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MD Research News

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Drug treatment

Ophthalmology. 2012 Nov 3. pii: S0161-6420(12)00763-4. doi: 10.1016/j.ophtha.2012.08.008. [Epub ahead of print]

Super-dose Anti-VEGF (SAVE) Trial: 2.0 mg Intravitreal Ranibizumab for Recalcitrant Neovascular Macular Degeneration-Primary End Point.

Brown DM, Chen E, Mariani A, Major JC Jr; SAVE Study Group.

Retina Consultants of Houston, The Methodist Hospital, Houston, Texas. Electronic address: dmbmd@houstonretina.com.

PURPOSE: To determine whether a higher dose of intravitreal ranibizumab could improve the anatomy and best-corrected visual acuity (BCVA) in eyes with neovascular age-related macular degeneration (AMD) with persistent disease activity despite monthly intravitreal anti-vascular endothelial growth factor (VEGF) injections.

DESIGN: Phase I to II multicenter, open-label, controlled clinical trial.

PARTICIPANTS: Eighty-seven patients with recalcitrant neovascular AMD, defined as having leakage on fundus fluorescein angiography or spectral domain optical coherence tomography (SD-OCT) despite monthly anti-VEGF injections.

METHODS: Patients were treated with 2.0-mg ranibizumab injections monthly for 3 doses and monitored with Early Treatment Diabetic Retinopathy Study (ETDRS) 4-m refractions, clinical examinations, and SD-OCT.

MAIN OUTCOME MEASURES: The mean change in baseline visual acuity (VA), the percentage of patients who experienced a loss or gain of 15 or more letters in ETDRS BCVA, the mean change in central retinal thickness, and the incidence of adverse events.

RESULTS: Eighty-seven patients with an average of 24 injections before enrollment and a mean of 10.4 injections in the preceding 12 months had a mean refracted VA of 69.2 ETDRS letters (20/41 Snellen) and a mean central subfield of 422 μm at baseline. Mean VA gain over baseline was +2.5 letters at day 7 (n = 82), +3.7 letters at month 1 (n = 87), +3.9 letters at month 2 (n = 87), and +3.3 letters at month 3 (20/36 Snellen; P = 0.001; n = 86). Anatomic outcomes showed a mean optical coherence tomography central subfield thickness improvement from baseline of -48.4 μm at day 7 (n = 84), -37.5 μm at month 1 (n = 87), -42.4 μm at month 2 (n = 85), and -33.1 μm at month 3 (P = 0.01; n = 86).

CONCLUSIONS: Intravitreal injections of 2.0 mg ranibizumab led to statistically significant VA gains and

anatomic improvement in patients with persistent intraretinal, subretinal, or subretinal pigment epithelial fluid during a previous regimen of chronic monthly 0.5-mg ranibizumab injections.

PMID: 23131717 [PubMed - as supplied by publisher]

Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2012 Nov 6. doi: 10.5507/bp.2012.066. [Epub ahead of print]

Progression of macular atrophy after PDT combined with the COX-2 inhibitor Nabumetone in the treatment of neovascular ARMD.

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Department of Ophthalmology, University Hospital Olomouc and Faculty of Medicine and Dentistry, Palacky University Olomouc, Czech Republic.

AIM: To evaluate photodynamic therapy (PDT) combined with the preferential the cyclooxygenase-2 (COX-2) inhibitor, nabumetone in the treatment of the neovascular age-related macular degeneration (ARMD).

METHODS: A prospective, double-blind, randomized study on 60 patients with subfoveal CNV secondary to ARMD without any previous treatment. Patients were divided into a nabumetone or placebo group. The main endpoints were the change of best-corrected visual acuity (BCVA), central macular thickness (CRT) and number of required PDT treatments.

RESULTS: In the nabumetone group, 27 patients (90%) and 28 (93%) in the placebo group completed the follow-up of 12 months. In the nabumetone group, the mean CRT decreased from 332 μm (SD 68 μm) to 220 μm (SD 46 μm). In the placebo group, CRT decreased from 331 μm (SD 72 μm) to 254 μm (SD 61 μm). The mean BCVA was 0.68 log MAR (SD 0.22 log MAR) in the nabumetone group and 0.62 log MAR (SD 0.23 log MAR) in the placebo group at baseline. This stabilised in the placebo group to 0.66 log MAR (SD 0.33) but deteriorated in the nabumetone group to 0.86 logMAR (SD 0.41 log MAR). There was a significant reduction in the number of required PDTs in the nabumetone group, but significant progression of the RPE atrophy area.

CONCLUSION: Combined PDT with oral intake of the COX-2 inhibitor, nabumetone reduced the number of required PDT retreatments, but worsening BCVA caused by macular atrophy progression. Therefore the combination of the PDT with the nabumetone is not recommended.

PMID: 23132511 [PubMed - as supplied by publisher]

Ophthalmic Res. 2012 Oct 30;49(1):43-48. [Epub ahead of print]

Comparative Analysis of Hyaluronan's Affinity for Antivascular Endothelial Growth Factor Agents.

Sugita I, Yoneda M, Iwaki M, Zako M.

Department of Ophthalmology, Aichi Medical University, Nagakute, Japan.

Background: Differences in the efficacy of bevacizumab, an antivascular endothelial growth factor (VEGF) agent, against retinopathy with neovascularization when injected into the vitreous cavity of vitrectomized and nonvitrectomized eyes suggests the involvement of hyaluronan, a major component of the vitreous body. This study aimed to compare the affinities of hyaluronan for anti-VEGF agents in vitro.

Methods: We examined the affinities of hyaluronan for 3 anti-VEGF agents (bevacizumab, pegaptanib and ranibizumab). Tritium [(3)H]-labeled hyaluronan was incubated separately with each anti-VEGF agent. The ratio of bound and unbound hyaluronan measured using solid and liquid phase methods was calculated.

Results: Hyaluronan demonstrated a significantly greater affinity for bevacizumab than for pegaptanib or ranibizumab.

Conclusions: The absence or presence of hyaluronan may be associated with the clinical efficacy of bevacizumab injected into the vitreous cavity due to the affinity of hyaluronan for bevacizumab.

PMID: 23128274 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2012 Nov 7. [Epub ahead of print]

Regression of rubeosis in the fellow eye after intravitreal ranibizumab injection.

Lüke J, Nassar K, Grisanti S, Lüke M.

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PMID: 23132337 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Stem Cells. 2012 Nov 6. doi: 10.1002/stem.1268. [Epub ahead of print]

Self-organising Neuroepithelium from Human Pluripotent Stem Cells Facilitates Derivation of Photoreceptors.

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Abstract: Retinitis pigmentosa, other inherited retinal diseases and age-related macular degeneration lead to untreatable blindness because of the loss of photoreceptors. We have recently shown that transplantation of mouse photoreceptors can result in improved vision. It is therefore timely to develop protocols for efficient derivation of photoreceptors from human pluripotent stem (hPS) cells. Current methods for photoreceptor derivation from hPS cells require long periods of culture and are rather inefficient. Here, we report that formation of a transient self-organised neuroepithelium from human embryonic stem (hES) cells cultured together with extracellular matrix (ECM) is sufficient to induce a rapid conversion into retinal progenitors in 5 days. These retinal progenitors have the ability to differentiate very efficiently into Crx(+) photoreceptor precursors after only 10 days and subsequently acquire rod photoreceptor identity within 4 weeks. Directed differentiation into photoreceptors using this protocol is also possible with human induced pluripotent stem (hiPS) cells, facilitating the use of patient specific hiPS cell lines for regenerative medicine and disease modelling.

PMID: 23132794 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2012 Nov 6. pii: iovs.12-10701v1. doi: 10.1167/iovs.12-10701. [Epub ahead of print]

Activity Limitation Due to a Fear of Falling in Older Adults with Eye Disease.

Wang MY, Rousseau J, Boisjoly H, Schmaltz H, Kergoat MJ, Moghadaszadeh S, Djafari F, Freeman EE.

Centre de Recherche, Hopital Maisonneuve-Rosemont, Montreal, Canada.

PURPOSE: To examine whether patients with age-related macular degeneration (AMD), glaucoma, or Fuchs corneal dystrophy report limiting their activity due to a fear of falling as compared to a control group of older adults with good vision.

METHODS: We recruited 345 patients (93 with AMD, 57 with Fuchs, 98 with glaucoma, and 97 controls) from the ophthalmology clinics of Maisonneuve-Rosemont Hospital (Montreal, Canada) to participate in a cross-sectional study from September, 2009 until July, 2012. Control patients who had normal visual acuity and visual field were recruited from the same clinics. Participants were asked if they limited their activity due to a fear of falling. Visual acuity, contrast sensitivity, and visual field were measured and the medical record was reviewed.

RESULTS: Between 40 and 50% of patients with eye disease reported activity limitation due to a fear of falling compared to only 16% of controls with normal vision. After adjustment for age, gender, race, number of comorbidities, cognition, and lens opacity, the Fuchs groups was most likely to report activity limitation due to a fear of falling (OR=3.07, 95% CI 1.33, 7.06) followed by the glaucoma group (OR=2.84, 95% CI 1.36, 5.96) and the AMD group (OR=2.42 95% CI 1.09, 5.35). Contrast sensitivity best explained these associations.

CONCLUSIONS: Activity limitation due to a fear of falling is very common in older adults with visually impairing eye disease. Although this compensatory strategy may protect against falls, it may also put people at risk for social isolation and disability.

PMID: 23132799 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2012 Nov 8. [Epub ahead of print]

Differences in spectral absorption properties between active neovascular macular degeneration and mild age related maculopathy.

Balaskas K, Nourrit V, Dinsdale M, Henson DB, Aslam T.

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Abstract: This study examines the differences in spectral absorption properties between the maculae of patients with active neovascular macular degeneration and those with early age related maculopathy (ARM). Patients attending for management of neovascular age related macular degeneration (AMD) underwent multispectral imaging with a system comprising of a modified digital fundus camera coupled with a 250-W tungsten-halogen lamp and a liquid crystal fast-tuneable filter. Images were obtained at 8 wavelengths between 496 and 700 nm. Aligned images were used to generate a DLA (differential light absorption, a measure of spectral absorption properties) map of the macular area. DLA maps were generated for both eyes of 10 sequential patients attending for anti-vascular endothelial growth factor injections. Each of these patients had active leaking neovascular AMD in one eye and early ARM or milder disease in the fellow eye. Eyes with neovascular AMD demonstrated lower average levels of DLA compared with their fellow eyes with early ARM (p=0.037, t test). The significant difference in DLA demonstrates the potential of multispectral imaging for differentiating the two pathologies non-invasively.

PMID: 23137662 [PubMed - as supplied by publisher]

Ophthalmology. 2012 Nov 5. pii: S0161-6420(12)00739-7. doi: 10.1016/j.ophtha.2012.07.076. [Epub ahead of print]

Retinal Pigment Epithelial Cell Loss Assessed by Fundus Autofluorescence Imaging in Neovascular Age-Related Macular Degeneration.

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PURPOSE: To characterize retinal pigment epithelial (RPE) cell loss as evidenced by autofluorescence imaging in patients with neovascular age-related macular degeneration (AMD).

DESIGN: Retrospective cohort study.

PARTICIPANTS: There were 162 eyes of 116 consecutive patients with neovascular AMD examined in a retinal practice.

METHODS: Each patient underwent a complete examination including autofluorescence imaging. Areas of confluent absence of autofluorescence signal of at least 0.5 mm in greatest linear diameter were measured within the macular area. Patient demographic and examination data were evaluated in relation to the autofluorescence data.

MAIN OUTCOME MEASURES: Prevalence and progression of confluent areas of absent autofluorescence and the relationship these areas had with visual acuity.

RESULTS: The mean age of the patients was 82.9 years, and the mean visual acuity was 20/71 (logarithm minimum angle of resolution [logMAR], 0.55). Confluent loss of autofluorescence was seen in 58.6% of eyes at baseline, and the median area of absent autofluorescence among those was 1.57 mm(2) (interquartile range [IQR], 0.62-4.32 mm(2)). Using generalized estimation equation modeling, the significant predictors for area of confluent absent autofluorescence at baseline were duration of disease and any previous treatment with photodynamic therapy. The significant predictor of baseline visual acuity was baseline area of confluent absent autofluorescence. Follow-up was available for 124 (76.5%) eyes, with a mean follow-up of 2.9 years. By then, the mean visual acuity was 20/90 (logMAR, 0.65), and 79% of eyes had confluent areas of absent autofluorescence, the large majority of which affected the central macula. The median area of absent autofluorescence was 3.61 mm(2) (IQR, 1.16-7.11 mm(2)). The best predictor of final visual acuity was the area of absent autofluorescence at the final follow-up.

CONCLUSIONS: Confluent absence of autofluorescence, a measure signifying RPE loss, was a significant predictor of visual acuity both at baseline and at final follow-up. This is the first study to document the prevalence, rate of progression, and factors associated with measures of confluent RPE loss in patients with neovascular AMD. Application of strategies to limit RPE cell loss may prove useful in eyes with neovascular AMD.

PMID: 23137630 [PubMed - as supplied by publisher]

Pathogenesis

Invest Ophthalmol Vis Sci. 2012 Nov 8. pii: iovs.12-10495v1. doi: 10.1167/iovs.12-10495. [Epub ahead of print]

Age-related susceptibility to apoptosis in human retinal pigment epithelial cells is triggered by disruption of p53-Mdm2 association.

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PURPOSE: Relatively little is known about the contribution of p53/Mdm2 signaling axis in apoptosis of retinal pigment epithelial (RPE) cells or its possible link to dysfunction of aging RPE or to related blinding disorders such as age-related macular degeneration (AMD).

METHODS: Age-associated changes in p53 activation were evaluated in primary RPE cultures from human donor eyes of various ages. Apoptosis was evaluated by activation of caspases and DNA fragmentation. Gene-specific siRNA was used to knock down expression of p53.

RESULTS: We observed that the basal rate of p53-dependent apoptosis increased in an age-dependent manner in human RPE. The age-dependent increase in apoptosis was linked to alterations in several aspects of the p53 pathway. p53 phosphorylation Ser15 was increased through the stimulation of ATM-Ser1981. p53 acetylation Acetyl-Lys379 was increased through the inhibition of SIRT1/2. These two post-translational modifications of p53 blocked the sequestration of p53 by Mdm2, thus, resulting in an increase in free p53 and of p53 stimulation of apoptosis through increased expression of PUMA and activation of caspase-3. Aged RPE also had reduced expression of anti-apoptotic Bcl-2, which contributed to the increase in apoptosis. Of particular interest in these studies was that pharmacologic treatments to block p53 phosphorylation, acetylation or expression were able to protect RPE cells from apoptosis.

CONCLUSIONS: Our studies suggest that aging in the RPE leads to alterations of specific checkpoints in the apoptotic pathway, which may represent important molecular targets for the treatment of RPE-related aging disorders such as AMD.

PMID: 23139272 [PubMed - as supplied by publisher]

Hum Mol Genet. 2012 Nov 8. [Epub ahead of print]

iPS cell modeling of Best disease: Insights into the pathophysiology of an inherited macular degeneration.

Singh R, Shen W, Kuai D, Martin JM, Guo X, Smith MA, Perez ET, Phillips MJ, Simonett JM, Wallace KA, Verhoeven AD, Capowski EE, Zhang X, Yin Y, Halbach PJ, Fishman GA, Wright LS, Pattnaik BR, Gamm DM.

Waisman Center, University of Wisconsin, Madison, Wisconsin.

Abstract: Best disease (BD) is an inherited degenerative disease of the human macula that results in progressive and irreversible central vision loss. It is caused by mutations in the retinal pigment epithelium (RPE) gene BESTROPHIN1 (BEST1), which, through mechanism(s) that remain unclear, lead to the accumulation of subretinal fluid and autofluorescent waste products from shed photoreceptor outer segments (POS). We employed human iPS cell (hiPSC) technology to generate RPE from BD patients and unaffected siblings in order to examine the cellular and molecular processes underlying this disease. Consistent with the clinical phenotype of BD, RPE from mutant hiPSCs displayed disrupted fluid flux and increased accrual of autofluorescent material after long-term POS feeding when compared to hiPSC-RPE from unaffected siblings. On a molecular level, RHODOPSIN degradation after POS feeding was delayed in BD hiPSC-RPE relative to unaffected sibling hiPSC-RPE, directly implicating impaired POS handling in the pathophysiology of the disease. In addition, stimulated calcium responses differed between BD and normal sibling hiPSC-RPE, as did oxidative stress levels after chronic POS feeding. Subcellular localization, fractionation, and co-immunoprecipitation experiments in hiPSC-RPE and human prenatal RPE further linked BEST1 to the regulation and release of endoplasmic reticulum calcium stores. Since calcium signaling and oxidative stress are critical regulators of fluid flow and protein degradation, these findings likely contribute to the clinical picture of BD. In a larger context, this report demonstrates the potential to use patient-specific hiPSCs to model and study maculopathies, an important class of blinding disorders in humans.

PMID: 23139242 [PubMed - as supplied by publisher]

Eur J Ophthalmol. 2012 Nov 6:0. doi: 10.5301/ejo.5000163. [Epub ahead of print]

Idiopathic macular telangiectasia type 2: the progressive vasculopathy.

Engelbert M, Yannuzzi LA.

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Purpose: To describe the complete sequence of the progressive vasculopathy in macular telangiectasia type 2.

Methods: This is a report of a case demonstrating the complete vasogenic sequence in macular telangiectasia type 2 over the course of 15 years, and representative images from a collective of 150 patients with macular telangiectasia type 2 employing fundus photography, fluorescein angiography, and optical coherence tomography.

Results: Macular telangiectasia may progress along a predictable vasogenic sequence which consists of nonproliferative stages, characterized by temporal loss of macular luteopigment and inner retinal volume loss in the absence of vascular changes, followed by a progressive proliferative vasculopathy, first involving the deep capillary plexus with eventual extension of the vascular changes circumferentially in the inner retinal capillary plexus. Late proliferative stages may become indistinguishable from advanced neovascular age-related macular degeneration.

Conclusions. While it is rare to observe the complete vasogenic sequence of macular telangiectasia type 2, a classification into nonproliferative and proliferative stages can be established, and may prove helpful as the mechanisms driving the pathogenic process through those stages are identified.

PMID: 23138663 [PubMed - as supplied by publisher]

Retina. 2012 Nov 6. [Epub ahead of print]

EXPRESSION OF SIRT1 IN CHOROIDAL NEOVASCULAR MEMBRANES.

Maloney SC, Antecka E, Granner T, Fernandes B, Lim LA, Orellana ME, Burnier MN Jr.

Department of Ophthalmology, Henry C. Witelson Ocular Pathology Laboratory, McGill University, Montreal, Canada.

PURPOSE: SIRT1 is a deacetylase that has been shown to be instrumental in embryonic and pathologic vascular formation. The purpose of this study was to evaluate the potential role of SIRT1 in the pathogenesis of choroidal neovascularization in age-related macular degeneration.

METHODS: The expression of SIRT1 was assessed via immunohistochemistry in nine excised human choroidal neovascularization membranes and seven non-age-related macular degeneration donor eyes. Enzyme-linked immunosorbent assay-based angiogenesis arrays were used to assess the potential of an SIRT1 inhibitor, nicotinamide, to reduce secretion of 10 unique proangiogenic cytokines from retinal pigment epithelial cells.

RESULTS: SIRT1 was expressed more frequently in choroidal neovascularization membranes than donor eyes about vascular endothelial cells (78 vs. 29% positive cases) and retinal pigment epithelial cells (57 vs. 14% positive cases). SIRT1 inhibition in retinal pigment epithelial cells correlated with significantly decreased secretion of three potent proangiogenic cytokines: angiogenin, platelet-derived growth factor BB, and vascular endothelial growth factor A.

CONCLUSION: SIRT1 levels appear elevated in human choroidal neovascularization membranes

compared with control eyes. Moreover, inhibition of SIRT1 activity is correlated with decreased secretion of potent proangiogenic cytokines. Collectively, these data support a potential role for SIRT1 in the pathogenesis of neovascular age-related macular degeneration.

PMID: 23135526 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2012 Nov 6. pii: iovs.12-10165v1. doi: 10.1167/iovs.12-10165. [Epub ahead of print]

Metallothionein-III deficiency exacerbates light-induced retinal degeneration.

Tsuruma K, Shimazaki H, Ohno Y, Inoue Y, Honda A, Imai S, Lee J, Shimazawa M, Satoh M, Hara H.

Department of Biofunctional Evaluation, Molecular Pharmacology, Gifu Pharmaceutical University, 1-25-4 Daigaku-nishi, Gifu, 501-1196, Japan.

Purpose: Retinal photoreceptor damage is a common feature of ophthalmic disorders such as age-related macular degeneration and retinitis pigmentosa. Oxidative stress plays a key role in these diseases. Metallothionein (MT) is a family of cysteine-rich proteins, and various physiological functions have been reported, including protection against metal toxicity and antioxidative potency. We investigated the functional role of MT-III in light-induced retinal damage.

Methods: The expression of retinal MT-I, -II, and - III mRNA was evaluated by real-time reverse-transcription PCR in retina exposed to light. Retinal damage in MT-deficient mice was induced by exposure to white light at 16,000 lx for 3 h after dark adaptation. Photoreceptor damage was evaluated histologically by measuring the thickness of the outer nuclear layer (ONL) 5 days after light exposure and by electroretinogram recording. In an in vitro experiment, the MT-III siRNAs were tested for their effects on light-induced mouse photoreceptor cell (661W) damage.

Results: The mRNAs of the MTs were significantly increased in murine retina after light exposure. The ONL thickness in the MT-III-deficient mice was remarkably thinner compared with light-exposure wild-type mice, and a- and b- wave amplitudes were decreased; the photoreceptor damage in the MT-I/-II-deficient mice was not observed. MT-III knockdown by siRNA in 661W exacerbated the cell damage and increased the production of reactive oxygen species in response to light exposure.

Conclusions: These findings suggest that MT-III can help protect against retinal damage compared with MT -I/II. Some of these effects may be exerted by its antioxidative potency.

PMID: 23132798 [PubMed - as supplied by publisher]

Int J Mol Med. 2012 Oct 26. doi: 10.3892/ijmm.2012.1164. [Epub ahead of print]

Retinal pigment epithelium, age-related macular degeneration and neurotrophic keratouveitis.

Bianchi E, Scarinci F, Ripandelli G, Feher J, Pacella E, Magliulo G, Gabrieli CB, Plateroti R, Plateroti P, Mignini F, Artico M.

Department of Sensory Organs, University of Rome 'La Sapienza', Rome, Italy.

Abstract: Age-related macular degeneration (AMD) is the leading cause of impaired vision and blindness in the aging population. The aims of our studies were to identify qualitative and quantitative alterations in mitochondria in human retinal pigment epithelium (RPE) from AMD patients and controls and to test the protective effects of pigment epithelium-derived factor (PEDF), a known neurotrophic and antiangiogenic substance, against neurotrophic keratouveitis. Histopathological alterations were studied by means of morphometry, light and electron microscopy. Unexpectedly, morphometric data showed that the RPE

alterations noted in AMD may also develop in normal aging, 10-15 years later than appearing in AMD patients. Reduced tear secretion, corneal ulceration and leukocytic infiltration were found in capsaicin (CAP)-treated rats, but this effect was significantly attenuated by PEDF. These findings suggest that PEDF accelerated the recovery of tear secretion and also prevented neurotrophic keratouveitis and vitreoretinal inflammation. PEDF may have a clinical application in inflammatory and neovascular diseases of the eye.

PMID: 23128960 [PubMed - as supplied by publisher]

Medicina (Kaunas). 2012;48(8):404-9.

Does matrix metalloproteinase-3 polymorphism play a role in age-related macular degeneration in patients with myocardial infarction?

Liutkevičienė R, Zaliaduonytė-Pekšienė D, Zaliūnienė D, Gustienė O, Jašinskas V, Lesauskaitė V, Tamošiūnas A, Zaliūnas R.

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OBJECTIVE: The aim of our study was to determine if the genotype of the matrix metalloproteinase-3 (MMP-3) gene might carry the risk of age-related macular degeneration (ARMD) in patients with myocardial infarction.

MATERIAL AND METHODS: A total of 499 patients with an acute myocardial infarction or with a history of myocardial infarction were enrolled into the study. They were subdivided into 2 groups: 273 patients with ARMD and 226 patients without ARMD. The control group comprised 560 persons from a random sample of the Lithuanian population. DNA was analyzed using real-time polymerase chain reaction to genotype polymorphism 5A/6A at a position -1171 of the MMP-3 gene promoter.

RESULTS: Of the 499 patients with myocardial infarction, 47% had early-stage ARMD. The patients with ARMD were older than the patients in the group without ARMD (62.1±10.8 vs. 59.6±11.1, P<0.01). The analysis of MMP-3 gene polymorphism did not reveal any differences in the distribution of 5A/5A, 5A/6A, and 6A/6A genotypes between the ARMD group, non-ARMD group, and the control group (24.2%, 52.5%, and 23.3% in the ARMD group; 28.7%, 51.9%, and 19.4% in non-ARMD group; and 25.7%, 49.3% and 25.0%, in the control group, respectively).

CONCLUSIONS: MMP-3 gene polymorphism had no predominant effect on the development of ARMD in patients with myocardial infarction.

PMID: 23128460 [PubMed - in process]

Adv Gerontol. 2012;25(2):239-43.

Adv Gerontol. 2012;25(2):232-8.

[Molecular-cellular mechanisms of retina pathology development in people of various age].

[Article in Russian]

[No authors listed]

The review considers the molecular-cellular mechanisms of retina pathology in people of various age. Dysfunction of retinal cells (retinal pigment epithelium, photoreceptors, neurons) causes the development of age-related macular degeneration, retinal ischemia and a variety of hereditary diseases. This is the description of involvement of genes and signaling molecules in the dysfunction of retinal cell types. It is

established that a breach of RPE65 gene expression leads to age-related macular degeneration, retinitis pigmentosa and Leber's congenital amaurosis. Mutations in the CRX gene are the cause of progressive states such as cone-rod dystrophy. In addition, more than 100 mutations in RHO have been identified, leading to different variants of retinitis pigmentosa. The involvement of TGF-(beta2 in the formation of retinal cells and the regulation of secretion of vascular endothelial growth factor VEGF, which synthesis is increased by ischemic lesions of the retina, is described.

PMID: 23130512 [PubMed - in process]

[The role of melatonin in progress of pathology of a retina in patients of senior age group].

[Article in Russian]

[No authors listed]

Abstract: Epiphysis cerebri and its hormone melatonin play a leading role in aging. Melatonin affects many biochemical processes in a human body. The authors assume that there is a correlation between the level of melatonin and development of macular degeneration by age.

PMID: 23130513 [PubMed - in process]

Genetics

Cold Spring Harb Perspect Med. 2012 Nov 1;2(11). pii: a006510. doi: 10.1101/cshperspect.a006510.

Common polymorphisms in angiogenesis.

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Vascular Biology Program, Children's Hospital, and Department of Surgery, Harvard Medical School, Boston, Massachusettes 02115.

Abstract: A wide variety of diseases have a significant genetic component, including major causes of morbidity and mortality in the western world. Many of these diseases are also angiogenesis dependent. In humans, common polymorphisms, although more subtle in effect than rare mutations that cause Mendelian disease, are expected to have greater overall effects on human disease. Thus, common polymorphisms in angiogenesis-regulating genes may affect the response to an angiogenic stimulus and thereby affect susceptibility to or progression of such diseases. Candidate gene studies have identified several associations between angiogenesis gene polymorphisms and disease. Similarly, emerging pharmacogenomic evidence indicates that several angiogenesis-regulating polymorphisms may predict response to therapy. In contrast, genome-wide association studies have identified only a few risk alleles in obvious angiogenesis genes. As in other traits, regulatory polymorphisms appear to dominate the landscape of angiogenic responsiveness. Rodent assays, including the mouse corneal micropocket assay, tumor models, and a macular degeneration model have allowed the identification and comparison of loci that directly affect the trait. Complementarity between human and animal approaches will allow increased understanding of the genetic basis for angiogenesis-dependent disease.

PMID: 23125197 [PubMed - in process]