Oxidative-Stress-Related Genetic Determinants of Skin Aging: Integrated Effects of *GSTM1*, *GSTT1*, *GSTP1*, *SOD2*, and *GPX1*

A Literature Review

Sabrina Frauenschuh[1], Magdalena Behensky[1], René Rohrmanstorfer[1], Thomas Dullnig[1], Daniel Wallerstorfer[1]

[1]*Laboratory, Novogenia GmbH, Salzburg, Austria*

Corresponding Author: Daniel Wallerstorfer (ceo@novogenia.com)

ABSTRACT

Background. Oxidative stress is a key biological driver of both intrinsic and extrinsic skin aging, connecting mitochondrial reactive oxygen species formation with lipid peroxidation, inflammatory signaling, and extracellular matrix degradation. In this context, the genes *GSTM1*, *GSTT1*, *GSTP1*, *SOD2*, and *GPX1* define a biologically coherent network centered on glutathione-dependent detoxification and mitochondrial antioxidant defense. Altered activity within these pathways directly influences the capacity of the skin to neutralize reactive intermediates and modulate susceptibility to cumulative oxidative damage and age-associated tissue changes (Rinnerthaler et al., 2015; Kammeyer and Luiten, 2015; Treiber et al., 2012).

Methods. A narrative review was undertaken to highlight evidence on oxidative-stress-related antioxidant pathways in skin aging. Particular emphasis was placed on studies addressing the physiological roles of *GSTM1*, *GSTT1*, *GSTP1*, *SOD2*, and *GPX1*, the functional consequences of deletion polymorphisms and single-nucleotide variants, and their relevance to cutaneous aging. Additional focus was placed on investigations of antioxidant and micronutrient-based interventions as modulators of redox homeostasis, tissue protection, and oxidative damage in skin biology. Studies were considered in relation to their ability to clarify molecular mechanisms of oxidative-stress regulation, including mitochondrial ROS handling, glutathione-dependent detoxification, and peroxide metabolism. Attention was also given to translational evidence linking these pathways to skin-relevant outcomes and to intervention strategies aimed at supporting antioxidant resilience in the context of genetically influenced redox vulnerability (Rinnerthaler et al., 2015; Kammeyer and Luiten, 2015; Sepetiene et al., 2023).

Results. The literature supports a substantial role for the investigated oxidative-stress-related variants in the regulation of cutaneous redox homeostasis. Variability in *GSTM1*, *GSTT1*, *GSTP1*, *SOD2*, and *GPX1* is functionally significant because these genes act at complementary levels of antioxidant defense, including the detoxification of reactive oxygen species, lipid hydroperoxides, and electrophilic oxidation products. Altered function within these pathways therefore influences the skin's ability to withstand ultraviolet radiation, pollution, and other environmental stressors that promote cumulative oxidative damage and age-associated tissue deterioration. In this context, alpha-lipoic acid, vitamin C, and vitamin E represent supportive

interventions owing to their antioxidant and redox-regenerative properties, whereas zinc and manganese are additionally relevant because of their contribution to endogenous antioxidant systems and enzymatic activity. Taken together, these observations establish that targeted antioxidant and micronutrient-based strategies support antioxidant defense when oxidative defense capacity is reduced (Rinnerthaler et al., 2015; Kammeyer and Luiten, 2015; Treiber et al., 2012).

Discussion. The available evidence indicates that variation in *GSTM1*, *GSTT1*, *GSTP1*, *SOD2*, and *GPX1* modifies key antioxidant and detoxification processes involved in cutaneous redox homeostasis. Because these genes participate in complementary steps of reactive oxygen species neutralization, peroxide metabolism, and glutathione-dependent detoxification, altered function within this network contributes to differences in susceptibility to environmentally induced oxidative damage and, consequently, to interindividual variability in skin-aging trajectories. Within this mechanistic context, vitamins C and E, alpha-lipoic acid, zinc, and manganese are relevant supportive interventions because of their roles in antioxidant regulation and cellular defense (Al-Niaimi and Chiang, 2017; Beitner, 2003; Rostan et al., 2002).

Subjects: Genetics, Beauty. **Keywords:** Genetics, Polymorphism, Beauty, Oxidative Stress.

INTRODUCTION

Skin aging results from the cumulative interaction of intrinsic senescence and extrinsic environmental damage, with oxidative stress representing one of the principal mechanistic links between these processes. In cutaneous tissue, reactive oxygen species (ROS) arise from mitochondrial respiration, ultraviolet radiation, pollution, inflammation, and normal cellular metabolism. When ROS production exceeds antioxidant buffering capacity, oxidative damage accumulates in lipids, proteins, DNA, and extracellular matrix components, thereby contributing to wrinkle formation, loss of elasticity, dyschromia, and impaired tissue repair (Rinnerthaler et al., 2015; Kammeyer and Luiten, 2015; Poljšak et al., 2012).

Within this mechanistic framework, particular attention is directed toward *GSTM1*, *GSTT1*, *GSTP1*, *SOD2*, and *GPX1*, a group of genes that collectively contribute to glutathione-dependent detoxification and mitochondrial antioxidant defense. These pathways are of direct relevance to cutaneous biology because the skin is continuously exposed to both endogenous and environmental oxidant-generating stimuli. Accordingly, this gene network constitutes the framework through which the influence of inherited variation in redox regulation on detoxification capacity, oxidative resilience, and susceptibility to age-associated structural and functional alterations in the skin can be examined. Functional perturbation within these pathways favours the persistence of reactive intermediates and amplifies lipid peroxidation, inflammatory signaling, and extracellular matrix remodeling. Because *GSTM1*, *GSTT1*, and *GSTP1* participate in glutathione-dependent neutralization of electrophilic by-products, whereas *SOD2* and *GPX1* regulate sequential mitochondrial ROS detoxification, variation across these loci is biologically positioned to influence multiple levels of

cutaneous redox homeostasis. This is of particular importance under conditions of chronic ultraviolet and environmental exposure, in which repeated oxidative challenge may accelerate collagen degradation and impair tissue maintenance. As a result, interindividual differences in these antioxidant-defense pathways determine variability in the rate and extent of visible and molecular skin-aging changes (Rinnerthaler et al., 2015; Kammeyer and Luiten, 2015; Poljšak et al., 2012).

REACTIVE OXYGEN SPECIES AND ANTIOXIDANT NETWORKS IN SKIN AGING

The oxidative-stress framework can be conceptualized as a stepwise biological process. Mitochondria generate superoxide during oxidative phosphorylation. This radical is converted by manganese superoxide dismutase, encoded by *SOD2*, into hydrogen peroxide, which is subsequently detoxified by glutathione peroxidase 1, encoded by *GPX1*. In parallel, glutathione S-transferases such as *GSTM1*, *GSTT1*, and *GSTP1* facilitate the conjugation of glutathione to reactive electrophilic compounds, including oxidized lipid derivatives and xenobiotic intermediates. If one or more components of this network are less efficient, oxidative injury may accumulate over time and contribute to inflammatory signaling, collagen degradation, cellular senescence, and impaired barrier maintenance (Treiber et al., 2012; Rinnerthaler et al., 2015). This framework is particularly relevant to skin aging because the skin is persistently exposed to oxidant-generating stimuli. Ultraviolet radiation and airborne pollutants increase ROS production, initiate lipid peroxidation, and stimulate matrix metalloproteinases that degrade collagen and elastin. Accordingly, inherited variation in antioxidant-defense genes may influence the threshold at which cumulative oxidative damage becomes clinically visible as premature or accelerated cutaneous aging (Rinnerthaler et al., 2015; Kammeyer and Luiten, 2015; Treiber et al., 2012).

ANTIOXIDANT GENE VARIANTS RELEVANT TO CUTANEOUS OXIDATIVE STRESS

Variation in genes involved in glutathione-dependent detoxification and mitochondrial reactive oxygen species handling influences the efficiency with which the skin responds to oxidative challenge. Of particular relevance are *GSTM1*, *GSTT1*, *GSTP1*, *SOD2*, and *GPX1*, which act at complementary stages of electrophile detoxification, superoxide conversion, and peroxide clearance. Functional differences across these loci may therefore contribute to interindividual variability in oxidative-stress susceptibility and in the molecular processes underlying cutaneous aging (Rinnerthaler et al., 2015; Kammeyer and Luiten, 2015; Treiber et al., 2012).

GLUTATHIONE-DEPENDENT SKIN DETOXIFICATION: *GSTM1* AND *GSTT1* VARIANTS

GSTM1 and *GSTT1* encode cytosolic glutathione S-transferases involved in phase II detoxification through the conjugation of glutathione to reactive electrophilic compounds. This reaction contributes to the neutralization and elimination of potentially harmful intermediates generated during endogenous oxidative processes as well as in response to environmental exposures. In cutaneous tissue, these enzymes are of particular relevance because oxidative stress gives rise to electrophilic secondary products, including lipid-peroxidation derivatives, that may disrupt structural

proteins, membranes, and redox-sensitive signaling pathways if not efficiently detoxified (Rinnerthaler et al., 2015; Kammeyer and Luiten, 2015; Ghelli et al., 2021).

The characterization of *GSTM1* and *GSTT1* deletion variants as biologically significant is well supported. In most cases, these polymorphisms reflect homozygous gene deletions and are therefore associated with absent enzyme expression. Functionally, such deletion states reduce the reserve capacity of glutathione-mediated detoxification pathways. Published studies have linked these variants to altered oxidative-stress responses and modified susceptibility to environmentally mediated damage, supporting their relevance as modulators of redox homeostasis beyond their established role in exposure-related disease association studies (McWilliams et al., 1995; Wenzlaff et al., 2005; Ghelli et al., 2021).

From the perspective of skin aging, the direct consequence of reduced *GSTM1* or *GSTT1* activity is a diminished ability to clear reactive by-products of oxidative stress over time. Under conditions of chronic exposure to ultraviolet radiation, tobacco smoke, or air pollution, this lower detoxification capacity favours cumulative molecular injury and contributes to increased susceptibility to oxidative components of cutaneous aging (Rinnerthaler et al., 2015; Kammeyer and Luiten, 2015; Poljšak et al., 2012).

GSTP1 (RS1695) AND GLUTATHIONE-DEPENDENT OXIDATIVE-STRESS SUSCEPTIBILITY IN SKIN

GSTP1 encodes glutathione S-transferase pi, an important enzyme within glutathione-dependent detoxification pathways. In contrast to *GSTM1* and *GSTT1*, in which structural gene deletions are of primary functional relevance, allelic variation at the rs1695 locus includes a missense change that can modify *GSTP1* enzymatic activity and substrate handling. In the literature, this allelic variant has been associated with altered catalytic behavior and differences in substrate handling, supporting its relevance as a functional determinant of oxidative-stress defense (Watson et al., 1998; Sreeja et al., 2008).

This distinction is important for scientific interpretation. Allelic variation at GSTP1 rs1695 can modify enzymatic activity and substrate handling. More favorable allelic constellations are associated with better detoxification capacity, whereas less favorable constellations may reduce GSTP1-mediated oxidative defense. Experimental and association studies support the view that *GSTP1* genotype influences oxidative susceptibility and lipid-peroxidation profiles (Watson et al., 1998; do Nascimento et al., 2021).

In cutaneous biology, reduced *GSTP1*-mediated detoxification efficiency impairs the neutralization of electrophilic oxidative by-products generated during repeated environmental stress. Over prolonged periods of exposure, even modest differences in detoxification capacity contribute to cumulative molecular damage, establishing *GSTP1* as a relevant modifier of oxidative-stress susceptibility in skin aging (Rinnerthaler et al., 2015; Kammeyer and Luiten, 2015; Poljšak et al., 2012).

MITOCHONDRIAL SUPEROXIDE DETOXIFICATION AND THE *SOD2* (RS4880) VARIANT

SOD2 encodes manganese superoxide dismutase, the principal mitochondrial enzyme responsible for converting superoxide anion into hydrogen peroxide. Because mitochondria are a major endogenous source of ROS, *SOD2* occupies an upstream position in the cellular antioxidant hierarchy. In skin, mitochondrial oxidative stress has been implicated in fibroblast dysfunction, senescence-associated signaling, and age-related deterioration of the extracellular matrix (Treiber et al., 2012; Rinnerthaler et al., 2015; Kammeyer and Luiten, 2015).

Allelic variation at *SOD2* rs4880 is functionally important because it is located in the mitochondrial targeting sequence of MnSOD. Functional studies have shown that allelic variation at this locus influences mitochondrial import efficiency and affects mRNA stability, thereby altering the effective antioxidant performance of the enzyme. Accordingly, the polymorphism is a functional modifier of mitochondrial ROS handling, not a marker variant (Sutton et al., 2003; Sutton et al., 2005; Paludo et al., 2014).

A less favorable *SOD2* genotype lowers the threshold at which mitochondrial oxidative burden accumulates during environmental or metabolic stress. In skin, where repeated oxidant exposure is common, such a genotype contributes to greater ROS persistence, enhanced downstream oxidative signaling, and more rapid accumulation of aging-associated damage. This is supported by the broader literature linking *SOD2* variation to oxidative-stress phenotypes and age-related biology (Treiber et al., 2012; Sørensen et al., 2009; Paludo et al., 2014).

GLUTATHIONE PEROXIDASE ACTIVITY AND THE *GPX1* (RS1050450) VARIANT

GPX1 encodes glutathione peroxidase 1, an antioxidant enzyme that reduces hydrogen peroxide and lipid hydroperoxides using glutathione as a substrate. Within the antioxidant cascade, GPx1 functions directly downstream of MnSOD: after superoxide is converted to hydrogen peroxide by *SOD2*, GPx1 limits the persistence of peroxides that would otherwise propagate oxidative injury (Arthur, 2000; Rinnerthaler et al., 2015).

Allelic variation at *GPX1* rs1050450 has been associated with altered enzyme activity and with context-dependent differences in oxidative-stress regulation. This is particularly relevant because GPx1 occupies a central position in peroxide detoxification, and variation at this locus therefore influences the efficiency with which oxidative intermediates are neutralized. At *GPX1* rs1050450, less favorable allelic constellations reduce oxidative protection (Chen et al., 2011; Cominetti et al., 2011; Karunasinghe et al., 2012).

In the context of skin aging, diminished GPx1 efficiency permits greater accumulation of hydrogen peroxide and lipid hydroperoxides, thereby contributing to membrane damage, inflammatory signaling, and oxidative modification of structural proteins. Because this gene acts in sequence with *SOD2*, the biological significance of *GPX1* variation is magnified when both loci are less favourable (Kammeyer and Luiten, 2015; McKeever et al., 2021; Rinnerthaler et al., 2015).

MECHANISM-BASED ANTIOXIDANT AND MICRONUTRIENT INTERVENTIONS FOR REDUCED OXIDATIVE-STRESS RESILIENCE

From a translational perspective, intervention strategies for reduced oxidative-stress resilience should be directed toward strengthening endogenous antioxidant defenses, attenuating the propagation of reactive oxygen species and lipid-peroxidation intermediates, and supporting cofactor-dependent pathways within mitochondrial and glutathione-mediated redox networks. This framework is particularly relevant when variation in *GSTM1*, *GSTT1*, *GSTP1*, *SOD2*, and *GPX1* is considered in combination, as functional alterations across multiple levels of oxidative defense may cumulatively compromise cutaneous resilience to ultraviolet exposure, pollution, and inflammatory stress. Within this context, vitamin C is of particular importance because it contributes to antioxidant defense and collagen homeostasis, vitamin E because it limits lipid-phase oxidative injury, and alpha-lipoic acid because of its broader redox-regenerative capacity; these compounds support cutaneous antioxidant function both through dietary intake and, when appropriately formulated, through topical delivery to the skin. Zinc and manganese are likewise important, primarily as nutritional factors that support endogenous antioxidant systems and enzymatic homeostasis, including pathways relevant to mitochondrial redox regulation (Rinnerthaler et al., 2015; Eberlein-König and Ring, 2005; Treiber et al., 2012).

Vitamin C

Vitamin C is a core supportive compound within this framework because it contributes directly to antioxidant defense while also supporting collagen homeostasis. In skin, it can reduce oxidative burden, participate in redox recycling, and promote matrix maintenance, which is essential in settings characterized by persistent oxidative challenge and cumulative tissue damage. In addition, ascorbate is functionally linked to collagen biosynthesis through its role in the enzymatic processing of procollagen, thereby connecting antioxidant defense with structural preservation of the dermal matrix. This dual relevance establishes vitamin C as a primary intervention in phenotypes where oxidative injury and extracellular matrix deterioration occur in parallel (Al-Niaimi and Chiang, 2017; Eberlein-König and Ring, 2005).

Vitamin E

Vitamin E is of particular interest because it acts predominantly within lipid-rich compartments, where it helps limit membrane-associated oxidative injury and lipid peroxidation. Its relevance is strengthened by its functional interaction with vitamin C, which contributes to antioxidant recycling and thereby supports maintenance of redox balance in cutaneous tissue exposed to chronic environmental stress. In mechanistic terms, vitamin E is especially pertinent to the protection of cell membranes and epidermal lipids, both of which are vulnerable targets of oxidative damage in photoaged skin. This lipid-phase activity supports its inclusion in intervention strategies aimed at limiting the propagation of free-radical-mediated tissue injury under sustained environmental exposure (Eberlein-König and Ring, 2005; Thiele et al., 2005).

Alpha-Lipoic Acid

Alpha-lipoic acid is a mechanistically central adjunct because of its broader redox-regenerative properties and its capacity to interact with multiple antioxidant systems. Experimental and clinical

findings demonstrate that it reduces oxidative burden in photoaged skin and supports dermal repair processes, establishing it as a primary adjunct in phenotypes characterized by diminished oxidative defense capacity. Its biological relevance is further strengthened by evidence demonstrating that alpha-lipoic acid contributes to antioxidant recycling and influences pathways involved in collagen synthesis and fibroblast function. Within a cutaneous aging framework, these properties establish it as a compound that acts at both the level of oxidative stress reduction and matrix preservation (Packer et al., 1995; Beitner, 2003; Tsuji-Naito et al., 2010).

Zinc

Zinc is an essential supportive micronutrient because it contributes to antioxidant defense, inflammatory regulation, and maintenance of skin homeostasis. Its biological functions establish its inclusion in strategies for improving resilience to cumulative oxidative injury. In addition to its role in redox regulation, zinc has been linked to processes relevant to barrier integrity, tissue repair, and cellular protection against oxidative damage (Rostan et al., 2002; Marreiro et al., 2017).

Manganese

Manganese is primarily relevant because of its association with *SOD2*-dependent mitochondrial antioxidant defense, given that MnSOD represents a central enzymatic barrier against superoxide accumulation. Within the present framework, manganese is therefore a mechanistically essential supportive factor for mitochondrial redox homeostasis, particularly where antioxidant capacity may be reduced at the level of superoxide handling. Given the central role of mitochondrial ROS in skin aging biology, adequate manganese availability is essential for strategies aimed at preserving redox balance in oxidatively stressed skin (Treiber et al., 2012; Rinnerthaler et al., 2015).

TABLE 1: SELECTED STUDIES INVESTIGATING OXIDATIVE-STRESS POLYMORPHISMS RELEVANT TO CUTANEOUS AGING AND REDOX HOMEOSTASIS

STUDY (AUTHOR, YEAR)	DESIGN · POPULATION · SNP	PRIMARY OUTCOME / KEY FINDINGS
Watson et al., 1998	**Design:** Functional genotype–phenotype study. **Population:** Human lung tissue samples. **SNP:** *GSTP1* rs1695.	Showed that *GSTP1* variation is associated with differences in enzyme activity, supporting a functional effect on detoxification capacity.
do Nascimento et al., 2021	**Design:** Molecular marker study. **Population:** Human blood-storage model. **SNP:** *GSTP1* rs1695; *SOD2* rs4880.	Identified oxidative-stress-related polymorphisms as correlates of lipid peroxidation, supporting their relevance to redox susceptibility.

STUDY (AUTHOR, YEAR)	DESIGN · POPULATION · SNP	PRIMARY OUTCOME / KEY FINDINGS
Sutton et al., 2003	**Design:** Functional in vitro study. **Population:** Rat liver mitochondrial import model. **SNP:** *SOD2* rs4880.	Demonstrated that the *SOD2* targeting-sequence polymorphism modulates mitochondrial import efficiency of MnSOD.
Sutton et al., 2005	**Design:** Functional molecular study. **Population:** Experimental cellular / molecular model. **SNP:** *SOD2* rs4880.	Showed that rs4880 influences both mitochondrial import and mRNA stability, reinforcing its functional significance in antioxidant defense.
Paludo et al., 2014	**Design:** Functional cellular study. **Population:** Peripheral blood mononuclear cells with and without lipopolysaccharide stimulation. **SNP:** *SOD2* rs4880.	Reported allele-dependent differences in intracellular reactive-species production, supporting a role in oxidative-stress regulation.
Sørensen et al., 2009	**Design:** Genetic association study. **Population:** Oldest-old human cohort. **SNP:** *SOD2* rs4880; *GPX1* rs1050450.	Linked both polymorphisms to aging and longevity phenotypes, supporting their broader relevance to age-related oxidative biology.
Chen et al., 2011	**Design:** Meta-analysis. **Population:** Human association studies. **SNP:** *GPX1* rs1050450.	Supported a functional contribution of the *GPX1* variant to biological susceptibility, consistent with altered oxidative defense.
Cominetti et al., 2011	**Design:** Nutrigenetic association study. **Population:** Obese women following Brazil nut consumption. **SNP:** *GPX1* rs1050450.	Showed that *GPX1* genotype is associated with differences in oxidative-stress-related biomarkers, supporting context-dependent functional effects.

CONCLUSION

GSTM1, *GSTT1*, *GSTP1*, *SOD2*, and *GPX1* have established functional roles in the regulation of cutaneous oxidative-stress defense. These genes occupy complementary positions within redox homeostasis, spanning glutathione-dependent detoxification of electrophilic by-products, mitochondrial superoxide conversion, and peroxide neutralization. As a result, functional variation across this network influences the threshold at which endogenous and environmentally induced oxidative

damage translates into inflammation, extracellular matrix disruption, and progressive age-associated changes in skin structure and function (Rinnerthaler et al., 2015; Kammeyer and Luiten, 2015; Treiber et al., 2012).

Importantly, the significance of these loci lies not only in their individual effects, but also in their combined contribution to overall oxidative resilience. When variation affects several components of the antioxidant system simultaneously, the cumulative reduction in redox buffering capacity is more informative than the interpretation of a single variant in isolation. This network-based perspective is particularly relevant in the skin, where chronic ultraviolet exposure, pollution, and other oxidant-generating stimuli impose repeated demands on mitochondrial and glutathione-mediated defense pathways. In this context, inherited differences in antioxidant gene function contribute to interindividual variability in susceptibility to oxidative-stress-related skin aging and provide the mechanistic basis for biological stratification (Rinnerthaler et al., 2015; Kammeyer and Luiten, 2015; Treiber et al., 2012).

From a translational perspective, these findings support the rationale for antioxidant- and micronutrient-based adjunctive strategies, particularly vitamin C, vitamin E, alpha-lipoic acid, zinc, and manganese, as components of a broader approach to preserving cutaneous redox balance. Their importance lies in the ability to support antioxidant defense, membrane stability, matrix preservation, and endogenous enzymatic function within a biologically vulnerable oxidative milieu. Rather than being interpreted in deterministic terms, variation in these genes is functionally meaningful information that strengthens the rationale for targeted supportive interventions and for more individualized prevention strategies. Further integration of genotype, skin phenotype, and intervention response will be important for defining how redox-related genetic profiles can be applied in a more precise and clinically useful manner in skin-aging management (Al-Niaimi and Chiang, 2017; Rostan et al., 2002; Sepetiene et al., 2023).

REFERENCES

- Rinnerthaler M, Bischof J, Streubel MK, Trost A, Richter K. Oxidative stress in aging human skin. Biomolecules. 2015;5(2):545-89.
- Kammeyer A, Luiten RM. Oxidation events and skin aging. Ageing Res Rev. 2015;21:16-29.
- Treiber N, Maity P, Singh K, Ferchiu F, Wlaschek M, Scharffetter-Kochanek K. The role of manganese superoxide dismutase in skin aging. Dermatoendocrinol. 2012;4(3):232-5.
- Sepetiene R, Patamsyte V, Valiukevicius P, Gecyte E, Skipskis V, Gecys D, et al. Genetical signature—an example of a personalized skin aging investigation with possible implementation in clinical practice. J Pers Med. 2023;13(9):1305.
- Al-Niaimi F, Chiang NYZ. Topical vitamin C and the skin: mechanisms of action and clinical applications. J Clin Aesthet Dermatol. 2017;10(7):14-17.
- Beitner H. Randomized, placebo-controlled, double blind study on the clinical efficacy of a cream containing 5% alpha-lipoic acid related to photoageing of facial skin. Br J Dermatol. 2003;149(4):841-9.
- Rostan EF, DeBuys HV, Madey DL, Pinnell SR. Evidence supporting zinc as an important antioxidant for skin. Int J Dermatol. 2002;41(9):606-11.
- Poljšak B, Dahmane RG, Godić A. Intrinsic skin aging: the role of oxidative stress. Acta Dermatovenerol Alp Pannonica Adriat. 2012;21(2):33-6.
- Ghelli F, Bellisario V, Squillacioti G, Panizzolo M, Santovito A, Bono R. Formaldehyde in hospitals induces oxidative stress: the role of *GSTT1* and *GSTM1* polymorphisms. Toxics. 2021;9(8):178.
- McWilliams JE, Sanderson BJS, Harris EL, Richert-Boe KE, Henner WD. Glutathione S-transferase M1 (*GSTM1*) deficiency and lung cancer risk. Cancer Epidemiol Biomarkers Prev. 1995;4(6):589-94.
- Wenzlaff AS, Cote ML, Bock CH, Land SJ, Schwartz AG. *GSTM1*, *GSTT1* and *GSTP1* polymorphisms, environmental tobacco smoke exposure and risk of lung cancer among never smokers: a population-based study. Carcinogenesis. 2005;26(2):395-401.
- Watson MA, Stewart RK, Smith GB, Massey TE, Bell DA. Human glutathione S-transferase P1 polymorphisms: relationship to lung tissue enzyme activity and population frequency distribution. Carcinogenesis. 1998;19(2):275-80.
- Sreeja L, Syamala V, Hariharan S, Syamala VS, Raveendran PB, Sivanandan CD, et al. Glutathione S-transferase M1, T1 and P1 polymorphisms: susceptibility and outcome in lung cancer patients. J Exp Ther Oncol. 2008;7(1):73-85.
- do Nascimento MR, Silva de Souza RO, Silva Junior AL, Lima ES, Gonçalves MS, Moura Neto JP. *GSTP1* rs1695 and rs1871042, and *SOD2* rs4880 as molecular markers of lipid peroxidation in blood storage. Blood Transfus. 2021;19(4):309-16.
- Sutton A, Khoury H, Prip-Buus C, Cepanec C, Pessayre D, Degoul F. The Ala16Val genetic dimorphism modulates the import of human manganese superoxide dismutase into rat liver mitochondria in vitro. Pharmacogenetics. 2003;13(3):145-57.
- Sutton A, Imbert A, Igoudjil A, Descatoire V, Cazanave SC, Pessayre D, et al. The manganese superoxide dismutase Ala16Val dimorphism modulates both mitochondrial import and mRNA stability. Pharmacogenet Genomics. 2005;15(5):311-9.
- Paludo FJO, Bristot IJ, Alho CS, Gelain DP, Moreira JCF. Effects of 47C allele (rs4880) of the *SOD2* gene in the production of intracellular reactive species in peripheral blood mononuclear cells with and without lipopolysaccharides induction. Free Radic Res. 2014;48(2):190-9.
- Sørensen M, Christensen K, Stevnsner TV, Christiansen L. The Mn-superoxide dismutase single nucleotide polymorphism rs4880 and the glutathione peroxidase 1 single nucleotide polymorphism rs1050450 are associated with aging and longevity in the oldest old. Mech Ageing Dev. 2009;130(5):308-14.
- Arthur JR. The glutathione peroxidases. Cell Mol Life Sci. 2000;57(13-14):1825-35.

- Chen J, Cao Q, Qin C, Shao P, Wu Y, Wang M, et al. GPx-1 polymorphism (rs1050450) contributes to tumor susceptibility: evidence from meta-analysis. J Cancer Res Clin Oncol. 2011;137(10):1553-61.
- Cominetti C, de Bortoli MC, Purgatto E, Ong TP, Moreno FS, Garrido AB Jr, et al. Associations between glutathione peroxidase-1 Pro198Leu polymorphism, selenium status, and DNA damage levels in obese women after consumption of Brazil nuts. Nutrition. 2011;27(9):891-6.
- Karunasinghe N, Han DY, Zhu S, Yu J, Lange K, Duan H, et al. Serum selenium and single-nucleotide polymorphisms in genes for selenoproteins: relationship to markers of oxidative stress in men from Auckland, New Zealand. Genes Nutr. 2012;7(2):179-90.
- McKeever L, Peterson SJ, Lateef O, Freels SA, Diamond AM, Braunschweig CA. Impact of MnSOD and GPx1 genotype at different levels of enteral nutrition exposure on oxidative stress and mortality: a post hoc analysis from the FeDOx trial. JPEN J Parenter Enteral Nutr. 2021;45(2):287-94.
- Eberlein-König B, Ring J. Relevance of vitamins C and E in cutaneous photoprotection. J Cosmet Dermatol. 2005;4(1):4-9.
- Thiele JJ, Hsieh SN, Ekanayake-Mudiyanselage S. Vitamin E: critical review of its current use in cosmetic and clinical dermatology. Dermatol Surg. 2005;31(7 Pt 2):805-13; discussion 813.
- Packer L, Witt EH, Tritschler HJ. Alpha-lipoic acid as a biological antioxidant. Free Radic Biol Med. 1995;19(2):227-50.
- Tsuji-Naito K, Ishikura S, Akagawa M, Saeki H. Alpha-lipoic acid induces collagen biosynthesis involving prolyl hydroxylase expression via activation of TGF-beta-Smad signaling in human dermal fibroblasts. Connect Tissue Res. 2010;51(5):378-87.
- Marreiro DDN, Cruz KJC, Morais JBS, Beserra JB, Severo JS, de Oliveira ARS. Zinc and oxidative stress: current mechanisms. Antioxidants (Basel). 2017;6(2):24.