Way to longevity: role of antioxidant defense gene polymorphisms in successful adaptation

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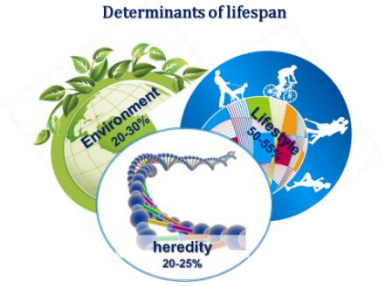
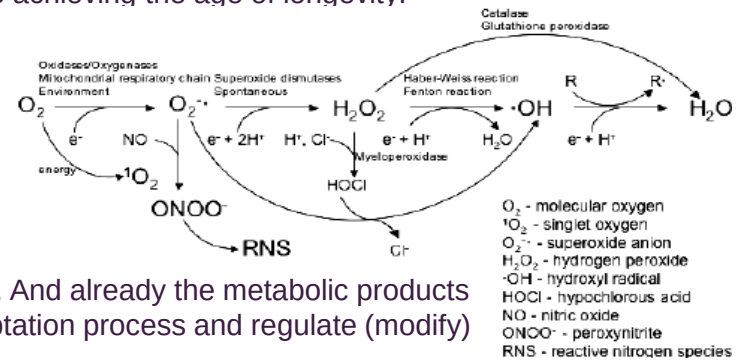
Motivation

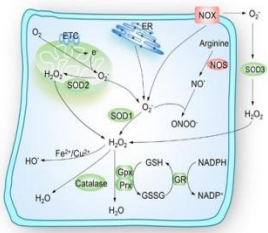


Longevity is a complex phenomenon of surviving to an age significantly exceeding the average species lifespan. Among possible causes of aging and longevity about 25% are genetic and 25% are external factors, while the majority - about 50% - is the way of carry out the interaction of exogenous and endogenous factors. To date, the question remains as to which particular combinations of factors of hereditary and environmental nature contribute to achieving the age of longevity.

An organism is an open system, therefore it is precisely those external agents (molecules, substances, ions) that primarily come into contact with it deserve special attention. First of all, it is oxygen participating in the energy exchange inside the cell. Getting into the body, it enters a chain of chemical transformations. And already the metabolic products of those structures are involved in the adaptation process and regulate (modify) homeostasis.



The enzyme activity level is determined by the genetic variation in the structure of their genes. Thus, individual genotypic features determine the variability of the enzymatic antioxidant system, and, therefore, the plasticity of chemical and physiological reactions that determine the range of adaptive capabilities of the body.



Aim

The purpose of the study was the analysis of the polymorphic markers of some genes-candidate of aging and longevity, which relate to the body's defense system against oxidative stress, considering ethnicity, age gradation and gender differentiation.

Table 1.Studied polymorphic loci

refSNP	Gene	Chr. location	Polymorphism	Protein mutation
rs2070424	***SOD1***	21q22.11	251A>G	–
rs4880	***SOD2***	6q25.3	116T>C	16V>A
rs1799895	***SOD3***	4p15.2	691C>G	231R>G
rs10098474	***MSRA***	8p23.1	–402C>T	–
rs1001179	***CAT***	11p13	*-262C>T*	–
rs1131341	***NQO1***	16q22.1	465C>T	139R>W,
rs1801133	***MTHFR***	1p36.22	c.677C>T	222A>V
rs1002149	***GSR***	8p21.1	-386G>T	–
rs1050450	***GPX1***	3p21.31	593C>T	197P>L
rs1695	***GSTP1***	11q13.2	313A>G	105I>V

Studied group

Total group (3664 people) included individuals living in the Republic of Bashkortostan and belonging to three ethnic groups – Russians, Bashkirs and Tatars and in age from 1 to 109 years old.

Methods

The biological material was DNA isolated from 8 ml of whole venous blood by standard phenol-chloroform extraction.

Allelic variants of the genes were identified by RT-PCR using TaqMan probes.

For statistical analysis of the results of the study, computer programs SPSS (v.13.0), GENEPOP, and Arlequin (v.3.0) were used.

Results

We found interethnic differences in the distribution of allele frequencies of superoxidedismutases 1 and 2 (Mn, Cu-SOD and Mn-SOD), catalase (CAT), NAD(P)H Quinone dehydrogenase 1 (NQO1) genes. To reach the age of longevity, genotypes *SOD1**A/A, *SOD1**A/G, *SOD2**A/A, *NQO1**C/T, *NQO1**C/C and *GPX1**L/L were significant among Russians, genotypes *SOD2**A/A, *SOD2**V/V, *SOD2**V/A, *CAT**C/T, *CAT**C/C were significant among Tatars, genotypes *MSRA**C/C, *CAT**C/C were significant among Bashkirs.

Table 2. Association analysis of polymorphic loci in antioxidant defense genes with age by the logistic regression method

Ethnic group	Genotype	Age period	AUC	P	OR	CI_{OR}
Total group (male and female)						
Russian	*SOD1**A/A	36-98	0.371	0.001	1.025	1.010-1.041
	*SOD1**A/G		0.631	0.001	0.975	0.960-0.990
	*SOD2**A/A	16-98	0.406	0.002	0.985	0.976-0.995
	*NQO1**C/T	16-98	0.376	0.007	0.980	0.966-0.995
	*NQO1**C/C		0.624	0.007	1.020	1.005-1.035
	*GPX1**T/T	45-98	0.368	0.013	0.966	0.940-0.993
Tatars	*CAT**C/T	36-80	0.571	0.001	1.022	1.009-1.035
	*CAT**C/C		0.430	0.010	0.979	0.967-0.991
Bashkirs	*MSRA**C/C	28-75	0.667	0.038	1.048	1.003-1.095
	*CAT**C/C	16-70	0.393	0.028	0.979	0.961-0.998
Male						
Tatars	*SOD2**C/C	22-89	0.428	0.029	0.989	0.980-0.999
	*SOD2**T/T		0.414	0.000	0.985	0.977-0.993
	*SOD2**T/C		0.631	0.000	1.023	1.015-1.032

Note. AUC – area under ROC curve, P – significance level, OR – odds ratio, CI_{OR} – confidence interval of OR

Based on modern ideas about the genes of aging and longevity, antioxidant defense genes related to “frailty genes”. A number of associative studies have shown the participation of antioxidant defense genes in the development of multifactorial and age-associated diseases that limit the lifespan. However, genetically determined functioning of the antioxidant defense enzyme system can become the key to the molecular base for the formation of an individual phenotype of longevity.

Acknowledgment

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