OPEN

SUBJECT AREAS:

BIOLOGICAL
ANTHROPOLOGY
MOLECULAR EVOLUTION

Received
30 October 2014

Accepted
14 January 2015

Published
11 February 2015

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A genetic contribution from the Far East into Ashkenazi Jews via the ancient Silk Road

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Contemporary Jews retain a genetic imprint from their Near Eastern ancestry, but obtained substantial genetic components from their neighboring populations during their history. Whether they received any genetic contribution from the Far East remains unknown, but frequent communication with the Chinese has been observed since the Silk Road period. To address this issue, mitochondrial DNA (mtDNA) variation from 55,595 Eurasians are analyzed. The existence of some eastern Eurasian haplotypes in eastern Ashkenazi Jews supports an East Asian genetic contribution, likely from Chinese. Further evidence indicates that this connection can be attributed to a gene flow event that occurred less than 1.4 kilo-years ago (kya), which falls within the time frame of the Silk Road scenario and fits well with historical records and archaeological discoveries. This observed genetic contribution from Chinese to Ashkenazi Jews demonstrates that the historical exchange between Ashkenazim and the Far East was not confined to the cultural sphere but also extended to an exchange of genes.

Consistent with their displaced ethno-history since the ancient Northern Kingdom of Israel was invaded and occupied by the Neo-Assyrian Empire¹, contemporary Jews, including Ashkenazi Jews, Sephardic Jews, North African Jews and Middle Eastern Jews², retain a genetic imprint of their Near Eastern ancestry, but have received a substantial contribution, to a variable extent, from their neighboring populations such as Europeans, Near Easterners, and North Africans^{2–8}. However, it has hitherto remained unclear whether Jews received any genetic contribution from populations outside western Eurasia. Intriguingly, frequent communication has been observed between Jews and Chinese since the early centuries of the Common Era, plausibly initiated by the Silk Road. For instance, Hebrew letters and prayers in the 8th century from ancient Jewish merchants were found in the northwestern region of China⁹. Some unearthed pottery figurines from the Tang Dynasty (618–907AD) have Semitic characteristics⁹, and synagogues were recorded in the epigraphy from the Ming (1368–1644AD) and Qing Dynasties (1644–1912AD)^{9,10}. Nonetheless, such connections, as revealed by the archaeological discoveries and historical records, have been confined to economic and cultural exchanges; so far, no direct evidence of a genetic contribution from Chinese into Jews has been reported.

To address the issue of whether Jews received any genetic contribution from the Far East, and thus shed more light on their ethno-origins, mitochondrial DNA (mtDNA) variation (mainly from the control region of the molecule, plus some coding-region variants) of 1,930 Jews and 21,191 East Asians, retrieved from previous studies as well as our unpublished data, were considered and analyzed, with especial attention to pinpointing eastern Eurasian haplogroups in Jews (Supplementary Table S1). Then, mtDNA control region variants of an additional 32,474 Eurasian individuals were analyzed to gain further insights into the phylogeographic distribution of M33c (Supplementary Table S1), so that the total number of Eurasian mtDNAs considered here was 55,595. Our results do reveal a direct genetic connection, as manifested by the sharing of some Eastern Eurasian haplogroups e.g. N9a, A, and M33c, between Jews and Chinese. Further analyses, including phylogeny reconstruction with the aid of new mtDNA genomes, confirm that this connection was established at least by a founder lineage M33c2. The differentiation time of this lineage is estimated to ~1.4 kilo-years ago (kya), which fits well with the historical records and, most importantly, indicates that the exchange between Jews and the Far East was not confined to culture but also extended to the demic.

Table 1 | The shared eastern Eurasian haplotypes between Ashkenazi Jews and Chinese

Sample ID	Haplogroup	HVS-I (16000+)	HVS-II	Population	Region/Country	Reference
AS2C5	A	182C 183C 189 193.1C 223 290 319 362	73 150 152 204 235 263	Ashkenazi	Hungary	32
472	N9a	129 223 257A 261	73 146 150 263	Ashkenazi	Russia	7
75916	N9a	129 223 257A 261	73 146 150 263 309.1C 309.2C 315.1C	Ashkenazi	Belarus	Family Tree DNA
110612	N9a	129 223 257A 261	73 146 150 263 309.1C 309.2C 315.1C	Ashkenazi	Belarus	Family Tree DNA
Bel 1 ^a	M33c	111 223 235 362 (519)	73 263 315.1C (489)	Ashkenazi	Belarus	This study
EU148486 ^a	M33c	111 223 235 362 (519)	73 263 315.1C (489)	Ashkenazi	Belarus	Family Tree DNA
4130 ^b	M33c	111 223 235 362 (519)	73 263 315.1C (489)	Ashkenazi	Belarus	Family Tree DNA
135479 ^b	M33c	111 223 235 362 (519)	73 263 315.1C (489)	Ashkenazi	Belarus	Family Tree DNA
266609 ^b	M33c	111 223 235 362 (519)	73 263 315.1C (489)	Ashkenazi	Western Ukraine	Family Tree DNA
N50366 ^b	M33c	111 223 235 362 (519)	73 263 315.1C (489)	Ashkenazi	Western Ukraine	Family Tree DNA
N105293 ^b	M33c	111 223 235 362 (519)	73 263 315.1C (489)	Ashkenazi	Western Ukraine	Family Tree DNA
50126 ^b	M33c	111 223 235 362 (519)	73 263 315.1C (489)	Ashkenazi	Russia	Family Tree DNA
289247	M33c	111 223 235 362 (519)	73 263 315.1C (489)	Ashkenazi	Russia	Family Tree DNA
403	M33c	111 223 235 362 (519)	73 263	Ashkenazi	Western Ukraine	Family Tree DNA
404	M33c	111 223 235 362 (519)	73 263	Ashkenazi	Belarus	7
405	M33c	111 223 235 362 (519)	73 263	Ashkenazi	Poland	7
406	M33c	111 223 235 362 (519)	73 263	Ashkenazi	Poland	7
Forum 1 ^{a,c}	M33c	111 223 235 362 (519)	73 263	Ashkenazi	Romania	7
			73 263 315.1C (489)	Jew	Belarus/Russia/Lithuania	A Genetic Genealogy Community
JQ702003 ^a	M33c	111 223 235 362 (519)	73 263 315.1C (489)	N.A.	N.A.	14
HN-SZ420 ^a	M33c	111 192 223 362 (519)	73 263 315.1C (489)	Han	Hunan, China	33, This study
HN-SZ167 ^a	M33c	111 223 235 356 362 (519)	73 263 309.1C 315.1C (489)	Han	Hunan, China	33, This study
HN-SZ104 ^a	M33c	111 223 235 362 (519)	73 263 308-310d 315.1C (489)	Han	Hunan, China	33, This study
HN-SZ527 ^a	M33c	111 223 235 362 (519)	73 263 309.1C 315.1C (489)	Han	Hunan, China	33, This study
JSH08058	M33c	111 129 223 235 284 300 362 (519)	73 150 263 315.1C	Han	Jiangsu, China	This study
K9534 ^a	M33c	111 129 140 223 235 300 362 (519)	73 150 263 309.1C 315.1C (489)	Han	Jilin, China	This study
K9511 ^a	M33c	111 192 223 235 362 (519)	73 263 315.1C 471 (489)	Han	Jilin, China	This study
H11694 ^a	M33c	104 111 223 362 (519)	73 263	Han	Shaanxi, China	This study
H11281 ^a	M33c	111 223 235 362 (519)	73 263 309.1C 315.1C	Han	Shaanxi, China	This study
DJY76 ^a	M33c	111 223 235 243 362 (519)	73 263 309.1C 315.1C	Han	Sichuan, China	This study
Zhuang21 ^a	M33c	093 104 111 223 235 362 (519)	73 263 309.1C 315.1C (489)	Zhuang	Guangxi, China	This study
Zhuang74	M33c	093 104 111 223 235 362 (519)	73 263 309.1C 315.1C (489)	Zhuang	Guangxi, China	This study
Zhuang9	M33c	093 104 111 223 235 362 (519)	73 263 315.1C (489)	Zhuang	Guangxi, China	This study
HN-SZ416	M33c	093 104 111 223 362 (519)	73 263 309.1C 315.1C (489)	Han	Hunan, China	33
Dongguan-65	M33c	093 104 111 223 235 311 362	73 263 210 309.1C 310 315.1C	Han	Guangdong, China	34
539	M33c	093 104 111 223 235 362		Han	Guangxi, China	35
129	M33c	093 104 111 223 235 362		Han	Guangxi, China	35
136	M33c	093 104 111 223 235 362		Han	Guangxi, China	35
499	M33c	093 104 111 223 235 362		Han	Guangxi, China	35
370	M33c	104 111 223 235 362		Han	Guangxi, China	35
149	M33c	111 223 235 362		Han	Guangxi, China	35
Viet0121	M33c	111 223 362 (519)	73 203 263 309.1C 309.2C 315.1C (489)	Vietnamese	Vietnam	36
GD7815 ^a	M33c	093 104 111 223 362	73 146 263 309.1C 315.1C	Han	Guangdong, China	13
Yao171 ^a	M33c	111 129 223 235 362 (519)	73 263 309.1C 309.2C 315.1C	Yao	Hunan, China	13
MK13	M33c	111 129 223 235 300 362		Kam-Tai	Guizhou, China	37
Kinh117	M33c	111 223 362 (519)		Kinh	Vietnam	38
(03B)045	M33c	093 104 111 223 235 362 (519)	73 263 309.1C 315.1C	Han	Guangdong, China	39
YZ-Tib05-23	M33c	092 104 111 223 362		Tibetan	Yunnan, China	40
YZ-Tib05-8	M33c	092 104 111 223 362		Tibetan	Yunnan, China	40

Table 1 | Continued

Sample ID	Haplogroup	HVS-I (16000+)	HVS-II	Population	Region/Country	Reference
MHN43	M33c	111 223 235 362		Miao	Hunan, China	41
YBP28	M33c	093 104 111 223 235 362		Yao	Guangdong, China	41
YLO22	M33c	093 104 111 223 235 305C 362		Yao	Guangxi, China	41
YLO03	M33c	111 223 235 362		Yao	Guangxi, China	41
YLO23	M33c	111 223 235 362		Yao	Guangxi, China	41
GD7821	M33c	093 104 111 223 235 362	73 263 309.1C 315.1C	Han	Guangdong, China	42
HG00457 ^a	M33c	111 223 362 (519)		Han	Hunan/Fujian, China	15
TL397	M33c	093 101 111 223 235 362 (519)		Thai	Thailand	43

^aThe whole-mtDNA genome information is displayed on the phylogenetic tree (Figure 2).

^bThe individual has coding region information confirming its haplogroup assignment from the Family Tree DNA (www.familytreedna.com).

^cThis sequence is from A Genetic Genealogy Community (http://eng.molgen.org/viewtopic.php?t=41&t=141).

N.A. = not available.

All the samples in this study have confirmed G2361A mutation when assigning their haplogroup. The mutations (e.g. 489 and 16519) outside HVS-I and HVS-II are listed in the parentheses. The haplogroups A and N9a mtDNAs in the Far East are not shown here.

Results and Discussion

Our analysis of the mtDNA variation in a total of 23,121 individuals from East Asian populations and Jews reveals that mtDNAs of four Ashkenazi Jewish individuals can be allocated into eastern Eurasian haplogroups A and N9a, suggesting that Ashkenazi Jews received a genetic contribution from East Asia (Table 1). Intriguingly, our results also disclose that 14 eastern Ashkenazi Jews belong to haplogroup M33c (Table 1), for which sister clusters, M33a, M33b and M33d, are prevalent in the Indian Subcontinent and thus most plausibly trace their origins there^{11,12}.

To achieve further insight into the phylogeographic distribution of M33c, mtDNA variants (mainly from the control region) of an additional 32,474 Eurasian individuals were analyzed, so that the total number of Eurasian mtDNAs considered here was 55,595. As shown in Table 1, besides the 14 Ashkenazi Jewish M33c lineages, an additional 38 M33c mtDNAs (with the specific control-region motif showing transitions at positions 16111, 16223, 16235, and 16362) were pinpointed, among which 34 are from China, 2 from Vietnam, and 1 from Thailand, with the remaining individual most likely from Europe but with ambiguous ancestry. Thus, despite the restricted distribution of M33a, M33b and M33d in South Asia, it is most likely that M33c originated, or at least differentiated, in eastern Asia. This notion receives clear support from the median network, in which virtually all of the diversity of this haplogroup is observed in China (Figure 1).

To shed light on the phylogeny within haplogroup M33c, 11 mtDNAs, covering the widest range of internal variation within the haplogroup, were chosen for whole-mtDNA genome sequencing. In good agreement with the previous result¹³, the resulting phylogenetic tree (Figure 2), incorporating five previously reported mtDNA genomes^{13–15} as well as one whose information was released online (A Genetic Genealogy Community; <http://eng.molgen.org>), confirms that M33c is defined by mutations at positions 3316, 4079, 5894, 8227, 8848, 16111, and 16235. Of note is that five clades within M33c appear respectively characterized by diagnostic coding-region variant(s), and these are named M33c1 to M33c5 here. With the exception of M33c2, all the samples in these clades are from China. The likely origin of M33 in South Asia and the restriction to China of M33c, dating to 10 kya according to the estimation based on whole-mtDNA genome, implies some dispersal from South to East Asia in the immediate postglacial.

Intriguingly, sub-haplogroup M33c2 (defined by three additional coding-region variants at positions 4182, 4577, and 7364) consists of three different haplotypes (one seen in three Ashkenazi Jews, another in a single Chinese individual and the third in the likely European with unknown ethnicity). Although there is no control-region variant in the defining motif of M33c2, multiple lines of evidence suggest that the pinpointed 14 Ashkenazi Jewish M33c mtDNAs most likely all belong to this clade: (1) all of the 14 mtDNAs share an identical control-region motif (Table 1); (2) the three completely sequenced Ashkenazi Jewish mtDNAs with this motif (EU148486, Bel 1 and Forum 1) belong to M33c2 (Figure 2); (3) M33c shows a virtually exclusive distribution in Ashkenazi Jews in western Eurasia, even though 55,595 mtDNAs have been checked (Table 1 and Supplementary Table S1). Thus, it is plausible that the unknown European individual (JQ702003) was in fact from a Jewish population or had Ashkenazi Jewish ancestry.

Age estimates for M33c2 are similar whether based either on the whole genome or on the control region alone (Table 2), and the age of ~1.4 kya fits well with the medieval operation of the Silk Road. We note that this is an upper bound for the gene flow event during which the lineage was assimilated into the Ashkenazim; it is the age of the subclade overall, which most likely arose within China, and indeed there is no variation at all within the Jewish lineages, suggesting a very recent event. If we assume that the unidentified European lineage belongs within the Ashkenazi diversity, we can date the

Ashkenazi origins are controversial¹⁸. According to recent archaeological evidence, the Jewish community of Cologne, mentioned by Emperor Constantine in 321AD, existed in the city continuously until they had to leave in 1423–1424AD¹⁹. This suggests that Ashkenazi Jewry may date to Roman times, possibly originating in

Extensive genetic admixture has been observed in populations residing around the ancient Silk Road region^{23,24}. Our currently observed genetic imprint echoes the previously observed ancient communications between Jews and Chinese and, most significantly, implies that such historical exchanges were not confined to the cultural realm but involved gene flow. This unexpected ancient genetic connection between Ashkenazi Jews and the Far East, as witnessed a

Figure 2 | Phylogenetic tree of haplogroup M33c. The nucleotide positions in the sequences are scored relative to the rCRS²⁷. Transversions are annotated by adding suffixes “A” and “T”. The recurrent variants are underlined and prefix @ designates a back mutational event; “s” means synonymous and “ns” means nonsynonymous mutation; “nc” refers to mutations at the intergenic noncoding regions in segments 577–16023; and “r” and “t” denote mutations in rRNA genes and tRNA genes, respectively. Length polymorphisms (e.g., 309.1C, 309.2C and 315.1C) are disregarded from the analysis. The newly sequenced samples in this study are marked in rectangles, while mtDNAs from the published literature are displayed in ellipses. Note: * This individual is from A Genetic Genealogy Community (<http://eng.molgen.org/viewtopic.php?f=41&t=141>).

least by mtDNA haplogroup M33c2, provides the first evidence for a significant genetic contribution from Chinese to eastern European Ashkenazi Jews that was most likely mediated by the Silk Road between around 640 and 1400 years ago. Although the involvement of male Jewish traders has been suggested before¹⁷, our results, focusing on the female line of descent, specifically point to the involvement also of women. Well-resolved evidence from the male-specific part of the Y chromosome and from the autosomes would help to further illustrate the rather complex, pan-Eurasian ethno-history of Jews.

Methods

mtDNA Data collection and mining. mtDNA variation (mainly from control region) of 23,121 East Asians and Jews, retrieved from previous studies as well as our unpublished data, were considered and analyzed, with especial attention to pinpointing the eastern Eurasian haplogroups in Jews. Then, additional 32,474 individuals were analyzed to gain further insights into the phylogeographic

distribution of M33c, leading the total number of Eurasian mtDNAs considered here to 55,595. The study project was approved by the Ethics Committee at Kunming Institute of Zoology, Chinese Academy of Sciences. Each participant was informed about the study and provided informed consent. All mtDNAs collected and considered in the present study were first allocated to haplogroups, based mainly on their control-region motifs, which were then further confirmed by typing specific coding-region variation according to the PhyloTree (mtDNA tree Build 16²⁵; <http://www.phylotree.org/>).

DNA amplification and sequencing. For haplogroups of interest, special attention was paid to the intrinsic phylogeny reconstructed on entire mitogenome information. In this way, entire mitogenomes for 11 selected representatives from haplogroup M33c were amplified, sequenced, and dealt with as described elsewhere^{13,26}. The sequencing outputs were edited and aligned by Lasergene (DNASTar Inc., Madison, Wisconsin, USA) and compared with the revised Cambridge Reference Sequence (rCRS)²⁷.

Data analysis. The median-joining network of M33c was constructed manually²⁸ and then confirmed using Network 4.612 (<http://www.fluxus-engineering.com/sharenet>).

Table 2 | Ages of the major clades of haplogroup M33c estimated from control-region and whole-mtDNA genome data with 95% confidence intervals

Haplogroup	Control region			Whole-mtDNA genome			
	Rho			Rho			Maximum Likelihood
	<i>n</i>	$\rho \pm \sigma$	Age (kya)	<i>n</i>	$\rho \pm \sigma$	Age (kya)	Age (kya)
M33c	52	1.13 ± 0.47	21.38 [4.1;38.7]	17	3.88 ± 0.76	10.29 [6.2;14.4]	8.95 [5.2;12.8]
M33c2	16	0.06 ± 0.06	1.18 [0;3.5]	5	0.60 ± 0.35	1.55 [0;3.3]	1.55 [0;3.3]
M33c2*	—	—	—	4	0.25 ± 0.25	0.64 [0;1.9]	0.64 [0;1.9]

M33c2*: the Chinese individual is not considered for the estimation.

htm). The most parsimonious phylogenetic tree (Figure 2) was reconstructed by hand as carried out previously^{13,26}. The coalescence ages were estimated by the $p \pm \sigma$ method^{29,30} and maximum likelihood (ML) analysis. Recently corrected calibrated mutation rates³¹ were adopted in the p statistic and the ML analysis.

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Acknowledgments

We thank Dr. Pedro Soares for his help in time estimation. This work was supported by grants from the National Natural Science Foundation of China (81272309, 31123005, 31322029) and the Chinese Academy of Sciences.

Author contributions

Q.-P.K. designed the research; Y.-C.L., W.Z. and Y.-G.Y. collected the samples; J.-Y.T., H.-W.W. and Y.-C.L. collected the data; J.-Y.T. and H.-W.W. performed the experiments; J.-Y.T., H.-W.W., Y.-C.L. and Q.-P.K. analyzed data; J.-Y.T., Y.-C.L., J.v.S., M.B.R. and Q.-P.K. wrote the paper.

Additional information

Accession codes All of the sequences obtained in this study have been deposited into GenBank, with accession codes KP313552–KP313562 (for whole mtDNA genomes) and KP313549–KP313551 (for control region sequences).

Supplementary information accompanies this paper at <http://www.nature.com/scientificreports>

Competing financial interests: The authors declare no competing financial interests.

How to cite this article: Tian, J.-Y. *et al.* A genetic contribution from the Far East into Ashkenazi Jews via the ancient Silk Road. *Sci. Rep.* **5**, 8377; DOI:10.1038/srep08377 (2015).

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