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MD Research News

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Drug treatment

Korean J Ophthalmol. 2011 Aug;25(4):231-7. Epub 2011 Jul 22.

Combined treatment of photodynamic therapy and bevacizumab for choroidal neovascularization secondary to age-related macular degeneration.

Kim HW, Kim JL, Lee MH, Yoo HG, Chung IY, Lee JE.

Department of Ophthalmology, Inje University College of Medicine, Busan, Korea.

PURPOSE: To evaluate the outcome of a combined photodynamic therapy and intravitreal injection of bevacizumab in choroidal neovascularization secondary to age-related macular degeneration.

METHODS: Photodynamic therapy (PDT) was administered to 28 eyes followed by 3 consecutive bevacizumab injections. Patients were followed-up for more than 12 months. At baseline, 1, 3, 6, and 12 months post PDT, visual acuity (VA) and central macular thickness were measured using optical coherence tomography.

RESULTS: The mean VA was significantly improved from logarithm of the minimal angle of resolution 0.86 at baseline to 0.69 at 1 month ($p = 0.011$), 0.63 at 3 months ($p = 0.003$), 0.64 at 6 months ($p = 0.004$) and 0.60 at 12 months ($p < 0.001$). Central macular thickness decreased significantly from 328.3 μm at baseline to 230.0 μm at 6 months and 229.9 μm at 1 year ($p < 0.001$). Reinjection mean number was 0.4 for 6 months and 0.8 for 12 months. By 1 year, retreatment was performed in 10 eyes (36%).

CONCLUSIONS: PDT combined with three consecutive intraviteal bevacizumab injections was effective in improving VA and reducing central macular thickness.

PMID: 21860568 [PubMed - in process] PMCID: PMC3149132

Int J Dev Biol. 2011;55(4-5):383-8.

From the discovery of Vascular Endothelial Growth Factor to the introduction of Avastin in clinical trials - an interview with Napoleone Ferrara.

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Abstract

Napoleone Ferrara and his colleagues at Genentech were the first to isolate and clone vascular endothelial growth factor (VEGF) in 1989. His laboratory has investigated many aspects of VEGF biochemistry and molecular biology. In 1993, Ferrara reported that inhibition of VEGF-induced angiogenesis by specific monoclonal antibodies resulted in dramatic suppression of the growth of a variety of tumors in vivo. These findings provided an important evidence that inhibition of angiogenesis may suppress tumor growth and blocking VEGF action could have therapeutic value for a variety of malignancies. A further development was the design in a rational fashion in 1997 of a humanized anti-VEGF monoclonal antibody (Avastin), now in clinical trials as a treatment for several solid tumors and also outside of cancer, in the treatment of age-related macular degeneration (AMD). Ferrara's work is revolutionizing quality of life for many of the estimated 1.2 million individuals in the US who have wet AMD. Upwards of a million AMD patients worldwide have already received anti-VEGF antibody therapy.

PMID: 21858763 [PubMed - in process]

Am J Ophthalmol. 2011 Aug 20. [Epub ahead of print]

Aqueous Humor Levels of Vascular Endothelial Growth Factor Before and After Intravitreal Bevacizumab in Type 3 vs Type 1 and 2 Neovascularization. A Prospective, Case-Control Study.

Dell'omo R, Cassetta M, Dell'omo E, Salvatore AD, Hughes JM, Aceto F, Porcellini A, Costagliola C.

Medical Retina Unit, Department of Health Science, University of Molise, Campobasso, Italy; Casa di Cura "Villa Maria", Campobasso, Italy.

PURPOSE: To determine the aqueous levels of vascular endothelial growth factor (VEGF) in patients with type 3 neovascularization (NV) secondary to age-related macular degeneration (AMD) and to compare the levels of those with type 1 and 2 NV secondary to AMD before and after administration of intravitreal bevacizumab (IVB).

DESIGN: Prospective, case-control study.

METHODS: Aqueous samples were collected from 29 eyes of 29 patients with untreated wet AMD at baseline (day of the first IVB), month 1 (day of the second IVB), and month 2 (day of the third IVB). Among them, 10 eyes presented with type 1, 9 with type 2, and 10 with type 3 NV. A group of 14 aqueous samples from 14 patients who underwent cataract surgery without other ocular or systemic disease comprised the controls. Main outcome measures were concentration of VEGF at baseline and after IVB in the 3 NV groups; secondary outcome measures included best-corrected visual acuity (BCVA) and central macular thickness (CMT) changes after IVB. Levels of VEGF were determined by commercially available enzyme-linked immunosorbent assay kits.

RESULTS: VEGF concentrations in aqueous humor at baseline were higher in patients with type 3 NV when compared to controls ($P = .0001$) and type 1 and 2 NV patients ($P = .002$ and $P = .0001$ respectively). At month 1, levels of VEGF were significantly reduced compared to baseline ($P < .05$) and significantly lower compared to the controls ($P < .005$) in each NV group. These low levels were maintained at the 2-month interval. BCVA significantly improved in type 1 and 2 NV groups ($P < .05$). CMT significantly reduced in each NV group compared to baseline ($P < .05$).

CONCLUSION: In eyes with untreated wet AMD, aqueous levels of VEGF are significantly higher in type 3 NV than in type 1 or 2 NV. Regardless of the type of NV, aqueous VEGF levels significantly reduce 1 month after IVB as compared to both the baseline measurements and the values recorded in age-matched controls. These decreases are maintained at 2 months after administering a second IVB 30 days after the initial injection.

PMID: 21861975 [PubMed - as supplied by publisher]

Retina. 2011 Aug 20. [Epub ahead of print]

PROSPECTIVE RANDOMIZED CONTROLLED TRIAL OF COMBINATION RANIBIZUMAB (LUCENTIS) AND BROMFENAC (XIBROM) FOR NEOVASCULAR AGE-RELATED MACULAR DEGENERATION: A Pilot Study.

Flaxel C, Schain MB, Hamon SC, Francis PJ.

From the *Macular Degeneration Center, Casey Eye Institute, Oregon Health & Science University, Portland, Oregon; and †Department of Statistical Genetics, Rockefeller University, New York, New York.

PURPOSE: To evaluate whether bromfenac eyedrops and ranibizumab intravitreal injections would provide added efficacy over ranibizumab alone.

METHODS: This was a single-site, multiinvestigator, prospective, open-label, interventional, Phase II study of patients with new or recurrent exudative/neovascular age-related macular degeneration. Thirty eyes were enrolled consecutively and were randomized in a ratio of 2:1 to combination therapy with intravitreal ranibizumab and topical bromfenac, and ranibizumab alone. All patients received ranibizumab monthly therapy for 4 months then as needed monthly in accordance with standard of care. Patients receiving bromfenac self-administered 1 drop twice a day for 12 months. Patients were followed for 12 months.

RESULTS: There were no safety concerns with the combination therapy. No statistically significant differences were identified in Early Treatment Diabetic Retinopathy Study best-corrected visual acuity or the number of injections required. However, the mean 12-month change in central macular thickness in the combination group was -81.56 μm while in the ranibizumab group alone the change was -42.50 μm (P = 0.03). The proportion of eyes experiencing a decrease in CMT of 50 μm or more was also significantly higher in those receiving combination therapy (P = 0.046).

CONCLUSION: This pilot study is the first to prospectively identify a biologic signal that may indicate combination therapy with an easily administered well-tolerated eyedrop and ranibizumab is efficacious for the treatment of neovascular age-related macular degeneration. Further studies are warranted to validate this finding.

PMID: 21862953 [PubMed - as supplied by publisher]

Retina. 2011 Aug 23. [Epub ahead of print]

PROGNOSTIC IMPLICATIONS OF PIGMENT EPITHELIAL DETACHMENT IN BEVACIZUMAB (AVASTIN)-TREATED EYES WITH AGE-RELATED MACULAR DEGENERATION AND CHOROIDAL NEOVASCULARIZATION.

Freeman WR, Kozak I, Yuson RM, Nigam N, Cheng L, Mojana F.

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PURPOSE: To evaluate the response to primary bevacizumab treatment of eyes with age-related macular degeneration (AMD) and choroidal neovascularization (CNV) with a large pigment epithelial detachment (PED) component and to compare the increase in visual acuity and reabsorption of retinal fluid in PED eyes with eyes with CNV in AMD with a minimal to no PED component.

METHODS: We reviewed 43 consecutive eyes with CNV and AMD on primary bevacizumab therapy. There were 13 eyes with a large PED component in AMD with CNV and 30 eyes with a minimal to no PED in CNV. Only patients with no previous treatment for AMD and those started on purely intravitreal bevacizumab treatment were taken in the study. Pigment epithelial detachment size, time to PED collapse, and retinal or subretinal fluid resolution were determined as was Early Treatment Diabetic Retinopathy

Study vision. Time to resolution of intraretinal and subretinal fluid was compared between the PED group and the non-PED group using survival analysis.

RESULTS: In AMD with CNV eyes having a large PED component, sub- and intraretinal fluid initially resolved faster than the sub-PED fluid (P = 0.03). The subretinal pigment epithelial fluid itself was highly resistant. Visual acuity improvement was similar in both groups.

CONCLUSION: Despite monthly intravitreal bevacizumab injections for neovascular AMD patients with a large component PED, the majority had minimal to no response of the PED. Sub- and intraretinal fluid response was faster in neovascular AMD without large PEDs, but after 7 months, vision change and reabsorption of intra- and subretinal fluid were similar in the two groups. Sub- and intraretinal fluid response did not appear to be related to PED size. Bevacizumab was very effective in reducing more of the sub- and intraretinal fluid than the PED fluid in AMD with CNV.

PMID: 21866073 [PubMed - as supplied by publisher]

BMJ. 2011 Aug 23;343:d5058. doi: 10.1136/bmj.d5058.

Cost comparison of ranibizumab and bevacizumab.

Jackson TL, Kirkpatrick L.

Department of Ophthalmology, King's College Hospital, London SE5 9RS, UK.

PMID: 21862536 [PubMed - in process]

Other treatment & diagnosis

Invest Ophthalmol Vis Sci. 2011 Aug 23. [Epub ahead of print]

Age-Related Eye Disease and Mobility Limitations in Older Adults.

Popescu ML, Boisjoly H, Schmaltz H, Kergoat MJ, Rousseau J, Moghadaszadeh S, Djafari F, Freeman EE.

Centre de Recherche, Hôpital Maisonneuve-Rosemont, Montréal, Canada;

Purpose: To examine the extent of mobility limitations in patients with age-related macular degeneration (AMD), glaucoma, or Fuchs corneal dystrophy as compared to a control group of older adults with good vision.

Methods: We recruited 272 patients (68 with AMD, 49 with Fuchs, 82 with glaucoma, and 73 controls) from the ophthalmology clinics of Maisonneuve-Rosemont Hospital (Montreal, Canada) to participate in a cross-sectional study from September 2009 until February 2011. Control patients who had normal visual acuity and visual field were recruited from the same clinics. Questionnaire (life space, falls, driving) and performance-based (one-legged balance test, timed Up and Go (TUG) test) mobility data were collected, visual acuity, contrast sensitivity, and visual field were measured, and the medical record was reviewed.

Results: The three eye diseases were associated with different patterns of mobility limitations. Patients with glaucoma had the most types of mobility limitations as they had reduced life space scores, had worse TUG scores, were less likely to drive, and were more likely to have poor balance than the control group ($P<0.05$). Compared to controls, patients with AMD and Fuchs corneal dystrophy had reduced life space scores and were less likely to drive ($P<0.05$).

Conclusions: Our results suggest that eye diseases, especially glaucoma, restrain the mobility of older people in many different ways. It is important to further explore the impact of eye disease on mobility in this

population in order to develop interventions that could help affected older adults maintain their independence.

PMID: 21862652 [PubMed - as supplied by publisher]

Cutan Ocul Toxicol. 2011 Aug 24. [Epub ahead of print]

Evaluation of proton beam radiation sensitivity of proliferating choroidal endothelial and retinal ganglion cells with clonogenic assay.

Balaiya S, Robert M, Wen H, Murthy RK, Chalam KV.

University of Florida, Jacksonville , FL , USA.

Context: Proton beam therapy offers the advantage of precise delivery with limited damage to the healthy tissue and is being tested in the management of exudative age-related macular degeneration (AMD). However, the dosages tested are empirical and not based on preclinical studies.

Objective: In this study we evaluated the effects of varying doses of proton beam radiation on choroidal endothelial cells (CECs) and retinal ganglion cells (RGCs) using clonogenic assay to determine differential sensitivity.

Materials and methods: Each cell type has different efficiency to replicate (plating efficiency (PE)). PE of CEC (RF/6A) and RGC (RGC-5) grown in culture flasks was determined by plating 250 cells each (without any treatment) and counting the number of colonies after 13 days. Radiation induced sensitivity was determined by exposing the semi-confluent RF/6A and RGC-5 cells to proton beam at the doses of 0 (control), 2, 4, 8 and 12 cobalt gray equivalent (CGE). The ability of the cells to repair and replicate to form colonies were analyzed 13 days after radiation with crystal violet stain and the survival ratio was calculated. The significance of survival was analyzed using ANOVA (Graphpad Instat.3).

Results: The PE of CEC and RGC was 12.96 ± 0.29% and 40.7 ± 1.48%, respectively. A survival ratio of CEC at 2, 4, 8 and 12 CGE proton radiation was 66.0 ± 8.6%, 44.3 ± 6.5%, 7.6 ± 0.3% and 1.14 ± 0.06% on exposure to 2, 4, 8 and 12 CGE proton radiation, respectively, $p < 0.01$). Survival ratio of RGC was 71.1 ± 22.4% ($p = 0.05$), 40.2 ± 7.9%, 8.89 ± 2.6% and 0.78 ± 0.31% at 2, 4, 8 and 12 CGE dosages ($p < 0.001$).

Discussion: CEC showed dose-dependent decrease in survival rate with values attaining significance at all radiation dosages. In contrast, RGC was comparatively radio resistant and were able to replicate at lower doses and sensitive at higher doses after proton beam radiation.

Conclusion: Since CECs proliferate during neovascularization, this clonogenic assay is a useful assay to assess the sensitivity of CEC to radiation. This study identified that CEC were more sensitive to proton beam radiation than RGC at all doses. This may provide a therapeutic window for administration of proton beam radiation in the management of AMD.

PMID: 21861774 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2011 Aug 23. [Epub ahead of print]

Simple Estimation of Clinically-Relevant Lesion Volumes using Spectral Domain-Optical Coherence Tomography in Neovascular Age-Related Macular Degeneration.

Heussen FM, Ouyang Y, Sadda SR, Walsh AC.

Doheny Eye Institute and the Department of Ophthalmology, Keck School of Medicine of the University of Southern California, Los Angeles, California.

Purpose: To evaluate simple methods of estimating the volume of clinically-relevant features in neovascular age-related macular degeneration (NVAMD) using spectral domain OCT (SD-OCT).

Methods: Using a database of NVAMD cases imaged with macular cube (512 x 128) SD-OCT scans from either a Cirrus HD-OCT (Carl Zeiss Meditec, Inc., Dublin, CA) or a 3D-OCT-1000 (Topcon, Inc., Tokyo, Japan), we retrospectively selected visits where CME, SRF or a PED were evident. Patients with single visits were analyzed in the cross-sectional analysis (CSA) and those with a baseline visit and 3 or more follow-up visits in the longitudinal analysis (LA). The volume of each feature was measured by manual grading using validated grading software (3D-OCTOR). Simplified measurements for each feature included: # of B-scans or A-scans involved, and maximum height. Automated measurements of total macular volume (MV) and foveal central subfield (FCS) were also collected from each machine. Correlations were performed between the volumes measured with 3D-OCTOR, automated measurements, and the simplified measures.

Results: Forty-five visits for 25 patients were included in this study: 26 cube scans from 26 eyes of 25 patients in the CSA and 24 scans from 5 eyes of 5 patients in the LA. The simplified measures that correlated best with manual grading in the CSA group were maximum lesion height for CME (r(2) value = 0.96) and B-scan count for SRF and PED volume (r(2) values of 0.88 and 0.70). In the LA group, inter-visit differences were correlated. Change in B-scan count correlated well with change in SRF volume (r(2)=0.97) while change in maximum height correlated with change in CME and PED volume (r(2)=0.98 and 0.43 respectively).

Conclusion: These data suggest that simplified estimators of some NVAMD lesion volumes exist and are accessible by clinicians without the need for specialized software or time-consuming manual segmentation. These simple approaches could enhance quantitative disease monitoring strategies in clinical trials and clinical practice.

PMID: 21862646 [PubMed - as supplied by publisher]

Ophthalmologica. 2011 Aug 25. [Epub ahead of print]

Imaging Geographic Atrophy in Age-Related Macular Degeneration.

Göbel AP, Fleckenstein M, Schmitz-Valckenberg S, Brinkmann CK, Holz FG.

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Abstract

Advances in retinal imaging technology have largely contributed to the understanding of the natural history, prognostic markers and disease mechanisms of geographic atrophy (GA) due to age-related macular degeneration. There is still no therapy available to halt or slow the disease process. In order to evaluate potential therapeutic effects in interventional trials, there is a need for precise quantification of the GA progression rate. Fundus autofluorescence imaging allows for accurate identification and segmentation of atrophic areas and currently represents the gold standard for evaluating progressive GA enlargement. By means of high-resolution spectral-domain optical coherence tomography, distinct microstructural alterations related to GA can be visualized.

PMID: 21865677 [PubMed - as supplied by publisher]

Epidemiology

Br J Ophthalmol. 2011 Aug 19. [Epub ahead of print]

Population-based incidence of exudative age-related macular degeneration and ranibizumab treatment load.

Geirsdottir A, Jonsson O, Thorisdottir S, Helgadottir G, Jonasson F, Stefansson E, Sigurdsson H.

Landspitali-The National University Hospital of Iceland, Reykjavik, Iceland.

Background/aims: The use of intravitreal vascular endothelial growth factor antibodies for exudative age-related macular degeneration (AMD) has stressed ophthalmology services and drug budgets throughout the world. The authors study the population-based incidence of exudative AMD in Iceland and the use of intravitreal ranibizumab in a defined population.

Methods: This is a prospective study of 439 consecutive patients aged 60 years and older with exudative AMD starting intravitreal ranibizumab for exudative AMD in Iceland from March 2007 to December 2009. All patients initially received three consecutive ranibizumab injections, with regular follow-up visits and re-treatment as needed.

Results: In total, 517 eyes from 439 patients received treatment for exudative AMD (mean age 79 years). The annual incidence of exudative AMD in the population 60 years and older is 0.29%. The incidence increased with advancing age, double for patients 85 years and older compared with those 75-79 years. Approximately 2400 ranibizumab injections per 100 000 persons aged 60 years and older were given each year for exudative AMD.

Conclusions: These data allow an estimation of the incidence of exudative AMD in a Caucasian population and the treatment load with ranibizumab, which may help plan anti-vascular endothelial growth factor treatment programmes and estimate costs.

PMID: 21856691 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2011 Aug 23. [Epub ahead of print]

Age-related macular degeneration: the importance of family history as a risk factor.

Shahid H, Khan JC, Cipriani V, Sepp T, Matharu BK, Bunce C, Harding SP, Clayton DG, Moore AT, Yates JR; for the Genetic Factors in AMD Study Group.

Cambridge Institute for Medical Research, University of Cambridge, Cambridge, UK.

Background: Family history is considered a risk factor for age-related macular degeneration (AMD). With the advent of effective therapy for the disease, the importance of family history merits further investigation. This study quantifies the risk associated with family history, first, by a case-control study of reported family history and, second, by examining the siblings of AMD cases.

Methods: The authors recruited cases with advanced AMD, spouses and siblings. All subjects were carefully phenotyped. Clinical findings in the siblings were compared with spouses. Information about family history was collected. The ORs for reported family history of AMD were calculated. Analyses were adjusted for age, smoking and genotype.

Results: 495 AMD cases, 259 spouses and 171 siblings were recruited. The OR for AMD was 27.8 (CI 3.8 to 203.0; p=0.001) with a reported family history of an affected parent and 12.0 (CI 3.7 to 38.6; p<0.0001) with a history of an affected sibling. ORs adjusted for age and smoking were higher. Examination of siblings confirmed their increased risk with 23% affected by AMD and an OR of 10.8 (4.5 to 25.8; p<0.0001). Adjusting for age increased the OR to 16.1 (6.2 to 41.8).

Conclusion: The risk of AMD is greatly increased by having an affected first-degree relative. Those at risk need to be made aware of this and AMD patients should advise siblings and children to seek prompt ophthalmological advice if they develop visual symptoms of distortion or reduced vision.

PMID: 21865200 [PubMed - as supplied by publisher]

Pathogenesis

Immunobiology. 2011 Jul 23. [Epub ahead of print]

Age-related macular degeneration and the complement system.

Khandhadia S, Cipriani V, Yates JR, Lotery AJ.

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Abstract

Age-related macular degeneration (AMD) is the leading cause of blindness in the developed world. It is a complex multifactorial disease, and despite new advances in treatment, many patients still succumb to visual impairment. The complement pathway has been implicated in the pathogenesis of many diseases, and recently variants in several genes encoding complement pathway proteins have been associated with AMD. Complement proteins have been found in histological specimens of eyes with AMD. Altered levels of both intrinsic complement proteins and activated products have been found in the circulation of patients with AMD. Complement activation may be triggered by oxidative stress, resulting from retinal exposure to incoming light; indeed an inter-play between these two pathological processes seems to exist. Finally, complement inhibitors are currently being evaluated in clinical trials. This article reviews the role of the complement system in AMD, and the potential of complement inhibition in preventing the devastating blindness resulting from this disease.

PMID: 21868123 [PubMed - as supplied by publisher]

Genetics

Recent Pat DNA Gene Seq. 2011 Aug 25. [Epub ahead of print]

Gene Patents Related to Common Diseases of the Eye.

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Abstract

Visual impairment and blindness impose substantial morbidity and premature mortality on the population [1]. The direct costs for vision disorders have been shown to be more than the cost of coronary heart disease, stroke, arthritis or depression and were estimated to be $9.85 billion in 2004 in Australia. Hence it is important to identify the causes of common eye diseases and understand their aetiology which in turn would allow determination of better management strategies and treatment options. Age related Macular Degeneration, Cataract, Diabetic Retinopathy, Glaucoma and uncorrected refractive errors represent the majority of the visual impairment and blindness in Australia and various parts of the world. This article reviews the gene patents available for these eye conditions and highlights the important discoveries that have so far contributed to our understanding of these diseases and provides valuable information as to where research will be heading in the future.

PMID: 21867478 [PubMed - as supplied by publisher]

Ophthalmology. 2011 Aug 17. [Epub ahead of print]

Association Assessment of Copy Number Polymorphism and Risk of Age-Related Macular Degeneration.

Sawitzke J, Im KM, Kostiha B, Dean M, Gold B.

SAIC-Frederick, Inc., Frederick, Maryland.

PURPOSE: We previously identified a genetic copy number polymorphism (CNP147) that was statistically associated with age-related macular degeneration (AMD) and that resides downstream of the complement factor H (CFH) gene. Factor H protein is polymorphic at amino acid 402, in which the resulting histidine containing moiety has been established to impart significant risk of AMD. We present a method to precisely determine the exact copy number of CNP147 and examine in more detail the association with AMD.

DESIGN: Case-control study.

PARTICIPANTS: A total of 421 Age-Related Eye Disease Study (AREDS) subjects, of whom approximately 35% were diagnosed with neovascular disease, 19% were diagnosed with geographic atrophy, 16% were diagnosed with both, 30% were diagnosed with large drusen, and 215 were controls.

METHODS: By using copy number assays available from Applied Biosystems Inc. (Carlsbad, CA), we examined 4 loci spanning CNP147 and neighboring CNP148 in an AREDS matched case-control sample set. We analyzed these data by copy number while controlling for 2 high-risk CFH variants, rs1061170 (Y402H) and rs1410996. We phased the high-risk CFH variants with CNP147 and analyzed haplotype frequencies in cases and controls. To further validate copy numbers, 6 Utah Centre D'etude du Polymorphism Humaine (CEPH) families were typed for CNP147, and the segregation was assessed.

MAIN OUTCOME MEASURES: Increased or decreased risk of AMD from genetic loci.

RESULTS: Having fewer than 2 copies of CNP147 was associated with an estimated 43% reduction in odds of having AMD in this sample set (adjusted odds ratio [OR] = 0.57, P=0.006). CNP148 variation is rare in Caucasians and was not statistically significant. Common haplotypes reveal that the risk alleles for rs1061170 and rs1410996 most frequently segregate with higher copy numbers for CNP147, but not exclusively, and that 1 haplotype that carried a deletion of CNP147 was highly protective (OR = 0.25 P=1.3×10(-13)) when compared with the reference.

CONCLUSIONS: In this matched subset of AREDS subjects, after adjusting for 2 known risk variants in CFH, CNP147 deletion statistically associates with diminished risk for AMD.

PMID: 21856016 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2011 Sep;152(3):499.

Polymorphisms in ARMS2 (LOC387715) and LOXL1 Genes in the Japanese With Age-Related Macular Degeneration.

Sakurada Y, Mabuchi F, Yoneyama S, Kubota T, Iijima H.

Yamanashi, Japan.

PMID: 21855673 [PubMed - in process]

Genomics. 2011 Aug 9. [Epub ahead of print]

Almost total protection from age-related macular degeneration by haplotypes of the Regulators of Complement Activation.

Williamson JF, McLure CA, Guymer RH, Baird PN, Millman J, Cantsilieris S, Dawkins RL.

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Abstract

Age-related macular degeneration (AMD) is the leading cause of blindness in developed countries. It has been proposed that the polymorphism encoding Y402H (T1277C) in the complement factor H gene (CFH) is one of the main determinants of disease. We genotyped the polymorphism at a number of loci in the region encompassing the Regulators of Complement Activation (RCA) on chromosome 1, including T1277C SNP, in 187 patients and 146 controls. Haplotypes have been classified as protective (P) or susceptible (S) with respect to AMD. This included the identification of an S haplotype with a T at 1277. The results show that no single locus should be assumed to be directly responsible for AMD, but rather argue for the existence of RCA haplotypes, which can be assigned meaningful predictive values for AMD. We conclude that the critical sequences are within a region 450kb centromeric to128kb telomeric of CFH.

PMID: 21855625 [PubMed - as supplied by publisher]

Exp Eye Res. 2011 Aug 16. [Epub ahead of print]

Cellular and 3D optical coherence tomography assessment during the initiation and progression of retinal degeneration in the Ccl2/Cx3cr1-deficient mouse.

Zhou Y, Sheets KG, Knott EJ, Regan CE Jr, Tuo J, Chan CC, Gordon WC, Bazan NG.

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Abstract

Retinal pathologies common to human eye diseases, including abnormal retinal pigment epithelial (RPE) cells, drusen-like accumulation, photoreceptor atrophy, and choroidal neovascularization, have been reported in the Ccl2/Cx3cr1-deficient mouse. The Ccl2 gene encodes the pro-inflammatory chemokine CCL2 (MCP-1), which is responsible for chemotactic recruitment of monocyte-derived macrophages to sites of inflammation. The Cx3cr1 gene encodes the fractalkine receptor, CX3CR1, and is required for accumulation of monocytes and microglia recruited via CCL2. Chemokine-mediated inflammation is implicated in retinal degenerative diseases such as diabetic retinopathy, age-related macular degeneration, retinitis pigmentosa, and uveoretinitis, and proper chemokine signaling from the RPE, Müller glia, and astrocytes is necessary to regulate leukocyte trafficking. Therefore, this mouse, possessing aberrant chemokine signaling coupled with retinal degenerative pathologies, presents an ideal opportunity to investigate the effect of altered signaling on retinal homeostasis and photoreceptor degeneration. Since this mouse is a recent development, more data covering the onset, location, and progression rate of pathologies is needed. In the present study we establish these parameters and show two photoreceptor cell death processes. Our observations of decreased glutamine synthetase and increased glial fibrillary acidic protein suggest that Müller cells respond very early within regions where lesions are forming. Finally, we suggest that retinal angiomatous proliferation contributes to pathological angiogenesis in this Ccl2/Cx3cr1-deficient mouse.

PMID: 21854772 [PubMed - as supplied by publisher]