TECHNICAL NOTE

Mary Walkinshaw,[1] Ph.D.; Leanne Strickland,[1] M.S.; Hayne Hamilton,[1] B.S.; Kristin Denning,[1] B.S.; and Todd Gayley,[2] Ph.D.

DNA Profiling in Two Alaskan Native Populations Using HLA-DQA1, PM, and D1S80 Loci

REFERENCE: Walkinshaw, M., Strickland, L., Hamilton, H., Denning, K., and Gayley, T., **"DNA Profiling in Two Alaskan Native Populations Using HLA-DQA1, PM, and D1S80 Loci,"** *Journal of Forensic Sciences,* JFSCA, Vol. 41, No. 3, May 1996, pp. 478–484.

ABSTRACT: Two Native Alaskan populations were sampled and DNA profiles were generated for 201 individuals. Ninety two blood samples were collected from the North Slope Borough region of Alaska and the remaining 109 blood samples came from Native Alaskans in the Bethel and Wade Hampton areas. Allele and genotype frequencies were established for the HLA-DQA1, LDLR, GYPA, HBGG, D7S8, Gc, and D1S80 loci. Native Alaskans are slightly less polymorphic than Caucasians at the HLA-DQA1 locus. In contrast, the PM loci appear to be nearly as informative in the Native Alaskan populations as in Caucasians for identity testing. The data clearly demonstrate that all the loci tested are highly informative for the Alaskan populations and fall well within Hardy-Weinberg expectations. There is little evidence for departure from expectation of independence of alleles across loci. The data demonstrate that estimates of multiple locus profile frequencies can be obtained from Native Alaskan populations using the product rule under the assumption of independence of loci. In addition, Native Alaskan databases were more similar to each other and to other Native American databases than they were to U.S. Caucasians and African Americans.

KEYWORDS: forensic science, population studies, DNA, genetic markers

Native people in Alaska can be divided into three large groups: Aleuts, Native American Indians and Eskimos. The Aleuts live on the Southwest peninsula that extends out the Aleutian Island chain (see Fig. 1 map). The Native Americans include the Athabaskan, the Tlingit and the Haida people. The vast interior of Alaska is homeland to the Athabaskan Indians. The other two groups of Indians, the Tlingit and Haida, live along the Southeast Gulf of Alaska. Most of the territory south of Controller Bay is home to the Tlingits. The Haidas live mainly on Prince of Wales Island and on Canada's Queen Charlotte Island. Each of these groups of Indians has their own language and culture (31).

[1]Criminalist III, Criminalist III, Criminalist III, and Criminalist II, respectively, Alaska State Crime Lab, Anchorage, AK.

[2]Software Engineer, Mathematical Applications, Wolfram Research Inc., Champaign, IL.

Received for publication 26 April 1995; revised manuscript received 29 Aug. 1995; accepted for publication 5 Sept. 1995.

Eskimos live along the western and northern coast of Alaska. Their homeland stretches from Bristol Bay around the coast and across northern Canada and parts of Greenland. Most Eskimos speak one of two languages, Inupiaq or Yupik. The linguistic boundary lies along the Norton Sound area. Inupiaq speakers live to the north of this boundary including the North Slope Borough region. Yupik speakers live to the south in the Bethel-Wade Hampton and other areas.

1990 census figures, compiled by the Alaskan Department of Labor, record 4336 Alaska Natives living in the North Slope Borough region. Census figures do not distinguish between the three main groups of Native Alaskans (American Indians, Aleuts and Eskimos). The 1990 figures report 11,370 Natives in the Bethel region and 5405 in the Wade Hampton region, for a total of 16,775 Native Alaskans in this area. This study focused on Native Alaskans from these regions because sufficient Alaskan Native blood samples were available to compile DNA databases. This study completed DNA profiles on 2% of the Native population from the North Slope Borough, and on 0.7% of the Native population from the Bethel Wade-Hampton area. These databases are extremely relevant to forensic case work investigated by the Alaska State Crime Laboratory.

Statistics compiled by the FBI and Uniform Crime Report (UCR) show that per capita, Alaska has ranked in the top five states of the Nation for the highest rate of reported rape for the past seventeen years. In all but five of these years, Alaska had the highest rate of reported rape per capita. Statistics compiled by the Alaska Department of Health and Human Services demonstrate that in 1993 Alaska had the highest per capita incidence of rape in the country—approximately twice the National average rate. 1992 figures reported by the Alaska Department of Public Safety show that 56% of offenders arrested for sexual assault were Native Alaskans, 36% were Caucasians and 8% were African Americans. These figures emphasize the urgent need for publication of databases containing allele and genotype frequencies for Native Alaskan populations.

No DNA profile information was available on Native Alaskans from the North Slope Borough or the Bethel-Wade Hampton areas prior to this study. Several sources have compiled population data on U.S. Caucasians, African Americans, Hispanics and Asians using PCR based technology. The most frequently applied PCR-based genetic markers include HLA-DQA1 (1–4), low density

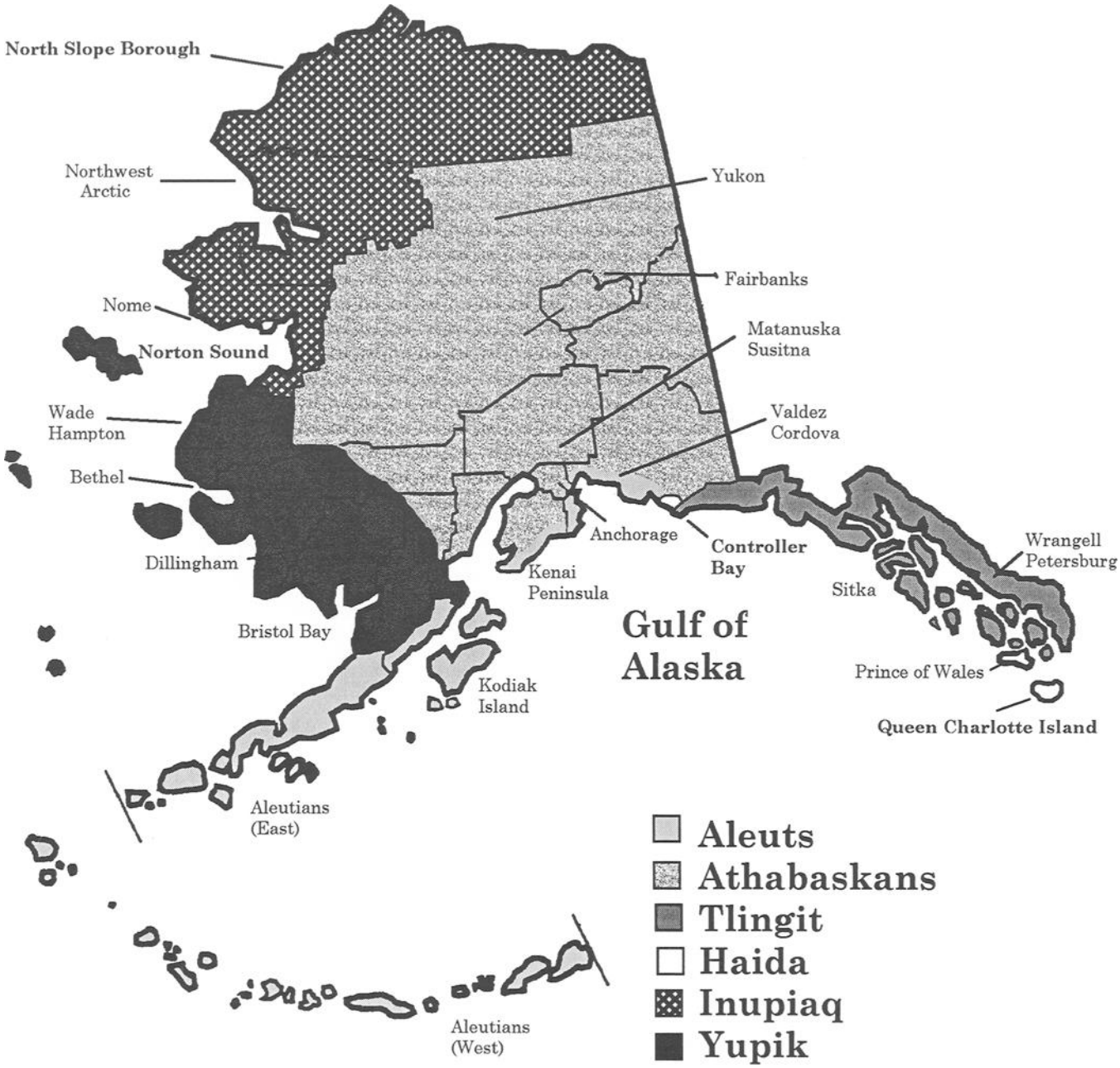

FIG. 1—*Alaska native populations.*

lipoprotein receptor (LDLR) (5), glycophorin A (GYPA) (6), hemoglobin G gammaglobin (HBGG) (7), D7S8 (8), group specific component (Gc) (9), and D1S80 (10–13).

Prior to the application of genetic markers in identity testing, it is necessary to compile allele/genotype data from relevant populations that allows the forensic scientist to provide an accurate estimate of the rarity of a given genetic profile. This paper provides population genetic data for seven loci in the Native Alaskan populations from the North Slope Borough region and the Bethel-Wade Hampton region.

In addition to providing vital information for law enforcement in Alaska, this study offers the opportunity to address criticisms leveled against the application of DNA typing to forensics. Lewontin and Hartl (30) have called for the examination of genetic variation among ethnic subgroups. Alaska Natives offer a unique set of small, relatively isolated populations that may offer some insight into these issues.

Materials and Methods

Sample Preparation

Whole blood was obtained in EDTA Vacutainer tubes by venipuncture from Native Alaskans from the North Slope Borough region and from Native Alaskans from the Bethel-Wade Hampton

region. Samples were collected by regional law enforcement agents or by the County Medical Examiners Office. Samples are predominately from suspects and victims from forensic cases or autopsy cases dating back to 1987. To ensure that each sample in the data base was represented only once, a search for duplicates was conducted using first and last names as well as date of birth.

DNA was extracted by the phenol-chloroform method of Comey et al. 1994 (14) or by the Chelex extraction method described in the Amplitype User Guide, Version 2 (Perkin Elmer Corporation, Norwalk, CT). The quantity of extracted DNA was estimated using the slot-blot procedure (Budowle et al. 15). One to five nanograms of DNA were used for PCR.

HLA-DOA1 Typing

DNA samples were amplified and typed for the HLA-DQA1 locus using the AmpliType HLA-DQα Forensic DNA Amplification and Typing Kit (Perkin Elmer Corporation, Norwalk, CT) according to the manufacturer's protocol. Amplification was carried out in a Perkin-Elmer DNA thermal cycler 480.

Polymarker Typing

DNA samples were amplified and typed for the PM loci using the Amplitype PM PCR Amplification and Typing Kit (Perkin Elmer Corporation, Norwalk, CT) according to the manufacturer's protocol. Amplification was carried out in a Perkin-Elmer DNA thermal cycler 480.

D1S80 Typing

The D1S80 locus was typed according to the method described in Budowle et al. (16, and Baechtel et al. (17)).

Statistical Analysis

The frequency of each allele for each locus was calculated from the numbers of each genotype in the sample set. Unbiased estimates for expected heterozygosity were computed as described by Edwards et al. 1992 (18). The expected numbers of distinct homozygous and heterozygous genotypes and their standard error were calculated according the method described by Chakraborty et al. (22). Possible divergence from Hardy-Weinberg expectations (HWE) was determined by calculating the unbiased estimate of the expected homozygote/heterozygote frequencies (19–21), the likelihood ratio test (22,23), and the exact test (24). An interclass correlation criterion (25) was used to detect potential disequilibrium between loci. Dependence across all loci was also determined by examining whether the observed variance of the number of heterozygous loci in the population sample is outside its confidence interval under the assumption of independence (26).

A 2 × C contingency table exact test was used to generate a G-statistic (1000 shuffling experiments) (27), to test for homogeneity between population samples. The program was kindly provided by R. Chakraborty (University of Texas School of Biomedical Sciences, Houston, Texas).

Results and Discussion

Tables 1–4 show the distribution of observed genotype and allelic frequencies for HLA-DQA1 and D1S80. 102 individuals from the North Slope Borough were typed for HLA-DQA1 and a subset of 92 of these were typed for D1S80. 115 individuals from the Bethel-Wade Hampton area were typed for HLA-DQA1 and a subset of 109 were typed for D1S80. For the D1S80 locus, there were 12 different nominal alleles observed in the North Slope Borough population and 13 alleles in the Bethel-Wade Hampton population.

TABLE 1—*Distribution of observed HLA-DQα genotypes in Alaskan Natives.*

Genotype	North Slope	Bethel-Wade
	Frequency $N = 102$	Frequency $N = 115$
1.1–1.1	0.010	0.000
1.1–1.2	0.000	0.000
1.1–1.3	0.000	0.000
1.1–2	0.000	0.000
1.1–3	0.147	0.043
1.1–4	0.128	0.017
1.2–1.2	0.010	0.000
1.2–1.3	0.000	0.000
1.2–2	0.000	0.000
1.2–3	0.020	0.017
1.2–4	0.059	0.000
1.3–1.3	0.000	0.000
1.3–2	0.000	0.000
1.3–3	0.020	0.000
1.3–4	0.010	0.000
2–2	0.000	0.000
2–3	0.010	0.000
2–4	0.020	0.000
3–3	0.098	0.139
3–4	0.284	0.426
4–4	0.186	0.357

NOTE:

	NSB	BWH
a) observed Homozygosity	0.304	0.496
b) Expected homozygosity (unbiased)	0.326	0.480
c) HWE: (P values)		
Homozygosity test	0.650	0.768
Likelihood ratio test	0.487	0.192
Exact test	0.575	0.235

TABLE 2—*HLA-DQα allele frequencies in two Alaskan Native populations.*

Allele	North Slope	Bethel-Wade Hampton
	Frequency $N = 102$	Frequency $N = 115$
1.1	0.147	0.030
1.2	0.049	0.009
1.3	0.015	0.000
2	0.015	0.000
3	0.338	0.383
4	0.436	0.578

The observed heterozygosities for these two loci in the North Slope Borough population are 70 and 73%, respectively. In the Bethel-Wade Hampton population the observed heterozygosity for HLA-DQA1 is 50% and for D1S80 is 80%. The values for D1S80 are comparable to heterozygosity values reported for Caucasians (16,28). Observed heterozygosities for both HLA-DQA1 and D1S80 are similar to other Native American data bases (29) and demonstrate that these Alaskan Native populations are highly polymorphic at these loci.

A test was performed for independence for the alleles within a

TABLE 3—*D1S80 allele frequencies in two Alaskan Native populations.*

Allele	North Slope	Bethel-Wade Hampton
	Frequency $N = 92$	Frequency $N = 109$
17	0.038	0.051
18	0.435	0.321
19	0.027	0.032
20	0.000	0.000
21	0.011	0.005
22	0.000	0.005
23	0.000	0.018
24	0.152	0.124
25	0.044	0.133
26	0.000	0.000
27	0.005	0.005
28	0.005	0.092
29	0.011	0.018
30	0.027	0.023
31	0.239	0.174
32	0.005	0.000

NOTE:

	NSB	BWH
a) observed homozygosity	0.272	0.202
b) Expected homozygosity (unbiased)	0.271	0.176
c) HWE: (P values)		
Homozygosity test	1.000	0.470
Likelihood ratio test	0.929	0.082
Exact test	0.935	0.062

TABLE 4—*Distribution of observed D1S80 genotypes in Alaskan Natives.*

Genotype	North Slope Borough	Bethel Wade Hampton
	Fequency $N = 92$	Fequency $N = 109$
17,17	0.000	0.009
17,18	0.043	0.018
18,18	0.174	0.092
18,19	0.043	0.046
18,21	0.011	0.000
18,23	0.000	0.028
18,24	0.163	0.110
17,24	0.011	0.000
19,24	0.000	0.009
21,24	0.000	0.009
24,24	0.022	0.018
17,25	0.000	0.046
18,25	0.043	0.073
24,25	0.011	0.000
18,27	0.000	0.009
17,28	0.000	0.009
18,28	0.011	0.028
19,28	0.000	0.009
24,28	0.000	0.009
25,28	0.000	0.028
28,28	0.000	0.028
18,29	0.011	0.000
25,29	0.011	0.009
28,29	0.000	0.018
18,30	0.011	0.000
24,30	0.000	0.009
25,30	0.000	0.018
28,30	0.000	0.009
29,30	0.000	0.009
30,30	0.011	0.000
17,31	0.022	0.009
18,31	0.174	0.148
19,31	0.011	0.000
21,31	0.011	0.000
22,31	0.000	0.009
24,31	0.076	0.037
25,31	0.022	0.037
27,31	0.011	0.000
28,31	0.000	0.018
30,31	0.022	0.000
31,31	0.065	0.046
18,32	0.011	0.000

locus, based on the number of distinct heterozygote and homozygote genotypes (Tables 1 and 3). There is no detectable deviation from expected values for either population. In addition the distribution of HLA-DQA1 and D1S80 genotypes do not deviate from HWE based on the homozygosity test (19), the likelihood ratio test (23) or the exact test (24) (Tables 1 and 3). The data support that HLA-DQA1 and D1S80 allele frequencies for these populations can be multiplied to estimate genotype frequencies.

Ninety-six individuals from the North Slope Borough (NSB) and 112 individuals from the Bethel-Wade Hampton (BWH) area were typed for the five polymarker loci. Both populations are polymorphic at all five loci. The observed heterozygosity in the NSB population ranged from 27% (for GYPA) to 68% (for Gc) (Table 5). The observed heterozygosity in the BWH population went from 28% (for HBGG) to 67% (for Gc) (Table 6). There is no detectable deviation from HWE for these loci based on the homozygosity test, likelihood ratio test and the exact test in either population (Tables 7 and 8). To the best of our knowledge this is the first published report of genotype and allelic distributions of HLA-DQA, D1S80 and polymarker loci for Alaskan Native populations.

Estimating the frequency of a DNA profile containing all seven loci by the direct count method with databases of this size, (N = 92 for NSB, N = 109 for BWH) does not provide a reliable estimate of the rarity of a multiple locus DNA profile. All of the loci examined in this study are on different chromosomes except for GYPA and GC which are both located on the q arm of chromosome 4. Therefore, it would be expected that genotypes at these loci occur independently. Even so, analyses were performed to determine whether or not there were any detectable associations between the 7 PCR based loci.

The first analysis was the inter-class correlation test (25), which demonstrates little evidence for correlation between the alleles at any of the pairs of loci (Tables 9 and 10). Two pairwise comparisons in the North Slope Borough population do show some deviation from expectation. The HBGG/D1S80 comparison results in a P value of 0.044, and the HLA-DQA1/D1S80 comparison gives a P value of 0.007. Of the loci tested, HLA-DQA1 and D1S80 have the greatest number of alleles. This polymorphism predisposes them to departures from expected values because one or more alleles from the loci may appear only once or not at all in a sample population data base. A significant P value in these loci may be due to the size of the sample population.

Based on the number of pairwise comparisons (that is, inter-locus association tests) the amount of deviation observed for the inter-class correlation test is no more than would be expected (2 observations out of 42 total comparisons = 4.8%), less than 5% departures. The data are consistent with 7 PCR based independent loci in both Native Alaskan populations.

The effect on two-locus frequency estimates due to the potential association between HBGG/D1S80 or HLA-DQA1/D1S80 can be

TABLE 5—*Distribution of PM marker genotypes from the North Slope Borough region.*

Genotype	LDLR	GYPA	HBGG	D7S8	Gc
AA	0.313	0.656	0.031	0.033	0.083
AB	0.479	0.271	0.292	0.469	0.094
BB	0.208	0.073	0.677	0.198	0.094
AC	NG[a]	NG	0.000	NG	0.302
BC	NG	NG	0.000	NG	0.281
CC	NG	NG	0.000	NG	0.146

NOTE: a) NG = There is no allele C with the AmpliType® PM PCR Amplification and Typing Kit (Perkin-Elmer Corporation, Norwalk, CT) for LDLR, GYPA, and D7S8; therefore no genotype can be detected.

b) LDLR—Observed homozygosity = 0.521; Expected homozygosity (unbiased) = 0.503; HWE—Homozygosity test (P = 0.843), Likelihood ratio test (P = 0.843), exact test (P = 0.843).

c) GYPA—Observed homozygosity = 0.729; Expected homozygosity (unbiased) = 0.668; HWE—Homozygosity test (P = 0.114), Likelihood ratio test (P = 0.114), Exact test (P = 0.114).

d) HBGG—Observed homozygosity = 0.708; Expected homozygosity (unbiased) = 0.707; HWE—Homozygosity test (P = 1.000), Likelihood ratio test (P = 1.000), Exact Test (P = 1.000).

e) D7S8—Observed homozygosity = 0.531; Expected homozygosity (unbiased) = 0.507; HWE = Homozygosity test (P = 0.660), Likelihood ratio test (P = 0.660), Exact test (P = 0.660).

f) Gc—Observed homozygosity = 0.323; Expected homozygosity (unbiased) = 0.346; HWE—Homozygosity test (P = 0.665), Likelihood ratio test (P = 0.118), Exact test (P = 0.124).

TABLE 6—*Distribution of PM marker genotypes from the Bethel-Wade Hampton region.*

Genotype	LDLR	GYPA	HBGG	D7S8	Gc
AA	0.357	0.384	0.018	0.295	0.098
AB	0.518	0.491	0.277	0.527	0.170
BB	0.125	0.125	0.705	0.179	0.107
AC	NG[a]	NG	0.000	NG	0.232
BC	NG	NG	0.000	NG	0.268
CC	NG	NG	0.000	NG	0.125

NOTE: a) NG = There is no allele C with the AmpliType® PM PCR Amplification and Typing Kit (Perkin-Elmer Corporation, Norwalk, CT) for LDLR, GYPA, and D7S8; therefore no genotype can be detected.

b) LDLR—Observed homozygosity = 0.482; Expected homozygosity (unbiased) = 0.525; HWE—Homozygosity test (P = 0.424), Likelihood ratio test (P = 0.344), Exact test (P = 0.424).

c) GYPA—Observed homozygosity = 0.509; Expected homozygosity (unbiased) = 0.531; HWE—Homozygosity test (P = 0.691), Likelihood ratio test (P = 0.691), Exact test (P = 0.691).

d) HBGG—Observed homozygosity = 0.723; Expected homozygosity (unbiased) = 0.735; HWE—Homozygosity test (P = 0.750), Likelihood ratio test (P = 0.750), Exact test (P = 1.000).

e) D7S8—Observed homozygosity = 0.473; Expected homozygosity (unbiased) = 0.505; HWE—Homozygosity test (P = 0.665), Likelihood ratio test (P = 0.665), Exact test (P = 0.665).

f) Gc—Observed homozygosity = 0.330; Expected homozygosity (unbiased) = 0.333; HWE—Homozygosity test (P = 1.000), Likelihood ratio test (P = 0.802), Exact test (P = 0.875).

examined by comparing the two locus genotype frequencies derived by the counting method (observed two-locus genotype frequency) with those derived by the product rule under the assumption of independence. Table 11 compares observed genotype frequencies with those estimated using the product rule for the HBGG and D1S80 genotypes. The estimates in Table 11 that are marked by an asterisk are occasions where the product rule yielded a lower frequency estimate than the counting method. If the product rule is used to estimate a multiple locus DNA profile

TABLE 7—*PM marker allele frequencies from 96 Alaska Natives from the North Slope Borough region.*

Allelle	LDLR	GYPA	HBGG	D7S8	Gc
A	0.552	0.792	0.177	0.568	0.281
B	0.448	0.208	0.823	0.432	0.281
C	NA[a]	NA	0.000	NA	0.438

NOTE: [a]Na = there is no C allele on the typing strips with the AmpliType® PM PCR Amplification and Typing Kit (Perkin-Elmer Corporation, Norwalk, CT) for LDLR, GYPA, and D7S8.

TABLE 8—*PM marker allele frequencies from 112 Alaskan Natives from the Bethel-Wade Hampton area.*

Allele	LDLR	GYPA	HBGG	D7S8	Gc
A	0.616	0.629	0.156	0.558	0.299
B	0.384	0.371	0.844	0.442	0.326
C	NA[a]	NA	0.000	NA	0.375

NOTE: [a]NA = there is no C allele on the typing strips with the AmpliType® PM PCR Amplification and Typing Kit (Perkin-Elmer Corporation, Norwalk, CT) for LDLR, GYPA, and D7S8.

TABLE 9—*Two locus inter-class correlation test for HLA-DQα, D1S80, and PM markers for 109 individuals from the Bethel-Wade Hampton area.*

Loci	Two-sided probability
LDLR/GYPA	0.282
LDLR/HBGG	0.749
LDLR/D7S8	1.000
LDLR/Gc	0.359
LDLR/DQα	0.700
GYPA/HBGG	0.957
GYPA/D7S8	0.695
GYPA/Gc	0.402
GYPA/DQα	0.314
HBGG/D7S8	0.819
HBGG/Gc	0.522
HBGG/DQα	0.360
D7S8/Gc	0.194
D7S8/DQα	0.816
Gc/DQα	0.386
LDLR/D1S80	0.370
GYPA/D1S80	0.768
HBGG/D1S80	0.341
D7S8/D1S80	0.371
Gc/D1S80	0.882
DQα/D1S80	0.803

NOTE: a) deviation at P = 0.05 level.

frequency, then the concern for potential wrongful bias in an estimate will be when the counting method yields a higher frequency estimate than the product rule.

In Table 11, 31% of the time the counting method results in a higher frequency estimate. In the case of HLA-DQA1/D1S80 (data not shown) 13% of the time the counting method results in a higher frequency estimate. The remainder of the time, application of the product rule results in the same or higher frequency estimate. The difference in frequency estimates by the two methods is marginal and does not result in a noticeable effect on a multiple locus frequency estimate. Since the product rule estimates for some of the double locus patterns in a multiple locus profile will be greater than those obtained by the counting method, any potential wrongful

TABLE 10—*Two locus inter-class correlation test for HLA-DQα, D1S80, and PM markers for 109 individuals from the North Slope Borough region.*

Loci	Two-Sided Probability
LDLR/GYPA	0.696
LDLR/HBGG	0.703
LDLR/D7S8	0.816
LDLR/Gc	0.910
LDLR/DQα	0.992
GYPA/HBGG	0.632
GYPA/D7S8	1.000
GYPA/Gc	0.539
GYPA/DQα	0.332
HBGG/D7S8	0.609
HBGG/Gc	0.187
HBGG/DQα	0.671
D7S8/Gc	0.165
D7S8/DQα	0.749
Gc/DQα	0.600
LDLR/D1S80	0.874
GYPA/D1S80	0.279
HBGG/D1S80	0.044*
D7S8/D1S80	0.267
Gc/D1S80	0.781
DQα/D1S80	0.007*

NOTE: * = deviation at $P = 0.05$ level.

TABLE 11—*Frequencies for the two-locus genotypes for D1S80 and HBGG in 92 Native Alaskans from the North Slope Borough region.*

Genotype D1S80	HBGG AA Counting	HBGG AA Product	HBGG AB Counting	HBGG AB Product	HBGG BB Counting	HBGG BB Product
17,18	0.000	0.001	0.000	0.013	0.044	0.029*
18,18	0.022	0.005*	0.044	0.051	0.109	0.118
18,19	0.000	0.001	0.022	0.013*	0.022	0.029
18,21	0.000	0.000	0.000	0.003	0.011	0.008*
17,24	0.000	0.000	0.011	0.003*	0.000	0.007
18,24	0.000	0.005	0.065	0.048*	0.098	0.110
24,24	0.000	0.001	0.022	0.006*	0.000	0.015
18,25	0.000	0.001	0.011	0.013	0.033	0.029*
24,25	0.000	0.000	0.011	0.003*	0.000	0.007
18,28	0.011	0.000*	0.000	0.003	0.000	0.007
18,29	0.000	0.000	0.011	0.003*	0.000	0.007
25,29	0.000	0.000	0.000	0.003	0.011	0.007*
18,30	0.000	0.000	0.000	0.003	0.011	0.007*
30,30	0.000	0.000	0.000	0.003	0.011	0.007*
17,31	0.000	0.001	0.011	0.006*	0.011	0.015
18,31	0.000	0.005	0.022	0.051	0.152	0.118*
19,31	0.000	0.000	0.011	0.003*	0.000	0.007
21,31	0.000	0.000	0.011	0.003*	0.000	0.007
24,31	0.000	0.002	0.011	0.003*	0.065	0.052*
25,31	0.000	0.001	0.000	0.006	0.022	0.015*
27,31	0.000	0.000	0.000	0.003	0.011	0.007*
30,31	0.000	0.001	0.000	0.006	0.022	0.015*
31,31	0.000	0.002	0.011	0.019	0.011	0.044
18,32	0.000	0.000	0.000	0.003	0.000	0.007

NOTE: *product rule frequency estimates that are less than the counting method.

bias will be minimized across several loci. For forensic purposes the application of the product rule provides a valid estimate of a multiple locus frequency. In instances of a rare genotype, application of the product rule will result in a higher frequency especially if the sample population is small. In these cases there is a good chance a rare genotype or profile will not be seen at all.

To confirm that there is little deviation from expectation when using the product rule to derive a multiple locus frequency estimate, an additional test for independence between the seven loci was run on each population using the procedure described by Brown et al. (26). This test, the s_k^2 criterion, has sufficient power to detect association of alleles across more than two loci that might have an impact on estimating multiple locus genotype frequencies using the product rule. There is no evidence of association for the seven loci in either the North Slope Borough Population or the Bethel Wade-Hampton Population. The s_k^2 value for the North Slope Borough population is 1.98316, the 95% confidence interval for this statistic is 1.13482–1.98468. The s_k^2 value for the Bethel Wade-Hampton Area is 1.84217, the 95% confidence interval is 1.17371–1.95203. Both values fall within their confidence interval.

Forensic geneticists have never argued that substructure does not exists in populations. The relevant issue is the significance of any potential substructure on the ability to generate DNA profile frequencies using the product rule. The statistical analyses employed in this study are sufficiently powerful enough to detect any substructure that would significantly impact profile frequency estimates. Given the number of tests performed in this study, and the comparatively large sample population size (2% from the North Slope Borough and 0.7% from the Bethel Wade-Hampton area), it is likely that existing significant associations between loci would have been detected.

Future plans include the expansion of current databases with more loci and larger sample size. As we increase the population sample any departures due to sample size should diminish. We are currently participating in the validation of subtyping at the HLA DQA1 4 allele. The predominance of the 4 allele in Native Alaskan populations holds promise for variability at the subtype level. Once validation is complete we will determine population frequencies of the known subtypes. In addition we hope to examine other Alaskan Native populations statewide.

The Native Alaskan population databases are statistically more similar to each other than they are to other published population data bases. However, these Native Alaskan populations are more similar to other Native American groups (29) than they are to Caucasians and African Americans. (Data not shown.)

In conclusion, two Alaskan Native population data bases have been established for seven PCR-based polymorphic loci. The distribution of the genotype frequencies for the various loci meet HWE and there is little evidence for departures from expectations of independence of alleles across loci. It is important to demonstrate polymorphism in isolated Native Alaskan populations at forensically relevant loci. Small isolated populations may be an area where the product rule might be least expected to hold, due to elevated inbreeding (32). It is noteworthy that these two populations appear to show no such effect. These results confirm that valid estimates of multiple locus profile frequencies can be derived from Native Alaskan databases using the product rule under the assumption of independence.

Acknowledgments

The authors gratefully acknowledge funding assistance provided by the Alaska Science and Technology Foundation. Perkin-Elmer

donated Amplitype PM kits used in this study. Dr. Bruce Budowle (FBI) Jill Smerick, and Barbara Koons generously provided training and guidance.

The authors would also like to thank the anonymous reviewers for their suggestions, which improved the manuscript considerably.

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Address requests for reprints or additional information to
Mary Walkinshaw, Ph.D.
Alaska State Scientific Crime Detection Lab
5500 E. Tudor Rd.
Anchorage, AK 99507