Letters to the Editor

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Genetic Evidence for the Expansion of Arabian Tribes into the Southern Levant and North Africa

To the Editor:

In a recent publication, Bosch et al. (2001) reported on Y-chromosome variation in populations from northwestern (NW) Africa and the Iberian peninsula. They observed a high degree of genetic homogeneity among the NW African Y chromosomes of Moroccan Arabs, Moroccan Berbers, and Saharawis, leading the authors to hypothesize that "the Arabization and Islamization of NW Africa, starting during the 7th century AD, … [were] cultural phenomena without extensive genetic replacement" (p. 1023). H71 (Eu10) was found to be the second-most-frequent haplogroup in that area. Following the hypothesis of Semino et al. (2000), the authors suggested that this haplogroup had spread out from the Middle East with the Neolithic wave of advance. Our recent findings (Nebel et al. 2000, 2001), however, suggest that the majority of Eu10 chromosomes in NW Africa are due to recent gene flow caused by the migration of Arabian tribes in the first millennium of the Common Era (CE).

In the sample of NW Africans (Bosch et al. 2001), 16 (9.1%) of the 176 Y chromosomes studied were of Eu10 (H71 on a haplogroup 9 background). Of these 16 chromosomes, 14 formed a compact microsatellite network: 7 individuals shared a single haplotype, and the haplotypes of the other 7 were one or two mutational steps removed. This low diversity may be indicative of a recent founder effect. Where did these chromosomes come from?

The highest frequency of Eu10 (30%–62.5%) has been observed so far in various Moslem Arab populations in the Middle East (Semino et al. 2000; Nebel et al. 2001). The most frequent Eu10 microsatellite haplotype in NW Africans is identical to a modal haplotype (DYS19-14, DYS388-17, DYS390-23, DYS391-11, DYS392-11, DYS393-12) of Moslem Arabs who live in a small area in the north of Israel, the Galilee (Nebel et al. 2000). This haplotype, which is present in the Galilee at 18.5%, was termed the modal haplotype of the Galilee (MH Galilee) (Nebel et al. 2000). Notably, it is absent from two distinct non-Arab Middle Eastern populations, Jews and Muslim Kurds, both of whom have significant Eu10 frequencies—18% and 12%, respectively (Nebel et al. 2001). Interestingly, this modal haplotype is also the most frequent haplotype (11 [~41%] of 27 individuals) in the population from the town of Sena, in Yemen (Thomas et al. 2000). Its single-step neighbor is the most common haplotype of the Yemeni Hadramaut sample (5 [~10%] of 49 chromosomes; Thomas et al. 2000). The presence of this particular modal haplotype at a significant frequency in three separate geographic locales (NW Africa, the Southern Levant, and Yemen) makes independent genetic-drift events unlikely.

It should be noted that the Yemeni samples (Thomas et al. 2000) were not typed for the binary markers (p12f2 and M172) that define Eu10. However, both Yemeni modal haplotypes are present on a haplogroup background compatible with Eu10. These haplotypes carry a DYS388 allele with a high number of repeats (i.e., 17). High repeat numbers of DYS388, $\geqslant$15, were found to occur almost exclusively on Hg9, which comprises Eu9 and Eu10. Furthermore, in a sample of a six Middle Eastern populations, chromosomes with 17 repeats are frequent (40%) in Eu10 and rare (7%) in Eu9 (Nebel et al. 2001).

The term "Arab," as well as the presence of Arabs in the Syrian desert and the Fertile Crescent, is first seen in the Assyrian sources from the 9th century BCE (Eph'al 1984). Originally referring to nomads of central and northern Arabia, the term "Arabs" later came to include the sedentary population of the south, which had its own language and culture. The term thus covers two different stocks that became linguistically and culturally unified yet retained consciousness of their discrete origins (Grohmann et al. 1960; Rentz 1960; Caskel 1966, pp. 19–47; Goldziher 1967, pp. 45–97, 164–190; Beeston 1995; also see Peters 1999). Migrations of southern Arabian tribes northwards have been recorded mainly since the 3d century CE. These tribes settled in various places in central and northern Arabia, as well as in the Fertile Crescent, including areas that are now part of Israel (Dussaud 1955; Ricci 1984). The emergence of Islam in the 7th century CE furthered the unification of the Arabian tribal populations. This unified Arab-Islamic community engaged in a large movement of expansion, the Fertile Crescent and Egypt being the first areas to have

been conquered. It is very difficult to trace the tribal composition of the Muslim armies, but it is known that tribes of Yemeni origin formed the bulk of those Muslim contingents that conquered Egypt in the middle of the 7th century CE. Egypt was the primary base for raids further west into the Maghrib. The conquest of North Africa was difficult and took a few decades to complete (Abun-Nasr 1987). The region was militarily and administratively attached to Egypt until the beginning of the 8th century CE. Arab tribes of northern origin entered North Africa as well, both as troops and as migrants. A major wave of migration of such tribes, the Banu Hilal and Banu Sulaym, occurred during the 11th century CE (Abun-Nasr 1987). Thus, the Arabs, both southern (Yemeni) and northern, added to the heterogeneous Maghribi ethnic melting pot.

Little is known of the origins of the indigenous population of the Maghrib, the Berbers, except that they have always been a composite people. After the 8th century CE, a process of Arabization affected the bulk of the Berbers, while the Arab-Islamic culture and population absorbed local elements as well. Under the unifying framework of Islam, on the one hand, and as a result of the Arab settlement, on the other, a fusion took place that resulted in a new ethnocultural entity all over the Maghrib. In addition, Berber tribes sometimes claimed Arab descent in order to enhance their prestige. For example, the Berber nomadic tribe of the western Sahara, the Lamtuna, claimed descent from one of the South Arabian eponyms, Himyar. One of the chiefs of this Berber tribe, Lamtuna, is sometimes referred to as Saharawi, meaning "one of the nomads" or "one who comes from the Sahara" (Ibn al-Athir 1898, p. 462; Ibn Khallikan 1972, pp. 113, 128–129; Lewicki 1986). In Arabic sources, however, the name Saharawi is seldom used and does not seem to refer to a specific genealogical group. In light of these historical data, it is not surprising to find, among the Berbers and contemporary Saharawis of northern Africa, Y chromosomes that may have been introduced by recurrent waves of invaders from the Arabian Peninsula.

These documented historical events, together with the finding of a particular Eu10 haplotype in Yemenis, Palestinians, and NW Africans, are suggestive of a recent common origin of these chromosomes. Remarkably, the only non-Arabs in whom this haplotype has been observed to date are the Berbers (Bosch et al. 2001). It appears that the Eu10 chromosome pool in NW Africa is derived not only from early Neolithic dispersions but also from recent expansions from the Arabian peninsula.

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Almut Nebel,[1,*] Ella Landau-Tasseron,[2] Dvora Filon,[1] Ariella Oppenheim,[1] and Marina Faerman[3]

[1]*Department of Hematology, The Hebrew University–Hadassah Medical School and Hadassah University Hospital,* [2]*The Institute for Asian and African Studies, The Hebrew University, and* [3]*Laboratory of Biological Anthropology and Ancient DNA, The Hebrew University–Hadassah School of Dental Medicine, Jerusalem*

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Address for correspondence and reprints: Dr. Marina Faerman, Laboratory of Biological Anthropology and Ancient DNA, Hebrew University–Hadassah School of Dental Medicine, Jerusalem 91120, Israel. E-mail: marinaf@pob.huji.ac.il

* Present affiliation: Division of Human Genetics, School of Pathology, National Health Laboratory Service (NHLS) and University of the Witwatersrand, Johannesburg, South Africa.

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SMN Dosage Analysis and Risk Assessment for Spinal Muscular Atrophy

To the Editor:

Feldkötter et al. (2002) recently reported a new method to determine, on the basis of real-time, quantitative PCR, copy numbers of *SMN1* (MIM 600354) and *SMN2* (MIM 601627). Their method allows a greater degree of automation and a faster turnaround time than do methods that have been described elsewhere (McAndrew et al. 1997; Chen et al. 1999; Wirth et al. 1999; Gérard et al. 2000; Scheffer et al. 2000; Ogino et al. 2001). Using their new method, they demonstrated that the copy number of *SMN2*—which is the centromeric homologue of *SMN1,* the disease gene for spinal muscular atrophy (SMA [MIM 253300 for type I; MIM 253550 for type II; and MIM 253400 for type III])—influences the severity of SMA in affected individuals with homozygous deletions of *SMN1*. They found that, the greater the copy number of *SMN2* was, the greater the likelihood was of a milder SMA type. Because this correlation is not absolute, they used Bayesian-type analyses to determine the posterior probabilities of developing each SMA type, with both a homozygous deletion of *SMN1* and a given copy number of *SMN2*. We discuss below several important ethical, prognostic, and technical issues raised in their article.

In table 6, Feldkötter et al. report "Probabilities That an Unaffected Who Has Been Tested after Birth and Has Been Found to Carry a Homozygous Absence of SMN1 Will Develop Type I, II, or III SMA, on the Basis of Number of SMN2 Copies." SMA is usually a childhood-onset disease, and testing of unaffected children is ethically problematic. We agree with the American Society of Human Genetics and the American College of Medical Genetics that "Timely medical benefit to the child should be the primary justification for genetic testing in children and adolescents" (American Society of Human Genetics Board of Directors and American College of Medical Genetics Board of Directors 1995, p. 1233). Since there are currently no effective treatments, presymptomatic or otherwise, for SMA, the timely medical benefit of the testing of unaffected children is unclear.

For the purpose of predicting SMA type from the *SMN2* copy number in unaffected children who lack *SMN1,* Feldkötter et al. perform Bayesian-type analyses by use of odds ratios, rather than conventional conditional probabilities. For the prior probabilities, they use the distribution of types of SMA among individuals affected with SMA: .51, for type I; .32, for type II; and .17, for type III. Even if one were to test unaffected children in this way, for this purpose, these prior probabilities would not be the correct ones to use for Bayesian or Bayesian-type analyses. If a child is asymptomatic at age 10 mo, for example, he or she is much less likely to have type I SMA than to have one of the other types (Zerres and Rudnik-Schöneborn 1995). One would have to incorporate the conditional probabilities of being asymptomatic at a particular age, for the hypothesis of each SMA type.

The data on *SMN2* copy number given by Feldkötter et al. could be used in prenatal testing, to predict SMA type. However, the prior probabilities that they use would be applicable only if the family history of SMA is of an unknown type. Although families with more than one type of SMA have been described—and are far from rare—knowing the type of SMA in an affected family member increases the prior probability of that type of SMA in a relative who is at risk of developing SMA. If the type of SMA in that affected family member is unknown, then the distribution of SMA types among all individuals with SMA would be relevant to the assignment of prior probabilities.

On the basis of all reported data, Feldkötter et al. state that, because two *SMN1* copies were found on 20/834 (2.4%) healthy chromosomes, "4.8% of normal individuals would be misinterpreted as noncarriers on the basis of the direct SMN1 test" (p. 365). Actually, these data imply that ~4.8% of noncarriers would have three copies of *SMN1* and that ~2.4% of carriers with an *SMN1* deletion on one chromosome 5 would have two *SMN1* copies on the other chromosome 5. We have referred to the latter as the "2 + 0" genotype (Chen et al. 1999). Taking into account the ~1.7% of carriers who