Data Article

Data on association of mitochondrial heteroplasmia with carotid intima-media thickness in subjects from Russian and Kazakh populations

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A B S T R A C T

The search for variants of mitochondrial genome associated with atherosclerosis, in particular, with carotid intima-media thickness (cIMT), is necessary to understand the role of the damage of mitochondrial genome in the development of atherosclerosis. Such data can be useful to provide novel genetic markers of predisposition to atherosclerosis and molecular targets for further development of technologies aimed to prevent age-related degenerative pathologies. Data presented in this article demonstrate the association of several heteroplasmic variants of mitochondrial DNA (mtDNA) previously described as proatherogenic ones with cIMT in 251 participants (190 participants from Novosibirsk, Russia, and 61 participant from Almaty, Kazakhstan). It was shown that the occurrence of some variants of mitochondrial genome is different
in samples derived from Russian and Kazakh populations; the level of mitochondrial heteroplasmy m.13513G > A correlates negatively with mean cIMT in both Russian and Kazakh participants.

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| List of abbreviations |
|-----------------------|
| CVD       cardiovascular disease |
| PCR       polymerase chain reaction |
| cIMT      carotid intima-media thickness |
| BMI       body mass index |
| SBP       systolic blood pressure |
| DBP       diastolic blood pressure |
| HDL       high-density lipoproteins |
| LDL       low-density lipoproteins |
| TG        triglycerides |

Specifications Table

| Subject                          | Cardiovascular diseases |
|---------------------------------|-------------------------|
| Specific subject area           | Genetic predisposition to carotid atherosclerosis |
| Type of data                    | Tables and figures |
| How data was acquired           | Pyrosequencing (PSQ HS96MA) |
|                                 | Ultrasound of carotid arteries (Sonoscape S6) |
| Data format                     | Raw and graphs |
| Parameters for data collection  | Blood samples and ultrasound images of carotid arteries from 190 subjects with subclinical atherosclerosis from Novosibirsk, Russia and 61 from Almaty, Kazakhstan were collected |
| Description of data collection | Mitochondrial heteroplasmy level m.13513G > A, m.3336T > C, m.12315G > A, m.5178C > A, m.14459G > A, m.14846G > A were determined, and their association with carotid intima-media thickness was analysed |
| Data source location            | Almaty, Kazakhstan |
|                                 | Novosibirsk, Russia |
| Data accessibility              | Raw data are provided with this article |

Value of the Data

- The presented data are useful since demonstrate the associations of mutations of mitochondrial genome and proatherosclerotic phenotype that can be shown in ethnically different populations, but may vary between populations.
- The data on association of mutations of mtDNA and carotid atherosclerosis are beneficial for scientists who investigate mitochondrial genetics of atherosclerosis in epidemiological trials at the population level.
- The data may contribute to the development of further research aimed to investigate the role of the damage of mitochondrial genome in the pathogenesis of atherosclerosis and provide novel genetic markers of predisposition to atherosclerosis and molecular targets for further development of technologies aimed to prevention of age-related degenerative pathologies.
- Associations of variants of mitochondrial heteroplasmy and carotid atherosclerosis can either be similar for different populations, or can have significant differences; therefore, it makes sense to carry out the search of the similar data in replication studies and verification studies in other populations, including ethnically different ones.
1. Data description

Table 1
Clinical and laboratory characteristic of subjects from Russian population.

|          | Women       | Men       | p   |
|----------|-------------|-----------|-----|
| Age, years | 57.8 (2.4)  | 58.9 (3.1) | 0.071 |
| BMI, kg/m² | 29.1 (4.9)  | 26.4 (4.5) | 0.004* |
| SBP, mm Hg | 125 (12)    | 128 (10)   | 0.221 |
| DBP, mm Hg | 81 (10)     | 83 (7)     | 0.371 |
| Total cholesterol, mg/dL | 234 (46) | 219 (38) | 0.081 |
| HDL, mg/dL | 49.5 (12.7) | 45.4 (8.5) | 0.088 |
| LDL, mg/dL | 163.8 (41.1) | 151.2 (34.1) | 0.117 |
| TG, mg/dL | 113.4 (68.1) | 101.1 (46.3) | 0.345 |
| Mean cIMT | 0.788 (0.109) | 0.760 (0.132) | 0.207 |

*, statistically significant difference at p < 0.05.

Table 2
Clinical and laboratory characteristic of subjects from Kazakh population.

|          | Women       | Men       | p   |
|----------|-------------|-----------|-----|
| Age, years | 57.1 (6.0)  | 56.9 (6.1) | 0.893 |
| BMI, kg/m² | 27.1 (3.1)  | 26.6 (2.6) | 0.553 |
| SBP, mm Hg | 120 (16)    | 127 (12)   | 0.068 |
| DBP, mm Hg | 77 (10)     | 83 (5)     | 0.015* |
| Total cholesterol, mg/dL | 207 (54) | 239 (37) | 0.016* |
| HDL, mg/dL | 45.0 (19.1) | 50.8 (16.2) | 0.244 |
| LDL, mg/dL | 142.9 (51.8) | 170.3 (40.1) | 0.036* |
| TG, mg/dL | 94.0 (48.2) | 87.5 (24.1) | 0.560 |
| Mean cIMT | 0.744 (0.107) | 0.795 (0.105) | 0.080 |

*, statistically significant difference at p < 0.05.

Table 3
Levels of mitochondrial heteroplasmy in subjects from Russian population.

|          | Women       | Men       | p   |
|----------|-------------|-----------|-----|
| m.13513G > A,% | 24.0 (12.3) | 20.8 (10.9) | 0.194 |
| m.3336T > C,% | 4.3 (11.2)  | 2.7 (2.2)  | 0.436 |
| m.12315G > A,% | 36.7 (24.8) | 31.6 (19.5) | 0.283 |
| m.5178C > A,% | 6.4 (15.3)  | 13.3 (25.3) | 0.045* |
| m.14459G > A,% | 3.4 (1.7)   | 4.7 (7.3)  | 0.045* |
| m.14846G > A,% | 16.6 (15.7) | 20.3 (25.8) | 0.303 |

*, statistically significant difference at p < 0.05.

Table 4
Levels of mitochondrial heteroplasmy in subjects from Kazakh population.

|          | Women       | Men       | P   |
|----------|-------------|-----------|-----|
| m.13513G > A,% | 12.9 (5.7)  | 10.6 (5.7) | 0.133 |
| m.3336T > C,% | 3.8 (5.0)   | 4.2 (5.5)  | 0.853 |
| m.12315G > A,% | 9.5 (10.3)  | 14.1 (10.4) | 0.234 |
| m.5178C > A,% | 21.2 (10.8) | 24.8 (3.6)  | 0.168 |
| m.14459G > A,% | 10.7 (13.0) | 7.9 (11.6)  | 0.401 |
| m.14846G > A,% | 22.1 (12.5) | 18.0 (9.4)  | 0.191 |
Table 3 demonstrates levels of mitochondrial heteroplasmy of subjects from Russian population indicating the differences between men and women.

Table 4 demonstrates levels of mitochondrial heteroplasmy of subjects from Kazakh population indicating the differences between men and women.

Table 5 presents clinical and laboratory characteristics (age, body mass index, arterial blood pressure, lipids profile, mean cIMT) of total groups of Russian and Kazakh subjects indicating statistical significance of the differences between populations.

Table 6 presents levels of mitochondrial heteroplasmy of total groups of Russian and Kazakh subjects indicating statistical significance of the differences between populations.

The analysis of samples derived from Russian (n = 190) and Kazakh (n = 61) populations demonstrates that levels of variants of heteroplasmy m.13513G > A and m.12315G > A mtDNA were significantly higher in Russian group, and heteroplasmy level of m.5178C > A and m.14459G > A was significantly higher in Kazakh group.

The association of analysed variants of mitochondrial heteroplasmy with mean carotid IMT of subjects from Russian and Kazakh populations in total groups and in men and women separately is presented in Table 7.

Pearson’s correlation analysis revealed significant association of mitochondrial heteroplasmy m.13513G > A with mean carotid IMT in both Russian and Kazakh groups. Upon subdivision of groups by sex, this correlation was significant only in women in both population-derived samples. In addition, negative correlation of m.5178C > A mitochondrial heteroplasmy with cIMT was found in male samples from Russian population, and positive correlation of m.12315G > A mitochondrial heteroplasmy was found in females from Kazakhstan. We have found no correlations of variants of mitochondrial heteroplasmy with traditional cardiovascular risk factors such as age, body mass index, blood pressure, blood cholesterol, triglycerides, high-density and low-density lipoprotein cholesterol in both groups.

Graphs of correlation of mitochondrial heteroplasmy m.13513G > A and mean carotid IMT in Kazakh and Russian population-derived samples are presented on Figs. 1 and 2, respectively.

Dataset is presented as supplementary material.

### Table 5
Comparison of clinical characteristics of Russian and Kazakh population-derived samples.

|                  | Russian, total | Kazakh, total | p  |
|------------------|----------------|---------------|----|
| Age, years       | 57.9 (2.6)     | 57.1 (6.0)    | 0.097 |
| BMI, kg/m²       | 28.7 (4.8)     | 26.9 (2.9)    | 0.008* |
| SBP, mm Hg       | 126 (12)       | 122 (15)      | 0.075 |
| DBP, mm Hg       | 81 (9)         | 79 (9)        | 0.118 |
| Total cholesterol, mg/dL | 232 (44)   | 218 (50)      | 0.040* |
| HDL, mg/dL       | 48.9 (12.2)    | 47.1 (18.5)   | 0.389 |
| LDL, mg/dL       | 161.8 (40.3)   | 152 (49.4)    | 0.152 |
| TG, mg/dL        | 111.4 (65.2)   | 91.7 (41.0)   | 0.027* |
| Mean cIMT        | 0.783 (0.113)  | 0.762 (0.108) | 0.219 |

*, statistically significant difference at p < 0.05.

### Table 6
Comparison of levels of mitochondrial heteroplasmy of Russian and Kazakh population-derived samples.

|                  | Russian, total | Kazakh, total | p      |
|------------------|----------------|---------------|--------|
| m.13513G > A,%   | 23.5 (12.1)    | 12.1 (5.8)    | <0.001*|
| m.3336T > C,%    | 4.0 (10.3)     | 3.9 (5.1)     | 0.943  |
| m.12315G > A,%   | 35.9 (24.1)    | 10.8 (10.4)   | <0.001*|
| m.5178C > A,%    | 7.5 (17.4)     | 22.4 (9.2)    | <0.001*|
| m.14459G > A,%   | 3.6 (3.3)      | 9.7 (12.5)    | <0.001*|
| m.14846G > A,%   | 17.2 (17.8)    | 20.6 (11.5)   | 0.175  |

*, statistically significant difference at p < 0.05.
2. Experimental design, materials and methods

The association of mitochondrial genome variation with cardiovascular disease is an extremely relevant issue of modern scientists nowadays [1–5]. Our previous data demonstrate the significant differences of mitochondrial heteroplasmy between unaffected and atherosclerotic areas of human aortic intima, and detected heteroplasmic variants of mitochondrial genome statistically related to atherosclerosis [6,7]. Furthermore, we have shown the association of several heteroplasmic mtDNA variants with carotid atherosclerosis in samples derived from Moscow population [8–10]. Our recent data show that the mutations of the mitochondrial genome are differently related to cardiovascular disease in genetically and clinically diverse populations, Russian and Mexican ones [11]. In this way, it seems to be important to make comparisons between ethnically different populations that have similar socio-economic conditions.

![Graph showing the correlation of mitochondrial heteroplasmy m.13513G > A and mean cIMT in Kazakh population-derived sample.](image)

**Table 7**

| Variable | Russian | Kazakh |
|----------|---------|--------|
|          | Total   | Women  | Men   | Total   | Women  | Men   |
| m.13513G > A | –0.235 | –0.313 | –0.087 | –0.412 | –0.445 | –0.276 |
|           | 0.001*  | <0.001* | 0.646 | 0.001*  | 0.005* | 0.214 |
| m.3336T > C | 0.030   | 0.018  | 0.232 | –0.031 | –0.177 | 0.208 |
|           | 0.686   | 0.819  | 0.217 | 0.861   | 0.397  | 0.564 |
| m.12315G > A | –0.018 | –0.021 | –0.053 | 0.262   | 0.420  | –0.235 |
|           | 0.808   | 0.797  | 0.779 | 0.128   | 0.036* | 0.514 |
| m.5178C > A | –0.078 | 0.084  | –0.476 | 0.045   | –0.106 | –0.039 |
|           | 0.286   | 0.291  | 0.008* | 0.747   | 0.537  | 0.876 |
| m.14459G > A | 0.001  | –0.073 | 0.111 | 0.011   | 0.033  | 0.047 |
|           | 0.985   | 0.361  | 0.558 | 0.932   | 0.844  | 0.837 |
| m.14846G > A | –0.025 | –0.016 | –0.026 | 0.081   | 0.062  | 0.263 |
|           | 0.727   | 0.839  | 0.891 | 0.546   | 0.720  | 0.237 |

r, Pearson's correlation coefficient and significance of correlation are shown.
*, statistical significance at p < 0.05.
In this article the association of heteroplasmy level of mitochondrial mtDNA variants with carotid atherosclerosis in Russian and Kazazh population-derived samples, was demonstrated. In total, data on 251 participants were analysed (190 participants from Novosibirsk, Russia, and 61 participants from Almaty, Kazakhstan). Men and women were aged 50–70 years old, and females were included on additional criterion, namely, more than 5 years after spontaneous (non-surgical) menopause. All participants were free of clinical manifestations of atherosclerosis-related diseases. The protocol met the standards of Declaration of Helsinki (the revised version of 1975 and the amendments of 1983, 1989, and 1996), and has been approved by the local ethical committee at the Institute for Atherosclerosis Research; all participants have provided written informed consent prior to inclusion.

Carotid arteries were examined by high-resolution B-mode ultrasound using a SonoScape S6 scanner (SonoScape, China) equipped with a 7.5 MHz linear array probe. Both left and right common carotid arteries were visualized in different projections (anterolateral, lateral, and posterolateral). The cIMT measurements were performed on the first centimeter of common carotid arteries before carotid bulb using dedicated M’Ath PACS software (IMT, France). The mean value of these measures was considered as an integral measure of intima-media thickness (mean cIMT).

Phenol-chloroform extraction was used for mitochondrial DNA isolation from blood leukocytes [12]. Polymerase chain reaction (PCR) was used to obtain DNA fragments covering the investigated variant nucleotide [6]. Pyrosequencing of PCR fragments was carried out by device PSQ HS96MA (Biotage, Sweden) to determine the heteroplasmy level as a percent of mtDNA mutant copies, as described elsewhere [6,13].

Data processing was performed by the IBM SPSS Statistics software, version 20.0 (SPSS IBM Inc., USA). Data are expressed in terms of means and standard deviation. The significance of differences was defined at the 95% level of confidence. Pearson’s correlation analysis was used to evaluate the association of mitochondrial heteroplasmy with cIMT.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dib.2020.105136.

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