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MD Research News

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Drug Management

Retina. 2010 Nov-Dec;30(10):1601-8.

Intravitreal infliximab in patients with macular degeneration who are nonresponders to antivascular endothelial growth factor therapy.

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Abstract

PURPOSE: The purpose of this study was to determine the efficacy and safety of intravitreal infliximab in the treatment of choroidal neovascularization secondary to age-related macular degeneration in patients who are nonresponders to antivascular endothelial growth factor therapy.

METHODS: Prospective, noncomparative, interventional case series. The primary inclusion criteria for patients consisted of previous treatment with five or more intravitreal injections of bevacizumab and/or ranibizumab, visual loss, angiographic leakage, and intraretinal and/or subretinal fluid on spectral domain optical coherence tomography. At Day 0, a single intravitreal injection of infliximab (2 mg/0.05 mL) was administered. Best-corrected visual acuity testing measured with Early Treatment Diabetic Retinopathy Study charts and spectral domain optical coherence tomography scans were performed on Days 0, 3, 7, 30, 60, and 90. Fluorescein angiography was performed at days 0 and 90. The development of systemic antibodies against infliximab (human antichimeric antibodies) was not sought. Main outcome measures were changes in best-corrected visual acuity, foveal thickness, and lesion size.

RESULTS: We included four patients. At Day 90, the best-corrected visual acuity change was -18, +3, +4, and -4 letters, respectively. Intraretinal and/or subretinal fluid on spectral domain optical coherence tomography scans was not significantly reduced in any case. Lesion size was not reduced in any case. Two patients developed intraocular inflammation with high intraocular pressure 3 and 5 weeks after the infliximab injection, respectively. One case was controlled with topical medication, and one case required posterior vitrectomy.

CONCLUSION: Intravitreal infliximab showed no significant visual or anatomical benefit for the treatment of choroidal neovascularization secondary to age-related macular degeneration in patients who were nonresponders to antivascular endothelial growth factor therapy. In addition, half of the cases developed intraocular inflammation.

PMID: 21060271 [PubMed - in process]

Genetics

PLoS One. 2010 Nov 1;5(11):e13786.

The ERCC6 Gene and Age-Related Macular Degeneration.

Baas DC, Despriet DD, Gorgels TG, Bergeron-Sawitzke J, Uitterlinden AG, Hofman A, van Duijn CM, Merriam JE, Smith RT, Barile GR, Ten Brink JB, Vingerling JR, Klaver CC, Allikmets R, Dean M, Bergen AA.

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Abstract

BACKGROUND: Age-related macular degeneration (AMD) is the leading cause of irreversible visual loss in the developed countries and is caused by both environmental and genetic factors. A recent study (Tuo et al., PNAS) reported an association between AMD and a single nucleotide polymorphism (SNP) (rs3793784) in the ERCC6 (NM_000124) gene. The risk allele also increased ERCC6 expression. ERCC6 is involved in DNA repair and mutations in ERCC6 cause Cockayne syndrome (CS). Amongst others, photosensitivity and pigmentary retinopathy are hallmarks of CS.

METHODOLOGY/PRINCIPAL FINDINGS: Separate and combined data from three large AMD case-control studies and a prospective population-based study (The Rotterdam Study) were used to analyse the genetic association between ERCC6 and AMD (2682 AMD cases and 3152 controls). We also measured ERCC6 mRNA levels in retinal pigment epithelium (RPE) cells of healthy and early AMD affected human donor eyes. Rs3793784 conferred a small increase in risk for late AMD in the Dutch population (The Rotterdam and AMRO-NL study), but this was not replicated in two non-European studies (AREDS, Columbia University). In addition, the AMRO-NL study revealed no significant association for 9 other variants spanning ERCC6. Finally, we determined that ERCC6 expression in the human RPE did not depend on rs3793784 genotype, but, interestingly, on AMD status: Early AMD-affected donor eyes had a 50% lower ERCC6 expression than healthy donor eyes (P=0.018).

CONCLUSIONS/SIGNIFICANCE: Our meta-analysis of four Caucasian cohorts does not replicate the reported association between SNPs in ERCC6 and AMD. Nevertheless, our findings on ERCC6 expression in the RPE suggest that ERCC6 may be functionally involved in AMD. Combining our data with those of the literature, we hypothesize that the AMD-related reduced transcriptional activity of ERCC6 may be caused by diverse, small and heterogeneous genetic and/or environmental determinants.

PMID: 21072178 [PubMed - in process]

Arch Ophthalmol. 2010 Nov;128(11):1462-71.

Prospective Study of Common Variants in the Retinoic Acid Receptor-Related Orphan Receptor {alpha} Gene and Risk of Neovascular Age-Related Macular Degeneration.

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Abstract

OBJECTIVES: The retinoic acid receptor (RAR)-related orphan receptor α gene (RORA) is implicated as a candidate for age-related macular degeneration (AMD) through a previous microarray expression study, linkage data, biological plausibility, and 2 clinic-based cross-sectional studies. We aimed to determine if common variants in RORA predict future risk of neovascular AMD.

METHODS: We measured genotypes for 18 variants in intron 1 of the RORA gene among 164 cases who developed neovascular AMD and 485 age- and sex-matched controls in a prospective, nested, case-control study within the Nurses' Health Study and the Health Professionals Follow-up Study. We determined the incidence rate ratios and 95% confidence intervals (CI) for neovascular AMD for each variant and examined interactions with other AMD-associated variants and modifiable risk factors.

RESULTS: We identified one single-nucleotide polymorphism (rs12900948) that was significantly associated with increased incidence of neovascular AMD. Participants with 1 and 2 copies of the G allele were 1.73 (CI, 1.32-2.27) and 2.99 (CI, 1.74-5.14) times more likely to develop neovascular AMD. Individuals homozygous for both the G allele of rs12900948 and ARMS2 A69S had a 40.8-fold increased risk of neovascular AMD (CI, 10.1-164; P = .017). Cigarette smokers who carried 2 copies of the G allele had a 9.89-fold risk of neovascular AMD but the interaction was not significant (P = .08). We identified a significant AMD-associated haplotype block containing the single-nucleotide polymorphisms rs730754, rs8034864, and rs12900948, with P values for ACA = 1.16 × 10(-9), ACG = 5.85 × 10(-12), and GAA = .0001 when compared with all other haplotypes.

CONCLUSIONS: Common variants and haplotypes within the RORA gene appear to act synergistically with the ARMS2 A69S polymorphism to increase risk of neovascular AMD. These data add further evidence of a high level of complexity linking genetic and modifiable risk factors to AMD development and should help efforts at risk prediction.

PMID: 21060049 [PubMed - in process]

Retina. 2010 Nov-Dec;30(10):1595-600.

TUMOR NECROSIS FACTOR-α GENE POLYMORPHISMS IN AGE-RELATED MACULAR DEGENERATION.

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Abstract

PURPOSE: The purpose of this study was to investigate tumor necrosis factor-α gene polymorphisms in unrelated Taiwan Chinese patients with wet age-related macular degeneration (AMD) and controls.

METHODS: In this retrospective case-control study, we enrolled 190 wet AMD patients and 180 age- and gender-matched controls. Genomic DNA was extracted from the peripheral blood obtained from wet AMD patients and control subjects. Polymerase chain reaction was performed to analyze 6 candidate single nucleotide polymorphisms in the tumor necrosis factor-α gene: -238 G/A, -308 G/A, +489 G/A, -857 C/T, -863 C/A, and -1031 T/C.

RESULTS: Among the 6 candidate single nucleotide polymorphisms of the tumor necrosis factor-α gene, only -1031 T/C was significantly associated with wet AMD. The distribution of the -1031 T/C genotypes was significantly different between wet AMD patients (homozygous T [TT], 64%; TC heterozygous [TC], 36%; homozygous C [CC] 0%) and controls (TT, 66%; TC, 28%; CC, 7%; P = 7 × 10). The genotype CC of -1031 T/C was significantly lower than that in controls (0 vs. 7%, P = 1.45 × 10, odds ratio = 14.70, 95% confidence interval = 1.90-33.59). No single haplotype was found to be significantly associated with either wet AMD patients or controls.

CONCLUSION: Our data indicate that the tumor necrosis factor-α -1031 T/C polymorphism may be associated with wet AMD in the Taiwan Chinese population.

PMID: 21060270 [PubMed - in process]

Other Management & Epidemiology

Invest Ophthalmol Vis Sci. 2010 Nov 11. [Epub ahead of print]

Fixation Stability during Binocular Viewing in Patients with Age-Related Macular Degeneration.

Tarita-Nistor L, Brent MH, Steinbach MJ, Gonzalez EG.

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Abstract

Purpose: We examined fixation stability of patients with age-related macular degeneration (AMD) and large interocular acuity differences, testing them in monocular and binocular viewing conditions. We also studied the relationship between fixation stability and visual performance during monocular and binocular viewing. Methods: Twenty patients with AMD participated. Their monocular and binocular distance acuities were measured with the ETDRS charts. Fixation stability of the better and worse eye were recorded monocularly with the MP-1 microperimeter and binocularly with the EyeLink eye-tracker. Additional recordings of monocular fixations were obtained with the EyeLink in viewing conditions when one eye viewed the target while the fellow eye was covered by an infra red filter so it could not see the target. Results: Fixation stability of the better eye did not change across viewing conditions. Fixation stability of the worse eye was 84 to 100% better in the binocular condition than in monocular conditions. Fixation stability of the worse eye was significantly larger ($p < .05$) than that of the better eye when recorded monocularly with the MP-1. This difference was dramatically reduced in the binocular condition, but remained marginally significant (95% CI: -.351 to -.006). For the better eye, there was a moderate relationship between fixation stability and visual acuity, both monocular and binocular, in all conditions in which this eye viewed the target. Conclusions: Fixational ocular motor control and visual acuity are driven by the better-seeing eye when patients with AMD and large interocular acuity differences perform the tasks binocularly.

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Invest Ophthalmol Vis Sci. 2010 Nov 11. [Epub ahead of print]

Effect of Cataract in Evaluation of Macular Pigment Optical Density Using Autofluorescence Spectrometry.

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Abstract

Purpose: To assess the effect of cataract on evaluation of the macular pigment optical density (MPOD) level in aged patients. Methods: We prospectively measured the MPOD level using autofluorescence spectrometry before and after cataract surgery. The Lens Opacities Classification System III was used to grade the cataracts at baseline. Results: Forty-five eyes of 41 subjects, who had no ocular disorders or fundus autofluorescence abnormalities, except for age-related nuclear cataract were included. The preoperative MPOD level was 0.350±0.117 density unit (DU). Regression analysis showed that a higher nuclear color grading score was correlated with a lower MPOD level (T=-2.90, P=0.0063). The preoperative MPOD prediction formula was MPOD = 0.545 - 0.069 × (nuclear color grading score). A higher nuclear color grading score was correlated significantly with failure to measure the MPOD (chi-square=5.08, P=0.0242). The mean postoperative MPOD level was 0.600 DU (95% confidence interval [CI]; 0.562-0.637), which was significantly (P<0.0001) higher than the preoperative level of 0.350 DU (95% CI; 0.313-0.388). Regression analysis showed that higher preoperative MPOD levels were correlated with higher postoperative MPOD levels (T=2.91, P=0.0061). Conclusions: Cataract, especially its nuclear component, affects the MPOD level measured by autofluorescence spectrometry. Care should be taken when using this

method in eyes with age-related macular maculopathy and age-related macular degeneration and in patients who are old enough to develop these diseases.

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Graefes Arch Clin Exp Ophthalmol. 2010 Nov 6. [Epub ahead of print]

Patient characteristics and treatment of neovascular age-related macular degeneration in France: the LUEUR1 observational study.

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Abstract

BACKGROUND: Age-related macular degeneration is the primary cause of blindness in developed countries. Current treatments of this degenerative disease mainly include laser, photodynamic therapy with verteporfin and administration of anti-vascular endothelial growth factors. The LUEUR (LUcentis® En Utilisation Réelle) study is composed of a cross-sectional part (LUEUR1), which examined the current management of wet AMD in France, and a follow-up part (LUEUR2), which will assess the development of patients treated for wet AMD over 4 years. Here we describe the results of LUEUR1.

METHODS: Patients with wet AMD were enrolled during a routine medical examination in LUEUR1, a cross-sectional, observational, prospective, multicentre study. Investigators recorded patient demographics, visual acuity, characteristics of wet AMD lesions, date of AMD diagnosis, comorbidities, previous treatments, treatments prescribed at inclusion, and low vision rehabilitation.

RESULTS: A total of 72 investigators recruited 1,019 patients with wet AMD, corresponding to 1,405 eyes affected by the disease. The mean age of patients was 78.7 ± 7.3 years. Most were female (62.3%) and non-smokers (66.9%). The mean visual acuity was 49.12 ± 24.18 Early Treatment Diabetic Retinopathy Study letters. Most eyes showed occult (52.8%) and subfoveal (84.6%) choroidal neovascularisation. Bilateral wet AMD affected 37.9% of patients. The median time since diagnosis was 12 months. Ranibizumab-based therapy (67.3%) and photodynamic therapy (29.8%) were the most frequent previous treatments. Prior to inclusion, 5.6% of patients had low vision rehabilitation. When a treatment was prescribed on the day of inclusion, it was most often ranibizumab (89.0% of all treatments at inclusion).

CONCLUSIONS: The results of this study illustrate the impact of anti-vascular endothelial growth factor therapies on the treatment of wet AMD in a real-life context. Specifically, ranibizumab-based therapy appears to have largely replaced laser photocoagulation and verteporfin-based photodynamic therapy.

PMID: 21057805 [PubMed - as supplied by publisher]

J Fr Ophtalmol. 2010 Nov 4. [Epub ahead of print]

[Outer retinal cysts in exudative age-related macular degeneration: A spectral domain OCT study.]

[Article in French]

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Abstract

PURPOSE: To describe the optical coherence tomography (OCT) findings and progression of peculiar retinal cysts that we identified in patients being followed up after anti-vascular endothelial growth factor (anti-VEGF) treatment.

METHODS: This is an observational case series. All relevant data (including best-corrected visual acuity and spectral domain OCT scans) concerning exudative age-related macular degeneration (AMD) patients treated with at least three anti-VEGF intravitreal injections (IVT) during the previous 12 months were collected over a period of four months.

RESULTS: A total of 376 consecutive choroidal neovascularization (CNV) patients (398 eyes) were examined. Of these patients, 18 (18 eyes, 4.5%), who underwent a mean of five (range, 3 to 15) anti-VEGF IVTs, had a cystic appearance of the retina on OCT scans. These cysts were usually multiple (2 to 7) and presented as optically empty spaces bordered by a mildly reflective rim. Tiny punctate spots were seen inside or along the inner border of the cyst. The presence of these two features allowed the differentiation of these cysts from CME cavities. Usually round, the cysts could be elongated in shape and simulate a serous retinal detachment (SRD). A thin layer of degenerate retina below the cysts helps differentiate them from SRD. The cysts, varying in size from 60 to 600μm, were always located below the outer plexiform layer and visualized over or contiguous to a fibrous and hyperreflective thickening of the choriocapillary/retinal pigment epithelial (CC/RPE) complex or over an atrophic portion of the CC/RPE complex. Their size did not change over time.

CONCLUSIONS: These retinal cysts are a newly reported SD-OCT finding in anti-VEGF-treated exudative AMD. They could correspond to active scavenger macrophages and must be differentiated from CME and SRD in order to avoid unnecessary anti-VEGF retreatment.

PMID: 21056515 [PubMed - as supplied by publisher]

Retina. 2010 Nov-Dec;30(10):1573-8.

Epidemiology of the association between anticoagulants and intraocular hemorrhage in patients with neovascular age-related macular degeneration.

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Abstract

PURPOSE: To determine the cumulative incidence and annual incidence of intraocular hemorrhage (subretinal hemorrhage or vitreous hemorrhage) in patients with neovascular age-related macular degeneration (AMD) and association with daily antiplatelet or anticoagulant (AP/AC) medication usage (aspirin, clopidogrel, and warfarin), age, gender, hypertension, diabetes mellitus, or bilateral neovascular AMD.

METHODS: Retrospective cross-sectional study in a tertiary university setting. Data on 195 eyes of 195 patients without previous intraocular hemorrhage examined over 73 months were reviewed.

RESULTS: Ninety-six of 195 patients (49.2%) were taking daily AP/ACs. Of patients taking daily AP/AC agents, 63.5% had hemorrhage compared with 29.2% of patients not taking (odds ratio = 4.21; 95% confidence interval = 1.42-8.46; P < 0.001). The overall annual incidence of intraocular hemorrhage was 0.14% per year. Among patients taking daily AP/AC, the cumulative incidence (61 of 96, 63.5%) and annual incidence (0.10%) of concurrent intraocular hemorrhage were significantly greater compared with patients not taking them (29 of 99, 29.2% and 0.04%, respectively; P < 0.0001). Fourteen of 18 patients (77%) taking more than 1 daily AP/AC had occurrence of intraocular hemorrhage. Antiplatelet or anticoagulant usage was an independent risk factor for the development of intraocular hemorrhage. The use of any agent resulted in a significantly increased risk of developing intraocular hemorrhage. Additionally, presence of bilateral neovascular AMD was a significant association in those taking daily AP/ACs, whereas age was a

significant association in those not taking daily AP/AC agents.

CONCLUSION: All three daily AP/AC types were significantly associated with an increased risk of the development intraocular hemorrhage in patients with neovascular AMD, whereas gender, hypertension, and diabetes were not. Age was not significantly associated with hemorrhage in patients taking daily AP/AC agents, whereas the presence of bilateral neovascular AMD was significantly associated with hemorrhage. These findings indicate that the AP/AC use may predispose patients with neovascular AMD to intraocular hemorrhage more so than age and duration of disease alone. While the risk that discontinuing these medicines would pose to the patients' health may be too great to justify, ensuring that an appropriate medication dosage is maintained should be a priority within this patient population.

PMID: 21060269 [PubMed - in process]

Ophthalmologica. 2010 Nov 12;225(3):144-149. [Epub ahead of print]

Early Markers of Choroidal Neovascularization in the Fellow Eye of Patients with Unilateral Exudative Age-Related Macular Degeneration.

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AIBILI - Association for Innovation and Biomedical Research on Light and Image, Coimbra, Portugal.

Abstract

Objective: To identify morphological and/or functional early markers of choroidal neovascularization (CNV) development in fellow eyes of patients with exudative age-related macular degeneration (AMD). Design: This is a single-center, prospective, observational, longitudinal 2-year study. Patients: Patients were enrolled with the diagnosis of neovascular AMD in 1 eye and early age-related maculopathy (ARM) in the fellow eye. Intervention or Methods: All patients completed the baseline assessment and were followed up for up to 24 months with repeated ophthalmic and imaging assessments performed at 6-month intervals. Main OutcomeMeasures: Each patient underwent a detailed ocular and medical history, a complete ophthalmologic examination with color fundus photography, fluorescein angiography, indocyanine green angiography (ICG), optical coherence tomography (OCT), fundus autofluorescence (FAF) imaging and retinal leakage analysis (RLA). Results: Sixty-two patients were enrolled in the study. Large or intermediate drusen were present in 100% of the study eyes and hyperpigmentation in 46% (24 eyes). Fifty-two patients completed the 2-year study follow-up. Large soft drusen (>125 μm) were observed in 15 out of 17 eyes (88%) that converted and developed CNV during the study and in 25 out of 35 eyes (71.4%) that did not develop CNV. Among the 17 eyes that developed CNV, 9 (53%) showed abnormal findings before conversion, on ICG. No particular FAF pattern was found to be correlated with conversion to wet AMD. OCT was able to document the presence of intra- or subretinal fluid at the time of conversion in all 17 eyes that developed CNV during the study. Alterations of the blood-retinal barrier were identified by RLA before conversion in 76% of the eyes that converted and 23% of the eyes that did not convert during the study. Conclusions: Characterization of early ARM phenotypes is challenging. By combining different imaging modalities of the macula and correlating this information, we were able to determine the presence of functional macular alterations in the fellow eye of patients with this disease before development of CNV.

PMID: 21071996 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2010 Nov 11. [Epub ahead of print]

Claudin-19 and the barrier properties of the human retinal pigment epithelium.

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Abstract

Purpose: The retinal pigment epithelium (RPE) separates photoreceptors from choroidal capillaries but in age-related macular degeneration (AMD) capillaries breach the RPE barrier. Little is known about human RPE tight junctions or the effects of serum on the retinal side of the RPE. Methods: Cultured human fetal RPE (hfRPE) was assessed by the transepithelial electrical resistance (TER) and the transepithelial diffusion of methylated polyethylene glycol (mPEG). Claudins and occludin were monitored by quantitative RT-PCR, immunoblotting, and immunofluorescence. Results: Similar to freshly isolated hfRPE, claudin-19 mRNA was 25× more abundant than claudin-3. Other detectable claudin mRNAs were found in even lesser amounts, as little as 3,000× less abundant than claudin 19. Claudin-1 and claudin-10b were only detected in subpopulations of cells whereas others were undetectable. Knockdown of claudin-19 by small interfering RNA (siRNA) eliminated the TER. siRNAs for other claudins had minimal effects. Serum affected tight junctions only when presented to the retinal side of the RPE. The TER increased 2× and the conductance of K(+) relative to Na(+) decreased without affecting the permeability of mPEG. These effects correlated with increased steady-state levels of occludin. Conclusion: Fetal human RPE is a claudin-19-dominant epithelium that has regional variations in claudin-expression. Apical serum decreases RPE permeability, which might be a defense mechanism that would retard the spread of edema due to AMD.

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Cell Mol Life Sci. 2010 Nov 9. [Epub ahead of print]

Expression and distribution of immunoglobulin G and its receptors in an immune privileged site: the eye.

Niu N, Zhang J, Sun Y, Wang S, Sun Y, Korteweg C, Gao W, Gu J.

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Abstract

It has recently been demonstrated that not only mature B lymphocytes, but also non-lymphoid cells, including cancer cells and neurons, express IgG. In the eye, an important immune privileged site, the presence of IgG has been ascribed to IgG entering the eye through breaches of the blood-ocular barrier. Here we demonstrate that the eye itself can produce IgG intrinsically. Applying immunohistochemistry, in situ hybridization, and RT-PCR, several intraocular structures were found to express proteins and mRNA transcripts of IgG heavy chains, light chains, V(D)J rearrangements, and enzymes required for V(D)J recombination. IgG receptors were also detected in the intraocular epithelium and endothelium. The extensive distribution of IgG and its receptors in intraocular structures indicates that locally produced IgG could play a significant role in maintaining the ocular microenvironment and protection of the eyes, and it might also be involved in the pathogenesis of age-related macular degeneration and some inflammatory diseases.

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Invest Ophthalmol Vis Sci. 2010 Nov 11. [Epub ahead of print]

Activation of P2X receptors induces apoptosis in human retinal pigment epithelium.

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Abstract

Purpose. The retinal pigment epithelium (RPE) is considered a primary site of pathology in age-related macular degeneration (AMD), which is the most prevalent form of irreversible blindness worldwide in the elderly population. Extracellular adenosine triphosphate (ATP) acts as a key signaling molecule in numerous cellular processes including cell death. The purpose of this study was to determine whether extracellular ATP induces apoptosis in cultured human RPE. Methods. RPE apoptosis was evaluated by caspase-3 activation, Hoechst staining, and DNA fragmentation. Intracellular Ca(2+) levels were determined by both a cell-based fluorometric Ca(2+) assay and a ratiometric Ca(2+) imaging technique. P2X(7) mRNA and protein expression were detected by reverse transcription-polymerase chain reaction (RT-PCR) and confocal microscopy, respectively. Results. We found that 1) both the endogenous P2X(7) agonist ATP and the synthetic, selective P2X(7) agonist 2',3'-O-(4-benzoylbenzoyl)-ATP (BzATP) induced RPE apoptosis, which was significantly inhibited by P2X(7) antagonist oxidized ATP (oATP), but not by the P2 receptor antagonist suramin; 2) both ATP and BzATP increase intracellular Ca(2+) via extracellular Ca (2+) influx; 3) both ATP- and BzATP-induced Ca(2+) responses were significantly inhibited by oATP, but not by suramin; 4) ATP-induced apoptosis was significantly inhibited or blocked by BAPTA-AM, low or no extracellular Ca(2+); and 5) P2X(7) receptor mRNA and protein were expressed in RPE cells. Conclusions. Our findings suggest that P2X receptors, especially P2X(7) receptors, contribute to ATP- and BzATP-induced Ca(2+) signaling and apoptosis in the RPE. Abnormal Ca(2+) homeostasis via activation of P2X receptors could cause dysfunction and apoptosis of RPE that underlie AMD.

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Zhonghua Yan Ke Za Zhi. 2010 Aug;46(8):708-713.

[Fundus autofluorescence patterns of drusen in age-related macular degeneration.]

[Article in Chinese]

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Abstract

OBJECTIVE: To investigate the characteristics of fundus autofluorescence (FAF) patterns of drusen in patients with nonexudative age-related macular degeneration (AMD).

METHODS: It was a retrospective case series study. Spatial distribution and intensity of FAF of 63 cases (78 eyes) with nonexudative AMD were recorded using a confocal scanning laser ophthalmoscopy (cSLO, Heidelberg Retina Angiograph 2, HRA2, Heidelberg, Germany), the excitation light used was at 488 nm (argon laser), emission light at 514 nm (barrier filter), and fundus field-of-view at 30-degrees. Color fundus photographs were obtained with Kowa Nonmyd 7. Three-dimensional fundus images were captured by spectral domain optical coherence tomography (Topcon, 3D OCT-1000, Japan).

RESULTS: The FAF changes did not correlate topographically with visible fundus changes and 3D-OCT images in 78 eyes with drusen in nonexudative AMD. The majority of these eyes (68 out of 78) showed abnormal FAF signal of drusen at the posterior pole, which could be classified into seven different patterns according to their different features: minimal, focal confluent, linear, patchy, lace-like, speckled and scattered changes. In the remaining 10 eyes, the small lesions presented in color fundus photos were not detected in FAF examination. Therefore, a homogeneous background signal similar to the normal fundus was obtained by FAF examination. In addition, 15 patients exhibited abnormal autofluorescence in both eyes, 13 of them showed asymmetrical FAF changes, indicating that asymmetrical lesions might be presented.

CONCLUSIONS: Various patterns of abnormal FAF can be clearly imaged with HRA2-cSLO in nonexudative AMD, reflecting different stages of this disease. Periodic observation of drusen with FAF examination is of great clinical value in the estimation of occurrence and development of AMD.

PMID: 21054995 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2010 Nov;150(5):752; author reply 752-3.

Choroidal neovascularization in pathologic myopia.

Dave V, Narayanan R.

Comment on:

Am J Ophthalmol. 2010 Mar;149(3):458-64.e1.

PMID: 21036211 [PubMed - indexed for MEDLINE]

Diet

Mol Biosyst. 2010 Nov 5. [Epub ahead of print]

Milk, revealed "silent" chemistry: new mode of cycloretinal synthesis.

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Abstract

Bovine milk is by far the most commonly consumed milk in the western world. The protein composition in milk consists of casein and whey proteins, of which β-lactoglobulin (BLG) is the principal constituent of the latter. Here we provide biochemical evidence that this milk protein, in purified form and in pasteurized store-bought milk, promotes the formation of cycloretinal (all-trans retinal dimer), and a variety of other cycloterpenals of biological relevance [Fishkin et al., Proc. Natl. Acad. Sci. U. S. A., 2005, 102, 7091-7096; Fishkin et al., Chirality, 2004, 16, 637-641; Kim et al., Proc. Natl. Acad. Sci. U. S. A., 2007, 104, 19273-19278]. Cycloretinal is an eye metabolite and among several toxic byproducts of the visual cycle firmly established to cause age-related macular degeneration. Experiments in rabbits further demonstrate that BLG/milk can survive the digestive system and promote this reaction in vivo [Caillard et al., Am. J. Physiol., 1994, 266(6), G1053-G1059]. Proteomic studies on age-related macular degeneration patients have detected BLG in the eye of these patients further suggesting that this milk protein could contribute to disease progression [Crabb et al., Proc. Natl. Acad. Sci. U. S. A., 2002, 99(23), 14682-14687].

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