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SHORT REPORT

Y chromosome evidence for a founder effect in Ashkenazi Jews

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Recent genetic studies, based on Y chromosome polymorphic markers, showed that Ashkenazi Jews are more closely related to other Jewish and Middle Eastern groups than to their host populations in Europe. However, Ashkenazim have an elevated frequency of R-M17, the dominant Y chromosome haplogroup in Eastern Europeans, suggesting possible gene flow. In the present study of 495 Y chromosomes of Ashkenazim, 57 (11.5%) were found to belong to R-M17. Detailed analyses of haplotype structure, diversity and geographic distribution suggest a founder effect for this haplogroup, introduced at an early stage into the evolving Ashkenazi community in Europe. R-M17 chromosomes in Ashkenazim may represent vestiges of the mysterious Khazars.
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Introduction

Ashkenazi Jews, who have resided in various European countries during the Diaspora, traditionally trace their origin to the Jewish people that lived in the Holy Land before the Roman exile. However, some studies claimed that a substantial part of Ashkenazim were descendants of Eastern European non-Jews. In particular, according to Middle Age historians, the Khazars from a small kingdom near the Caspian Sea converted en masse to Judaism[1] and therefore might have contributed to the composition of the emerging Ashkenazi community. Yet, recent genetic studies, based on Y chromosome polymorphic markers, clearly showed that Ashkenazim are more closely related to other Jewish and Middle Eastern groups than to their host populations in Europe.[2–4] Those findings argue against large-scale male-mediated gene flow into the Ashkenazi community during the Diaspora. The male admixture proportion of Europeans in Ashkenazi Jews was estimated to be 0.5% per generation,[3] indicating that Ashkenazim remained, to a large extent, genetically isolated throughout their history.

Ashkenazim were found to have a significantly higher frequency of the R-M17 haplogroup compared with Sephardic and Kurdish Jews.[4,5] Interestingly, Behar *et al*[6] reported R-M17 to be the dominant haplogroup in Ashkenazi Levites (~52%), although rare in Ashkenazi Cohanim (1.3%) and Israelites (4%). R-M17, the most common haplogroup in Eastern Europe, was suggested to

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have originated and started to expand in the Ukraine, probably in a Paleolithic population after the Last Glacial Maximum about 13 000 years ago.[5,7]

Our present study demonstrates that R-M17 is a distinctive feature of the Ashkenazim in general and not only of Levites, as reported previously.[6] Furthermore, we provide evidence for a founder effect of this haplogroup in Ashkenazim, dated to the first millennium CE.

Subjects and methods

A total of 495 DNA samples, from different sources (Table 1), were collected from paternally unrelated male Ashkenazi Jews, irrespective of their religious status (Cohen, Levite, Israelite).

The typing of the Y chromosome biallelic marker M17 and the six microsatelllite loci (DYS19, DYS388, DYS390, DYS391, DYS392 and DYS393) was conducted following Thomas *et al*.[8] Statistical analyses were performed as previously described.[4] The study was approved by the ethics review committees of the respective institutions.

Results and discussion

In total, 495 DNA samples from different collections (Table 1) were screened for the Y chromosome polymorphism M17. The average frequency of the haplogroup R-M17 in Ashkenazi Jews (11.5%, 57 individuals) is significantly higher ($P<0.05$) than that in Sephardic Jews (3.9%), Kurdish Jews (4%) and Palestinian Arabs (1.4%). To date, comparable frequencies of R-M17 in other Middle Eastern populations have been reported in Moslem Kurds, Syrians and Lebanese (Table 2). However, the haplotype distribution within R-M17, available only for Moslem Kurds, is very different from that of Ashkenazim.[4] These data suggest that the increase in R-M17 in Ashkenazim occurred after they had gone into the Diaspora.

Table 1 Frequencies of haplogroup R-M17 in Ashkenazi Jews sampled from various DNA collections

		R-M17	
Collection	*Sample size*	*Number of chromosomes*	*Frequency (%)*
A	79	10	12.7
B	46	4	8.7
C	156	19	12.2
D	44	4	9.0
E	62	7	11.3
F	20	3	15.0
G	88	10	11.3
Total	495	57	11.5

Note: collection A – previous study[4]; B – Metabolic Disease Research Unit, Shaarei Zedek Medical Center, Jerusalem; C – Department of Endocrinology, Hadassah Medical Center, Jerusalem; D, E and F – Department of Hematology, Hadassah Medical Center, Jerusalem (studies of leukemias and lymphomas, thalassemias, blood clotting disorders); G –MRC/NHLS/Wits Human Genomic Diversity and Disease Research Unit, University of the Witwatersrand, Johannesburg.

Table 2 Haplogroup R-M17 frequencies in Middle Eastern and European populations

Population	*Number of chromosomes*	*R-M17 frequency (%)*	*Reference*
Jews			
Ashkenazi Jews	495	11.5	This study
Ashkenazi Jews	82	9.7	5
Sephardic Jews	78	3.9	4
Sephardic Jews	85	3.5	5
Kurdish Jews	99	4.0	4
Middle Easterners			
Moslem Kurds	95	11.6	4
Palestinians	143	1.4	4
Lebanese	31	10.0	7
Syrians	20	9.7	7
Europeans			
North Caucasians[a]	140	2.9	**21**
Russians	49	43.0	22
Ukrainians	82	50.0	5
Byelorussians	306	51.0	6
Poles	97	59.7	5
Hungarians	49	59.1	5
Czech and Slovaks	88	32.9	5
Lithuanians	37	35.1	13
Germans	88	12.5	6
Dutch	27	3.7	7
French	23	0	7

[a]Pooled sample comprising five North Caucasian populations.

Variation within R-M17 was examined by analysing 56 of the 57 chromosomes for six microsatellite loci. Apart from one singleton (haplotype H9), the other 13 haplotypes form a compact network (Figure 1). The star-like pattern and the low level of diversity are indicative of a founder effect. The most common R-M17 haplotype in the total Ashkenazi sample (~45%), haplotype 6 (H6), is most likely the ancestral haplotype of this haplogroup among Ashkenazim. The time to the most recent common ancestor of R-M17 in Ashkenazim[9] was estimated to 62.7 generations ago (excluding H9), using the previously published mutation rate for the six microsatellite loci studied here ($\mu = 1.8 \times 10^{-3}$ with 95% CI 9.8×10^{-4}–3.1×10^{-3}).[10] Assuming a generation time of 25 years, this amounts to 1567 years ago (95% CI 2877–910 years ago).

If R-M17 had been present in substantial frequency in the pre-Diaspora Y chromosome pool, one would expect to observe the ancestral haplotype H6 in other Jewish groups and in Palestinians who share a large portion of their Y chromosomes with Jews.[3,4,11] However, in a combined non-Ashkenazi sample of 320 individuals (Sephardic, Kurdish Jews and Palestinians),[4] H6 was found only in a single Sephardic Jew (0.3%; Figure 1). This finding strongly

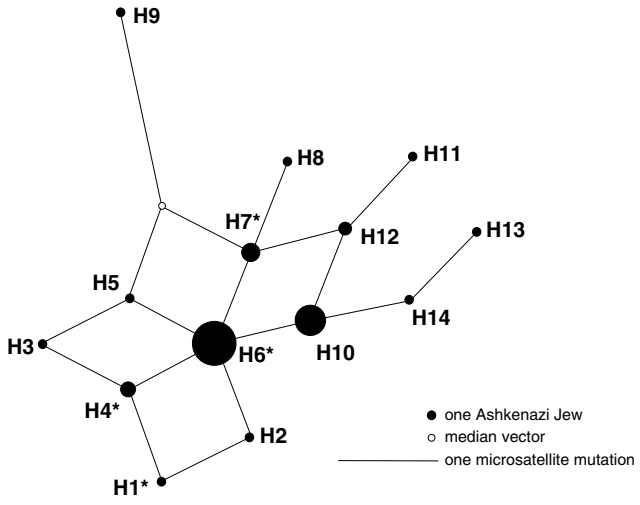

Figure 1 MJ network of haplogroup R-M17 in Ashkenazim. The network shows the relationships of the 14 haplotypes (56 individuals) found in Ashkenazi Jews. Haplotypes were constructed on the basis of six microsatellite loci (DYS19, DYS388, DYS390, DYS391, DYS392 and DYS393). The MJ ($\varepsilon = 0$) was calculated on the data preprocessed by the RM algorithm ($r = 2$). Circle size is proportional to haplotype frequency. Haplotype numbers refer to the supplementary information. At the centre of the network is H6 (16-12-25-10-11-13), the likely founding haplotype of this haplogroup in Ashkenazim. Those haplotypes marked with an asterisk were also observed in other Jewish groups and Moslem Palestinians[4] (H6 and H7 – one Sephardic Jew each; H4 – one Moslem Palestinian; H1 – two Kurdish Jews and one Sephardic Jew).

suggests gene flow from an external population into the Ashkenazi gene pool.

Where did the R-M17 chromosomes in Ashkenazim come from? The haplogroup R-M17 has a wide geographic distribution in Europe, West Asia and the Middle East, with the highest frequencies in Eastern European populations (Table 2). Haplotype H6 is also present at considerable frequencies in various Eastern European populations,[5,12,13] but is absent or found only at very low frequencies in Central and West Asians and in Middle Easterners.[14,15] Thus, R-M17 in Ashkenazi Jews could represent gene flow from Eastern European populations. This scenario is supported by the lower haplotype diversity measures (h) in Ashkenazim (0.735 ± 0.05) compared to those of Eastern European populations[5] (ranging from 0.894 ± 0.022 to 0.919 ± 0.026), and by the fact that in a combined Ashkenazi–European network, Jews present only a subset of the haplotypes (not shown).

The widespread distribution of R-M17 in Europe might suggest multiple gene flow events from the European host populations into Ashkenazim. However, we observed that the frequencies of R-M17 in Jews from various countries (Germany, Lithuania, Czechoslovakia, Hungary, Romania, Poland, Russia and the Ukraine) ranged from 12–13% in Russia and Ukraine to 22% in Germany and Lithuania, and did not differ from one another ($P > 0.05$). Likewise, the haplotypes of Jews from these countries showed very similar distribution patterns in a network (not shown). Furthermore, the frequencies of R-M17 in different Ashkenazi communities did not correspond to the east–west cline seen in Europeans. Altogether, these results support the hypothesis of a single male founder who introduced R-M17 into the Ashkenazi gene pool at the beginning of the Jewish Diaspora in Europe. Since then this haplogroup has expanded and spread among the Jewish communities across Europe.

Noteworthy, Behar *et al*,[6] in their sample of Ashkenazi Levites, found R-M17 at a frequency of 52% and its modal haplotype (identical to H6 in the present study) at 74% within this haplogroup. They suggested a founder event specific to this particular group as a result of intrusion of one or a few European Y chromosomes into the forming Ashkenazi community. The present study does not necessarily contradict that of Behar *et al*,[6] but rather indicates that R-M17 is characteristic of the general Ashkenazi population and not restricted to the Levites. The proportion of Levites in different Jewish populations has been estimated to range from 0.25[16] to 3.4%.[17] Thus, their contribution to the overall frequency of R-M17 in Ashkenazim could not exceed 2%, while the frequency observed in the present study is 11.5%. Similar frequency (9.7%) was also reported by Passarino *et al*.[5] Furthermore, the haplotype diversity in the Ashkenazi Levites (0.451)[6] is lower than in the sample of Ashkenazi Jews described here, suggesting that R-M17 drifted to high frequency in the Levites more recently than in the general Ashkenazi population.

It is historically well documented that the Khazar King Bulan and his court converted to Judaism at the end of the 8th century CE.[1] The Khazars were originally a Turkic tribe from Central Asia who settled in the northern Caucasus and later spread to southern Russia and eastern Ukraine. Some authors argue that after the fall of their kingdom in the second half of the 10th century CE, the Khazar converts were absorbed by the emerging Ashkenazi Jewish community in Eastern Europe.[18,19] Since R-M17 haplogroup is also found at moderate to high frequencies in Central Asia[20] and southern Russia/Ukraine,[5] this haplogroup could have been present in the Khazars. However, if the R-M17 chromosomes in Ashkenazi Jews do indeed represent the vestiges of the mysterious Khazars then, according to our data, this contribution was limited to either a single founder or a few closely related men, and does not exceed $\sim$12% of the present-day Ashkenazim.

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Supplementary Information accompanies the paper on European Journal of Human Genetics website (http://www.nature.com/ejhg)