Original paper

The role of Cat -262C/T, GPX1 Pro198Leu and Sod1+35A/C gene polymorphisms in a development of primary open-angle glaucoma in a Polish population

Katarzyna Malinowska[1], Michał Kowalski[2], Jerzy Szaflik[3], Jerzy P. Szaflik[3], Ireneusz Majsterek[1]

[1]Department of Clinical Chemistry and Biochemistry, Medical University of Lodz, Lodz, Poland
[2]Medical Centre Sal-Med, Lodz, Poland
[3]Department of Ophthalmology, Medical University of Warsaw, Warsaw, Poland

The development of glaucoma may be connected with a long-term exposure to oxidative stress caused by free radical (ROS). The main aim of this work was an analysis of associations of Cat-262C/T, GPX1 Pro198Leu and SOD1 35 A/C gene polymorphisms of antioxidant enzymes with a risk of open-angle glaucoma (POAG) in a Polish population.
DNA samples collected from 209 patients with POAG and 191 healthy controls were used in this study. Polymorphisms were determined by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). We found that the +35A/C polymorphisms of SOD1 were not associated with a risk of POAG. We found that C/T genotype (1-GPX1Pro198Leu, 2-Cat C262T) is associated with increased risk of open angle glaucoma (1-OR = 2.24; 95% CI: 1.46-3.44; p = 0.0001, 2-OR = 2.16; 95% CI: 1.35-3.34; p = 0.001). We also found that T/T genotype is a risk factor for progression of POAG (1-OR = 3.86; 95% Cl: 1.36-10.96; p = 0.007, 2-OR = 6.37; 95% CI: 1.39-29.28; p = 0.007). Finally our data suggest that gene polymorphisms of GPX1 Pro198Leu and CAT C262T may have a protective role in the development of primary open-angle glaucoma in a Polish population.

Key words: open-angle glaucoma, gene polymorphism, CAT, GPX1, SOD1.

Introduction

Around 70 million people currently suffer from glaucoma [1, 2] and although no comprehensive data exists, it is estimated that around 800.000 people in Poland are affected [3, 4]. Glaucoma is a dangerous, chronic, progressive eye disease characterized by optic neuropathy leading to complete vision loss. It occurs as a result of impaired outflow of aqueous humor caused by an increase in intraocular pressure. This increased pressure can lead to the destruction of retinal ganglion cells and the optic nerve. Pressure is relative, but the development of glaucoma is determined by several factors, including genetic predisposition or risk of blood circulation disorders.

Glaucoma is the most common cause of blindness, and the leading cause of irreversible blindness worldwide [5, 6]. Primary open angle glaucoma (POAG) is the most common type of glaucoma. Its incidence depends on age and is characterized by progressive loss of retinal ganglion cells (RGCs) and their axons, leading to the pathognomonic cupping of the optic nerve head [7]. Recently, epidemiological studies have indicated that apart from elevated intraocular

pressure (IOP) and age, the risk of POAG might also be associated with ethnic origin, the presence of diabetes mellitus and most significantly, genetic predisposition [8, 9, 10]. In addition, oxidative stress is a very dangerous condition that can lead to the development of glaucoma, together with many other diseases [11, 12]. Oxidative stress is defined as a shift in the pro-oxidant antioxidant balance in favor of the former caused by the production of *inter alia* reactive oxygen species (ROS) [13]. The increase in fluid volume causes an increase in intraocular pressure, which in turn results in the destruction of retinal ganglion cells and the optic nerve. Although the development of glaucoma is known to be associated with genetic predisposition and the risk of blood circulatory disorders, ROS production may also play a role. Increased levels of free radicals have been shown to lead to oxidative modification of proteins and lipid peroxidation in the circulatory system of the eye [14].

In addition, ROS and reactive nitrogen levels have been found to be elevated in various parts of the eye during glaucoma, indicating that free radical damage is associated with the progressive deterioration of the optic nerve in open angle glaucoma [15].

As the antioxidant enzyme pathway is considered the most important mechanism involved in the repair of ROS-induced damage, the present study examines the possible association between polymorphisms of superoxide dismutase (*SOD1*), catalase (*CAT*), and glutathione peroxidase (*GPX1*) genes and the development of age-related glaucoma [16]. These significant genetic variations related to oxidative stress have already been studied extensively, including the single nucleotide polymorphisms (SNP) 35 A/C of the *SOD1* gene (rs2234694), -262C/T in the promoter region of the *CAT* gene (rs1001179), and *GPX1* Pro198Leu gene (rs1050450). *SOD1* 35A/C, *CAT* -262C/T and *GPX1*.

The Pro198Leu polymorphisms can significantly influence the levels and activity of most common antioxidant enzymes, which can lead to reduced protection against oxidative stress [17, 18, 19, 20, 21].

The *SOD1*-gene has five exons. The +35A/C polymorphism (rs2234694) is adjacent to the splicing point (exon3/intron3) [16], being related to the *SOD1*-activity – AA-genotype having the higher *SOD1*-activity [22].

GPX represent one of the most important defenses of enzymatic antioxidants [23]. They serve to protect cells against oxidative damage by reducing hydrogen peroxide and a wide range of organic peroxidases to H_2O with reduced glutathione [24]. This enzyme is encoded by the *GPx1* gene, which is located at chromosome 3p21 and contains two exons within a 1.42 kb region [25]. A transition of C to T (rs:1050450) is known to exist at nucleotide 594 in exon 2 of the *GPx1* gene, corresponding to an amino acid change from proline (Pro) to leucine (Leu) at codon 198 (Pro-198Leu) [26]. Selenium enhances *GPX1* expression and increases cellular antioxidant capacity.

Catalase (CAT, EC 1.11.1.6), another component of the antioxidant system, is a tetrameric enzyme weighing 240 kDa [27]. CAT reacts very efficiently with H_2O_2, converting it to water and molecular oxygen [28]. This enzyme is largely located within cells in peroxisomes and is most abundant in erythrocytes, hepatocytes and kidney tissue [25]. The *CAT* gene itself is located on chromosome 11p13 and contains 13 exons [29, 30]. A frequently-occurring polymorphism is often present in the promoter region, consisting of a C to T (rs1001179) substitution at position -262 in the 50 region. This polymorphism influences transcription factor binding, reporter gene transcription and is correlated with blood *CAT* levels [30, 31].

It is assumed that polymorphic variations in these antioxidant genes modify the risk of glaucoma, especially when oxidative stress is increased and non-enzymatic antioxidants are deficient [32]. The purpose of the study was to evaluate the possible association between *SOD1* 35A/C, *CAT* -262A/T and *GPX1* Pro198Leu polymorphisms and the risk of age-related glaucoma in a Polish population.

Material and methods

The study analyzes *SOD1* 35A/C, *CAT* -262A/T and *GPX1* Pro198Leu polymorphisms in patients with age-related glaucoma and healthy age-matched controls. In total, a group of 400 unrelated subjects were included in the study. Peripheral blood samples were taken, and the material for DNA tests was isolated from the lymphocytes (Table I). The study group consisted of 209 unrelated patients with diagnosed POAG (79 males and 130 females; mean age 64 ±11) and a control group of 191 unrelated patients without glaucoma symptoms (90 males and 101 females; mean age 66 ±15). All patients and controls were matched on age. All subjects underwent ophthalmic examination, including best-corrected visual acuity, intraocular pressure, slit-lamp examination, gonioscopy, and fundus examination using non-contact and fundus contact lenses with a slit lamp. In the group of glaucomatous patients, the diagnosis of POAG was stated prior to enrolment, in accordance with the guidelines of European Glaucoma Society (Terminology and Guidelines for Glaucoma, Second Edition, Dogma, Savona 2003, Italy). The patients with POAG at the time of enrolment in the study were treated topically with typical anti-glaucoma medication, such as beta blockers (Timolol), prostaglandin analogs (Latanoprost), carbonic anhydrase inhibitors (Dorzolamide) or α2 agonists (Brimonidine), either alone or in combination.

Participants were enrolled from the Department of Internal Medicine, Chair of Clinical Ophthalmol-

Table I. The characteristic of open-angle glaucoma (POAG) patients

Patients	Age (years)	POAG diagnosis (years)	Intraocular pressure, IOP (mmHg)	Best corrected visual acuity, BCVA
Mean	64 ±11	9.55 ±3.4	12.2 ±1.8	0.5 ±0.12
	Gender male/female	Hypertension*	Low blood pressure**	POAG in family relatives
Number	66/130	68	31	34

** Systolic pressure ≥ 140; Diastolic pressure ≥ 90 mmHg*

*** Systolic pressure < 90; Diastolic pressure < 60 mmHg*

ogy of the Medical University of Warsaw, Poland. All subjects included into the study were Caucasian and had been recruited from the Warsaw area. This project was approved by the Ethics Committee of the Medical University of Lodz. In accordance with the Declaration of Helsinki, each subject was informed of the detailed study protocol, and gave their informed consent to take part.

Polymorphism analysis

DNA was extracted from peripheral blood lymphocytes using DNA Blood Mini Kits (A&A Biotechnology, Gdynia, Poland). Genotypes were determined by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). PCR was carried out in a volume of 25 μl. The reaction mixture consisted of 100 ng of genomic DNA, 1U Taq polymerase (Thermo Scientific), 1.5 mmol $MgCl_2$, 200 μmol dNTPs, and 0.5 μmol of each primer [33, 34]. PCR conditions were as follows. *SOD1*+35A/C: initial denaturation two minutes at 94°C, 32 cycles – 40 s at 94°C, 40 s at 55°C, 40 s at 72°C, ending with a final elongation of one minute at 72°C. RFLP was performed in a 20 μl total reaction containing 5 U of *HhaI* (Fermentas) Samples *CAT -262C/T* initial denaturation two minutes at: 94°C for 30 s, 68°C –0.5 for 45 s, 72°C for one minute, 17 cycles, then 94°C for 30 s, 60°C for 45 s, 72°C for one minute, 25 times. The final extension step was 10 minutes at 72°C. RFLP was performed in a 20 μl total reaction containing 10 U of *Sma I* (Fermentas). The PCR cycling for *GPX1* Pro198Leu initial denaturation two minutes at 95°C for three minutes, followed by 35 cycles at 95°C for 30 s, 58°C for 30 s, and 72°C for 90 s, with a final extension step at 72°C for 10 minutes. RFLP was performed in a 20 μl total reaction containing 10 U of *Apa I* (Fermentas). After digestion, the products were separated on a 2% agarose gel stained with ethidium bromide. The primers, length of PCR products and restriction enzymes are summarized in Table II.

Statistical analysis

The allele frequencies were estimated by gene counting and genotypes were scored. The χ^2 test was used to compare the observed numbers of genotypes with those expected for a population according to the Hardy-Weinberg equilibrium, and to test the significance of the differences of observed alleles and genotypes between groups. The odds ratios (ORs) and 95% confidence intervals (CIs) were calculated.

The Pearson correction was used to calculate probability, and if the expected cell values were less than five, Fisher's exact test was used. A P-value of < 0.05 was taken as statistically significant. The *t*-test was used to compare normally-distributed parameters between the two groups, and the Mann-Whitney test to compare non-normally distributed parameters. A p-value of < 0.05 was taken as statistically significant. STATISTICA 6.0 software (Statsoft, Tulsa, OK, USA) was used to perform the analyses.

Results

Analysis of polymorphisms

The genotype, allele frequency and odds ratios of the *CAT* -262C/T, *GPX1* Pro198Leu and *SOD1*+35A/C gene polymorphisms in open angle

Table II. The primers, length of PCR products and restriction enzymes

Polymorphism	Primers	Product length	Restriction enzyme
+35A/CSOD1	F: 5'-CTATCCAGAAAACACGGTGG GCC-3' R: 5'-TCTATAT TCAAT CAAATG CTACAAAACC-3'	277 bp	*Hha I* (37°C)
Cat -262C/T	F: 5'-AGA GCC TCG CCC CGC CGG ACC G-3' R: 5'-TAA GAG CTG AGA AAG CAT AGC T-3'	185 bp	*Sma* I (37°C)
GPX1 Pro198Leu	F: 5'-TGT GCC CCT ACG GTA CA-3' R: 5'-CCA AAT GAC AAT GAC ACA GG-3'	338 bp	*Apa I* (37°C)

glaucoma patients and controls are given in Tables III and IV. The observed genotype frequency of *CAT* -262C/T ($p > 0.05$: $\chi^2 = 0.0052$), *GPX1* Pro198Leu ($p > 0.05$; $\chi^2 = 0.0048$) and SOD1 35 A/C ($p > 0.05$; $\chi^2 = 0.86$) in the control group were in agreement with the Hardy-Weinberg equilibrium (HWE).

The genotype distributions of the *S0D1*+35A/C polymorphism were 92%(A/A), 6%(A/C) and 1%(C/C) in patients, and 91%(A/A), 8%(A/C) and 1%(C/C) in controls. The allele frequencies of *S0D1* for the +35A and +35C were 95% and 5% in controls, compared with 95% and 5% in patients ($p = 0.92$). The distribution of genotypes of the *GPX1* Pro198Leu polymorphism were 50% (C/C), 43 % (C/T) and 7% (T/T) for patients, and 71% (C/C), 27% (C/T) and 3% (T/T) for controls. The respective allele frequencies for -198C and -198T were 72% and 28% in patients and 84% and 16% in controls ($p < 0.0001$). The distribution of genotypes of the *Cat* -262C/T polymorphism were 63% (C/C), 32% (C/T) and 5% (T/T) for patients, and 89% (C/C), 19% (C/T) and 1% (T/T) for controls. The allele frequencies for the -262C and -262T were 79% and 21% in patients and 90% and 10% in controls ($p < 0.0001$).

Logistical regression analysis was used to assess the relationship between all the investigated polymorphisms and the risk of developing glaucoma. Subjects carrying the +35A/C (OR = 0.77 [0.34-1.57]; p = 0.42) and = 35C/C (OR = 0.13 [0.03-2.91]; p = 0.35) genotypes of *S0D1* had no significant risk of developing POAG. A significant relationship was found between the combined genotypes of CT/AA (OR = 0.37, 95% CI: 0.23-0.59), CT/CC *S0D1*+35A/C /*GPx1* Pro198Leu (OR = 0.04, 95% CI: 0.005-0.29) and TT/AA (OR = 0.23, 95% CI: 0.11-0.45) *S0D1*+35A/C /*GPx1* Pro198Leu. The genotype CC/AC *S0D1*+35A/C/*CAT*-262C/T was also observed (OR = 0.09, 95% CI: 0.036-0.25). We conclude that these genotypes reduce the risk of developing glaucoma.

Discussion

The present study examines the relationship between the risk of glaucoma in a Polish population and the occurrence of the *S0D1*, *CAT* and *GPX1*-198 C/T gene polymorphisms. It also attempts to determine their influence on the activity of antioxidant enzymes, resulting in synergistic effects of glaucoma-

Table III. Genotype and allele frequencies for *Cat -262C/T*, *GPX1* Pro198Leu and *S0D1*+35A/C in primary open-angle glaucoma (POAG) patients and control subjects

Genotype/Allele	Patients (POAG) (n = 209) (frequency)	Controls (n = 191) (frequency)	OR (95% CI)	P value
S0D1				
A/A	193 (0.92)	174 (0.91)	Ref	
A/C	13 (0.06)	16 (0.08)	0.73 (0.34-1.57)	0.42
C/C	3 (0.01)	1 (0.01)	0.13 (0.03-2.91)	0.35
A	399 (0.95)	364 (0.95)	Ref	
C	19 (0.05)	18 (0.05)	0.96 (0.49-1.86)	0.92
GPX1Pro198Leu	**Patients (n = 209)**	**Controls (n = 191)**	**OR (95% CI)**	**P value**
C/C	105 (0.50)	135 (0.71)	Ref	
C/T	89 (0.43)	51 (0.27)	**2.24 (1.46-3.44)**	**0.0001**
T/T	15 (0.07)	5 (0.03)	**3.86 (1.36-10.96)**	**0.007**
C	299 (0.72)	321 (0.84)	Ref	
T	119 (0.28)	61 (0.16)	**2.09 (1.48-2.96)**	< 0.0001
Cat -262C/T	**Patients (n = 209)**	**Controls (n = 191)**	**OR (95% CI)**	**P value**
C/C	131 (0.63)	153 (0.89)	Ref	
C/T	67 (0.32)	36 (0.19)	**2.16 (1.35-3.44)**	**0.0001**
T/T	11 (0.05)	2 (0.01)	**6.37 (1.39-29.28)**	**0.007**
C	331 (0.79)	342 (0.90)	Ref	
T	89 (0.21)	40 (0.10)	**2.29 (1.54-3.43)**	< 0.0001

Table IV. The distribution of double-combined genotypes of the *Sod1+35A/C/GPXPro198Leu and Sod1+35A/C/Cat-262C/T* of primary open-angle glaucoma (POAG) patients and control subjects.

Genotype	Patients (POAG) (n = 209) (frequency)	Controls (n = 191) (frequency)	OR (95% CI)	P value
Sod1+35A/C/GPXPro198Leu				
CC/AA	97 (0.46)	43 (0.23)	Ref	
CC/AC	5 (0.02)	0 (0.00)	–	
CC/CC	103 (0.50)	0 (0.00)	–	
CT/AA	86 (0.41)	103 (0.54)	**0.37 (0.23-0.59)**	**< 0.0001**
CT/AC	2 (0.01)	0 (0.00)	–	
CT/CC	1 (0.00)	12 (0.06)	**0.04 (0.005-0.29)**	**< 0.0001**
TT/AA	17 (0.08)	33 (0.17)	**0.23 (0.11-0.45)**	**< 0.0001**
TT/AC	0 (0.00)	0 (0.00)	–	
TT/CC	0 (0.00)	0 (0.00)	–	
Sod1+35A/C/Cat-262C/T	**Patients (n = 209)**	**Controls (n = 191)**		
CC/AA	130 (0.62)	103 (0.54)	Ref.	
CC/AC	5 (0.02)	42 (0.22)	**0.09 (0.036-0.25)**	**< 0.0001**
CC/CC	1 (0.00)	0 (0.00)	-	
CT/AA	49 (0.23)	25 (0.13)	1.55 (0.89-2.68)	0.147
CT/AC	14 (0.07)	20 (0.10)	0.55 (0.27-1.15)	0.157
CT/CC	7 (0.03)	0 (0.00)	–	
TT/AA	0 (0.00)	1 (0.01)		
TT/AC	3 (0.01)	0 (0.00)	–	
TT/CC	0 (0.00)	0 (0.00)	–	

induced oxidative damage. The *CAT* -262C/T, *GPX1* Pro198Leu and *SOD1* +35A/C polymorphisms were associated with an increased risk of glaucoma. These findings support the hypothesis that genetic variations in antioxidant defense may modify the risk of glaucoma among individuals with elevated oxidative stress or decreased antioxidant capacity [33, 34, 35, 36].

The present study examines the effect of serum SOD1, GPX and CAT1 level on the eye. The *CAT* gene encodes catalase, a common enzyme found in nearly all living organisms exposed to oxygen. It maintains the oxidative status of the body and plays an important role in protecting eukaryotic cells from entering premature apoptosis. Catalase is a heme aerobic cells. The enzyme is present in almost all paroxysms and reduces the toxic activity of hydrogen peroxide ROS by converting them to water and oxygen [37].

Recent studies indicate that free radicals play a crucial role of in the pathogenesis of many diseases, including such diseases of the eye as cataract, glaucoma and age-related macular degeneration. Free radicals are formed in trace amounts as by-products of metabolism and cause premature cell death. In addition, the amount of dangerous free radicals increases following trauma or neurodegenerative diseases [38, 39, 40, 41, 42].

Parkinson's disease, Alzheimer's or multiple sclerosis (MS) are some of the most common neurodegenerative diseases [43]. These are associated with progressive damage to the pigment cells of the substantial nigra midbrain: cells which are responsible for the synthesis of dopamine under physiological conditions, which they use as a neurotransmitter [44, 45, 46, 47, 48, 49]. Patients with Alzheimer's and Parkinson's disease are more likely to suffer from glaucoma than healthy people, and severe adverse reactions location biochemical, i.e. glycosylation, formation and carbonylation AEGs. During glycosylation, protein molecules bind to glucose molecules, leading to the formation of damaged and dysfunctional structures with reduced biological activity. Many age-related diseases such as hardening of the arteries, cataracts and neurological diseases arise, at least in part, due to glycosylation. The accumulation

of protein in tissue is a clear sign of disease. An ideal supplement for people with an increased risk of such degenerative diseases, or who have suffered from them, is carnosine. It has been found to prevent the formation of these radicals, and is known to be effective against both oxidative stress and the resulting synuclein [50].

Izzotti *et al*. analyzed the frequency of mitochondrial (mtDNA) DNA damage in primary open angle glaucoma. Oxidative damage is known to play an important role in the pathogenesis of glaucoma, and their results indicate that mitochondria are targeted by the effects of glaucoma. These findings may be valuable for the development of new molecular biomarkers of glaucoma and to identify potential patients at high risk [51]. One of the most influential factors regarding individual susceptibility to complex diseases is represented by the presence of SNPs. Since ROSs have a high potential to interact with genetic material, SNPs in genes coding for antioxidant enzymes may have an important influence on individual differences in the ability to maintain the integrity of the human genome. Genetic polymorphisms in *CAT*, *GPx1* and *SOD* have been associated with the potential to develop various diseases including cancer [46, 47, 48].

The presence of the C/T genotype (1-*GPX1* Pro198Leu, 2-*CAT* C262T) was found to be associated with an increased risk of open angle glaucoma (OR = 2.24, p = 0.0001, OR = 2.16, p = 0.001). Our findings indicate that the combined genotypes CT/AA, CT/AC and CT/CC of Sod1+35A/C *GPX1* Pro198Leu may be associated with a reduced risk of POAG among the Polish population. In addition, in contrast to earlier research, they indicate that the prevalent polymorphisms *CAT* -262C/T, *GPX1* Pro198Leu and *SOD1*+35A/C in the Polish population have toxicogenetic effects.

There is currently a lack of research into the gene-gene interactions and the role of the *SOD1*-251A, *CAT* G/T and T-21A *GPX1*-198C polymorphisms of antioxidant enzymes in patients with open-angle glaucoma. Recent studies have indicated that the *SOD1*-251 A/G polymorphism is associated with reduced antioxidant capacity [52, 53]. Therefore, our findings indicate that individuals with impaired antioxidant activity may have a predisposition to diseases associated with oxidative stress. Our study provides a framework for future studies concerning the role of polymorphic variants of *CAT*, *SOD1* and *GPX1* antioxidant enzymes in the development of glaucoma associated with long-term exposure to free radicals. Most importantly, our findings indicate that the *GPX1* Pro198Leu and *SOD1*+35A/C gene polymorphisms may play a protective role in the risk of glaucoma development in a Polish population.

The authors declare no conflict of interest.

References

1. Quigley HA, Broman AT. The number of people with glaucoma worldwide in 2010 and 2020. Br J Ophthalmol 2006; 90: 262-267.
2. Czajkowski J. W poszukiwaniu skutecznego farmakologicznego leczenia jaskry pierwotnej otwartego kąta [Looking for effective primary open angle glaucoma pharmacological treatment]. Okulistyka 2009; 1: 19-23.
3. Szaflik J, Zaleska-Żmijewska A, Ambroziak AM, et al. Epidemiologia jaskry – dane światowe [Worldwide data on glaucoma epidemiology]. Okulistyka 2008; 1: 13-14.
4. Cook C, Foster P. Epidemiology of glaucoma: what's new? Can J Ophthalmol 2012; 47: 223-226.
5. Kowalski M, Walczak A, Majsterek I. Matrix metalloproteinases (MMPs): Modern molecular markers of open-angle glaucoma diagnosis and therapy. Postepy Hig Med Dosw (Online) 2008; 62: 582-592.
6. Nizankowska MH, Kaczmarek R. Prevalance of glaukoma in the Wroclaw population. The Wroclaw epidemiological study. Ophthalmic Epidemiol 2005; 12: 363-371.
7. Markiewicz L, Majsterek I, Przybylowska K, et al. Gene polymorphisms of the MMP1, MMP9, MMP12, IL-1β and TIMP1 and the risk of primary open-angle glaucoma. Acta Ophthalmol 2013; 91: 516-523.
8. Flammer J, Orgul S, Costa VP, et al. The impact of ocular blood flow in glaucoma. Prog Retin Eye Res 2002; 21: 359-393.
9. Marcic TS, Belyea DA, Katz B. Neuroprotection in glaucoma: a model for neuroprotection in optic neuropathies. Curr Opin Ophthalmol 2003; 14: 353-356.
10. Waliszek-Iwanicka A, Waliszek M, Banach MM, et al. Assessment of blood flow in posterior ciliary arteries and its correlation with intraocular and arterial blood pressures in patients with open angle glaucoma. Med Sci Monit 2010; 16: 501-509.
11. Spector A. Oxidative stress-induced cataract: mechanism of action. FASEB J 1995; 9: 1173-1182.
12. Rajkumar S, Praveen MR, Gajjar D, et al. Activity of superoxide dismutase isoenzymes in lens epithelial cells derived from different types of age-related cataract. J Cataract Refract Surg 2008; 34: 470-474.
13. Betteridge DJ. What is oxidative stress? Metabolism 2000; 49: 3-8.
14.
15. Mariani E, Polidori MC, Cherubini A, et al. Oxidative stress in brain aging, neurodegenerative and vascular diseases: an overview. J Chromatogr B Analyt Technol Biomed Life Sci 2005; 827: 65-75.
16. Cuchra M, Szymanek K, Szaflik JP, et al. Rola polimorfizmów 751lys/genuXPD oraz 939lys/glin genu XPC w rozwoju jaskry pierwotnej otwartego kąta [The role of the 751Lys/Gln XPD and 939 Lys/Gln XPC genes polymorphism in the pathogenesis of primary open-angle glaucoma]. Okulistyka 2015; 18: 13-18.
17. Lal MA, Brismar H, Eklof AC, et al. Role of oxidative stress in advanced glycation end product-induced mesangial cell activation. Kidney Int 2002; 61: 2006-2014.
18. Cebrian A, Pharoah PD, Ahmed S, et al. Tagging Single-Nucleotide Polymorphisms in Antioxidant Defense Enzymes and Susceptibility to Breast Cancer. Cancer Res 2006; 66: 1225-1233.
19. Ukkola O, Erkkilae PH, Savolainen MJ, et al. Lack of association between polymorphisms of catalase, copper-zinc superoxide dismutase (SOD), extracellular SOD and endothelial nitric oxide synthase genes and macroangiopathy in patients with type 2 diabetes mellitus. J Intern Med 2001; 249: 451-459.
20. Tiwari AK, Prasad P, Kumar BKT, et al. Oxidative stress pathway genes and chronic renal insufficiency in Asian Indians with Type 2 diabetes. J Diabetes Complications 2009; 23: 102-111.

21. Rajaraman P, Hutchinson A, Rothman N, et al. Oxidative response gene polymorphisms and risk of adult brain tumors. Neuro Oncol 2008; 10: 709-715.
22. Bastaki M, Huen K, Manzanillo P, et al. Genotype-activity relationship for Mn-superoxide dismutase, glutathione peroxidase 1 and catalase in humans. Pharmacogenet Genomics 2006; 16: 279-286.
23. Tan AL, Forbes JM, Cooper ME. AGE, RAGE, and ROS in diabetic nephropathy. Semin Nephrol 2007; 27: 130-143.
24. Arthur JR. The glutathione peroxidases. Cell Mol Li Sci 2000; 57: 1825-1835.
25. Flohe L. Glutathione peroxidase. Basic Life Sci 1998; 49: 663-668.
26. Ishida K, Morino T, Takagi K, et al. Nucleotide sequence of a human gene for glutathione peroxidase. Nucleic Acids Res 1987; 15: 10051.
27. Forsberg L, de Faire U, Morgenstern R. Low yield of olymorphisms from EST blast searching: analysis of genes related to oxidative stress and verification of the P197L polymorphism in GPX1. Hum Mutat 1999; 13: 294-300.
28. Mates JM, Perez-Gomez C, Nunez de Castro CL. Antioxidant enzymes and human diseases. Clin Biochem 1990; 32: 595-603.
29. Mueller CS, Riedel HD, Stremmel W. Direct evidence for catalase as the predominant H_2O_2-removing enzyme in human erythrocytes. Blood 1997; 90: 4973-4978.
30. Forsberg L, de Faire U, Morgenstern R. Oxidative stress, human genetic variation, and disease. Arch Biochem Biophys 2001; 389: 84-93.
31. Quan F, Korneluk RG, Tropak MB, Gravel RA. Isolation and characterization of the human catalase gene. Nucleic Acids Res 1986; 14: 5321-5335.
32. Forsberg L, Lyrenas L, de Faire U, et al. A common functional C-T substitution polymorphism in the promoter region of the human catalase gene influences transcription factor binding, reporter gene transcription and is correlated to blood catalase levels. Free Radic Biol Med 2001; 30: 500-505.
33. Malinowska K, Gacek M, Zaleska A, et al. Suplementacja melatoniną oraz związek statusu antyoksydacyjnego z patogenezą jaskry pierwotnej otwartego kąta [Supplementation of melatonin and the role of total antioxidant status]. Okulistyka 2011; 1: 97-100.
34. Panduru NM, Cimponeriu D, Cruce M, et al. Association of +35A/C (intron3/exon3) polymorphism in SOD1-gene with diabetic nephropathy in type 1 diabetes. Rom J Morphol Embryol 2010; 51: 37-41.
35. Suzen HS, Gucyener E, Sakalli O, et al. CAT -262C/T and GPX1 Pro198Leu polymorphisms, in a Turkish population. Mol Biol Rep 2010; 37: 87-92.
36. Malinowska K, Szaflik JP, Majsterek I, et al. Procesy pro- i antyoksydacyjne w medycynie ze szczególnym uwzględnieniem jaskry [Pro- and antioxidant processes in medicine with particular emphasis on glaucoma]. Okulistyka 2012; 2: 60.
37. Zhang Y, Zhang L, Sun D, et al. Genetic polymorphisms of superoxide dismutases, catalase, and glutathione peroxidase in age-related cataract. Mol Vis 2011; 17: 2325-2332.
38. Majsterek I, Malinowska K, Stanczyk M, et al. Evaluation of oxidative stress markers in pathogenesis of primary open-angle glaucoma. Exp Mol Pathol 2011; 90: 231-237.
39. Forsberg L, Faire U, Morgenstern R. Oxidative stress, human genetic variation, and disease. Arch Biochem Biophys 2001; 389: 84-93.
40. Tang H, Dong X, Day RS, et al. Antioxidant genes, diabetes and dietary antioxidants in association with risk of pancreatic cancer. Carcinogenesis 2010; 31: 607-613.
41. Flekac M, Skrha,J, Hilgertova J, et al. Gene polymorphisms of superoxide dismutases and catalase in diabetes mellitus. BMC Med Genet 2008; 9: 30.
42. Cebrian A, Pharoah PD, Ahmed S, et al. Tagging single-nucleotide polymorphisms in antioxidant defense enzymes and susceptibility to breast cancer. Cancer Res 2006; 66: 1225-1233.
43. Juronen E, Tasa G, Veromann S, et al. Polymorphic glutathione S-transferases as genetic risk factors for senile cortical cataract in Estonians. Invest Ophthalmol Vis Sci 2000; 41: 2262-2267.
44. Lin TL, Beal MF. Mitochondrial dysfunction and oxidative stress in neurodegenerative diseases. Nature 2006; 443: 787-795.
45. Truscott RJW. Age-related nuclear cataract-oxidation is the key. Exp Eye Res 2005; 80: 709-725.
46. Faschinger, Schmut O, Wachswender C, et al. Glaucoma and oxidative stress. Determination of malondialdehyde-a product of lipid peroxidation. Ophthalmologe 2006; 103: 953-959.
47. Tezel G. Oxidative stress in glaucomatous neurodegeneration mechanisms and consequences. Prog Retin Eye Res 2006; 25: 490-513.
48. Tezel G, Luo C, Yang X. Accelerated aging in glaucoma immunohistochemical assessment of advanced glycation end products in the human retina and optic nerve head. Invest Ophthalmol Vis Sci 2007; 48: 1201-1211.
49. Brennan lM, Kantorow M. Mitochondrial function and redox control in the aging eye Role of MsrA and other repair systems in cataract and macular degenerations. Exp Eye Res 2009; 88: 195-203.
50. Hollyfield JG, Bonilha VL, Rayborn ME, et al. Oxidative damage-induced inflammation initiates age-related macular degeneration. Nat Med 2008; 14: 194-198.
51. Hegde KR, Varma SD. Prevention of oxidative stress to the retina by pyruvate. A preliminary report. Ophthalmologica 2008; 222: 194-198.
52. Izzotti A, Longobard M, Cartiglia IC, et al. Proteome alterations in primary open angle glaucoma aqueous humor. J Proteome Res 2010; 9: 4831-4838.
53. Tiwari AK, Prasad P, Kumar BKT, et al. Oxidative stress pathway genes and chronic renal insufficiency in Asian Indians with Type 2 diabetes. J Diabetes Complications 2009; 23: 102-111.
54. Rajaraman P, Hutchinson A, Rothman N, et al. Oxidative response gene polymorphisms and risk of adult brain tumors. Neuro Oncol 2008; 10: 709-715.

Address for correspondence

Katarzyna Malinowska
Department of Chemistry and Clinical Biochemistry
Medical University of Lodz
Hallera 1 square
90-647 Lodz, Poland
e-mail: modmal@wp.pl