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REVIEW ARTICLE

APPLICATION ASPECTS OF ANIMAL AND HUMAN MITOCHONDRIAL GENOMICS

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Abstract. Currently, extensive investigations are being carried out in the area of mitochondrial genomics. Mitochondrial DNA is used in many fields of science, e.g. evolutionism, phylogeography, anthropology, archaeology, forensics, medical diagnostics, veterinary medicine, molecular ecology, population genetics, and animal breeding. Mitochondrial markers, haplotypes, or haplogroups are associated with pathogenesis of diseases, evolution and origin of organisms, and identification of species. An interesting direction based on mitochondrial DNA sequences is the research into polymorphisms/mutations that can be related to economically important utility traits of livestock. The use of mtDNA has drawbacks due to the low power of discrimination and pattern of inheritance. Still, mtDNA has many advantages as a marker; therefore, it is often used in both basic and applied research.

Key words: breeding, judiciary, medicine, mitochondrial genomics, molecular ecology, mtDNA

Introduction

Achievements of bioinformatics have facilitated global analysis of the organization of the genetic information in individual species, i.e. genomes, thereby contributing to emergence of a new scientific discipline – genomics, which is an

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interdisciplinary area of knowledge concerning the structural and functional characteristics of genomes [Świtoński 2008, Ślaska 2010].

Within genomics, three main branches have developed, i.e. structural genomics (concerning the genome sequence and organization), functional genomics (comprising processes associated with gene expression), and epigenomics. An important role is also played by interspecific comparative analyses referred to as comparative genomics [Świtoński 2008, Ślaska 2010].

The genome is a set of genetic data contained in the gamete, i.e. the nuclear DNA (nDNA) and mitochondrial DNA (mtDNA). Since the mtDNA molecule is very small compared with the haploid set of chromosomes, the term ”genome“ is typically generalised and refers to nuclear DNA.

In the recent years, extensive research has been carried out concerning the mitochondrial genome and the relationships between mitochondrial haplotypes and haplogroups and physiological (aging, acclimation) and pathological states, which can be collectively called “civilisation diseases”. These include e.g. human and canine malignancies, neurodegenerative diseases, and diabetes. To emphasise the fact that the research concerns the small but extremely important mitochondrial DNA molecules rather than nuclear DNA, the branch of science investigating the mtDNA structure and function is called mitochondrial genomics. One of the most important branches of mitochondrial genomics is oncogenomics, which analyses the relationship between mtDNA haplotypes and the neoplastic transformation process.

Mitochondria and mitochondrial genome

Mitochondria are one of the most important organelles in the cytoplasm of all eukaryotic cells. According to the endosymbiotic theory, mitochondria descended from bacteria that had been absorbed by the ancestors of today’s eukaryotic cells. The conserved mitochondrial genome as well as the arrangement of RNA and protein biosynthesis is a remainder of the evolutionary past [Higuchi 2007]. The number of mitochondria in a single eukaryotic cell depends on tissue energy demand [Moraes 2001, Tsang and Lemire 2002].

The primary function of mitochondria is their involvement in the cellular respiration process, which is essential for release and storage of free energy in high-energy bonds in ATP. The synthesis of ATP is possible through a combination of Krebs cycle reactions occurring in the mitochondrial matrix with oxidative phosphorylation taking place in the inner mitochondrial membrane. Mitochondria contain enzymes of both the respiratory chain and the tricarboxylic acid cycle [Leonard and Schapira 2000, Pebay-Peyroula et al. 2003].

Mammalian mitochondrial DNA has a length of about 15 000–17 000 base pairs [www.ncbi.nlm.nih.gov]. The small size is compensated for by the large number of copies (a single human cell contains from 1000 to 10 000 mitochondria with 2–10 copies of mtDNA in each) [Leonard and Schapira 2000, Higuchi 2007]. The mitochondrial genome of animals comprises 37 genes in total: two ribosomal RNA genes, 22 RNA transport genes, and 13 genes encoding the respiratory chain proteins. MtDNA is composed of two, light L and heavy H, strands. Strand H encodes all RNAs and proteins except the *ND6* protein and 8 tRNA, which are encoded on strand L. Absence of introns and gene-separating sequences is a characteristic feature of mtDNA. The only non-coding sequence in the mitochondrial DNA is the *D-loop* comprising a promoter of strand H and L transcription and a signal triggering H-strand replication. It is composed of two hypervariable regions (HV1, HV2) with a total length of approx. 1100 bp, which accounts for less than 7% of the mitochondrial genome. Additionally, the *D-loop* sequence is characterised by the highest degree of polymorphism [mitomap.org/MITOMAP].

Absence of recombination is a characteristic feature of mitochondrial DNA. Changes occurring in mtDNA over years are only related to mutations. Consequently, the mitochondrial genome is a single haplotype inherited in the maternal line; hence, mtDNA is often used in phylogenetic studies of the origin of humans and many animal species. It is possible to analyse the evolution of mitochondrial DNA from the emergence of mankind and identify its sequence polymorphisms that have accumulated over the years. Sets of polymorphisms derived from a common ancestor are referred to as mitochondrial haplogroups. The haplogroups are indicated by uppercase letters and the accompanying numbers denote subhaplogroups. The phylogenetic distribution of haplotypes indicates an African origin of human mtDNA with seven major groups named sequentially from L0 to L6 [mitomap.org/MITOMAP].

The development of mitochondrial genomics has become a cornerstone for a new branch of research analysing the relationship between the mitochondrial haplogroup and the phenotype of the individual. There are many reasons for the common use of mtDNA markers in the genetic analysis of animal populations. The mitochondrial genome is characterised by a small size, which combined with the conservative gene arrangement facilitates development of universal primers for amplification of various mtDNA fragments in vertebrates and invertebrates. In practice, this implies that genetic information can frequently be acquired without prior knowledge of the mtDNA sequence in analysed species. Additionally, despite the conservative gene arrangement, the mtDNA mutation rate is 5–10–fold higher than that in the nuclear genome. The high frequency of mtDNA mutations results from lack of a protective effect of histones, a less efficient DNA repair system, and proximity of the respiratory chain, i.e. the main source of ROS in

the cell. The high density of encoded information resulting from absence of intron sequences leads to mitochondrial aberrations induced by mutations in the encoding region and manifested by substitutions in the sequences of the respiratory chain, tRNA, or rRNA subunits. In turn, mutations in the *D-loop* region may affect mtDNA replication and transcription. Irrespective of the cause, the high mutation rate results in high mtDNA polymorphism and presence of multiple genetic lineages within populations [mitomap.org/MITOMAP].

Mitochondrial DNA is used in various fields of research, e.g. evolutionism, phylogeography, anthropology, archaeology, forensics, medical diagnostics, veterinary medicine, molecular ecology, population genetics, animal breeding, etc.

Mitochondrial DNA in animal husbandry

Intensive development of biotechnological techniques employed in animal husbandry programmes has contributed to rapid identification and selection of most valuable individuals for further breeding. However, genomic selection involves only nuclear markers. Investigations of the relationship between mtDNA mutations and livestock animal utility traits have been conducted for only a few years (Table 1). Raccoon dogs (*Nyctereutes procyonoides*) are one of fur–bearing animals bred species in Poland [Ślaska and Grzybowska-Szatkowska 2011]. Analyses of mitochondrial DNA genes revealed 4 haplotypes in farmed animals, which were not found in wild–living raccoon dogs. Simultaneously, no mitochondrial haplogroup of the wild–living raccoon dogs was found in the farmed animals. The diversity of the haplogroups may have been one of the factors inducing changes in selected utility traits in the phenotype of farmed raccoon dogs within a relatively short time. Compared with wild–living raccoon dogs, the emergence of new haplotypes and haplogroups in the bred animals implied appearance of adaptive mutations [Ślaska and Grzybowska-Szatkowska 2011]. In consecutive investigations, Ślaska et al. [2014] determined the relationship between polymorphisms of mitochondrial genes and the utility traits of raccoon dogs. The authors identified a candidate gene *COII* possibly associated with the coat quality, which in turn was found to be significantly influenced by polymorphism m.A7446G. Raccoon dogs with the m.G7446 genotype were characterised by significantly higher quality of the coat, compared with animals with the m.A7446 genotype. Moreover, animals with haplotype B and C (with substitution m.G7446) exhibited significantly better coat quality than raccoon dogs with haplotype A. The authors suggested that the analysis of mtDNA polymorphisms could be useful in selection aimed at improvement of coat quality in raccoon dogs.

Sutarno et al. [2002] carried out investigations aimed at demonstrating a relationship between the polymorphism identified in the gene encoding NADH de-

Table 1. Examples of application of mitochondrial DNA in animal husbandry

Tabela 1. Przykłady wykorzystania mitochondrialnego DNA w hodowli zwierząt

Species	Gene Gen	Literature Piśmiennictwo
Raccoon dogs Jenoty	*CYTB*, *COI*, *COII*, *D-loop*	Ślaska and Grzybowska-Szatkowska 2011, Ślaska et al. 2014 Ślaska i Grzybowska-Szatkowska 2011, Ślaska i in. 2014
Cattle Bydło	*ND5*, *D-loop*, 16S rRNA	Sutarno et al. 2002, Mannen et al. 2003 Sutarno i in. 2002, Mannen i in. 2003
Pigs Świnie	*D-loop*	Yen et al. 2007 Yen i in. 2007
Sheep Owce	*CYTB*, *D-loop*	Reicher et al. 2012 Reicher i in. 2012

hydrogenase subunit 5 (*ND5*) and in the control (*D-loop*) region and reproductive traits in cattle. The analyses revealed statistically significant differences between the calving rate and the mitochondrial haplotypes identified. Similarly, Mannen et al. [2003] demonstrated a correlation between polymorphism in several mtDNA encoding regions and meat quality in Japanese Black cattle. A significant effect of a substitution in 16S rRNA on the size of the longest muscle and the degree of meat marbling was identified. Yen et al. [2007] carried out investigations of the relationship between *D-loop* polymorphism and reproductive traits in Meishan pigs. Their analyses showed significant differences between the analysed haplotypes and body weight of piglets on day 21. Reicher et al. [2012] studied the correlations between polymorphisms in the *D-loop* and *CYTB* with production and reproductive traits in a group of Afec-Assaf sheep. The authors reported significant differences between mitochondrial haplogroups and reproduction performance in the sheep.

Mitochondrial DNA in molecular ecology

Several mitochondrial haplotypes can be distinguished within various animal species. Point mutations, a simple inheritance pattern, and absence of recombination facilitate observation of the mechanisms of haplotype differentiation, which in turn allows observation of changes in the size of the population and colonisation as well as assessment of the level of genetic variability and the direction and rate of gene flow (Table 2). If no common haplotypes are found in analysed populations, long-term isolation between the populations or appearance of adaptive mutations can be assumed. In turn, differences in haplotype sequences between different populations of the same species may indicate that they belong to different evolutionary lineages [Rutkowski et al. 2009, Ślaska and Grzybowska-Szatkowska

2011]. This approach is often applied in ornithology. MtDNA analyses were used e.g. in the research of the Polish population of the wood grouse, in which no common haplotypes were found for the southern and north–eastern regions of Poland. It was additionally reported that the wood grouse population from the northern Lubelszczyzna region was isolated from other Polish populations [Rutkowski et al. 2009].

Table 2. Examples of application of mitochondrial DNA in molecular ecology and animal forensics

Tabela 2. Przykłady wykorzystania mitochondrialnego DNA w ekologii molekularnej i genetyce sądowej zwierząt

Research branch Kierunek badań	Organism Organizm	Gene Gen	Literature Piśmiennictwo
Phylogenesis Filogeneza	Raccoon dog Jenot	*CYTB*, *COI*, *COII*	Ślaska and Grzybowska-Szatkowska 2011 Ślaska i Grzybowska-Szatkowska 2011
	Horse Koń	*D-loop*	Kracíková et al. 2010 Kracíková i in. 2010
	Roe deer Sarna	*CYTB*	Karpiński et al. 2008 Karpiński i in.. 2008
Species identification, taxonomy Identyfikacja gatunkowa, taksonomia	Bison Żubr	*CYTB*	Prusak et al. 2004 Prusak i in.2004
	Fish Ryba	*COI*	Ward et al. 2005 Ward i in. 2005
	Bird Ptak	*COI*	Hebert et al. 2004 a Hebert i in. 2004 a
	Butterfly Motyl	*COI*	Hebert et al. 2004 b Hebert i in. 2004 b
Protection of endangered and protected species Ochrona gatunków zagrożonych i chronionych	Elephant Słoń	12S rRNA, *CYTB*	Comstock et al. 2003, Wozney and Wilson 2012 Comstock i in. 2003, Wozney i Wilson 2012
	Wood grouse Głuszec	*D-loop*	Rutkowski et al. 2009 Rutkowski i in. 2009
	Snake Wąż	*CYTB*	Singh et al. 2012 Singh i in. 2012
	Fish Ryba	*CYTB*	Ludwig et al. 2002 Ludwig i in. 2002

Identification of mtDNA haplotypes is also used in phylogenetic analyses of many farmed animal species e.g. for determination of the genetic distances between species and populations. This type of analyses was performed in a population of Old Kladruber horses. The analyses distinguished 16 different haplotypes [Kracíková et al. 2010]. Sequence analysis of the cytochrome b encoding gene (*CYTB*, cytochrome b) has confirmed that although the American bison and the European bison are closely related species, classification thereof into the same subspecies is questionable. This hypothesis is important for addressing the problems of the genetic purity and diversity of both species [Prusak et al. 2004]. Karpiński et al. [2008] conducted investigations aimed at estimation of genetic

parameters of two roe deer sub-populations based on the *CYTB* gene. The variability of the parameters was assessed and the most polymorphic loci helpful in estimation of the genetic variation of the species were identified. In turn, in his study of ancient DNA (aDNA) of the aurochs, Słomski [2011] used mitochondrial DNA for comparative analyses of domestic and wild cattle. The results of the analyses not only initiated a public debate on the aurochs but also facilitated identification of the relatives of this species. Using mitochondrial DNA sequences (*CYTB*, *COI*, *COII*), mitochondrial haplogroups characteristic for farmed and wild-living raccoon dogs were determined [Ślaska and Grzybowska-Szatkowska 2011].

It is estimated that there are from 10 to 100 million species in the world, and only approximately 1.5 million have been described. This creates a possibility of potential identification of hitherto undescribed organisms [Mayer et al. 2007]. A breakthrough in the identification research on many animal species was the development of the genetic barcoding method (DNA barcoding) based on the sequence analysis of the 648-bp gene fragment encoding the mitochondrial cytochrome c oxidase subunit I (*COI*). The choice of this gene was prompted by the low intraspecific variability and high interspecific variability. Barcoding is used for identification of new species and those that are difficult to identify with conventional methods as well as for identification of species in developmental stages that are hardly recognisable using conventional methods [http://www.barcodeoflife.org/]. Hebert et al. [2004 a] identified the nucleotide sequence of the *COI* fragment for 260 bird species in North America. It was found on the basis of the sequences that the differences between closely related species were on average 18–fold greater than the differences within the same species. Additionally, four probably new bird species were found. The high interspecific variability and the low intraspecific variability observed by the authors confirmed the effectiveness of barcoding based on the *COI* gene fragment in identification of bird species. Hebert et al. [2004 b] carried out investigations on 484 Costa Rican *Astraptes fulgerator* butterflies originally classified as one species. Morphological traits and barcoding helped to distinguish 10 different butterfly species in this group.

Mitochondrial DNA in forensic medicine and judiciary

The usefulness of mtDNA sequences in forensic genetics is limited by its low power of discrimination. Therefore, mtDNA analyses facilitate only exclusion of the compatibility of sequences obtained. They are, however, performed when identification of the genetic profile on the basis of microsatellite sequences is difficult or impossible. Mitochondrial DNA exhibits considerable higher resistance to degradation than nuclear DNA and is present in a large number of

copies in the cell. It may therefore be used for analysis of the so-called ancient DNA [Morling 2004]. MtDNA may be present in the cell in thousands of copies, which is particularly favourable in the case of highly degraded hair material devoid of bulbs or old bones. MtDNA markers are also used in clinical identification of missing persons or unidentified bodies and in genealogy for reconstruction of the history of the female part of the humankind, given exclusive inheritance down the maternal line. Interpretation of mtDNA analysis results involves comparison of mtDNA sequences from trace material and reference material sampled from a suspect. The next step is determination of the frequency of occurrence of a given mtDNA haplotype in the population, which is facilitated by enlarging mtDNA databases, e.g. EMPOP (Group's mitochondrial DNA Population Database Project, http://empop.org/).

Analyses of mitochondrial DNA are applicable in criminal investigations of trafficking endangered and protected species (Table 2). Comstock et al. [2003] developed a molecular test for determination of the species origin of ivory. 16 microsatellite loci and 2 fragments of mitochondrial genes (12S rRNA and *CYTB*) were selected as molecular markers. The molecular tests proved useful in identification of illegally imported ivory products derived from African elephants, which are protected under the Convention on International Trade in Endangered Species of Wild Fauna and Flora called the CITES Red List. Given their high accuracy of species identification, such analyses also contribute to monitoring of the range of endangered and protected species trafficking. Similar investigations aimed at developing an identification test for samples originating from international ivory trade were conducted on the Indian elephant, the African elephant, and the woolly mammoth by Wozney and Wilson [2012]. A specific real-time PCR test based on the mitochondrial *CYTB* gene product was developed. It can be applied to identify the origin of illegally traded products traded on the international market. The problem also applies to the illegal trade of snakes. Despite strict protection, a large number of snakes are killed in India for the venom and skin. After ivory, dried snake venom is the second product smuggled onto the international market. Although the Indian Wildlife Protection Act protects all snakes (with the Indian cobra as a priority), the fight against illegal trade is problematic due to the failure of reliable identification of the snake species from which venom is acquired. Singh et al. [2012] designed molecular tests based on a *CYTB* gene fragment, which helped to distinguish the Indian venomous snakes, including the Indian cobra.

Analyses aimed at determination of species affinity are also performed in the case of illegal trafficking of the most valuable freshwater fish species from the families Acipenseridae and Polyodontidae. Intensive fishing for these species in order to acquire eggs for production of caviar has caused a sharp decline in the fish numbers. Therefore, trade of the species and their products has been subjected to

CITES protection since 1998 [Ludwig et al. 2002]. Using the molecular biology techniques, Ludwig et al. [2002] analysed the *CYTB* gene of 22 Acipenseridae and Polyodontidae species. It was found that the use of 7 restriction endonucleases helped to distinguish 17 Acipenseridae species based on the characteristic band patterns. Since caviar is one of the most valuable products derived from aquatic organisms, identification of the product origin is essential for monitoring caviar trade and protecting the consumers from poachers trafficking caviar of illegally caught fish (Table 2).

Mitochondrial DNA in medicine

Knowledge of the major mitochondrial haplogroups and identification of their relationships with various physiological and pathological states is a rapidly developing branch of medical research (Table 3). Many experiments have been carried out in order to demonstrate the relationship between the affinity to a specified haplogroup and prevalence of diseases, including cancers. Affinity to a specific haplogroup may determine greater or lesser risk of cancer development [Petros et al. 2005, Lu et al. 2009, Czarnecka and Bartnik 2011, Grzybowska-Szatkowska and Ślaska 2012 a, 2012 b]. For instance, European haplogroups N are at the greatest risk of breast cancer, whereas the mitochondrial group U is exposed to a two-fold higher threat of developing prostate cancer [Grzybowska-Szatkowska and Ślaska 2012 a]. Tan et al. [2002] analysed mtDNA in order to identify mutations in breast cancer. In 74% of the tumour tissues, at least 1 somatic mutation was detected. The mutations were detected in the *D-loop*, *ATP6*, *ND2*, and *16S1*. Analyses of the mitochondrial genome performed by Liu et al. [2001] identified mutations in 60% of cancers. The 16S rRNA, 12S rRNA, *CYTB*, and *D-loop* regions were found to be preferred by mitochondrial mutations in ovarian cancer. The authors argue that the high frequency of mtDNA mutations provides evidence for their significant role in neoplastic transformation. Similar investigations focused on determination of the role of mtDNA mutations in carcinogenesis were also conducted on prostate [Petros et al. 2005], head and neck [Zhou et al. 2007], and colon [Ericson et al. 2012] cancers. Identification of the correlation between changes in mtDNA and development of cancers has also been performed in dogs [Ślaska et al. 2013 b, 2013 c].

The mitochondrial theory of aging implies that intracellular reactive oxygen species increase damage to cell components, including the mitochondrial genome. The respiratory chain is the primary site of reactive oxygen species (ROS) production. MtDNA damage associated with accumulation of mutations may induce production of proteins with impaired function, which in turn may result in development of neurodegenerative (Parkinson's, Alzheimer's) diseases and accelerated

Table 3. Examples of application of mitochondrial DNA in medicine

Tabela 3. Przykłady wykorzystania mitochondrialnego DNA w medycynie

Pathological/physiological state Stan patologiczny/fizjologiczny	Literature Piśmiennictwo
Malignant human and canine cancers (breast, prostate, ovary, head and neck, colon) Nowotwory złośliwe człowieka i psa (sutka, gruczołu krokowego, jajnika, prostaty, głowy i szyi, jelita grubego)	Tan et al. 2002, Liu et al. 2001, Petros et al. 2005, Zhou et al. 2007, Ericson et al. 2012, Grzybowska-Szatkowska and Ślaska 2012 a, b, Slaska et al. 2013 a, b, Ślaska et al. 2013 Tan i in. 2002, Liu i in. 2001, Petros i in. 2005, Zhou i in. 2007, Ericson i in. 2012, Grzybowska-Szatkowska i Ślaska 2012 a, b, Slaska i in. 2013 a, b, Ślaska i in. 2013
Mitochondrial diseases Choroby mitochondrialne	Czarnecka and Bartnik 2011, Grzybowska-Szatkowska and Ślaska 2013 a, Ślaska et al. 2013 a Czarnecka i Bartnik 2011, Grzybowska-Szatkowska i Ślaska 2013 a, Ślaska i in. 2013 a
Neurodegenerative diseases (Parkinson's, Alzheimer's) Choroby neurodegeneracyjne (Parkinsona, Alzheimera)	Simon et al. 2000, Ghezzi et al. 2005, Coscun et al. 2004, Da Sylva et al. 2005 Simon i in. 2000, Ghezzi i in. 2005, Coscun i in. 2004, Da Sylva i in. 2005
Diabetes Cukrzyca	Brągoszewski and Ostrowski 2009, Alcolado et al. 2002, Mohlke et al. 2005 Brągoszewski i Ostrowski 2009, Alcolado i in. 2002, Mohlke i in. 2005
Aging Starzenie	Czarnecka and Bartnik 2011, Niemi et al. 2003, Da Sylva et al. 2005, Tońska et al. 2009, Trifunovic et al. 2005 Czarnecka i Bartnik 2011, Niemi i in. 2003, Da Sylva i in. 2005, Tońska i in. 2009, Trifunovic i in. 2005
Acclimation to environmental conditions, adaptive mutations Aklimatyzacja do warunków środowiskowych, mutacje adaptacyjne	Grzybowska-Szatkowska and Slaska 2012 a, Ślaska and Grzybowska-Szatkowska 2011 Grzybowska-Szatkowska i Slaska 2012a, Ślaska i Grzybowska-Szatkowska 2011

aging of the organism [Da Sylva et al. 2005, Trifunovic et al. 2005]. Research on the organism aging process has been focused on e.g. determination of the relationship between longevity and specific mtDNA variants and some mitochondrial haplogroups (haplogroups U and J in particular) [Niemi et al. 2003, Da Sylva et al. 2005].

Research focused on identification of specific mtDNA mutations in patients with Parkinson's disease was conducted by Simon et al. [2000]. Their investigations demonstrated presence of mutations in the analysed mtDNA fragments. The authors found that the high level of mitochondrial DNA mutations did not have a significant role in the pathogenesis of Parkinson's disease. However, it was not proved that mutations occurring at a low frequency could induce development of the disease. Ghezzi et al. [2005] attempted at identification of the role of polymorphism 10398G, common to haplogroups J and K, in the susceptibility of the Italian population to Parkinson's disease. The authors reported that the frequency

of haplogroup K was significantly lower in patients affected by the disease, which implies that the haplogroup is associated with a lower disease risk.

Alzheimer's disease is another health problem induced by disturbances in the mitochondrial respiratory chain. Coscun et al. [2004] found that a mutation at position T414G was reported in 65% of patients with the disease, but not in the control group. The authors observed a higher frequency of heteroplasmic mutations in patients affected by Alzheimer's disease and patients over 80 years of age. Additionally, the analyses demonstrated a reduced level of the *ND6* transcript and lower numbers of mtDNA copies in the cell, which may impair oxidative phosphorylation. This, in turn, may cause defects observed in Alzheimer's disease patients [Coscun et al. 2004].

Type 2 diabetes is another disease resulting from impaired energy metabolism. Due to the key role of mitochondria in glucose metabolism and ATP production, mtDNA mutations may contribute to development of diabetes. Alcolado et al. [2002] showed that a mutation at position 3243 the mt-tRNA gene was responsible for ca. 1% of diabetes cases. Additionally, attempts were made to determine the correlation between the affinity to a specified mitochondrial haplogroup and the risk of developing diabetes. Type 2 diabetes was found to be associated with haplogroup J [Mohlke et al. 2005].

REFERENCES

Alcolado J.C., Laji K., Gill-Randall R., 2002. Maternal transmission of diabetes. Diabet. Med. 19, 89–98.

Brągoszewski P., Ostrowski J., 2009. Medycyna mitochondrialna [Mitochondrial medicine]. Post. Nauk Med. 2, 138–148 [in Polish].

Comstock K.E., Ostrander E.A., Wasser S.K., 2003. Amplifying Nuclear and Mitochondrial DNA from African Elephant Ivory: a Tool for Monitoring the Ivory Trade. Conserv. Biol. 17(6), 1840–1843.

Coscun P.E., Beal M.F., Wallace D.C., 2004. Aizheimer's brain harbor somatic mtDNA control-region mutations that suppress mitochondrial transcription and replication. Proc. Natl. Acad. Sci. USA 101(29), 10726–10731.

Czarnecka A.M., Barnik E., 2011. The role of the mitochondria genome in ageing and carcinogenesis. Aging Res. DOI: 10.4061/2011/136435.

Da Sylva T.R., Connor A., Mburu Y., Keystone E., Wu G.E., 2005. Somatic mutations in the mitochondria of rheumatoid arthritis synoviocytes. Arthritis Res. Ther. 7, 844––851.

Ericson N.G., Kulawiec M., Vermulst M., Sheahan K., O'Sullivan J., Salk J.J., Bielas J.H., 2012. Decreased mitochondrial DNA mutagenesis in human colorectal cancer. PLoS Genet. DOI: 10.1371/journal.pgen.1002689.

Ghezzi D., Marelli C., Achilli A., Goldwurm S., Pezzoli G., Barone P., Pellecchia M.T., Stanzione P., Brusa L., Bentivoglio A.R., Bonuccelli U., Petrozzi L., Abbruzzese G., Marchese R., Cortelli P., Grimaldi D., Martinelli P., Ferrarese C., Garavaglia B.,

Sangiorgi S., Carelli V., Torroni A., Albanese A., Zeviani M., 2005. Mitochondrial DNA haplogroup K is associated with a lower risk of Parkinson's disease in Italians. Eur. J. Hum. Genet. 13, 748–752.

Grzybowska-Szatkowska L., Ślaska B., 2012 a. Mitochondrial DNA and carcinogenesis (Review). Mol. Med. Rep. 6, 923–930.

Grzybowska-Szatkowska L., Ślaska B., 2012 b. Polymorphisms in genes encoding mt-tRNA in female breast cancer in Poland. Mitochondrial DNA 23 (2), 106–111.

Hebert P.D.N., Penton E.H., Burns J.M., Janzen D.H., Hallwachs W., 2004 b. Ten species in one: DNA barcoding reveals cryptic species in the neotropical skipper butterfly *Astraptes fulgerator*. Proc. Natl. Acad. Sci. USA 101(41), 14812–14817.

Hebert P.D.N., Stoeckle M.Y., Zemlak T.S., Francis C.M., 2004 a. Identification of Birds through DNA Barcodes. PLoS Biology 2 (10), 1657–1663.

Higuchi M., 2007. Regulation of mitochondrial DNA content and cancer. Mitochondrion 7, 53–57.

http://www.barcodeoflife.org/ (access: 15.05.2014)

http://empop.org/ (access: 17.05.2014)

http://www.mitomap.org/MITOMAP (access: 10.05.2014)

http://www.ncbi.nlm.nih.gov/ (access: 05.05.2014)

Karpiński M., Adaszek Ł., Drozd L., Winiarczyk S., Czyżowski P., 2008. Polimorfizm długości fragmentów restrykcyjnych mitochondrialnego DNA u sarny (*Capreolus capreolu*) [Restriction fragment length polymorphism of the mitochondrial DNA in roe deer (*Capreolus capreolus*)]. Annales UMCS 3, 24–32 [in Polish].

Kracíková O., Czerneková V., Melčová S., Kott T., Majzlík I., Čapková Z., Andrejsová L., 2010. Mitochondrial DNA analysis of the gene reserve of the Old Kladruber horse. Acta Fytotech. Zootech. 1, 19–23.

Leonard J.V., Schapira A.H.V., 2000. Mitochondrial respiratory chain disorders I: mitochondrial DNA defects. Lancet 355, 299–304.

Liu V.W.S., Shi H.H., Cheung A.N.Y., Chiu P.M., Leung T.W., Nagley P., Wong L.C., Ngan H.Y.S., 2001. High Incidence of Somatic Mitochondrial DNA Mutations in Human Ovarian Carcinomas. Cancer Res. 61, 5998–6001.

Lu J., Sharma L.K., Bai Y., 2009. Implications of mitochondrial DNA mutations and mitochondrial dysfunction in tumorigenesis. Cell Res. 19, 802–815.

Ludwig A., Debus L., Jenneckens I., 2002. A molecular approach to control the international trade in black caviar. Int. Rev. Hydrobiol. 87 (5–6), 661–674.

Mannen H., Morimoto M., Oyama K., Mukai F., Tsuji S., 2003. Identification of mitochondrial DNA substitutions related to meat quality in Japanese Black cattle. J. Anim Sci. 81, 68–73.

Mayer F., Dietz C., Kiefer A., 2007. Molecular species identification boosts bat diversity. Front Zool. 4, 4.

Mohlke K.L., Jackson A.U., Scott L.J., Peck E.C., Suh Y.D., Chines P.S., Watanabe R.M., Buchanan T.A., Conneely K.N., Erdos M.R., Narisu N., Enloe S., Valle T.T., Tuomilehto J., Bergman R.N., Boehnke M., Collins F.S., 2005. Mitochondrial polymorphisms and susceptibility to type 2 diabetes-related traits in Finns. Hum. Genet. 118, 245–54.

Moraes C.T., 2001. What regulates mitochondrial DNA copy number in animal cells? Trends Genet. 17(4), 199–205.

Morling N., 2004. Forensic genetics. The Lancet, 364, 10–11.

Niemi A.K., Hervonen A., Hurme M., Karhunen P.J., Jylhä M., Majamaa K., 2003. Mitochondrial DNA polymorphisms associated with longevity in a Finnish population. Hum. Genet. 112, 29–33.

Pebay-Peyroula E., Dahout-Gonzalez C., Kahn R., Trézéguet V., Lauquin G.J., Brandolin G., 2003. Structure of mitochondrial ADP/ATP carrier in complex with carboxyatractyloside. Nature 426, 39–44.

Petros J.A., Baumann A.K., Ruiz-Pesini E., Amin M.B., Sun C.Q., Hall J., Lim S., Issa M.M., Flanders W.D., Hosseini S.H., Marshall F.F., Wallace D.C., 2005. mtDNA mutations increase tumorigenicity in prostate cancer. Proc. Natl. Acad. Sci. USA 102 (3), 719–724.

Prusak B., Grzybowski T., Zięba G., 2004. Taxonomic position of *Bison bison* (Linnaeus 1758) and *Bison bonasus* (Linnaeus 1758) as determined by means of *CYTB* gene sequence. Anim. Sci. Pap. Rep. 22 (1), 27–35.

Reicher S., Seroussi E., Weller J. I., Rosov A., Gootwine E., 2012. Ovine mitochondrial DNA sequence variation and its association with production and reproduction traits within an Afec-Assaf flock. J. Anim. Sci. 90, 2084–2091.

Rutkowski R., Zawadzka D., Jagołkowska P., Zawadzki J., 2009. Badania genetyczne głuszca – weryfikacja danych ekologicznych i kierunków ochrony [Genetic study of the capercaillie – verified ecological data and direction of protection]. Stud. Mater. Centr. Eduk. Przyr.-Leśnej 2 (21), 75–83 [in Polish].

Simon D.K., Mayeux R., Marder K., Kowall N.W., Beal M.F., Jonson R.D., 2000. Mitochondrial DNA mutations in complex I and tRNA genes in Parkinson's disease. Neurology 54 (3), 703–709.

Singh C.S., Gaur A., Sreenivas A., Singh L., 2012. Species Identification from Dried Snake Venom. J. Forensic Sci. 57 (3), 826–828.

Słomski R., 2011. Tur od nowa [Aurochs again]. Pan. Inż. Genet. 3 (27), 4–7 [in Polish].

Sutarno, Cummins J.M., Greeff J., Lymbery A.J., 2002. Mitochondrial DNA polymorphisms and fertility in beef cattle. Theriogenology 57, 1603–1610.

Ślaska B., 2010. Genomika strukturalna jenota (*Nyctereutes procyonoides procyonoides*) [Structural genomics of the raccoon dog (*Nyctereutes procyonoides procyonoides*)]. Rozpr. Nauk. Uniw. Przyr. w Lublinie, 348.

Ślaska B., Grzybowska-Szatkowska L., 2011. Analysis of the mitochondrial haplogroups of farm and wild-living raccoon dogs in Poland. Mitochondrial DNA 22 (4), 105–110.

Ślaska B., Grzybowska-Szatkowska L., Bugno-Poniewierska M., Surdyka M., Śmiech A., 2013 a. Nuclear and mitochondrial DNA mutation in human and canine tumors. Med. Weter. 4, 195–202.

Ślaska B., Grzybowska-Szatkowska L., Nisztuk S., Surdyka M., Rozanska D., 2013 b. Mitochondrial DNA polymorphism in genes encoding ND1, *COI* and *CYTB* in canine malignant cancers. Mitochondrial DNA. DOI: 10.3109/19401736.2013.840594.

Ślaska B., Grzybowska-Szatkowska L., Surdyka M., Nisztuk S., Rozanska D., Rozanski P., Smiech A., Orzelski M., 2013 c. Mitochondrial *D-loop* mutations and polymorphisms are connected with canine malignant cancers. Mitochondrial DNA. DOI: 10.3109/19401736.2013.792054.

Ślaska B., Zięba G., Jeżewska-Witkowska G., Nisztuk S., Horecka B., Zoń A., 2014. Mitochondrialne DNA a cechy użytkowe jenotów [Mitochondrial DNA and raccoon

dogs utility traits]. Mat. Konf. Zjazd Katedr Genetyki i Metod Hodowli Zwierząt. Poznań 1–3 lipca 2014 [in Polish].

Świtoński M., 2008. Postępy genomiki zwierząt domowych [Advances in domestic animal genomics]. Nauka 1, 27–43 [in Polish].

Tan D-J., Bai R-K., Wong L-J.C., 2002. Comprehensive Scanning of Somatic Mitochondrial DNA Mutations in Breast Cancer. Cancer Res. 62, 972–976.

Tońska K., Sołyga A., Bartnik E., 2009. Mitochondria and aging: innocent bystanders or guilty parties? J. Appl. Genet. 50, 55–62.

Trifunovic A., Hansson A., Wredenberg A., Rovio A.T., Dufour E., Khvorostov I., Spelbrink J.N., Wibom R., Jacobs H.T., Larsson L–G., 2005. Somatic mtDNA mutations cause aging phenotypes without affecting reactive oxygen species production. Proc. Natl. Acad. Sci. U S A 102(50), 17993–17998.

Tsang W.Y., Lemire B.D., 2002. Mitochondrial genome content is regulated during nematode development. Biochem. Biophys. Res. Commun. 291, 8–16.

Ward R.D., Zemlak T.S., Innes B.H., Last P.R., Hebert P.D., 2005. DNA barcoding Australia's fish species. Phil. Trans. R. Soc. B: Biol Sci., 360 (1462), 1847–1857.

Wozney K.M., Wilson P.J., 2012. Real-time PCR detection and quantification of elephantid DNA: Species identification for highly processed samples associated with the ivory trade. Forensic Sci. Int. 219, 106–112.

Yen N-T., Lin C-S., Ju C-C., Wang S-C., Huang M-C., 2007. Mitochondrial DNA Polymorphism and Determination of Effects on Reproductive Traits in Pigs. Reprod. Domest. Anim. 42, 387–392.

Zhou S., Kachhap S., Sun W., Wu G., Chuang A., Poeta L., Grumbine L., Mithani S.K., Chatterjee A., Koch W., Westra W.H., Maitra A., Glazer C., Carducci M., Sidransky D., McFate T., Verma A., Califano J.A., 2007. Frequency and phenotypic implications of mitochondrial DNA mutations in human squamous cell cancers of the head and neck. Proc. Natl. Acad. Sci. USA 104 (18), 7540–7545.

ASPEKTY APLIKACYJNE GENOMIKI MITOCHONDRIALNEJ ZWIERZĄT I CZŁOWIEKA

Streszczenie. Obecnie prowadzone są intensywne badania z zakresu genomiki mitochondrialnej. Mitochondrialny DNA znajduje zastosowanie w wielu dziedzinach, takich jak: ewolucjonizm, filogeografia, antropologia, archeologia, medycyna sądowa, diagnostyka medyczna, medycyna weterynaryjna, ekologia molekularna, genetyka populacji i hodowla zwierząt. Markery, haplotypy lub haplogrupy mitochondrialne związane są z patogenezą chorób, ewolucją i pochodzeniem organizmów oraz identyfikacją gatunków. Interesującym kierunkiem badań, bazującym na sekwencjach mitochondrialnego DNA, jest poszukiwanie polimorfizmów/mutacji, które mogą mieć związek z ważnymi z ekonomicznego punktu widzenia cechami użytkowymi zwierząt gospodarskich. Wykorzystanie mtDNA ma wady, ze względu na niski stopień siły dyskryminacji i sposób dziedziczenia. Mimo to, mtDNA jako marker ma również wiele zalet, dzięki czemu jest często wykorzystywany w badaniach poznawczych, ale w głównej mierze – aplikacyjnych.

Słowa kluczowe: ekologia molekularna, genomika mitochondrialna, hodowla, medycyna, mtDNA, sądownictwo

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