0.828080
rs7982 x rs616147	1.000000	0.565880	0.507900	0.440310	0.120060
rs7982 x rs10139154	0.934810	0.373150	0.775730	0.297270	0.672920
rs4236673 x rs3818361	NA	0.581130	0.475580	0.780040	0.727350
rs4236673 x rs3764650	1.000000	0.164830	0.894830	0.071150	1.000000
rs4236673 x rs4575098	0.401630	0.270730	0.931250	0.427290	0.540770
rs4236673 x rs7935829	0.191150	0.159810	0.161750	0.728830	0.857100
rs4236673 x rs16984239	0.474420	0.116540	0.863190	0.763080	0.257270

rs4236673 x rs4363506	0.233400	0.342790	0.413540	0.536710	0.845790
rs4236673 x rs5014235	0.127060	0.459290	0.384540	0.650960	0.779330
rs4236673 x rs7976059	1.000000	0.888380	0.976920	0.696250	0.700810
rs4236673 x rs616147	1.000000	0.654400	0.816670	0.221770	0.252940
rs4236673 x rs10139154	0.934020	0.548210	0.618190	0.332230	0.558080
rs3818361 x rs3764650	NA	0.211380	0.113100	0.622730	0.467150
rs3818361 x rs4575098	NA	0.337830	0.090250	0.831060	0.233060
rs3818361 x rs7935829	NA	0.734900	0.517520	0.615520	1.000000
rs3818361 x rs16984239	NA	0.683710	1.000000	0.400400	0.063770
rs3818361 x rs4363506	NA	0.175460	1.000000	0.119000	0.300850
rs3818361 x rs5014235	NA	0.453420	0.454730	0.063690	0.074440
rs3818361 x rs7976059	NA	0.777170	0.107600	0.545540	0.298600
rs3818361 x rs616147	NA	0.916690	0.174080	0.311440	1.000000
rs3818361 x rs10139154	NA	0.896080	0.028560	0.297210	0.623900
rs3764650 x rs4575098	0.400900	0.835440	0.115270	0.439040	0.455310
rs3764650 x rs7935829	0.197710	0.307460	0.300000	0.108750	0.849830
rs3764650 x rs16984239	1.000000	0.054500	1.000000	0.084900	0.430190
rs3764650 x rs4363506	0.450350	0.018600	0.236670	0.726850	0.469060
rs3764650 x rs5014235	1.000000	1.000000	0.675730	0.819210	0.874040
rs3764650 x rs7976059	0.452540	1.000000	0.484270	0.092770	0.809270
rs3764650 x rs616147	1.000000	0.610190	0.837210	0.234480	0.864400
rs3764650 x rs10139154	1.000000	0.300020	0.745580	0.438630	0.808920
rs4575098 x rs7935829	0.683210	0.056500	0.613790	0.890060	0.281940
rs4575098 x rs16984239	0.211940	0.600750	0.819960	1.000000	0.003650
rs4575098 x rs4363506	0.250710	0.799210	0.546130	0.472790	0.098480
rs4575098 x rs5014235	0.651350	0.788670	0.536150	0.250400	0.716420
rs4575098 x rs7976059	0.097980	0.458960	0.945750	0.966330	0.366900
rs4575098 x rs616147	0.490170	0.370880	0.925920	0.427020	1.000000
rs4575098 x rs10139154	0.814130	0.953210	0.872980	0.692630	0.698000
rs7935829 x rs16984239	0.369630	0.903380	0.328290	0.067830	0.324350
rs7935829 x rs4363506	0.679980	0.833750	0.735080	0.798290	0.725100
rs7935829 x rs5014235	0.368420	1.000000	0.737790	0.642790	0.671310
rs7935829 x rs7976059	0.840830	0.247850	0.279460	0.066080	0.889600
rs7935829 x rs616147	0.466040	0.817440	0.048350	0.852060	1.000000
rs7935829 x rs10139154	0.599630	0.702520	0.285560	0.880920	0.884350
rs16984239 x rs4363506	0.099630	0.888400	0.010290	0.640130	0.088270
rs16984239 x rs5014235	1.000000	0.678210	0.465380	1.000000	0.593190
rs16984239 x rs7976059	1.000000	0.402020	0.772730	0.000150	0.543850
rs16984239 x rs616147	0.572420	0.637420	0.364100	1.000000	0.880500
rs16984239 x rs10139154	0.190560	0.030130	0.084580	1.000000	0.335250
rs4363506 x rs5014235	1.000000	0.851790	0.773040	0.371580	0.369290
rs4363506 x rs7976059	0.632920	0.916310	0.620380	0.982210	0.274750
rs4363506 x rs616147	0.692230	0.654560	0.404850	0.000230	0.801150

rs4363506 x rs10139154	0.210750	0.030460	0.659230	0.780730	0.776650
rs5014235 x rs7976059	0.710310	1.000000	0.280400	0.350830	0.062250
rs5014235 x rs616147	1.000000	0.327100	0.030940	0.188630	0.453040
rs5014235 x rs10139154	1.000000	0.856420	0.671750	0.055900	0.191630
rs7976059 x rs616147	0.306880	0.040790	0.646150	0.712400	0.016150
rs7976059 x rs10139154	0.312730	0.704170	0.027650	0.879850	0.101290
rs616147 x rs10139154	0.489540	0.952920	0.211040	0.204810	0.599960

NA, Not Available due to one of the markers being monomorphic.