Data Article

Data on association of mitochondrial heteroplasmy and cardiovascular risk factors: Comparison of samples from Russian and Mexican populations

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Abstract
Despite the fact that the role of mitochondrial genome mutations in a number of human diseases is widely studied, the effect of mitochondrial heteroplasmy in the development of cardiovascular disease has not been adequately investigated. In this study, we compared the heteroplasmy levels of mtDNA from leukocytes for m.3256C>T, m.3336T>C, m.12315G>A, m.5178C>A, m.13513G>A, m.14459G>A, m.14846G>A, m.15059G>A, m.652insG and m.1555A>G mutations in CVD-free subjects and CVD patients in samples derived from Russian and Mexican populations. It was demonstrated that heteroplasmy level of m.5178C>A was associated with CVD in Russian men, and m.14459G>A – in Russian women. Mitochondrial heteroplasmy

List of Abbreviations: CVD, cardiovascular disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MI, myocardial infarction; HDL, high-density lipoproteins; LDL, low-density lipoproteins; TG, triglycerides

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level of m.13513G > A and m.652insG were associated with CVD in Mexican men, and only m.652insG– in Mexican women. The levels of heteroplasmy for mitochondrial mutations m.3336T > C, m.5178C > A, m.14459G > A, m.14846G > A and m.1555A > G were significantly higher in CVD-free Mexican men, and for m.3256C > T, m.3336T > C, and m.14459G > A – in CVD-free Mexican women.

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Specifications Table

| Subject area                        | Cardiovascular diseases                        |
|-------------------------------------|------------------------------------------------|
| More specific subject area          | Genetic predisposition to cardiovascular disease|
| Type of data                        | Tables                                          |
| How data was acquired               | Pyrosequencing, clinical data, biochemical analysis |
| Data format                         | Analysed                                       |
| Experimental factors               | Not applicable                                  |
| Experimental features              | Mitochondrial mutations m.1555A > G, m.3256C > T, m.3336T > C, m.5178C > A, m.12315G > A, m.13513G > A, m.14459G > A, m.14846G > A, m.15059G > A, m.652insG were determined using pyrosequencing technology, and their association with CVD was analysed |
| Data source location               | Rostov-on-Don, Russia                           |
|                                    | Moscow, Russia                                  |
|                                    | Villahermosa, Mexico                            |
| Data accessibility                 | Data are provided in this article               |

Value of the data

- The study shows that in genetically and clinically diverse populations, Russian and Mexican ones, the mutations of the mitochondrial genome are differently related to cardiovascular disease.
- In samples from Russian population, mitochondrial heteroplasmy level of m.5178C > A and m.14459G > A were significantly higher in men and women with CVD, respectively. In samples from Mexican population, heteroplasmy level of these mutations was significantly higher in CVD-free study participants. More, in Mexican population, heteroplasmy levels of m.13513G > A and m.652insG were associated with CVD in males, and m.652insG– in females. Higher level of heteroplasmy of mutations m.3336T > C, m.5178C > A, m.14459G > A, m.14846G > A and m.1555A > G was demonstrated in healthy men, and that of m.3256C > T, m.3336T > C, and m.14459G > A – in healthy women.
- Estimation of the associations of as much as possible mitochondrial mutations with risk factors and clinical signs of coronary heart disease and atherosclerosis provides an important source for further investigation of the role of mitochondrial heteroplasmy level in the development of cardiovascular pathology.

1. Data

Clinical and laboratory characteristics of Russian and Mexican study participants are presented in Tables 1 and 2.
Table 3 demonstrates statistical significance of the differences in clinical and biochemical characteristics between Russian and Mexican study participants.

Mitochondrial heteroplasmy level in Russian and Mexican study participants is presented in Tables 4 and 5.

In samples from Russian population, heteroplasmy level of m.5178C > A is significantly higher in male study participants with CVD than in healthy men; heteroplasmy level of m.14459G > A prevails significantly in women with CVD.

In the sample from Mexican population, heteroplasmy level of m.13513G > A and m.652insG prevails significantly in men with CVD, heteroplasmy level of m.3336T > C, m.5178C > A, m.14459G > A, m.14846G > A and m.1555A > G are significantly higher in healthy men; m.652insG is significantly higher in female study participants with CVD, and m.3256C > T, m.3336T > C, m.14459G > A – in CVD-free women.

Table 6 demonstrates statistical significance of the difference of mitochondrial heteroplasmy level between Russian and Mexican study participants.
### Table 3
Comparison of Russian and Mexican populations.

| Variable          | Men              |          | Women             |          |
|-------------------|------------------|----------|-------------------|----------|
|                   | Healthy, p       | CVD, p   | Healthy, p        | CVD, p   |
| Age, years        | .093             | .955     | .508              | .659     |
| BMI, kg/m²        | .001             | .569     | .002              | .118     |
| SBP, mm Hg        | .002             | .001     | .657              | .319     |
| DBP, mm Hg        | .021             | .005     | .055              | .256     |
| Smoking, %        | .001             | <.001    | .056              | .089     |
| Diabetes, %       | .210             | .001     | .026              | .020     |
| ML %              | .001             | .009     |                    |          |
| Total cholesterol, mg/dL | .019      | <.001    | .001              | <.001    |
| HDL, mg/dL        | <.001            | <.001    | <.001             | .009     |
| LDL, mg/dL        | .011             | <.001    | <.001             | .241     |
| TG, mg/dL         | <.001            | .396     | <.001             | .241     |

* Statistically significant difference at \( p < .05 \).

### Table 4
Mitochondrial heteroplasmy level of Russian participants.

| Mitochondrial heteroplasmy, % | Men |          | Women |          |
|-------------------------------|-----|----------|-------|----------|
|                               | Healthy | CVD     | \( p \) | Healthy | CVD     | \( p \) |
| m.12315G > A                  | 27.8(22.9) | 26.6(16.1) | .803 | 32.4(15.7) | 34.0(15.0) | .777 |
| m.3256C > T                   | 21.2(16.8) | 18.9(10.2) | .561 | 22.2(12.3) | 23.5(14.8) | .770 |
| m.3336T > C                   | 7.9(5.6) | 10.5(21.3) | .452 | 7.8(7.9) | 8.5(3.5) | .762 |
| m.5178C > A                   | 10.5(12.1) | 17.9(15.9) | .044 | 16.0(4.2) | 18.3(5.8) | .185 |
| m.13513G > A                  | 27.8(24.6) | 31.0(21.4) | .619 | 23.8(13.2) | 21.4(13.1) | .609 |
| m.14459G > A                  | 38.5(26.7) | 31.9(26.9) | .362 | 18.5(9.2) | 28.7(16.9) | .019 |
| m.14846G > A                  | 14.1(17.1) | 15.7(17.8) | .731 | 16.5(19.8) | 13.1(4.8) | .575 |
| m.15059G > A                  | 35.2(32.5) | 23.1(14.0) | .636 | 36.3(13.1) | 43.7(11.0) | .106 |
| m.652insG                     | 28.6(22.5) | 26.8(19.3) | .752 | 15.7(17.2) | 15.6(16.5) | .994 |
| m.1555A > G                   | 17.4(16.4) | 17.2(9.5)  | .954 | 16.7(8.9)  | 18.3(10.1) | .637 |

Mean (SD) values are shown.

* Statistically significant difference at \( p < .05 \).

### Table 5
Mitochondrial heteroplasmy level of Mexican participants.

| Mitochondrial heteroplasmy, % | Men |          | Women |          |
|-------------------------------|-----|----------|-------|----------|
|                               | Healthy | CVD     | \( p \) | Healthy | CVD     | \( p \) |
| m.12315G > A                  | 5.4(8.5) | 4.0(3.4) | .260 | 2.7(2.6)  | 2.7(1.8)  | .998 |
| m.3256C > T                   | 10.5(19) | 10.1(2.1) | .364 | 10.4(19)  | 9.4(17)   | .043 |
| m.3336T > C                   | 2.6(0.8) | 1.7(0.5)  | <.001 | 2.6(9.6)  | 1.6(5.6)  | <.001 |
| m.5178C > A                   | 10.3(27.7) | 1.7(0.8) | .017 | 1.6(6.8)  | 7.6(20.7) | .122 |
| m.13513G > A                  | 18.3(7.2) | 27.8(9.8) | <.001 | 20.0(6.6) | 23.2(7.2) | .098 |
| m.14459G > A                  | 3.1(0.2) | 2.8(0.2)  | <.001 | 3.2(2.5)  | 2.7(0.2)  | <.001 |
| m.14846G > A                  | 11.5(4.9) | 10.0(1.8) | .034 | 10.9(2.7) | 9.8(2.2)  | .106 |
| m.15059G > A                  | 3.1(0.6) | 3.6(1.5)  | .085 | 3.1(0.6)  | 3.4(0.7)  | .216 |
| m.652insG                     | 20.0(7.1) | 26.0(17.6) | <.001 | 21.1(7.3) | 27.5(7.4) | .003 |
| m.1555A > G                   | 30.0(43.6) | 12.1(5.8) | .002 | 15.7(7.9) | 21.8(29.2) | .285 |

Mean (SD) values are shown.

* Statistically significant difference at \( p < .05 \).
2. Experimental design, materials and methods

Previously we have developed a quantitative assay of mutant allele measurement for mitochon-
drdial heteroplasmic mutations [1] and demonstrated significant differences between unaffected areas
and atherosclerotic lesions in human aortic intima [2]. Further the association of mitochondrial
genetic variation with vascular diseases and carotid atherosclerosis has been demonstrated [3–6].

In this study, the association of heteroplasmy level of mitochondrial mutations with CVD in
Russian and Mexican populations was estimated. In total, 300 participants (150 in Russia, and 150 in
Mexico) were included in the study. Men and women aged from 55 to 79 years (for women – at least
five years after menopause). Study participants were divided into CVD-free and CVD group by the
results of cardiological examination. CVD group included patients who have been observed by a
 cardiologist with diagnosed CVD.

The observed levels of heteroplasmy did not reach the necessary level for the development of
mitochondrial disorders in this study, since it is known that the level of mitochondrial heteroplasmy
in patients should exceed 50% to evolve clinical manifestations [7].

The study was conducted in accordance with the Helsinki Declaration of 1975 as revised in 1983;
all participants gave their written informed consent prior to their inclusion in the study.

Mitochondrial DNA was isolated by phenol-chloroform extraction [8]. Polymerase chain reaction
(PCR) was used in order to obtain DNA fragments containing the region of the investigated mutations
[1]. Analysis of the heteroplasmy level was carried out in the investigated mutations using the origi-
nal quantitative method previously developed on the basis of pyrosequencing technology [9]. The
level of heteroplasmy, i.e. % mutant copies of mtDNA from their total amount in the sample was
estimated.

Statistical analysis was performed using the IBM SPSS 20.0 software (IBM Inc., USA). Data are
expressed in terms of means and standard deviation.

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Transparency document. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.
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