Macular Degeneration Foundation™
Our focus is your vision

MD Research News

Issue 99

Monday September 24 , 2012

This free weekly bulletin lists the latest published research articles on macular degeneration (MD) as indexed in the NCBI, PubMed (Medline) and Entrez (GenBank) databases. These articles were identified by a search using the key term “macular degeneration”.

If you have not already subscribed, please email Rob Cummins at **research@mdfoundation.com.au** with ‘Subscribe to MD Research News’ in the subject line, and your name and address in the body of the email.

You may unsubscribe at any time by an email to the above address with your ‘unsubscribe’ request.

Drug treatment

Retina. 2012 Sep 17. [Epub ahead of print]

INTRAVITREAL RANIBIZUMAB FOR POLYPOIDAL CHOROIDAL VASCULOPATHY IN NON-ASIAN PATIENTS.

Marcus DM, Singh H, Lott MN, Singh J, Marcus MD.

*Southeast Retina Center, Augusta, Georgia †Department of Ophthalmology, University of South Carolina School of Medicine, Columbia, South Carolina ‡Mayo Clinic Health System, Waycross, Georgia §Department of Ophthalmology, Northwestern University, Chicago, Illinois.

PURPOSE: To determine safety, tolerability, and efficacy of intravitreal ranibizumab in the treatment of polypoidal choroidal vasculopathy in a non-Asian population.

METHODS: Phase I/II, prospective, open-label, single-center, nonrandomized, uncontrolled, consecutive, interventional case series of 20 eyes in 19 patients with exudative active polypoidal choroidal vasculopathy. Eyes received 3 monthly intravitreal ranibizumab injections (0.3 or 0.5 mg), with additional ranibizumab injections, observation, or alternative treatments at investigators' discretion, through 24 months. Main outcome measures were ocular and systemic safety and mean change from baseline in best-corrected visual acuity and center point thickness.

RESULTS: Visually significant ocular adverse events included cataract progression (n = 3), mild vitreous hemorrhage (n = 2), and macular hole (n = 1). No systemic drug-related adverse events were observed. Mean baseline best-corrected visual acuity was 20/127 (range, 20/16-20/500) and center point thickness was 298 μm. Mean best-corrected visual acuity increased from baseline by 1.2 Snellen lines at 12 months and 24 months. Mean center point thickness decreased by 53 μm and 67 μm from baseline at 12 months and 24 months, respectively.

CONCLUSION: Intravitreal ranibizumab was well tolerated in non-Asian patients with polypoidal choroidal vasculopathy; the majority of eyes experienced improvements in best-corrected visual acuity and center point thickness after ranibizumab treatment.

PMID: 22990319 [PubMed - as supplied by publisher]

Retina. 2012 Sep 17. [Epub ahead of print]

EFFICACY OF ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY IN SUBRETINAL

NEOVASCULARIZATION SECONDARY TO MACULAR TELANGIECTASIA TYPE 2.

Narayanan R, Chhablani J, Sinha M, Dave V, Tyagi M, Pappuru RR, Kuppermann BD.

*Smt. Kanuri Santhamma Vitreoretinal Center, L V Prasad Eye Institute, Hyderabad, India †Shiley Eye Center, University of California, San Diego, La Jolla, California ‡Gavin Herbert Eye Institute, University of California, Irvine, Irvine, California.

PURPOSE: To evaluate the efficacy of intravitreal anti-vascular endothelial growth factor monotherapy in the treatment of naive subretinal neovascular membrane (SRNVM) secondary to macular telangiectasia (Mactel) Type 2.

METHODS: A retrospective chart review of consecutive patients with naive SRNVM secondary to Mactel who were examined between January 2007 and April 2011 was performed. Eyes with diabetic retinopathy, age-related macular degeneration, or any other macular pathology were excluded. Demographic data, medical history, and ocular history were recorded. The mean change in best-corrected visual acuity at the final visit was the primary outcome measure. The mean number of intravitreal injections, retinal thickness on optical coherence tomography, and intraocular pressure were the secondary outcomes.

RESULTS: A total of 16 eyes of 16 patients were included in the study. Of 16 eyes, 4 were treated with intravitreal ranibizumab monotherapy and 12 with intravitreal bevacizumab monotherapy. The average follow-up duration was 12 months (range, 3-43 months). The mean baseline visual acuity was 0.17 ± 0.16 (Snellen equivalent 20/120) (range, 0.001-0.5), and the mean final visual acuity was 0.27 ± 0.14 (Snellen equivalent 20/70) (range, 0.05-0.66), and this difference was statistically significant (P = 0.02). The mean number of intravitreal injections was 1.9 (range, 1-3), and there were no injection-related complications.

CONCLUSION: Intravitreal anti-vascular endothelial growth factor monotherapy appears to be effective and safe in treatment-naive SRNVM secondary to Mactel.

PMID: 22990322 [PubMed - as supplied by publisher]

Retina. 2012 Sep 17. [Epub ahead of print]

CLINICAL PREDICTORS OF SUSTAINED INTRAOCULAR PRESSURE ELEVATION DUE TO INTRAVITREAL ANTI-VASCULAR ENDOTHELIAL GROWTH FACTOR THERAPY.

Hoang QV, Tsuang AJ, Gelman R, Mendonca LS, Della Torre KE, Jung JJ, Freund KB.

*Vitreous Retina Macula Consultants of New York, New York, New York †LuEsther T. Mertz Retinal Research Center, Manhattan Eye, Ear, and Throat Institute, New York, New York ‡Department of Ophthalmology, Edward S. Harkness Eye Institute, Columbia University College of Physicians and Surgeons, New York, New York §Department of Ophthalmology, New York University Medical Center, New York, New York.

PURPOSE: We assess for frequency and predictive factors related to sustained intraocular pressure (IOP) elevation in eyes with neovascular age-related macular degeneration receiving intravitreal injections of ranibizumab and/or bevacizumab.

METHODS: A total of 328 patients with neovascular age-related macular degeneration (449 eyes) who presented to a single physician over a 6-month period were retrospectively assessed for baseline demographic/clinical information, total number of bevacizumab and/or ranibizumab injections, and sustained IOP elevation on 2 or more consecutive visits (absolute IOP >25 mmHg, increase above baseline >10 mmHg, or IOP of >21 mmHg and increase of >5 mmHg). Cox regression survival analysis and multivariate logistic regression were performed to assess the influence of intravitreal injections on experiencing sustained IOP elevation.

RESULTS: Overall, 32 eyes (7.1%) experienced sustained IOP elevation. Survival analysis showed a significant effect of the number of anti-vascular endothelial growth factor injections on sustained IOP elevation (hazard ratio, 1.085; 95% confidence interval: 1.06-1.11, P < 0.001). Also, there was an increased odds ratio (16.1, P = 0.008) of sustained IOP elevation in eyes receiving ≥29 injections compared with ≤12 injections. After controlling for the confounder (prior intravitreal steroid injection), total number of injections still showed a statistically significant association (P = 0.002).

CONCLUSION: A greater number of intravitreal anti-vascular endothelial growth factor injections is associated with an increased risk for sustained IOP elevation in eyes with neovascular age-related macular degeneration receiving intravitreal ranbizumab and/or bevacizumab.

PMID: 22990314 [PubMed - as supplied by publisher]

Bioconjug Chem. 2012 Sep 21. [Epub ahead of print]

Comparative binding of disulfide-bridged PEG-Fabs.

Brocchini S, Khalili H, Godwin A, Choi JW, Lever R.

Abstract

Protein PEGylation is the most clinically validated method to improve the efficacy of protein-based medicines. Antibody fragments such as Fabs display rapid clearance from blood circulation and therefore are good candidates for PEGylation. We have developed PEG-bis-sulfone reagents 1 that can selectively alkylate both sulfurs derived from a native disulfide. Using PEG-bis-sulfone reagents 1, conjugation of PEG specifically targets the disulfide distal to the binding region of the Fab (Scheme 2). PEG-bis-sulfone reagents 1 (10-40 kDa) were used to generate the corresponding PEG-mono-sulfones 2 that underwent essentially quantitative conjugation to give the PEG-Fab product 4. Four Fabs were PEGylated: Fabbeva, Fab'beva, Fabrani and Fabtrast. Proteolytic digestion of bevacizumab with papain gave Fabbeva, while digestion of bevacizumab with IdeS gave F(ab')2-beva, which after reaction with DTT and PEG-mono-sulfone 2 gave PEG2-Fab'beva. Ranibizumab, which is a clinically used Fab, was directly PEGylated to give PEG-Fabrani. Trastuzumab was proteolytically digested with papain and its corresponding Fab was PEGylated to give PEG-Fabtrast. Purification of the PEGylated Fabs was accomplished by a single ion exchange chromatography step to give pure PEG-Fab products as determined by silver stained SDS-PAGE. No loss of PEG was detected post conjugation. A comparative binding study by SPR using Biacore with low ligand immobilisation density was conducted using (i) VEGF165 for the bevacizumab and ranbizumab derived products or (ii) HER2 for the trastuzumab derived products. VEGF165 is a dimeric ligand with two binding sites for bevacizumab. HER2 has one domain for the binding of trastuzumab. Binding studies with PEG-Fabbeva indicated that the apparent affinity was 2-fold less compared to the unPEGylated Fabbeva. Binding properties of the PEG-Fabbeva products appeared to be independent of PEG molecular weight. Site-specific conjugation of two PEG molecules gave PEG2×20-Fab'beva, whose apparent binding affinity was similar to that observed for PEG-Fabbeva derivatives. The kd values were similar to the unPEGylated Fabbeva, hence once bound, PEG-Fabbeva remained bound to the same degree as Fabbeva. Biacore analysis indicated that both Fabrani and PEG20-Fabrani did not dissociate from the immobilised VEGF at 25 °C, but ELISA using immobilised VEGF showed 2-fold less apparent binding affinity for PEG20-Fabrani compared to the unPEGylated Fabrani. Additionally, the apparent binding affinities for trastuzumab and Fabtrast were comparable by both Biacore and ELISA. Biacore results suggested that trastuzumab had a slower association rate compared to Fabtrast, however both molecules displayed the same apparent binding affinity. This could have been due to enhanced rebinding effects of trastuzumab as it is a bivalent molecule. Analogous to PEG-Fabbeva products, PEG20-Fabtrast displayed 2-fold lower binding compared to Fabtrast when evaluated by ELISA. The variations in the apparent affinity for the PEGylated Fab variants were all related to the differences in the association rates (ka) rather than the dissociation rates (kd). We have shown that (i) Fabs are well matched for site-specific PEGylation with our bis-alkylation PEG reagents, (ii) PEGylated Fabs display only a 2-fold reduction in

apparent affinity without any change in the dissociation rate, and (iii) the apparent binding rates and affinities remain constant as the PEG molecular weight is varied.

PMID: 22994419 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2012 Sep 20. doi: 10.1111/j.1755-3768.2012.02525.x. [Epub ahead of print]

Topical Ranibizumab inhibits inflammatory corneal hem- and lymphangiogenesis.

Bucher F, Parthasarathy A, Bergua A, Onderka J, Regenfuß B, Cursiefen C, Bock F.

Department of Ophthalmology, University of Cologne, Cologne, Germany Department of Ophthalmology, University of Erlangen-Nürnberg, Erlangen, Germany Cornea Service, Clinical Research Centre, Vasan Eye Care Hospital, Chennai, India T.N Shukla Eye Hospital, Ranjhi, Jabalpur, India.

Purpose: Ranibizumab (Lucentis(®)) is a Fab-Fragment of a recombinant, humanized, monoclonal VEGF (anti-vascular endothelial growth factor) antibody. This study analyzed the ability of topical Ranibizumab to inhibit lymphangiogenesis in addition to hemangiogenesis after acute corneal inflammation in vivo. In addition, the effect of Ranibizumab on the proliferation of human lymphatic endothelial cells (LECs) and blood endothelial cells (BECs) in vitro was studied.

Methods: The inhibitory effect of Ranibizumab on LECs and BECs was studied in vitro using a proliferation enzyme-linked immunosorbent assay (ELISA) assay. To study the in vivo effects of Ranibizumab, the mouse model of suture induced inflammatory corneal neovascularization was used. Study mice received topical Ranibizumab as eye drops. After 1 week excised corneas were stained with LYVE-1 and CD31. Hemangiogenesis and lymphangiogenesis were analyzed morphometrically by using a semiautomatic method based on the image analyzing program Cell^F.

Results: An antiproliferative effect of Ranibizumab was seen in vitro on both human BECs and LECs with a significance of $p < 0.0001$ and $p < 0.0004$, respectively. In vivo experiments showed that topical application of Ranibizumab significantly inhibits both hemangiogenesis ($p = 0.0026$) and lymphangiogenesis ($p = 0.0026$) in the cornea.

Conclusion: Ranibizumab is a potent inhibitor of inflammatory corneal hemangiogenesis and lymphangiogenesis in vivo with a direct inhibitory effect on both endothelial cell types in vitro. This study for the first time demonstrates an inhibitory effect of Ranibizumab on lymphatic vessels which could have a wider range of clinical applications.

PMID: 22994268 [PubMed - as supplied by publisher]

Vestn Oftalmol. 2012 Jul-Aug;128(4):75-7.

[Safety aspect of age macular degeneration treatment].

[Article in Russian]

[No authors listed]

PMID: 22994114 [PubMed - in process]

Acta Ophthalmol. 2012 Sep 19. doi: 10.1111/j.1755-3768.2012.02546.x. [Epub ahead of print]

Effects of repeated intravitreal bevacizumab injections on the inner retinal function in neovascular age-related macular degeneration.

Kim HD, Kim SH, Cho IH, Moon CH, Ohn YH, Park TK.

Department of Ophthalmology, Soonchunhyang University College of Medicine, Bucheon, Korea.

PMID: 22989051 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Vestn Oftalmol. 2012 Jul-Aug;128(4):48-51.

[The effect of yellow filter intraocular lens on the macula after cataract phacoemulsification in patients with age macular degeneration]. [Article in Russian]

[No authors listed]

Abstract

Macula changes diagnosed with optical coherence tomography (OCT) within a year after cataract phacoemulsification (PE) with intraocular lens implantation with and without yellow filter are presented. 32 patients (36 eyes) with early stages of age macular degeneration (AMD) were included into the experimental group and 35 patients (36 eyes) served as controls. IOLs with yellow filter were implanted in 21 eyes, and in 15 cases IOLs without filter were used in each group. According to OCT data thickening of fovea and increasing of macula volume developed within 6 months after cataract PE. Implantation of yellow filter IOLs reduced the intensity of these changes after surgery in patients with AMD. The progression of early AMD into advanced stages within a year after PE was not observed.

PMID: 22994108 [PubMed - in process]

Phys Med Biol. 2012 Sep 21;57(20):6371-6380. [Epub ahead of print]

Gold nanoparticle enhancement of stereotactic radiosurgery for neovascular age-related macular degeneration.

Ngwa W, Makrigiorgos GM, Berbeco RI.

Department of Radiation Oncology, Division of Medical Physics and Biophysics, Brigham and Women's Hospital, Dana-Farber Cancer Institute and Harvard Medical School, Boston, MA 02115, USA.

Abstract

Age-related macular degeneration (AMD) is the leading cause of blindness in developed countries for people over the age of 50. In this work, the dosimetric feasibility of using gold nanoparticles (AuNP) as radiosensitizers to enhance kilovoltage stereotactic radiosurgery for neovascular AMD is investigated. Microdosimetry calculations at the sub-cellular level were carried out to estimate the radiation dose enhancement to individual nuclei in neovascular AMD endothelial cells (nDEF) due to photon-induced photo-/Auger electrons from x-ray-irradiated AuNP. The nDEF represents the ratio of radiation doses to the endothelial cell nuclei with and without AuNP. The calculations were carried out for a range of feasible AuNP local concentrations using the clinically applicable 100 kVp x-ray beam parameters employed by a commercially available x-ray therapy system. The results revealed nDEF values of 1.30-3.26 for the investigated concentration range of 1-7 mg g(-1), respectively. In comparison, for the same concentration range, nDEF values of 1.32-3.40, 1.31-3.33, 1.29-3.19, 1.28-3.12 were calculated for 80, 90, 110 and 120 kVp x-rays, respectively. Meanwhile, calculations as a function of distance from the AuNP showed that the dose enhancement, for 100 kVp, is markedly confined to the targeted neovascular AMD endothelial cells where AuNP are localized. These findings provide impetus for considering the application of AuNP to enhance therapeutic efficacy during stereotactic radiosurgery for neovascular AMD.

PMID: 22995994 [PubMed - as supplied by publisher]

Pathogenesis

J Neurosci. 2012 Sep 19;32(38):13010-21.

Loss of Retinoschisin (RS1) Cell Surface Protein in Maturing Mouse Rod Photoreceptors Elevates the Luminance Threshold for Light-Driven Translocation of Transducin But Not Arrestin.

Ziccardi L, Vijayasarathy C, Bush RA, Sieving PA.

G. B. Bietti Foundation, Istituto di Ricovero e Cura a Carattere Scientifico (IRCCS), 00198 Rome, Italy, Section on Translational Research for Retinal and Macular Degeneration, National Institute on Deafness and Other Communication Disorders, and National Eye Institute, National Institutes of Health, Bethesda, Maryland 20892.

Abstract

Loss of retinoschisin (RS1) in Rs1 knock-out (Rs1-KO) retina produces a post-photoreceptor phenotype similar to X-linked retinoschisis in young males. However, Rs1 is expressed strongly in photoreceptors, and Rs1-KO mice have early reduction in the electroretinogram a-wave. We examined light-activated transducin and arrestin translocation in young Rs1-KO mice as a marker for functional abnormalities in maturing rod photoreceptors. We found a progressive reduction in luminance threshold for transducin translocation in wild-type (WT) retinas between postnatal days P18 and P60. At P21, the threshold in Rs1-KO retinas was 10-fold higher than WT, but it decreased to <2.5-fold higher by P60. Light-activated arrestin translocation and re-translocation of transducin in the dark were not affected. Rs1-KO rod outer segment (ROS) length was significantly shorter than WT at P21 but was comparable with WT at P60. These findings suggested a delay in the structural and functional maturation of Rs1-KO ROS. Consistent with this, transcription factors CRX and NRL, which are fundamental to maturation of rod protein expression, were reduced in ROS of Rs1-KO mice at P21 but not at P60. Expression of transducin was 15-30% lower in P21 Rs1-KO ROS and transducin GTPase hydrolysis was nearly twofold faster, reflecting a 1.7- to 2.5-fold increase in RGS9 (regulator of G-protein signaling) level. Transduction protein expression and activity levels were similar to WT at P60. Transducin translocation threshold elevation indicates photoreceptor functional abnormalities in young Rs1-KO mice. Rapid reduction in threshold coupled with age-related changes in transduction protein levels and transcription factor expression are consistent with delayed maturation of Rs1-KO photoreceptors.

PMID: 22993419 [PubMed - in process]

Adv Exp Med Biol. 2013;734:301-13.

Complement in action: an analysis of patent trends from 1976 through 2011.

Yang K, Deangelis RA, Reed JE, Ricklin D, Lambris JD.

Department of Pathology and Laboratory Medicine, University of Pennsylvania, 401A Stellar-Chance Building, 422 Curie Blvd, Philadelphia, PA, 19104, USA.

Abstract

Complement is an essential part of the innate immune response. It interacts with diverse endogenous pathways and contributes to the maintenance of homeostasis, the modulation of adaptive immune responses, and the development of various pathologies. The potential usefulness, in both research and clinical settings, of compounds that detect or modulate complement activity has resulted in thousands of publications on complement-related innovations in fields such as drug discovery, disease diagnosis and treatment, and immunoassays, among others. This study highlights the distribution and publication trends of patents related to the complement system that were granted by the United States Patent and Trademark Office from 1976 to the present day. A comparison to complement-related documents published by the

World Intellectual Property Organization is also included. Statistical analyses revealed increasing diversity in complement-related research interests over time. More than half of the patents were found to focus on the discovery of inhibitors; interest in various inhibitor classes exhibited a remarkable transformation from chemical compounds early on to proteins and antibodies in more recent years. Among clinical applications, complement proteins and their modulators have been extensively patented for the diagnosis and treatment of eye diseases (especially age-related macular degeneration), graft rejection, cancer, sepsis, and a variety of other inflammatory and immune diseases. All of the patents discussed in this chapter, as well as those from other databases, are available from our newly constructed complement patent database: www.innateimmunity.us/patent .

PMID: 22990712 [PubMed - in process]

Aging Clin Exp Res. 2012 Sep 13. [Epub ahead of print]

THE IMPACT OF INFLAMMATION TO THE ANTIOXIDANT DEFENSE PARAMETERS IN AMD PATIENTS.

Colak E, Majkic-Singh N, Zoric L, Radosavljevic A, Kosanovic-Jakovic N.

Institute of Medical Biochemistry, Clinical Center of Serbia, School of Pharmacy, University of Belgrade, Serbia.

Objective: Oxidative stress and inflammation are postulated to be involved in the pathogenesis of the age-related macular degeneration (AMD) although the mechanism linking the oxidation and inflammation is still unknown. The aim of this study was the analysis of the antioxidant capacity measured by levels of the antioxidant enzymes: superoxide dismutase (SOD), glutathione peroxidase (GPx), glutathione reductase (GR) and total antioxidant status (TAS) along with the inflammatory markers such as Creactive protein (CRP), interleukin-6 (IL-6) and fibrinogen in AMD patients in order to analyze the relationship of the inflammatory markers with the antioxidant parameters and their association with AMD.

Material and methods: The cross-sectional study, carried out in the University clinical setting, included 84 patients with the age-related macular degeneration, aged 71.25±7.14 years and 84 aged-matched control subjects (CG).

Results: Statistical analysis revealed significantly lower GR (P=0.007) and TAS (P<0.000) values in the group of AMD patients compared to the controls. Logistic regression analysis showed that higher values of the inflammatory markers (CRP>3 mg/L, IL>4.9 pg/mL, fibrinogen >3.8 g/L) and lower values of the antioxidative parameters (SOD<900 U/gHb, GR<55 U/L and TAS <1.15 mmol/L) were significantly associated with AMD (ORCRP:1.29, 95% CI 0.54-3.12, P<0.05; ORIL-6: 3.53; 95% CI 1.16-10.75, P=0.024; ORFIB: 3.06 95% CI 1.78-7.92, P=0.019; ORSOD: 2.39; 95% CI 0.78-7.35, P<0.05; ORGR: 4.04, 95% CI 1.28-12.73, P=0.013 and ORTAS: 2.9, 95% CI 1.4-6.3, P=0.032).

Conclusions: Based on the obtained results, it may be concluded that the antioxidant defense system was significantly reduced in patients with AMD and the probability to develop AMD was higher in older individuals with lower values of the antioxidant parameters and higher values of the inflammatory markers.

PMID: 22982945 [PubMed - as supplied by publisher]

J Neuroinflammation. 2012 Sep 19;9(1):221. [Epub ahead of print]

Small interfering RNA-mediated suppression of Ccl2 in Muller cells attenuates microglial recruitment and photoreceptor death following retinal degeneration.

Rutar MV, Natoli RC, Provis JM.

BACKGROUND: The recruitment and activation of inflammatory cells is thought to exacerbate photoreceptor death in retinal degenerative conditions such as age-related macular degeneration (AMD). We investigated the role of Muller cell-derived chemokine (C-C motif) ligand (Ccl)2 expression on monocyte/microglia infiltration and photoreceptor death in light-mediated retinal degeneration, using targeted short interfering (si)RNA.

METHODS: Adult Sprague--Dawley rats were injected intravitreally with 1 mug of either Ccl2 siRNA or scrambled siRNA, and were then exposed to 1000 lux of light for a period of 24 hours. The mice were given an overdose of barbiturate, and the retinas harvested and evaluated for the effects of bright-light exposure. Ccl2 expression was assessed by quantitative PCR, immunohistochemistry, and in situ hybridization. Monocytes/microglia were counted on retinal cryostat sections immunolabeled with the markers ED1 and ionized calcium binding adaptor (IBA)1, and photoreceptor apoptosis was assessed using terminal dUTP nick end labeling.

RESULTS: Intravitreal injection of Ccl2 siRNA significantly reduced the expression of Ccl2 following light damage to 29 % compared with controls. In retinas injected with Ccl2 siRNA, in situ hybridization and immunohistochemistry on retinal cryostat sections showed a substantial decrease in Ccl2 within Muller cells. Cell counts showed significantly fewer ED1-positive and IBA1-positive cells in the retinal vasculature and outer nuclear layer of Ccl2 siRNA-injected retinas, compared with controls. Moreover, there was significantly less photoreceptor apoptosis in Ccl2 siRNA-injected retinas compared with controls.

CONCLUSIONS: Our data indicate that Ccl2 expression by Muller cells promotes the infiltration of monocytes/microglia, thereby contributing to the neuroinflammatory response and photoreceptor death following retinal injury. Modulation of exaggerated chemokine responses using siRNA may have value in reducing inflammation-mediated cell death in retinal degenerative disease such as AMD.

PMID: 22992301 [PubMed - as supplied by publisher]

Klin Monbl Augenheilkd. 2012 Sep 19. [Epub ahead of print]

[Macrophages in the Ultrastructure of PDR Membranes and Subretinal AMD Membranes - A Possible Role in Neoangiogenesis.] [Article in German]

Vidinova CN, Vidinov KN.

Department of Ophthalmology, Military Medical Academy, Sofia, Bulgaria.

Background and Purpose: Proliferative diabetic retinopathy (PDR) and age-related macular degeneration (AMD) are sight-threatening diseases with high social impact. The aim of our study is to compare the ultrastructure of PDR membranes and those in AMD with a special focus on the macrophages.

Material and Methods: In our study 24 PDR patients and 11 AMD patients were enrolled. They all underwent complete ophthalmological examination including OCT. In all cases pars plana vitrectomy with excision of epiretinal or subretinal membranes was performed. Proliferations taken directly from the eye have been studied by transmission and scanning electron microscopy and with safranin O.

Results: The fibrovascular proliferations in PDR consisted mostly of fibroblasts and occasional macrophages near the blood vessels. The prevailing type of blood vessels had one thin layer of endothelial cells, very thin basal membrane and no pericytes. Subretinal membranes in AMD patients consisted mainly of fibroblasts, isolated RPE cells and elements of the blood. Numerous macrophages and leukocytes in groups and clusters were found around the capillaries of subretinal blood vessels. The cells showed some peculiarities: diminished number of pseudopodia, altered shape. Groups of cytofilaments became visible in macrophages cell periphery. The number of proteoglycans in the matrix was increased.

Conclusion: Our results point out that macrophages play a key role in the formation of the fibrovascular proliferations in both PDR and AMD. Inflammation is assumed to act in the pathogenesis of both diseases.

Probably the senescence of macrophages, which we found in our study, is responsible for their proangiogenic response and promotion of new vessel formation. It is reasonable to expect that anti-inflammatory therapy might be helpful in patients with AMD and PDR.

PMID: 22996633 [PubMed - as supplied by publisher]

High Alt Med Biol. 2012 Sep;13(3):169-75.

Hypoxia in the eye: a two-sided coin.

Grimm C, Willmann G.

1 Laboratory for Retinal Cell Biology, Department of Ophthalmology, Zurich Centre for Integrative Human Physiology (ZIHP), and Neuroscience Centre (ZNZ), University of Zurich , Zurich, Switzerland .

Abstract

Tissue oxygenation in general and hypoxia in particular are important regulators of retinal physiology and pathophysiology. Reduced oxygen tension and hypoxia-inducible transcription factors along with some of their target genes are critically involved in retinal development, and especially in the generation of a normal retinal vasculature. Well-timed hypoxia is thus vital for the young eye to establish proper retinal function and vision. However, when hypoxia is ill-timed, reduced oxygen tension may be associated with the development of retinal pathologies, including retinopathy of prematurity, diabetic retinopathy, glaucoma, age-related macular degeneration, or high altitude retinopathy. Here, reduced oxygen tension activates a hypoxic response that culminates in an increased expression of vascular endothelial growth factor. This causes pathological neovascularization of the delicate neuronal retina, a process that may ultimately lead to loss of vision. In contrast, preconditioning by well-defined and controlled short-term hypoxia is not devastating for the retina but instead induces a molecular response that provides protection to neuronal cells. Detailed investigation of hypoxic mechanisms during development and adulthood may thus reveal factors, which may be targeted by therapeutic approaches to save and preserve vision in patients.

PMID: 22994516 [PubMed - in process]

Epidemiology

J Gerontol A Biol Sci Med Sci. 2012 Sep 14. [Epub ahead of print]

A Population-Based Examination of the Visual and Ophthalmological Characteristics of Licensed Drivers Aged 70 and Older.

Owsley C, McGwin G Jr, Searcey K.

Address correspondence to Cynthia Owsley, Department of Ophthalmology, University of Alabama at Birmingham, 700 S. 18th Street, Suite 609, Birmingham, AL 35294-0009. E-mail: owsley@uab.edu.

BACKGROUND: Safe driving performance depends on visual skills yet little is known about the prevalence of vision impairments in older drivers and the eye conditions that cause them. This study is a population-based examination of the prevalence of vision impairment and major ophthalmological conditions among drivers aged 70 and older.

METHODS: The source population was a random sample of 2,000 licensed drivers aged 70 and older residing in north central Alabama. All had driven within the past 3 months. Binocular visual acuity and contrast sensitivity were assessed. The Useful Field of View subtest 2 and Trails B assessed visual processing speed. Ophthalmological diagnoses for cataract, intraocular lens placement, glaucoma, diabetic retinopathy, age-related macular degeneration, and diabetic retinopathy were obtained through medical

records from the most recent eye examination.

RESULTS: Ninety-two percent of drivers had visual acuity of 20/40 or better; only two drivers (0.1%) had acuity worse than 20/100. Ninety-three percent had normal contrast sensitivity (≥1.5). About 40% had slowed visual processing speed (44%, Useful Field of View; 38%, Trails B). The most common eye condition was cataract, with more than half having cataract in one or both eyes (56%); yet by the 80s and 90s, the prevalence was low, with most drivers having undergone cataract surgery and intraocular lens placement.

CONCLUSIONS: This population-based study suggests that serious impairment in central vision-visual acuity or contrast sensitivity-is rather uncommon in older drivers; however, slowed visual processing speed is common.

PMID: 22982690 [PubMed - as supplied by publisher]