Am. J. Hum. Genet. 56:1450–1455, 1995

Mitochondrial and Nuclear Genetic Contribution of Female Founders to a Contemporary Population in Northeast Quebec

Evelyne Heyer

Institut Interuniversitaire de Recherches sur les Populations, Université du Québec à Chicoutimi, Chicoutimi

Summary

A common challenge in population genetics is to reconstruct the evolutionary history of populations on the basis of current allele frequencies. Through pedigree analysis, we have the opportunity to study the genetic contribution of founders to the contemporary population. This contribution over many generations accounts for the probable introduction, survival, and extinction of genes in the population. I use this method to follow nuclear and mitochondrial genes in the Saguenay population of northeast Quebec by tracing back ascending genealogies of 160,315 individuals born between 1950 and 1971 by using the BALSAC database. This study leads us to conclude that even in a growing population, the loss rate of mtDNA is high. The survival of mtDNA in the population is independent of the time of introduction in the population. The number of copies of a particular mtDNA gene in the contemporary population is higher for genes introduced earlier, but the correlation between these two variables is low (the relation is not linear). Compared to nuclear contribution, mitochondrial contribution is higher, but the loss rate of nuclear DNA is lower. The differential contribution (the fact that few founders contribute a lot) is the same proportion for nuclear and mtDNA, but only 592 female founders contribute 50% of the mtDNA gene pool of the contemporary cohort, compared to 994 for nuclear DNA. Since we have no molecular data on founders' haplotypes, these results cannot give us the diversity level in the population. However, this study enables us to compare the evolutionary fates of nuclear and mitochondrial genes in this expanding population.

Introduction

A common challenge in population genetics is to reconstruct the evolutionary history of populations on the basis of current allele frequencies. Nuclear or mitochondrial DNA can be used for this purpose. Although molecular markers are mostly used to infer such long historical processes as the peopling of America, information on a small time scale can help us understand long-term changes of frequencies. Here, I shall compare the evolution of nuclear and mitochondrial DNA allele frequencies in a population through its 150 years of history. In particular, I will address the following questions: what is the mitochondrial genome contribution of founders to the contemporary population compared with their nuclear genome contribution? What is the loss rate of mtDNA and nuclear genes?

Where vital statistics are available, an effective means of investigating the process by which nuclear alleles are distributed within a population is to track the genetic contribution of each founder to descending gene pools (Roberts 1968; Roberts and Bear 1980; Cazes 1986). This contribution over many generations accounts for the probable introduction, survival, and extinction of nuclear genes in the population.

In contrast to the nuclear genome, the mitochondrial genome has a haploid behavior (Sartoris et al. 1988) and is inherited unchanged through maternal lineage (Giles et al. 1980), and no recombination events have been observed as yet. This makes the mitochondrial genome even easiest to follow: for a female founder, her mitochondrial contribution is simply equal to her number of descendants through the maternal lineage.

The Saguenay population in northern Quebec is well suited for this study due to the existence of a large computerized data bank. Interuniversity Institute for Population Research (IREP) started the collection of vital records in 1972, and family reconstruction is still going on today (Bouchard et al. 1990). These records come from Catholic parish registers of baptisms, marriages, and burials. To date, all Saguenay parish registers before 1971 have been collected and computerized, and the families have been reconstructed into a genealogically linked database. Altogether, this database includes around 500,000 individuals.

Elsewhere, working with this material, we have calculated for each founder the number of contemporary descendants and their expected nuclear genetic contribution. This analysis first described the amount of immi-

Received November 15, 1994; accepted for publication February 27, 1995.

Address for correspondence and reprints: Dr. Evelyne Heyer, Institut Interuniversitaire de Recherches sur les Populations, 555 Boulevard de l'Université, Quebec, Canada G7H 2B1.

0002-9297/95/5606-0024$02.00

gration through time and then the genetic contribution of founders to the contemporary population with regard to their period of entrance in the region. It also revealed that few founders made a large contribution to the actual population (Heyer, in press).

In the present study, I will follow the same methodology to evaluate the number of female founders who contributed to the contemporary mtDNA pool as well as the probability of a female founder having contributed, taking into account her year of entrance in the population. In order to compare nuclear versus mitochondrial contributions, I shall only focus on female founders. To evaluate their contribution to the actual population, I shall compare all their descendants to those from maternal lineage.

Historical Background

The French colonization of the province of Quebec began in 1608 and continued until English control began in 1760. Of the >30,000 colonists who came from France (Boleda 1984), only an estimated 8,000–10,000 established themselves permanently in the province (Charbonneau et al. 1987). This colonization can be referred to as the first founder effect (Bouchard et al. 1988).

These colonists settled along the St. Lawrence River banks, taking advantage of the rich soil of the valley. The valley is fairly narrow, however, and by the beginning of the 19th century it was quite densely occupied. By the mid-19th century, overpopulation stimulated migration out of the older established areas toward the United States and to more remote regions of Quebec, such as the Saguenay (Pouyez et al. 1983).

The population of the Saguenay was created through a combination of migration and rapid intrinsic growth. As early as 1870, the growth of the population was mostly intrinsic. But immigration still remained a strong process: 56% of all the married people who could be identified from the parish records before 1911 were born outside the Saguenay (Gauvreau et al. 1987). Despite the intense immigration, considerable emigration occurred as well, and since 1921 net quinquennial migration rates are negatives.

Methodology

We define the contemporary population as all individuals born in the Saguenay between 1950 and 1971. We traced back the ancestors of all individuals born in the Saguenay after 1950 and before 1971 (160,315 individuals). The maternal ancestors of 91.4% of these individuals entered the region before 1950.

The year of entrance of a female founder is defined by the first vital certificate in which she is recorded. Some of the founders, in fact, never lived in the region but are included because they are registered in the marriage record of a child. I have decided to include them as founders, rather than their children, in order to keep track of first-order relationships—in the case, for example, of sisters moving to Saguenay.

Through ascending pedigrees, I identified 9,944 female founders who settled before 1950. Since 20,755 female founders entered Saguenay before 1950, <50% of them have a descendant born in the area after 1950.

For each founder, we calculated the number of descendants born after 1950 and the genetic contribution of the founder to this cohort. The nuclear genetic contribution of each founder to each descendant in the contemporary cohort was estimated by using the method of Roberts (1968), which was also used by Roberts and Bear (1980) and later by O'Brien et al. (1988). The probability that an individual received a gene from a founder via a particular path is $(1/2)^i$, where i is the number of generations separating a founder from a descendant through a pedigree path. The total contribution of a founder to a descendant cohort is then given by summing over all pedigree paths p for all members of the descendant cohort k:

$$\sum_k \sum_p (1/2)^i .$$

This formula gives an expectation of the genetic contribution. Because of random genetic sampling and dependency among genealogical paths, there is a variance about this expectation. It also indicates the expected number of copies of a particular gene carried by a founder in the descendant cohort.

The mitochondrial contribution of a female founder is simply the number of descendants in the contemporary population who are reached through the female lineage. I use the term *mtDNA copies* to refer to the founder-specific mtDNA contribution to the contemporary population. If each female founder is taken to represent a mitochondrial lineage, her genetic contribution in the contemporary population is the frequency of this lineage in the contemporary population. We have no data on mtDNA haplotype differences among female founders, so we cannot infer directly what diversity level should be found in the contemporary population. Using nuclear and mitochondrial genetic contributions, we can compare the evolutionary fates of nuclear and mitochondrial genes in the population.

Results

Genes' Survival

Figure 1 shows the proportion of female founders who transmitted nuclear DNA and the proportion who transmitted mtDNA. On average, 47.9% (see table 1) of

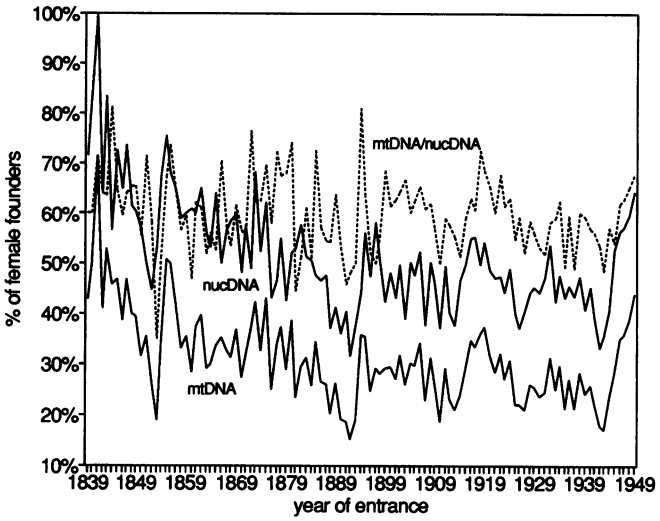

Figure 1 Percent of female founders transmitting mtDNA and nuclear DNA. Female founders who have transmitted at least one copy of their mtDNA are represented by the lower undotted curve. Female founders who have a nonzero probability of transmitting nuclear genes are represented by the higher undotted curve. The ratio between these two values is represented by the dotted curve.

female founders have descendants in the contemporary population and have transmitted nuclear genes to the contemporary population. However, only 28.5% of them have transmitted mtDNA. The dotted line shows the proportion of founders who have transmitted mtDNA among founders who transmit nucDNA. This proportion is on average 59.6%.

It is normally expected to find a smaller number of female founders who transmitted their mtDNA genes compared to the number of females transmitting nuclear DNA, because, by definition, an individual who transmits mtDNA also transmits nuclear DNA.

The extinction of mitochondrial genes in the population results from two facts: 52% of female founders have no descendants in the contemporary population, and among the remaining 48%, only 60% have transmitted genes through maternal lineage. Of course, nuclear genes transmission is only affected by the first phenomenon. But one should always keep in mind that the transmission of nuclear genes is calculated in terms of probability. So, the proportion of female founders who have transmitted nuclear genes is the proportion of female founders who have a nonzero probability of transmitting genes (a genetic contribution >0). But, in fact, for a specific gene, we can only calculate the expected number of copies in the contemporary population. This figure can be very low (0.001, for example)—and then the gene is transmitted—or being high (5.12, for example)—and then the gene is lost. On the other hand, the calculations on mtDNA are exact values. When it is estimated from pedigrees that a female has a mtDNA contribution of 10 in the contemporary population, this figure reflects precisely the reality (barring pedigree errors).

Table 1

Female Founders Who Entered Saguenay Before 1950, According to Their Transmission of Nuclear and Mitochondrial DNA to the Contemporary Population

Female Founders Who Entered Saguenay . . .	*n* (%)
Before 1950	20,755 (100)
Without any contemporary descendants	10,811 (52.1)
With contemporary descendants	9,944 (47.9)
Without any contemporary descendants through maternal lineage	4,022 (19.4)
With contemporary descendants through maternal lineage	5,922 (28.5)

NOTE.—The contemporary population is defined as all the individuals born in the Saguenay between 1950 and 1971.

mtDNA and Nuclear DNA Contribution

The mitochondrial contribution in the contemporary population is higher than the nuclear for most of the 5,922 founders who transmitted at least one mtDNA copy (see fig. 2). On average, the ratio of mtDNA copies to nuclear DNA copies is 2.891. The female founders transmitted on average 24.7 copies of mtDNA and 9.7 copies of nuclear DNA.

On the other hand, 4,022 female founders have descendants in the contemporary population but transmitted no mtDNA. These founders have an average genetic contribution of 3.6. We can point out, for example, the

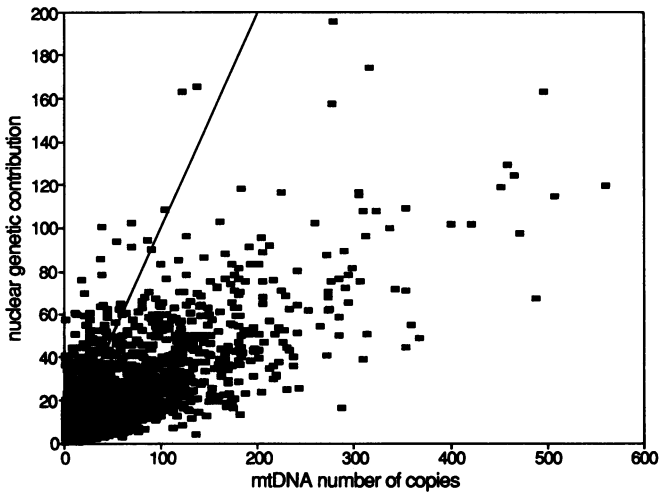

Figure 2 Nuclear genetic contribution and mitochondrial genetic contribution for female founders who transmitted at least one copy of mtDNA. The straight line shows the expected value for the same contribution for both genetic systems.

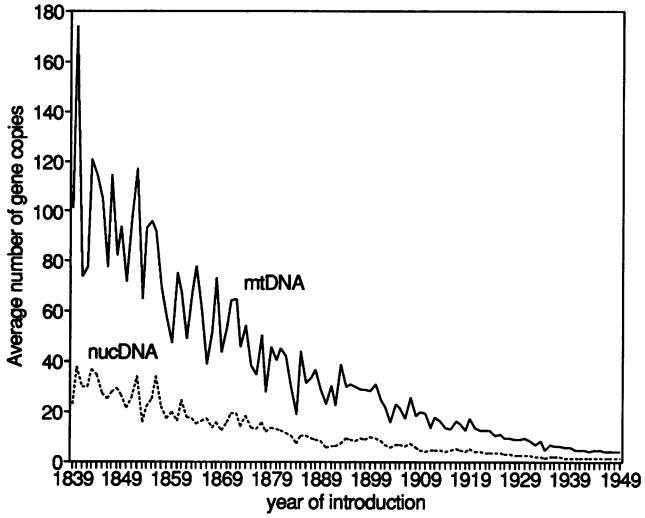

Figure 3 Average number of gene copies in the contemporary population, according to the year of introduction.

case of a female founder who had 3,407 descendants (a genetic contribution of 128.6) but transmitted no mtDNA.

Variability of Genetic Contribution

Eight-five percent of founders with descendants in the contemporary population (n = 9,944) have a genetic contribution of <13 nuclear DNA copies and <24 mtDNA copies. The highest value is 195 for nuclear DNA and 560 for mtDNA. The range of genetic contribution is larger for mtDNA than for nuclear DNA.

Another way of representing this variability is to look at the cumulative percentage of female founders in relation to their genetic contribution. The highest 10% of the 9,944 female founders accounts for 54% of the nuclear DNA contribution, and the highest 10% of the 5,922 female founders who have a mtDNA contribution accounts for 55% of the mitochondrial contribution. So, the fact that few female founders make a large genetic contribution to the contemporary gene pool follows the same pattern either for nuclear or mitochondrial DNA. But if we look at these values in absolute terms, the concentration is higher for mtDNA than for nuclear DNA: 592 female founders contribute >50% of the mitochondrial pool; for the nuclear pool, 994 founders are needed to reach the same percentage.

Genetic Contribution and Year of Entrance

As figure 3 shows, conditional to its survival, the frequency of a gene is higher when it has been introduced earlier in the population. This is true for both nuclear DNA and mtDNA, but the effect is greater for mtDNA. The advantage in terms of genetic contribution of first founders in comparison with the latest ones is explained by the fact that first founders have a higher number of descendants in the contemporary population. As I have explained elsewhere (author's unpublished data), the demographic advantage of first founders compensates for the lower nuclear genetic contribution of one of these founders to each of his contemporary descendants.

Table 2 presents the correlations between year of entrance, number of descendants, and genetic contribution. The nuclear genetic contribution is highly correlated with the number of descendants, but the mtDNA contribution is less correlated with this variable. Besides, there is a year-of-entrance effect: mtDNA contribution and nuclear DNA contribution are both negatively correlated with the year of entrance. This correlation is stronger for nuclear DNA contribution than for mtDNA contribution. The correlation is not very strong: r^2 = .348 for mtDNA contribution in table 2 part B, meaning that only 34.8% of the variance in mtDNA contribution is explained by the year of entrance. This is explained by the fact that the relation between these two variables is not clearly linear (see fig. 3).

Figure 4 shows that the year-of-entrance effect is almost the same for the two systems. The relative genetic contribution of first founders in comparison with the latest ones is equivalent for mtDNA and for nuclear DNA. Female founders who entered the population before 1870 account for 50% of the total genetic contribution either for mtDNA or nuclear DNA.

Discussion

mtDNA Genes' Survival

Avise et al. (1984) have calculated through simulation that during the population-expansion phase, most

Table 2

Correlation (r) between Year of Entrance, Number of Descendants, Nuclear Genetic Contribution, and Number of mtDNA Copies

	mtDNA	Nuclear DNA	Year	Descendants
A. For the 9,944 Female Founders Who Have Descendants in the Contemporary Population				
mtDNA	1	.76992	−.4480	.7252
Nuclear DNA	...	1	−.5834	.9295
Year	...	...	1	−.5772
Descendants	...	...	...	1
B. For the 5,922 Female Founders Who Have Transmitted at Least One Copy of mtDNA				
mtDNA	1	.8008	−.5906	.7764
Nuclear DNA	...	1	−.6523	.9300
Year	...	...	1	−.6251
Descendants	...	...	...	1

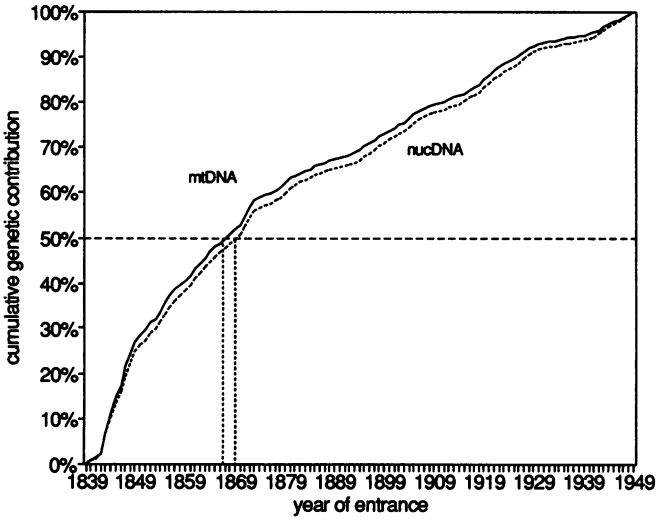

Figure 4 Cumulative genetic contributions of female founders, by year of entrance in the population.

mtDNA lineages survive. We have shown that even through a few (six to eight) generations, in a population in expansion, only 28.3% of the female founders have transmitted mtDNA to the contemporary population. If each founding female is taken to represent a mitochondrial lineage, the loss rate in this expanding population would be 71.7%.

The loss rate occured because 50% of the female founders had no contemporary descendants in the Saguenay. Even among founders who have descendants in the contemporary population, 40% have no descendant through maternal lineage. Avise et al. (1984) have also shown the negative effect of variance of family size on the survival of mtDNA genes. We therefore expected that this value would be high in the Saguenay population, which has been confirmed by a demographical analysis (Tremblay and Heyer 1993).

Avise et al. (1984) also concluded that low mtDNA-sequence diversity is not necessarily linked to a bottleneck effect. Since our findings show that the loss rate is important on a short time scale in an expanding population, we can expect on a larger time scale high loss rate without any bottleneck phenomenon.

Effect of Year of Entrance

The survival probability is not linked to the year of entrance. A gene introduced by earlier founders has almost the same survival probability as a gene introduced later. But, conditional to their survival, older genes will reach a higher frequency in the contemporary population. This result is in complete accordance with the results of Thompson et al. (1992). But the correlation calculated is not strong enough to conclude that the relation is linear.

Nuclear DNA versus mtDNA

The loss rate is higher for mtDNA than for nuclear DNA: only 60% of female founders who have transmitted nuclear DNA to the present population also transmitted mtDNA. This is explained by the fact that mtDNA is subject to sex-ratio fluctuation processes. On the other hand, conditional to their survival, mtDNA genes reach a higher frequency in the population. This result has some implications with respect to inherited disorders: if a disorder is associated with mtDNA mutation, it follows that it could reach a higher frequency in the population. Elsewhere, (author's unpublished data), I showed that the pedigree structure of the population allowed for an increase in nuclear gene frequency through its 150 years of history. This phenomenon is even stronger for mtDNA genes.

To infer the diversity level in the population (mtDNA haplotypes differences), we need molecular data on female founders. Since this population is Caucasian with a common European ancestry, sequencing of the D-loop would be required to show any difference among founders haplotypes.

Acknowledgments

I express my thanks to Marie-Christine Thibeault of Centre Hospitalier Universitaire Laval, to Marc Tremblay and Gérard Bouchard of IREP for their comments on the manuscript. I also thank two anonymous reviewers for their helpful comments and Arthur Connings for his help with English usage. This research was supported by Fonds pour la Formation de Chercheurs et l'Aide, Québec.

References

Avise JC, Neigel JE, Arnold J (1984) Demographic influences on mitochondrial DNA lineage survivorship in animal populations. J Mol Evol 20:99–105

Boleda M (1984) Les migrations au Canada sous le régime français (1608–1760) Cah Québécois Demogr 13:23–39

Bouchard G, Laberge C, Scriver CR (1988) Reproduction démographique et transmission génétique dans le nord-est de la province de Québec (18e–20e siècles). Eur J Popul 4:39–67

Bouchard G, Roy R, Casgrain B, Bourque M (1990) L'état civil saguenayen et la reconstitution automatique des familles à l'aide du système SOREP. In: Bouchard G, De Braekeleer M (eds) Histoire d'un Génome. Presses de l'Université du Québec, Quebec, pp 21–46

Charbonneau H, Guillemette A, Légaré J, Desjardins B, Landry Y, Nault F (1987) Naissance d'une population. Les Presses de l'Université de Montréal, Montreal

Cazes MH (1986) Genetic origins of the Dogon population in the Arrondissement of Boni (Mali). Am J Hum Genet 39:96–111

Gauvreau D, Jetté R, Bourque M (1987) Migration in the

Saguenay Region: evidence from reconstituted families, 1838–1911. Historical Methods 20:143–154

Giles RE, Blanc H, Cann HM, Wallace DC (1980) Maternal inheritance of human mitochondrial DNA. Proc Natl Acad Sci USA 77:6715–6719

Heyer E. Genetic consequences of differential demographic behavior in the Saguenay Region, Québec. Am J Phys Anthropol (in press)

O'Brien E, Jorde LB, Ronnlof B, Fellman JO, Eriksson AW (1988) Founder effect and genetic disease in Sottunga, Finland. Am J Phys Anthropol 77:335–346

Pouyez C, Lavoie Y, Bouchard G, Roy R, Simard J-P, St-Hilaire M (1983) Les Saguenayens. Presses de l'Université du Québec, Sillery, Quebec

Roberts DF (1968) Genetic effects of population size reduction. Nature 220:1084–1088

Roberts DF, Bear JC (1980) Measures of genetic change in an evolving population. Hum Biol 52:773–786

Sartoris S, Varetto O, Migone N, Capello N, Piazza A, Ferrara GB, Cappellini R (1988) Mitochondrial DNA polymorphism in four Sardinian villages. Ann Hum Genet 52:327–340

Thompson EA, Neel JV, Smouse PE, Barrantes R (1992) Microevolution of the Chibcha-speaking peoples of lower Central America: rare genes in an Amerindian complex. Am J Hum Genet 51:609–626

Tremblay M, Heyer E (1993) Fécondité et reproduction des femmes nées entre 1860 et 1870 au Saguenay-Lac-Saint-Jean. Cah Québécois Demogr 22:263–283