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MD Research News

Issue 5 Wed Dec 1, 2010

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Drug Treatment

1. Eye (Lond). 2010 Nov 19. [Epub ahead of print]

Comparing fixation location and stability in patients with neovascular age-related macular degeneration treated with or without Ranibizumab.

Pearce E, Sivaprasad S, Chong NV.

Laser and Retinal Research Unit, King's College Hospital, University of London, London, UK.

Abstract

Purpose: To compare fixation location and stability in patients with neovascular age-related macular degeneration (AMD) treated with or without ranibizumab.

Methods: Patients were recruited from the Macular Clinic of the King's College Hospital in London. Two groups of patients with neovascular AMD with at least 12 months of follow-up were included in the study. The treated group was treated with ranibizumab while the untreated group did not have any treatment. Best corrected visual acuity (BCVA) with modified ETDRS chart, fixation location and stability as measured with Nidek MP1, central retinal thickness as measured by Zeiss Cirrus SD-optical coherent tomography (OCT), and lesion size as measured by Topcon TRC-50IX camera were analysed and correlated.

Results: In total, 102 eyes were included in the study with 76 in the ranibizumab-treated group and 26 in the untreated group. There were no significantly demographic differences between the two groups. However, as expected, the treated group has significantly better vision (48.5 vs15.5 letters, P<0.0001) and smaller lesions (10.8 vs18.3 mm(2), P=0.004), the central macular thickness as measured by OCT also showed a trend of normalised macular thickness (252 vs282 microns, P=0.07). The location of fixation was significantly more central in the ranibizumab-treated group ($\chi(2)$ 17.9, P<0.0001) with over 50% of eyes with predominantly central fixation. Majority (84.6%) of the patients in the untreated group had predominantly eccentric fixation. Fixation stability was significantly better in the ranibizumab-treated group as compared with the untreated group, using both the software provided by the MP1 machine ($\chi(2)$ 21.8, P<0.0001) and the mean log bivariate contour ellipse area calculated from the raw data obtained from the machine (3.64 vs4.39 in treated and untreated group respectively, P<0.0001).

Conclusion:Low vision rehabilitation strategy for this group of patients in the ranibizumab era will be very different from those used in untreated patients with dense central scotoma. Further studies on the visual rehabilitation in the ranibizumab-treated patients should consider fixation characteristics of the patients.Eye advance online publication, 19 November 2010; doi:10.1038/eye.2010.167.

PMID: 21102492 [PubMed - as supplied by publisher]

Genetics

2. Acta Ophthalmol. 2010 Nov 25. doi: 10.1111/j.1755-3768.2010.02040.x. [Epub ahead of print]

Genetic association study of age-related macular degeneration in the Spanish population.

Brión M, Sanchez-Salorio M, Cortón M, De La Fuente M, Pazos B, Othman M, Swaroop A, Abecasis G, Sobrino B, Carracedo A; for the Spanish multi-centre group of AMD.

Genetics of Cardiovascular and Ophthalmologic Diseases, Hospital-University Complex of Santiago (CHUS), Santiago de Compostela, Spain Genomics Medicine Group, University of Santiago de Compostela, CIBERER Santiago de Compostela, Spain Instituto Gallego de Oftalmología (INGO), Santiago de Compostela, Spain Departments of Ophthalomology and Visual Sciences and Human Genetics, University of Michigan, Ann Arbor, Michigan, USA Neurobiology, Neurodegeneration & Repair Laboratory, National Eye Institute, National Institutes of Health, Bethesda, Maryland, USA Department of Biostatistics, Center for Statistical Genetics, University of Michigan, Ann Arbor, Minnesota, USA National Genotyping Center (CEGEN), University of Santiago de Compostela, Santiago de Compostela, Spain.

Abstract

Purpose: To investigate new genetic risk factors and replicate reported associations with advanced age-related macular degeneration (AMD) in a prospective case-control study developed with a Spanish cohort.

Methods: Three hundred and fifty-three unrelated patients with advanced AMD (225 with atrophic AMD, 57 with neovascular AMD, and 71 with mixed AMD) and 282 age-matched controls were included. Functional and tagging SNPs in 55 candidate genes were genotyped using the SNPlex(TM) genotyping system. Single SNP and haplotype association analysis were performed to determine possible genetic associations; interaction effects between SNPs were also investigated.

Results: In agreement with previous reports, ARMS2 and CFH genes were strongly associated with AMD in the studied Spanish population. Moreover, both loci influenced risk independently giving support to different pathways implicated in AMD pathogenesis. No evidence for association of advanced AMD with other previous reported susceptibility genes, such as CST3, CX3CR1, FBLN5, HMCN1, PON1, SOD2, TLR4, VEGF and VLDLR, was detected. However, two additional genes appear to be candidate markers for the development of advanced AMD. A variant located at the 3' UTR of the FGF2 gene (rs6820411) was highly associated with atrophic AMD, and the functional SNP rs3112831 at ABCA4 showed a marginal association with the disease.

Conclusion: We performed a large gene association study in advanced AMD in a Spanish population. Our findings show that CFH and ARMS2 genes seem to be the principal risk loci contributing independently to AMD in our cohort. We report new significant associations that could also influence the development of advanced AMD. These findings should be confirmed in further studies with larger cohorts.

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PMID: 21106043 [PubMed - as supplied by publisher]

3. Ann Med. 2010 Nov 22. [Epub ahead of print]

Genetic variants in BCMO1 and CD36 are associated with plasma lutein concentrations and macular pigment optical density in humans.

Borel P, de Edelenyi FS, Vincent-Baudry S, Malezet-Desmoulin C, Margotat A, Lyan B, Gorrand JM, Meunier N, Drouault-Holowacz S, Bieuvelet S.

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Abstract

Abstract: Lutein is recovered at high concentration in the human macula lutea. Recent studies suggest that this micronutrient might be implicated in prevention of age-related macular degeneration.

Objective: To identify genes which affect blood and retina lutein concentrations among candidate genes (intestinal sterol transporters and carotenoid oxygenases).

Design: A comparative plus an observational study. Participants. Twenty-nine healthy subjects for the comparative study and 622 subjects for the observational study. Intervention and methods. All the participants were genotyped for single nucleotide polymorphisms (SNPs) in the candidate genes. Fasting plasma lutein concentrations were measured in all the participants and after 6 months' supplementation, with either a lutein-rich supplement or a placebo, in the 29 subjects who participated in the comparative study. Macular pigment optical density (MPOD), which is a measure of macula concentration of lutein, was measured before and after the dietary intervention in the 29 subjects. Associations between SNPs and plasma lutein and MPOD were assessed by partial least square (PLS) regression followed by univariate analysis. Observed associations between SNPs and plasma lutein were verified by haplotype-based association analysis in the cohort of 622 subjects. Main outcome measures. Plasma lutein levels and MPOD.

Results: Six SNPs in four genes (ABCG8, BCMO1, CD36, and NPC1L1) explained 25% and 38% of the plasma and MPOD variance, respectively. Subjects with TT at the BCMO1 rs7501331 locus had lower ($P < 0.05$) plasma lutein than CT subjects. Subjects with CC at the CD36 rs13230419 locus had lower ($P < 0.05$) plasma lutein than subjects who carried a T allele. The association between CD36 and plasma lutein was confirmed in the cohort of 622 subjects. Subjects with TT at the BCMO1 rs7501331 locus had a higher ($P < 0.05$) MPOD, and subjects with GG at rs1761667 CD36 locus had a higher ($P < 0.05$) MPOD than those with an A allele.

Conclusions: These results suggest that BCMO1 and CD36 are implicated in plasma and retina concentrations of lutein and that genetic variants in these genes can modulate blood and retina concentrations of lutein.

PMID: 21091228 [PubMed - as supplied by publisher]

Other Management & Epidemiology

4. Conf Proc IEEE Eng Med Biol Soc. 2010;1:4100-3.

Towards automatic detection of age-related macular degeneration in retinal fundus images.

Liang Z, Wong DW, Liu J, Chan KL, Wong TY.

Institute for Infocomm Research, A*STAR, Singapore.

Abstract

Age-related macular degeneration (AMD) is a leading cause of blindness worldwide. The disease is highly associated with age, and becoming increasingly prevalent in our aging societies. Drusen is a pathological feature that is well-associated with AMD. In this paper, we present a method of detecting drusen in retinal fundus images. The method first determines the location of the macula, which is used as a landmark for a clinical drusen grading overlay. Subsequently, regions of drusen are identified though a maximal region-based pixel intensity approach via RGB and HSV channels. Methods of reducing the effect of retinal and choroidal vessels are also described. The system is tested on a sample set of 16 fundus images from a clinical study, with half having drusen. Experiments on the results show a sensitivity and specificity of 0.75 on the test image set.

PMID: 21096627 [PubMed - in process]

5. Conf Proc IEEE Eng Med Biol Soc. 2010;1:5363-6.

In vivo snapshot hyperspectral image analysis of age-related macular degeneration.

Lee N, Wielaard J, Fawzi AA, Sajda P, Laine AF, Martin G, Humayun MS, Smith RT.

Heffner Biomedical Imaging Laboratory (HBIL) and the Department of Biomedical Engineering, Columbia University, New York, 10027 USA.

Abstract

Drusen, the hallmark lesions of age related macular degeneration (AMD), are biochemically heterogeneous and the identification of their biochemical distribution is key to the understanding of AMD. Yet the challenges are to develop imaging technology and analytics, which respect the physical generation of the hyperspectral signal in the presence of noise, artifacts, and multiple mixed sources while maximally exploiting the full data dimensionality to uncover clinically relevant spectral signatures. This paper reports on the statistical analysis of hyperspectral signatures of drusen and anatomical regions of interest using snapshot hyperspectral imaging and non-negative matrix factorization (NMF). We propose physical meaningful priors as initialization schemes to NMF for finding low-rank decompositions that capture the underlying physiology of drusen and the macular pigment. Preliminary results show that snapshot hyperspectral imaging in combination with NMF is able to detect biochemically meaningful components of drusen and the macular pigment. To our knowledge, this is the first reported demonstration in vivo of the separate absorbance peaks for lutein and zeaxanthin in macular pigment.

PMID: 21096261 [PubMed - in process]

6. Br J Ophthalmol. 2010 Nov 25. [Epub ahead of print]

Evolution of reticular pseudodrusen.

Sarks J, Arnold J, Ho IV, Sarks S, Killingsworth M.

Prince of Wales Hospital, Randwick, Sydney, Australia.

Abstract

Aims: To report observations relating to the clinical recognition and possible basis of reticular pseudodrusen (RPD).

Methods: This retrospective study reports the evolution of RPD in 166 patients who had follow-up of over 1 year using multiple imaging techniques. Mean age when first seen was 73.3 years and the mean period of observation was 4.9 years (range 1-18 years). Associated macular changes were recorded.

Results: RPD were first identified in the upper fundus as a reticular network, which then became less obvious, developing a diffuse yellowish appearance. RPD also faded around choroidal neovascularisation (CNV). RPD therefore could be transient but the pattern often remained visible outside the macula or nasal to the discs. Manifestations of age-related macular degeneration (AMD) were present in nearly all eyes and there was a particularly high association with CNV (52.1%). In one clinicopathological case abnormal material was found in the subretinal space.

Conclusions: The prevalence of RPD may be underestimated because their recognition depends upon the imaging method used, the area of fundus examined and the confusion with typical drusen. The pathology of one eye suggests that RPD may correspond to material in the subretinal space.

PMID: 21109695 [PubMed - as supplied by publisher]

7. Acta Ophthalmol. 2010 Nov 25. doi: 10.1111/j.1755-3768.2010.02051.x. [Epub ahead of print]

The prevalence and clinical characteristics of Charles Bonnet Syndrome in Danish patients with neovascular age-related macular degeneration.

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Department of Ophthalmology, Copenhagen University Hospital, Roskilde, Denmark.

Abstract

Purpose: To investigate the prevalence and clinical characteristics of the Charles Bonnet Syndrome (CBS) in a group of Danish patients with neovascular age-related macular degeneration (AMD) and to study whether CBS is associated with a specific retinal morphology.

Methods: Three-hundred consecutive patients with neovascular AMD attending assessment consultations following variable series of ranibizumab therapy were actively asked whether they had symptoms of CBS. If they responded positively, a detailed questionnaire was orally administered to inquire into the details of the symptoms. Detailed optical coherence tomography and autofluorescence was performed. A comparison was made between retinal morphology of a randomly selected equal number of patients without CBS to patients with CBS.

Results: Twenty-five (8.3%) patients of 300 had hallucinations attributable to CBS. The median lesion size - measured as total area with increased autofluorescence - in the CBS group (median 14.2 mm(2)) was not significantly different from the non-CBS group (median 16.2 mm(2)); however, the patients with CBS had significantly larger areas of geographic atrophy (median 2 mm(2)) compared to patients without CBS (median 0.3 mm(2)) (p = 0.002).

Conclusion: CBS is not uncommon in an unselected population with neovascular AMD, and symptoms of CBS may be associated with larger areas of geographic atrophy.

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PMID: 21106047 [PubMed - as supplied by publisher]

8. J Biol Chem. 2010 Nov 19. [Epub ahead of print]

{alpha}B-crystallin is found in detergent resistant membrane microdomains and is secreted via exosomes from human retinal pigment epithelial cells.

Gangalum RK, Atanasov IC, Zhou ZH, Bhat SP.

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Abstract

αB-crystallin (αB) is known as an intracellular Golgi membrane-associated small heat shock protein. Elevated levels of this protein have been linked with a myriad of neurodegenerative pathologies including Alzheimer's disease, Multiple Sclerosis and age-related macular degeneration (AMD). The membrane association of αB has been known for more than three decades yet its physiological import has remained unexplained. In this investigation we show that αB is secreted from human adult retinal pigment epithelial cells (ARPE) via microvesicles (exosomes), independent of the ER-Golgi protein export pathway. The presence of αB in these lipoprotein structures was confirmed by its susceptibility to digestion by Proteinase K only when exosomes were exposed to Triton X-100. Transmission Electron Microscopy was used to localize αB in immunogold labeled intact and permeabilized microvesicles. The saucer-shaped exosomes, with a median diameter of 100-200 nm, were characterized by the presence of Flotillin-1, α-Enolase and

Hsp70, the same proteins that associate with detergent resistant membrane microdomains (DRMs), which are known to be involved in their biogenesis. Notably, using polarized ARPE, we show that the secretion of αB is predominantly apical. Using Optiprep gradients we demonstrate that αB resides in the DRM fraction. The secretion of αB is inhibited by the cholesterol depleting drug, methyl β-cyclodextrin (MBCD) suggesting that the physiological function of this protein and the regulation of its export through exosomes may reside in its association with DRMs/lipid rafts.

PMID: 21097504 [PubMed - as supplied by publisher]

9. Ophthalmology. 2010 Nov 18. [Epub ahead of print]

Documentation of Intraretinal Retinal Pigment Epithelium Migration via High-Speed Ultrahigh-Resolution Optical Coherence Tomography.

Ho J, Witkin AJ, Liu J, Chen Y, Fujimoto JG, Schuman JS, Duker JS.

New England Eye Center, Tufts Medical Center, Boston, Massachusetts; Boston University School of Medicine, Boston, Massachusetts.

Abstract

PURPOSE: To describe the features of intraretinal retinal pigment epithelium (RPE) migration documented on a prototype spectral-domain, high-speed, ultrahigh-resolution optical coherence tomography (OCT) device in a group of patients with early to intermediate dry age-related macular degeneration (AMD) and to correlate intraretinal RPE migration on OCT to RPE pigment clumping on fundus photographs.

DESIGN: Retrospective, noncomparative, noninterventional case series.

PARTICIPANTS: Fifty-five eyes of 44 patients seen at the New England Eye Center between December 2007 and June 2008 with early to intermediate dry AMD.

METHODS: Three-dimensional OCT scan sets from all patients were analyzed for the presence of intraretinal RPE migration, defined as small discreet hyperreflective and highly backscattering lesions within the neurosensory retina. Fundus photographs also were analyzed to determine the presence of RPE pigment clumping, defined as black, often spiculated, areas of pigment clumping within the macula. The en face OCT images were correlated with fundus photographs to demonstrate correspondence of intraretinal RPE migration on OCT and RPE clumping on fundus photography.

MAIN OUTCOME MEASURES: Drusen, dry AMD, intraretinal RPE migration, and RPE pigment clumping.

RESULTS: On OCT scans, 54.5% of eyes (61.4% of patients) demonstrated intraretinal RPE migration. Of the fundus photographs, 56.4% demonstrated RPE pigment clumping. All eyes with intraretinal RPE migration on OCT had corresponding RPE pigment clumping on fundus photographs. The RPE pigment migrated most frequently into the outer nuclear layer (66.7% of eyes) and less frequently into more anterior retinal layers. Intraretinal RPE migration mainly occurred above areas of drusen (73.3% of eyes).

CONCLUSIONS: The appearance of intraretinal RPE migration on OCT is a common occurrence in early to intermediate dry AMD, occurring in 54.5% of eyes, or 61.4% of patients. The area of intraretinal RPE migration on OCT always correlated to areas of pigment clumping on fundus photography. Conversely, all but 1 eye with RPE pigment clumping on fundus photography also had areas of intraretinal RPE migration on OCT. The high incidence of intraretinal RPE migration observed above areas of drusen suggests that drusen may play physical and catalytic roles in facilitating intraretinal RPE migration in dry AMD patients.

FINANCIAL DISCLOSURE(S): Proprietary or commercial disclosure may be found after the references.

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PMID: 21093923 [PubMed - as supplied by publisher]

10. Ophthalmology. 2010 Nov 20. [Epub ahead of print]

Vitreomacular Interface in Typical Exudative Age-Related Macular Degeneration and Polypoidal Choroidal Vasculopathy.

Nomura Y, Ueta T, Iriyama A, Inoue Y, Obata R, Tamaki Y, Yamaguchi T, Yanagi Y.

Department of Ophthalmology, University of Tokyo School of Medicine, Tokyo, Japan.

Abstract

PURPOSE: To investigate the association in Japanese between posterior vitreous attachment and the pathologies of typical age-related macular degeneration (AMD) and polypoidal choroidal vasculopathy (PCV), 2 major forms of exudative AMD.

DESIGN: Retrospective observational case series.

PARTICIPANTS: A total of 378 eyes from 302 subjects (132 with typical AMD, 126 with PCV, 120 controls) from the University of Tokyo Hospital.

METHODS: Posterior vitreous detachment (PVD) and vitreomacular adhesion (VMA) were investigated by B-mode ultrasonography and spectral-domain optical coherence tomography (SD-OCT), respectively. The greatest linear dimension (GLD) of initial photodynamic therapy (PDT) in a subset of the patients (n=92) receiving PDT was also investigated.

MAIN OUTCOME MEASURES: Number of eyes with complete PVD and with VMA. The GLD of initial PDT.

RESULTS: In typical AMD eyes, the frequency of complete PVD was significantly lower (63 [56.8%] of 111 eyes) than in the controls (52 [70.3%] of 74 eyes, risk ratio [RR] 0.76, P=0.021) and the frequency of VMA tended to be higher (14/115 [12.2%] in typical AMD eyes and 6/86 [7.0%] in the controls, RR 2.15, P=0.099). The frequency of complete PVD [77 [63.1%] of the 122 eyes] and VMA (9/108 [8.3%]) in PCV eyes was the same as the controls (RR 0.91, P=0.415 and RR 1.29, P=0.615). In patients with unilateral exudative AMD, the frequency of complete PVD was lower in typical AMD eyes than in fellow eyes (odds ratio [OR] 0.111, P=0.026) and VMA was observed in 7 (17.5%) and 3 (7.5%) typical AMD and fellow eyes, respectively (OR 2.33, P=0.34), whereas in PCV eyes, the frequency of complete PVD was higher (OR 8.00, P=0.045) and the frequency of VMA was the same as in the fellow eyes (OR 0.80, P=1.00). The GLD of the eyes without complete PVD or with VMA was significantly larger than that in the eyes with complete PVD in typical AMD eyes (P=0.042) and the same as that in the eyes with complete PVD in PCV eyes (P=0.67).

CONCLUSIONS: There is an association between posterior vitreous attachment and typical AMD. However, this association is not evident in PCV.

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PMID: 21095010 [PubMed - as supplied by publisher]

11. Conf Proc IEEE Eng Med Biol Soc. 2010;1:3065-8.

ORIGA(-light): An online retinal fundus image database for glaucoma analysis and research.

Zhang Z, Yin FS, Liu J, Wong WK, Tan NM, Lee BH, Cheng J, Wong TY.

Institute for Infocomm Research, A*STAR, Singapore.

Abstract

Retinal fundus image is an important modality to document the health of the retina and is widely used to diagnose ocular diseases such as glaucoma, diabetic retinopathy and age-related macular degeneration.

However, the enormous amount of retinal data obtained nowadays mostly stored locally; and the valuable embedded clinical knowledge is not efficiently exploited. In this paper we present an online depository, ORIGA(-light), which aims to share clinical groundtruth retinal images with the public; provide open access for researchers to benchmark their computer-aided segmentation algorithms. An in-house image segmentation and grading tool is developed to facilitate the construction of ORIGA(-light). A quantified objective benchmarking method is proposed, focusing on optic disc and cup segmentation and Cup-to-Disc Ratio (CDR). Currently, ORIGA(-light) contains 650 retinal images annotated by trained professionals from Singapore Eye Research Institute. A wide collection of image signs, critical for glaucoma diagnosis, are annotated. We will update the system continuously with more clinical ground-truth images. ORIGA(-light) is available for online access upon request.

PMID: 21095735 [PubMed - in process]

12. Semin Ophthalmol. 2010 Sep-Nov;25(5-6):206-13.

Fundus autofluorescence in geographic atrophy: a review.

Choudhry N, Giani A, Miller JW.

Massachusetts Eye & Ear Infirmary, Harvard Medical School, Boston, MA, USA.

Abstract

Fundus autofluorescence is a noninvasive imaging technology that provides information on the distribution of lipofuscin within the retinal pigment epithelial cell monolayer. Progressive accumulation of lipofuscin within retinal pigment epithelial cells is involved in the pathogenesis of geographic atrophy in age-related macular degeneration. This review contains an introduction to fundus autofluorescence, review of currently available imaging methods, and discussion of the role of autofluorescence imaging in geographic atrophy progression. The recent classification of geographic atrophy phenotypes by the Fundus Autofluorescence in Age-related Macular Degeneration Study (FAM) and the association of phenotype and atrophy progression are also summarized.

PMID: 21091001 [PubMed - in process]

Diet

13. Aging (Albany NY). 2010 Nov 9. [Epub ahead of print]

CD36 plays an important role in the clearance of oxLDL and associated age-dependent sub-retinal deposits.

Picard E, Houssier M, Bujold K, Sapieha P, Lubell W, Dorfman A, Racine J, Hardy P, Febbraio M, Lachapelle P, Ong H, Sennlaub F, Chemtob S.

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Abstract

Age-related macular degeneration (AMD) represents the major cause of vision loss in industrialized nations. Laminar deposits in Bruch's membrane (BM) are among the first prominent histopathologic features, along with drusen formation, and have been found to contain oxidized lipids. Increases in concentrations of oxidized LDL (oxLDL) in plasma are observed with age and high fat high (HFHC) cholesterol diet. CD36 is the principal receptor implicated in uptake of oxLDL, and is expressed in the retinal pigment epithelium (RPE). We determined if CD36 participates in oxLDL uptake in RPE and correspondingly in clearance of sub-retinal deposits. Uptake of oxLDL by RPEin vitro and in vivo was CD36

-dependent. CD36 deficiency in mice resulted in age-associated accumulation of oxLDL and sub-retinal BM thickening, despite fed a regular diet. Conversely, treatment of HFHC-fed ApoE null mice with a CD36 agonist, EP80317 (300 µg/kg/day), markedly diminished thickening of BM, and partially preserved (in part) photoreceptor function. In conclusion, our data uncover a new role for CD36 in the clearance of oxidized lipids from BM and in the prevention of age-dependent sub-retinal laminar deposits.

PMID: 21098885 [PubMed - as supplied by publisher]

Pre-clinical

14. Retina. 2010 Nov 17. [Epub ahead of print]

POSTERIOR VITREOUS DETACHMENT WITH MICROPLASMIN ALTERS THE RETINAL PENETRATION OF INTRAVITREAL BEVACIZUMAB (AVASTIN) IN RABBIT EYES.

Goldenberg DT, Giblin FJ, Cheng M, Chintala SK, Trese MT, Drenser KA, Ruby AJ.

From the *Associated Retinal Consultants, Royal Oak, Michigan; and †Eye Research Institute, Oakland University, Rochester, Michigan.

Abstract

PURPOSE: Intravitreal bevacizumab (BV) (Avastin) is frequently used for the treatment of age-related macular degeneration. Previous studies have demonstrated full-thickness retinal penetration. Intravitreal recombinant microplasmin (MP) has been shown to successfully induce a posterior vitreous detachment (PVD) and vitreous liquefaction in animals. It has been suggested that a PVD may alter the retinal penetration of molecules in the vitreous cavity. The aim of this study was to compare BV retinal penetration in rabbit eyes with and without an MP-induced PVD.

METHODS: Twelve adult rabbits were injected with 0.1 mL (0.4 mg) of MP into the vitreous cavity of 1 eye. One week later, the rabbits were injected with 0.05 mL (1.25 mg) of BV into both eyes. Both eyes of 3 rabbits were harvested at 6 hours, 12 hours, 24 hours, and 72 hours after the BV injection. Frozen retinal cross sections were prepared, and BV retinal penetration was evaluated with immunohistochemistry using a fluorescence-labeled antibody against BV. Two eyes from one rabbit were not injected with either agent and used as controls to compare the background autofluorescence. Peripapillary retinal sections were recorded with a digital camera, and intraretinal BV fluorescence-labeled antibody was measured by qualitative photographic interpretation. Two additional rabbits received an intravitreal injection of 0.1 mL of MP in 1 eye. One week later, both eyes from each rabbit were enucleated, and frozen retinal sections were prepared and analyzed with light microscopy to evaluate histologic damage.

RESULTS: Full-thickness BV retinal penetration was observed throughout the retina in both eyes of each rabbit. All the MP-injected eyes exhibited increased antibody labeling in retinas evaluated at 6 hours, 12 hours, and 24 hours after BV injection when compared with the contralateral non-MP-injected eyes. By 3 days after BV injection, all eyes demonstrated decreased antibody labeling compared with earlier periods. At 3 days, 1 rabbit showed increased antibody labeling in the retina of the non-MP-injected eye compared with the contralateral MP-injected eye, and 2 rabbits exhibited similar antibody labeling in both eyes. When compared with control eyes, light microscopy demonstrated normal retinal histologic findings in eyes injected only with MP.

CONCLUSION: Increased BV retinal penetration is observed initially in eyes with an MP-induced PVD, and the mechanism is likely multifactorial. By 3 days, retinal penetration is similar in eyes with and without a PVD. Although it is difficult to directly extrapolate to humans, our study suggests that a PVD may alter the retinal penetration of BV.

PMID: 21099453 [PubMed - as supplied by publisher]

15. Conf Proc IEEE Eng Med Biol Soc. 2010;1:6761-4.

Retinal ganglion cell (RGC) responses to different voltage stimulation parameters in rd1 mouse retina.

Ye JH, Ryu SB, Kim KH, Goo YS.

Department of Physiology, Chungbuk National University School of Medicine, Cheongju, 361-763, Republic of Korea.

Abstract

Retinal prostheses are being developed to restore vision for the blind with retinal diseases such as retinitis pigmentosa (RP) or age-related macular degeneration (AMD). Since neural prostheses depend upon electrical stimulation to control neural activity, optimal stimulation parameters for successful encoding of visual information are one of the most important requirements to enable visual perception. Therefore, in this paper, we focused on RGC responses to different stimulation parameters in degenerated retina. For this purpose, we used in vitro preparation of rd1 mice retina on microelectrode arrays. When the neural network of rd1 mice retinas is stimulated with voltage-controlled pulses, RGCs in degenerated retina also respond to voltage amplitude or voltage duration modulation as well in wild-type RGCs. But the temporal pattern of RGCs response is very different; in wild-type RGCs, single peak within 100 ms appears while in RGCs in degenerated retina multiple peaks (~4 peaks) with ~10 Hz rhythm within 400 ms appear. The threshold charge densities for activation of RGCs in rd1 mouse retinas were on average 70.50 ~ 99.87 μC/cm(2) in the experiment of voltage amplitude modulation and 120.5 ~ 170.6 μC/cm(2) in the experiment of voltage duration modulation.

PMID: 21095834 [PubMed - in process]

16. Acta Ophthalmol. 2010 Nov 23. doi: 10.1111/j.1755-3768.2010.02047.x. [Epub ahead of print]

Clearance of dying ARPE-19 cells by professional and nonprofessional phagocytes in vitro-implications for age-related macular degeneration (AMD).

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Abstract

Purpose: Failure of retinal pigment epithelial (RPE) cells and macrophages to engulf different dying cells in the retina may result in accumulation of debris and development of age-related macular degeneration (AMD). The dynamics and influence of different treatments on this clearance process can be studied in vitro using human ARPE-19 cells and macrophages as phagocytes modelling dry and wet type of AMD, respectively.

Methods: Death through extracellular matrix detachment using polyHEMA-coated surfaces (anoikis) and UV irradiation (apoptosis) was induced in ARPE-19 cells. Two-coloured phagocytic assays were performed to quantify the amount of dying cells phagocytes engulfed (flow cytometry) and for visualization (fluorescent and scanning electron microscopy). The effect of phosphatidylserine inhibition with recombinant annexin-V and glucocorticoid (triamcinolone) treatment on the phagocytic process was tested.

Results: The clearance of anoikic and apoptotic cells by nondying ARPE-19 cells over 8 hr of co-incubation increased over time (at 8 hr, over 53% and 35% of the phagocytes contained engulfed dying cells, respectively). The human macrophages engulfed the anoikic and apoptotic ARPE-19 cells with seven

and four times lower capacity, respectively. Phosphatidylserine appearance on the dying cells did not affect, but triamcinolone treatment enhanced the phagocytosis of the dying cells by macrophages.

Conclusions: ARPE-19 cells are more efficient in clearing anoikic than UV-induced apoptotic cells. Macrophages are less efficient in the clearance process than ARPE-19 cells. The present model can be used for studying both dry and wet type of AMD in vitro and for testing different pharmacological aspects affecting this disease.

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PMID: 21091941 [PubMed - as supplied by publisher]

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Sphingosine-1-phosphate antibodies as potential agents in the treatment of cancer and age-related macular degeneration.

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Abstract

Sphingosine-1-phosphate (S1P) is a pleiotropic bioactive lipid thought to be dysregulated in a variety of disease conditions. In this review, we discuss the roles of S1P in cancer and in wet age-related macular degeneration (AMD). We also explore potential treatment strategies for these disorders, including the utility of ant-S1P antibodies acting as molecular sponges to neutralize dysregulated S1P in relevant tissues.

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PMID: 21091645 [PubMed - as supplied by publisher]