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UNDERSTANDING THE GENETIC INTERSECTION: EYE DISEASES AND GENETIC DISORDERS

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Annotation. Relevance. Recent advancements in genetic research have illuminated the intricate intersection between eye diseases and genetic disorders. Understanding the genetic basis of various eye diseases is crucial for developing targeted therapies and improving patient outcomes. It is important to delve into the intricate relationship between genetic mutations and eye disorders, shedding light on the underlying mechanisms and potential treatment avenues. **Purpose of the study.** The aim of this article is to provide a comprehensive overview of the genetic factors contributing to eye diseases and how they intersect with broader genetic disorders. **Materials and methods.** A comprehensive review of peer-reviewed articles, scientific journals, and databases such as PubMed and Google Scholar will be conducted to gather relevant information on the genetic basis of eye diseases and genetic disorders. In addition, relevant genetic data, including common mutations associated with various eye diseases and genetic disorders, will be compiled and analyzed to identify patterns and intersections. **Results and conclusion.** The intricate relationship between eye diseases and genetic disorders underscores the importance of comprehensive genetic analysis in both diagnosis and treatment. By delving into the genetic intersection, we gain crucial insights into the underlying mechanisms driving these conditions, paving the way for personalized therapies and preventive measures. Moving forward, continued research and collaboration are essential to unraveling the complexities of these disorders and improving outcomes for affected individuals worldwide.

Key words: inheritance, mutations, monogenic, dominant, recessive, autosomal, phenotypic, epigenetic, heterozygous, photoreceptor.

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KO'Z KASALLIKLARI VA IRSIY KASALLIKLAR O'RTASIDAGI O'ZARO BOG'LIQLIKNING MOHIYATI

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Annotatsiya. Dolzarbligi. Genetik tadqiqotlardagi so'nggi yutuqlar ko'z kasalliklari va genetik kasalliklar o'rtasidagi murakkab bog'liqlikka oydinlik kiritdi. Turli xil ko'z kasalliklarining genetik asoslarini tushunish maqsadli (target) davolash usullarini ishlab chiqish va davolash natijalarini yaxshilash uchun juda muhimdir. Asosiy mexanizmlar va potentsial davolash usullariga e'tibor qaratgan holda genetik mutatsiyalar va ko'z kasalliklari o'rtasidagi bog'liqlikni o'rganish muhim ahamiyatga ega. **Tadqiqot maqsadi.** Ushbu maqolaning maqsadi ko'z kasalliklariga olib keluvchi genetik omillar va ularning boshqa genetik kasalliklar bilan bog'liqligi haqida to'liq ma'lumot berishdir. **Materiallar va usullar.** Ko'z kasalliklari va irsiy kasalliklarning genetik asoslari bo'yicha tegishli ma'lumotlarni to'plash uchun ekspertlar tomonidan ko'rib chiqilgan maqolalar, ilmiy jurnallar, PubMed va Google Scholar kabi ma'lumotlar bazalaridan foydalaniladi. Bundan tashqari, turli xil ko'z kasalliklari va irsiy kasalliklar bilan o'zaro mutanosib genetik ma'lumotlar, jumladan, keng tarqalgan mutatsiyalar turli ular o'rtasidagi bog'liqliklarni aniqlash uchun tahlil qilinadi. **Natijalar va xulosa.** Ko'z kasalliklari va genetik kasalliklar o'rtasidagi bog'liqlik diagnostika va davolashda keng qamrovli genetik tahlilning muhimligini ta'kidlaydi. Genetik bog'liqlikni o'rganish orqali biz ushbu kasalliklarni qo'zg'atuvchi asosiy mexanizmlar haqida muhim ma'lumotlarga ega bo'lamiz hamda terapiya va profilaktika choralariga keng yo'l ochamiz. Kelgusida davom etayotgan tadqiqotlar va hamkorliklar ushbu kasalliklarning murakkabliklarini ochish va butun dunyo bo'ylab azyiat chekayotgan bemorlar davolash natijalarini yaxshilash uchun juda muhimdir.

Kalit so'zlar: irsiy, mutatsiyalar, monogen, dominant, retsessiv, autosomal, fenotipik, epigenetik, geterozigota, fotoretseptor.

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СУТЬ ГЕНЕТИЧЕСКОГО ПЕРЕСЕЧЕНИЯ: ГЛАЗНЫЕ ЗАБОЛЕВАНИЯ И ГЕНЕТИЧЕСКИЕ НАРУШЕНИЯ

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Аннотация. Актуальность. Последние достижения в области генетических исследований пролили свет на сложную взаимосвязь между заболеваниями глаз и генетическими нарушениями. Понимание генетической основы различных заболеваний глаз имеет решающее значение для разработки таргетной терапии и улучшения результатов лечения пациентов. Важно углубиться в сложную взаимосвязь между генетическими мутациями и заболеваниями глаз, обращая внимание на основные механизмы и потенциальные пути лечения. **Цель исследования.** Цель этой статьи – предоставить всесторонний обзор генетических факторов, способствующих заболеваниям глаз, и того, как они пересекаются с более широкими генетическими нарушениями. **Материалы и методы.** Будет проведен комплексный обзор рецензируемых статей, научных журналов и баз данных, таких как PubMed и Google Scholar, для сбора соответствующей информации о генетической основе глазных заболеваний и генетических нарушений. **Результаты и заключение.** Сложная взаимосвязь между заболеваниями глаз и генетическими нарушениями подчеркивает важность комплексного генетического анализа как для диагностики, так и для лечения. Углубляясь в генетическое пересечение, мы получаем важную информацию о лежащих в основе этих состояний механизмах, открывая путь для персонализированной терапии и профилактических мер. В дальнейшем продолжение исследований и сотрудничества имеет важное значение для раскрытия сложностей этих расстройств и улучшения результатов для пострадавших людей во всем мире.

Ключевые слова: наследование, мутации, моногенный, доминантный, рецессивный, аутосомный, фенотипический, гетерозиготный, фоторецептор.

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Genetic diseases often manifest in various parts of the body, and the eyes are no exception. The intricate interplay between genetics and ocular health can lead to a range of eye diseases, impacting vision and overall well-being. Through a systematic analysis of current research and clinical findings, the intricate interplay between genetic factors and ocular pathologies is elucidated. Emphasis is placed on elucidating the molecular mechanisms underlying these diseases, which encompass various structures of the eye, such as the cornea, lens, retina, and optic nerve. Additionally, the impact of genetic testing and advancements in genomic technologies on diagnosis, prognosis, and personalized treatment strategies for individuals with eye-damaging genetic diseases is discussed. By unraveling the complexities of genetic determinants in ocular disorders, this article aims to facilitate a deeper understanding of these conditions and pave the way for the development of targeted therapeutic interventions and precision medicine approaches in ophthalmology.

Hereditary eye diseases are a group of genetic pathologies characterized by dysfunction of the visual organs. It is associated with the subtleties of certain genes that code for proteins, process structures, structures and functions of parts of the visual system. They include:

Aniridia is a rare genetic disorder characterized by the absence or partial absence of the iris, the colored

part of the eye. The genetic origin of aniridia is primarily associated with mutations in the PAX6 gene located on chromosome 11p13. The PAX6 gene plays a crucial role in the development of various structures in the eye, including the iris, cornea, lens, and retina, central nervous system, and pancreas.

During embryonic development, PAX6 guides the formation and differentiation of eye tissues. Mutations in the PAX6 gene can disrupt the normal development of the iris, leading to the characteristic absence or underdevelopment of this eye structure in individuals with aniridia.

In most cases, aniridia follows an autosomal dominant pattern of inheritance, meaning that a mutation in one copy of the PAX6 gene (inherited from either parent) is sufficient to cause the disorder. However, de novo mutations (spontaneous mutations not inherited from either parent) can also give rise to aniridia.

Beyond the iris abnormalities, aniridia is often associated with other eye abnormalities, including foveal hypoplasia (underdevelopment of the central part of the retina), glaucoma, and cataracts.

Retinitis pigmentosa (RP) stands as a paradigmatic example of an eye-damaging genetic disease, characterized by progressive degeneration of photoreceptor cells in the retina. Its etiology is complex, with both monogenic and polygenic inheritance

patterns identified. Monogenic forms, which constitute the majority of cases, result from mutations in over 70 genes, each encoding proteins vital for photoreceptor function, survival, or maintenance of retinal structure. These genes govern various cellular processes, including phototransduction, photoreceptor development, and maintenance of the retinal pigment epithelium.

The inheritance patterns of RP can be autosomal dominant, autosomal recessive, or X-linked, with variable expressivity and penetrance adding further complexity. Autosomal dominant RP often results from mutations in genes encoding structural components of photoreceptor cells, such as rhodopsin (RHO) or peripherin (PRPH2), leading to protein misfolding or aggregation. Autosomal recessive forms, on the other hand, typically arise from loss-of-function mutations in genes involved in photoreceptor function or metabolism, including the ciliary protein RPGRIP1 or the visual cycle enzyme RPE65. X-linked RP, associated with mutations in the RPGR gene or its interacting partners, predominantly affects males due to hemizygoty of the X chromosome.

Polygenic inheritance, involving the interplay of multiple genetic variants and environmental factors, has also been implicated in a subset of RP cases, contributing to the variable phenotypic presentation and disease progression observed among affected individuals. Additionally, genetic modifiers and epigenetic factors further modulate the clinical manifestations of RP, influencing the age of onset, rate of progression, and severity of vision loss.

Choroideremia is another inherited eye disorder associated with impaired vision in the dark and loss of its acuity due to disruption of the integrity of the retina and photoreceptors of the eye. It is caused by mutations of the CHM gene located on the X chromosome, which lead to disruption of prenylation processes and deficiency of transmitter proteins. This gene provides instructions for making a protein called Rab escort protein-1 (REP-1), which plays a role in intracellular transport. Mutations in the CHM gene lead to the absence or dysfunction of REP-1, disrupting the normal function of cells in the retina, choroid, and other tissues of the eye. As a result, individuals with choroideremia experience progressive vision loss, beginning with peripheral vision and eventually leading to tunnel vision or complete blindness. Choroideremia is inherited in an X-linked recessive pattern, meaning it predominantly affects males, who have only one X chromosome. However, females who carry a mutated CHM gene on one of their X chromosomes can be carriers and may experience milder symptoms or be unaffected.

Stargardt disease, also known as Stargardt macular dystrophy or fundus flavimaculatus, represents the most common form of inherited juvenile macular degeneration. This condition typically manifests during childhood or adolescence and is characterized by

progressive central vision loss due to degeneration of the macula, the central part of the retina responsible for sharp, central vision.

The genetic origin of Stargardt disease predominantly involves mutations in the ABCA4 gene, located on chromosome 1p22.1. The ABCA4 gene encodes a transmembrane protein primarily expressed in the outer segments of photoreceptor cells, where it functions as an ATP-binding cassette transporter involved in the clearance of toxic retinoid byproducts generated during the visual cycle. Mutations in ABCA4 disrupt the normal function of this transporter, leading to the accumulation of lipofuscin-like fluorophores and toxic retinoid derivatives within the retinal pigment epithelium and photoreceptor cells. This accumulation triggers a cascade of cellular events, including oxidative stress, inflammation, and ultimately, photoreceptor cell death.

The inheritance pattern of Stargardt disease is typically autosomal recessive, meaning that individuals must inherit two copies of the mutated ABCA4 gene (one from each parent) to develop the condition. However, compound heterozygous mutations, where each allele carries a different disease-causing variant, can also lead to disease manifestation. The phenotypic variability observed in Stargardt disease, including differences in age of onset, disease severity, and rate of progression, can be attributed to the diverse spectrum of pathogenic mutations in the ABCA4 gene, as well as the influence of genetic modifiers and environmental factors.

In addition to mutations in the ABCA4 gene, rare cases of Stargardt disease have been associated with mutations in other genes, such as ELOVL4, PROM1, and PRPH2, highlighting the genetic heterogeneity of this condition. These genes are involved in various cellular processes, including lipid metabolism, photoreceptor development, and maintenance of retinal structure and function.

Leber congenital amaurosis (LCA) is a severe inherited retinal dystrophy characterized by early-onset visual impairment, often present at birth or within the first few months of life. The condition is associated with significant visual impairment or blindness due to abnormalities in the structure and function of the retina, particularly affecting the photoreceptor cells.

The genetic origin of LCA is highly heterogeneous, with mutations identified in at least 25 different genes to date. These genes encode proteins involved in various aspects of retinal function, including phototransduction, photoreceptor development, maintenance of the retinal pigment epithelium, and ciliary function. Mutations in these genes disrupt the normal cellular processes critical for vision, leading to the progressive degeneration of photoreceptor cells and subsequent vision loss.

One of the most commonly implicated genes in LCA is GUCY2D, which encodes guanylate cyclase 2D, an enzyme involved in the phototransduction cascade

in rod and cone photoreceptor cells. Mutations in GUCY2D impair the production of cyclic guanosine monophosphate (cGMP), a key signaling molecule in photoreceptor cells, leading to photoreceptor dysfunction and degeneration.

Another frequently mutated gene in LCA is RPE65, which encodes a protein essential for the isomerization of vitamin A in the visual cycle. Mutations in RPE65 disrupt the normal recycling of visual pigments in the retina, resulting in the accumulation of toxic byproducts and subsequent photoreceptor degeneration.

Other genes implicated in LCA include CRB1, AIPL1, RDH12, CRX, and SPATA7, among others, each playing crucial roles in retinal development, structure, or function. The inheritance pattern of LCA varies depending on the gene involved, with autosomal recessive inheritance being the most common, although autosomal dominant and X-linked forms have also been reported.

Chronic external ophthalmoplegia (CEP) is a rare disorder characterized by progressive weakness of the muscles that control eye movement. This condition can have a genetic basis, with mutations occurring in either mitochondrial DNA or nuclear DNA. Mitochondrial DNA mutations are a significant cause of CEP, particularly affecting genes involved in mitochondrial function. Mutations in mitochondrial DNA can disrupt the production of energy within cells, leading to muscle weakness and dysfunction in the eye muscles. Some of the mitochondrial genes commonly implicated in CEP include MT-ND4, MT-ND6, and MT-TL1. In addition to mitochondrial DNA mutations, nuclear DNA mutations can also contribute to CEP. These mutations often affect genes responsible for maintaining mitochondrial function and integrity. Disruption of these nuclear genes can impair mitochondrial function, leading to muscle weakness and ophthalmoplegia. The genetic basis of these syndromes involves complex interactions between mitochondrial and nuclear DNA mutations.

Norrie disease is a rare X-linked recessive disorder characterized by congenital blindness, progressive hearing loss, and developmental abnormalities of the eye. The genetic origin of Norrie disease lies in mutations in the NDP gene, located on the short arm of the X chromosome (Xp11.3). The NDP gene encodes a protein called Norrin, which plays a crucial role in eye and vascular development.

Mutations in the NDP gene disrupt the normal function of Norrin, leading to aberrant signaling pathways during embryonic development. Norrin normally interacts with the Frizzled-4 (FZD4) receptor and the low-density lipoprotein receptor-related protein

5 (LRP5) co-receptor to activate the Wnt signaling pathway, which is essential for vascularization and retinal development.

In individuals with Norrie disease, the absence or dysfunction of Norrin disrupts Wnt signaling, leading to abnormal development of the retinal vasculature and the formation of a fibrovascular mass behind the lens, known as a retrolental mass or Norrie disease pseudoglioma. These vascular abnormalities compromise the blood supply to the retina, resulting in retinal ischemia, retinal detachment, and ultimately, blindness.

Norrie disease follows an X-linked recessive inheritance pattern, meaning that the condition primarily affects males, who have only one copy of the X chromosome. Females, who have two X chromosomes, are typically carriers of the mutated NDP gene and may exhibit milder symptoms or be asymptomatic.

Age-related macular degeneration is an inherited retinal disease that causes rapidly progressive vision loss. Associated with mutations of more than thirty genes responsible for the formation of the inner lining of the eye. AMD has a complex genetic origin, with both genetic and environmental factors playing a role. Several genes have been identified as associated with AMD, including complement factor H (CFH), complement factor B (CFB), complement component 2 (C2), complement factor I (CFI), and ARMS2/HTRA1. Variations in these genes can increase the risk of developing AMD, particularly the late-stage form known as geographic atrophy or neovascular AMD. However, genetic factors alone do not determine the development of AMD, and lifestyle factors such as smoking, diet, and exposure to sunlight also contribute significantly to its risk.

This list is not exhaustive, since hereditary eye diseases are a very large group of pathologies of the visual organs, which is constantly updated with discoveries in the field of medicine. Prevention methods include reducing eye strain, special exercises, reducing the duration of use of gadgets, organizing the lighting regime of the room and annual preventive examinations. If parents are diagnosed with hereditary diseases of the organs of vision, then genetic analysis is necessary to assess the risk of transmitting them to the child.

Methods of early diagnosis, thanks to which timely treatment is possible that improves the patient's standard of living, include: measuring visual acuity and refraction, examining the fundus of the eye and determining the reserve of accommodation.

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