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MD Research News

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Drug treatment

Ophthalmic Surg Lasers Imaging. 2011 Oct 13:1-7. doi: 10.3928/15428877-20111006-01. [Epub ahead of print]

Ranibizumab for Eyes Previously Treated With Pegaptanib or Bevacizumab Without Clinical Response.

Kaiser RS, Gupta OP, Regillo CD, Ho AC, Fineman MS, Vander JF, McNamara JA, Brown GC.

BACKGROUND AND OBJECTIVE: To assess the safety and efficacy of ranibizumab in patients who had inadequate response to pegaptanib or bevacizumab.

PATIENTS AND METHODS: In this single-center study, 19 patients with subfoveal choroidal neovascularization secondary to age-related macular degeneration (AMD) previously treated with pegaptanib (n = 1), bevacizumab (n = 13), or both (n = 5) received 12 monthly ranibizumab injections (0.5 mg). Outcomes were measured from start of previous therapy (baseline) to start of ranibizumab treatment (day 0) through 12 months.

RESULTS: No drug- or injection-related adverse events and no serious adverse events were reported. At 6 and 12 months, 4 and 5 patients gained 3 or more lines of VA, respectively; 3 patients lost less than 3 lines of VA at 6 months, and 6 patients lost less than 3 lines at 12 months. At 6 and 12 months, VA increased by a mean (± standard error of the mean) of 2.06 ± 1.23 and 1.17 ± 0.62 lines, respectively. Central retinal thickness decreased by a mean of 62.65 ± 22.46 and 62.16 ± 29.20 μm at months 6 and 12, respectively. When stratified by pigment epithelial detachment (PED) status, patients without PED had better visual and anatomical outcomes than patients with PED.

CONCLUSION: Ranibizumab has favorable safety and efficacy profiles for patients with AMD without previous response to pegaptanib or bevacizumab.

PMID: 21986085 [PubMed - as supplied by publisher]

Am J Ophthalmol. 2011 Oct 11. [Epub ahead of print]

Bevacizumab for Neovascular Age-Related Macular Degeneration Using a Treat-and-Extend Regimen: Clinical and Economic Impact.

Shienbaum G, Gupta OP, Fecarotta C, Patel AH, Kaiser RS, Regillo CD.

Retina Service, Wills Eye Institute, Thomas Jefferson University, Philadelphia, Pennsylvania.

PURPOSE: To evaluate the visual outcomes, number of injections, and direct medical cost of a treat-and-extend regimen in managing neovascular age-related macular degeneration with intravitreal bevacizumab.

DESIGN: Retrospective, interventional, consecutive case series.

METHODS: Seventy-four eyes of 73 patients with treatment-naïve neovascular age-related macular degeneration from a single clinical practice were treated monthly with intravitreal bevacizumab until no intraretinal or subretinal fluid was observed on optical coherence tomography. The treatment intervals then were lengthened sequentially by 2 weeks until signs of exudation recurred and then were reduced accordingly to maintain an exudation-free macula. Main outcomes measured included mean change from baseline visual acuity, proportion of eyes losing fewer than 3 and gaining 3 or more Snellen visual acuity lines at 1 year of follow-up, annual mean number of injections, optical coherence tomography mean central retinal thickness change from baseline, mean maximum period of extension, adverse events, and mean direct annual medical cost.

RESULTS: The mean follow-up period was 1.41 years. Mean Snellen visual acuity improved from 20/230 at baseline to 20/109 at 12 months ($P < .001$) and 20/106 at 24 months ($P < .001$). The mean number of injections over the first year was 7.94. The mean optical coherence tomography central retinal thickness decreased from 316 to 239 μm at 12 months ($P < .001$). The mean direct medical cost over the first year was $3493.85.

CONCLUSIONS: Eyes with neovascular age-related macular degeneration experienced significant visual improvements on average when managed with intravitreal bevacizumab using a treat-and-extend regimen with fewer patient visits and injections along with lower costs compared with a fixed, monthly dosing regimen.

PMID: 21996309 [PubMed - as supplied by publisher]

Ophthalmic Surg Lasers Imaging. 2011 Oct 13;42:e100-2. doi: 10.3928/15428877-20111006-02.

Severe intraocular pressure fluctuation after intravitreal anti-vascular endothelial growth factor injection.

Martel JN, Han Y, Lin SC.

Abstract

A 65-year-old man with unilateral exudative age-related macular degeneration presented initially with hypotony and a shallow choroidal detachment 5 days after an intravitreal ranibizumab injection. This was followed by an acute increase in intraocular pressure (IOP) to 60 mm Hg despite open angles, no evidence of intraocular inflammation, and no corticosteroid use. Ultrasound biomicroscopy showed a focal atrophic area in the ciliary body from the 7- to 9-o'clock positions, corresponding to the site of intravitreal injection. The IOP elevation was successfully treated with aqueous suppressants and resolved spontaneously after 48 hours. This report describes a patient with a rare case of labile IOP secondary to angle changes following ranibizumab injection. Injury to angle structures following intravitreal ranibizumab injection is a rare but potentially severe complication. Ultrasound biomicroscopy may be helpful in elucidating angle changes in the setting of labile IOP following intravitreal ranibizumab injection.

PMID: 21986163 [PubMed - in process]

Other treatment & diagnosis

Trials. 2011 Oct 11;12(1):221. [Epub ahead of print]

The Chronic Care for age-related macular degeneration study (CHARMED): Study protocol for a randomized controlled trial.

Frei A, Woitzek K, Wang M, Held U, Rosemann T.

BACKGROUND: Neovascular age-related macular degeneration is the leading cause of irreversible blindness in people 50 years of age or older in the developed world. As in other chronic diseases, several effective treatments are available, but in clinical daily practice there is an evidence performance gap. The Chronic Care Model represents an evidence-based framework for the care of chronically ill patients and aims at closing that gap. However, no data are available regarding patients with neovascular age-related macular degeneration.

METHODS: CHARMED is a multicenter randomised controlled trial. The study challenges the hypothesis that the implementation of core elements of the Chronic Care Model (patient empowerment, delivering evidence based information, clinical information system, reminder system with structured follow up and frequent monitoring) via a specially trained Chronic Care Coach in Swiss centres for neovascular age-related macular degeneration results in better visual acuity (primary outcome) and an increased disease specific quality of life (secondary outcome) in patients with neovascular age-related macular degeneration. According to the power calculation, a total sample size of 352 patients is needed (drop out rate of 25%). 14 specialised medical doctors from leading ophtalmologic centres in Switzerland will include 25 patients. In each centre, a Chronic Care Coach will provide disease specific care according to the Chronic Care Model for intervention group. Patients from the control group will be treated as usual. Baseline measurements will be taken in month III - XII, starting in March 2011. Follow-up data will be collected after 6 months and 1 year.

DISCUSSION: Multiple studies have shown that implementing Chronic Care Model elements improve clinical outcomes as well as process parameters in different chronic diseases as osteoarthritis, depression or e.g. the cardiovascular risk profile of diabetes patients. This study will be the first to assess this approach in neovascular age-related macular degeneration. If our hypothesis will be confirmed, the implementation of this approach in routine care for patients with with neovascular age-related macular degeneration should be considered. Trial Registration Current controlled trials ISRCTN32507927.

PMID: 21985296 [PubMed - as supplied by publisher]

Optom Vis Sci. 2011 Oct 6. [Epub ahead of print]

Multifocal Pupillographic Assessment of Age-Related Macular Degeneration.

Sabeti F, Maddess T, Essex RW, James AC.

*PhD †MBBS ARC Centre of Excellence in Vision Science and Centre for Visual Sciences, Research School of Biology, The Australian National University, Canberra, ACT, Australia (FS, TM, RWE, ACJ), and Ophthalmology Department, The Australian National University, Canberra Hospital, ACT, Australia (RWE).

PURPOSE: To investigate retinal function in subjects with unilateral exudative age-related macular degeneration (AMD) using multifocal pupillographic objective perimetry (mfPOP) and to assess the diagnostic accuracy of this technique.

METHODS: We tested each of 20 exudative AMD patients and 20 control subjects with 4 different mfPOP stimulus variants. Multifocal stimuli consisting of 24 or 44 independent stimulus regions per eye extending from fixation to 15° eccentricity were presented dichoptically. The aperiodic stimuli were presented at 1 or 4 s mean intervals. Video cameras recorded pupil responses under infrared illumination. Test duration consisted of 8 segments of 30 s. Stimuli were presented at a luminance of 250 cd/m and a background of 10

cd/m. Peak regional contraction amplitudes, time to peaks, and a linear combination of these were used to produce receiver operator characteristic (ROC) curves to measure the diagnostic accuracy of this method.

RESULTS: Mean constriction amplitudes of exudative AMD subjects were decreased by 0.77 ± 0.15 dB ($p < 5 \times 10$). Stimulus ensembles with 44 regions and faster presentation rates produced the largest effect on response sizes ($t = 3.63$; $p < 0.0002$). When comparing the control eyes to exudative AMD eyes, the area under the curve of ROC plots was 0.96 ± 0.03 (mean ± SE). This was achieved for asymmetry analysis of the difference in response amplitudes obtained from the two eyes at each point in the visual field.

CONCLUSIONS: The mean effect of exudative AMD on contraction amplitudes reflected the severity of disease, and ROC analysis from amplitude deviations improved the sensitivity of detection of exudative AMD. A longitudinal investigation into the mfPOP responses of patients with non-exudative AMD may detect and classify visual fields with poor prognosis.

PMID: 21983122 [PubMed - as supplied by publisher]

Can J Ophthalmol. 2011 Oct;46(5):391-398.e1. Epub 2011 Aug 4.

The impact of cataract surgery on patients from a low-vision clinic.

Kuo IC, Broman AT, Massof RW, Park W.

Wilmer Eye Institute and Department of Ophthalmology, Baltimore, Md.

OBJECTIVE: To evaluate the effects of cataract extraction with intraocular lens implantation (CE-IOL) in low-vision patients.

DESIGN: Prospective, interventional case series.

PARTICIPANTS: Twenty low-vision patients (30 eyes) underwent CE-IOL by 1 surgeon at an academic institution.

METHODS: Pre- and post-CE-IOL visual acuities and responses to a 23-page survey (self-reported functioning in general vision, mobility, illumination, and ability to see faces) were compared.

RESULTS: Sixteen patients had age-related macular degeneration (AMD); 1 patient each had rod-cone dystrophy, oculocutaneous albinism, retinitis pigmentosa, or cerebrovascular accident. The average age was 78 years (range: 53-96 years). Preoperative best-corrected visual acuity (BCVA) ranged from 20/70 to count fingers; postoperative BCVA at 8 weeks was 20/40 to 20/400, with improvement in 25 (83%) eyes of 15 patients, and no change in the rest. The average change in logMAR of BCVA in the 1 eye or in the eye with better preoperative vision in bilateral surgery was an improvement of 0.6 logMAR units ($p = 0.0001$). Seventeen (85%) patients noted an improvement in visual function and would consent to CE-IOL again. Twelve patients completed the survey pre- and post-CE-IOL at 3 months. More patients could read with a magnifier after surgery. On average, self-reported functioning was improved.

CONCLUSIONS: In this small study, CE-IOL offered subjective and objective benefits to patients from a low vision clinic, many of whom may have been dissuaded from CE-IOL. Most patients had moderately dense cataracts and moderate to advanced AMD, and these features may help form clinical recommendations. Expectations are important to elicit preoperatively. Postoperatively, patients may be more receptive to low-vision services and devices when the prognosis for visual rehabilitation is better.

PMID: 21995980 [PubMed - in process]

Neuropsychol Dev Cogn B Aging Neuropsychol Cogn. 2011 Oct 12. [Epub ahead of print]

Rehabilitation of reading in older individuals with macular degeneration: A review of effective training programs.

Pijnacker J, Verstraten P, van Damme W, Vandermeulen J, Steenbergen B.

a Radboud University Nijmegen, Behavioural Science Institute , Nijmegen , The Netherlands.

Abstract

Abstract Macular degeneration (MD) is the most common cause of visual impairment among older adults. It severely affects reading performance. People with MD have to rely on peripheral vision for reading. In this review, we considered several training programs that aim to improve peripheral reading, with a focus on eccentric viewing, oculomotor control, or perceptual learning. There was no strong support in favor of one particular training method for rehabilitation of reading in MD, but there is evidence that older individuals with MD can be trained to improve reading performance, even within limited time.

PMID: 21992418 [PubMed - as supplied by publisher]

Pathogenesis

Nanotechnology. 2011 Oct 11;22(44):445101. [Epub ahead of print]

Efficient nanoparticle mediated sustained RNA interference in human primary endothelial cells.

Mukerjee A, Shankardas J, Ranjan AP, Vishwanatha JK.

Department of Molecular Biology & Immunology and Institute for Cancer Research, Graduate School of Biomedical Sciences, University of North Texas Health Science Center, Fort Worth, TX 76107, USA.

Abstract

Endothelium forms an important target for drug and/or gene therapy since endothelial cells play critical roles in angiogenesis and vascular functions and are associated with various pathophysiological conditions. RNA mediated gene silencing presents a new therapeutic approach to overcome many such diseases, but the major challenge of such an approach is to ensure minimal toxicity and effective transfection efficiency of short hairpin RNA (shRNA) to primary endothelial cells. In the present study, we formulated shAnnexin A2 loaded poly(D,L-lactide-co-glycolide) (PLGA) nanoparticles which produced intracellular small interfering RNA (siRNA) against Annexin A2 and brought about the downregulation of Annexin A2. The per cent encapsulation of the plasmid within the nanoparticle was found to be 57.65%. We compared our nanoparticle based transfections with Lipofectamine mediated transfection, and our studies show that nanoparticle based transfection efficiency is very high (~97%) and is more sustained compared to conventional Lipofectamine mediated transfections in primary retinal microvascular endothelial cells and human cancer cell lines. Our findings also show that the shAnnexin A2 loaded PLGA nanoparticles had minimal toxicity with almost 95% of cells being viable 24 h post-transfection while Lipofectamine based transfections resulted in only 30% viable cells. Therefore, PLGA nanoparticle based transfection may be used for efficient siRNA transfection to human primary endothelial and cancer cells. This may serve as a potential adjuvant treatment option for diseases such as diabetic retinopathy, retinopathy of prematurity and age related macular degeneration besides various cancers.

PMID: 21990205 [PubMed - as supplied by publisher]

Mol Med. 2011 Oct 5. doi: 10.2119/molmed.2011.00256. [Epub ahead of print]

Notch signaling in ocular vasculature development and diseases.

Dou GR, Wang L, Wang YS, Han H.

Department of Ophthalmology, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, China Department of Medical Genetics and Developmental Biology, Fourth Military Medical University, Xi'an 710032, China.

Abstract

Ocular angiogenesis, characterized by the formation of new blood vessels in the avascular area in eyes, is a highly coordinated process involved in retinal vasculature formation and several ocular diseases such as age-related macular degeneration (AMD), proliferative diabetic retinopathy (PDR) and retinopathy of prematurity (ROP). This process is orchestrated by complicated cellular interactions and vascular growth factors, during which endothelial cells acquire heterogeneous phenotypes and distinct cellular destinations. To date, while vascular endothelial growth factor has been identified as the most critical angiogenic agent with a remarkable therapeutic value, the Notch signaling pathway appears to be a similarly important regulator in several angiogenic steps. Recent progress has highlighted the involvement, mechanisms, and therapeutic potential of Notch signaling in retinal vasculature development and pathological angiogenesis-related eye disorders, which may cause irreversible blindness.

PMID: 21989947 [PubMed - as supplied by publisher]

Exp Eye Res. 2011 Oct 6. [Epub ahead of print]

Enhanced retinal pigment epithelium regeneration after injury in MRL/MpJ mice.

Xia H, Krebs MP, Kaushal S, Scott EW.

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Abstract

Regenerative medicine holds the promise of restoring cells and tissues that are destroyed in human disease, including degenerative eye disorders. However, development of this approach in the eye has been limited by a lack of animal models that show robust regeneration of ocular tissue. Here, we test whether MRL/MpJ mice, which exhibit enhanced wound healing, can efficiently regenerate the retinal pigment epithelium (RPE) after an injury that mimics the loss of this tissue in age-related macular degeneration. The RPE of MRL/MpJ and control AKR/J mice was injured by retro-orbital injection of sodium iodate at 20 mg/kg body weight, which titration studies indicated was optimal for highlighting strain differences in the response to injury. Five days after sodium iodate injection at this dose, electroretinography of both strains revealed equivalent retinal responses that were significantly reduced compared to untreated mice. At one and two months post-injection, retinal responses were restored in MRL/MpJ but not AKR/J mice. Bright field and fluorescence microscopy of eyecup cryosections indicated an initial central loss of RPE cells and RPE65 immunostaining in MRL/MpJ and AKR/J mice, with preservation of peripheral RPE. Phalloidin staining of posterior eye whole mounts confirmed this pattern of RPE loss, and revealed a transition region characterized by RPE cell shedding and restructuring in both strains, suggesting a similar initial response to injury. At one month post-injection, central RPE cells, RPE65 immunostaining and phalloidin staining were restored in MRL/MpJ but not AKR/J mice. BrdU incorporation was observed throughout the RPE of MRL/MpJ but not AKR/J mice after one month of administration following sodium iodate treatment, consistent with RPE proliferation. These findings provide evidence for a dramatic regeneration of the RPE after injury in MRL/MpJ mice that supports full recovery of retinal function, which has not been observed previously in mammalian eyes. This model should prove useful for understanding molecular mechanisms that underlie regeneration,

and for identifying factors that promote RPE regeneration in age-related macular degeneration and related diseases.

PMID: 21989111 [PubMed - as supplied by publisher]

Epidemiology

Am J Ophthalmol. 2011 Oct 11. [Epub ahead of print]

Clinical Characteristics of Reticular Pseudodrusen in Korean Patients.

Lee MY, Yoon J, Ham DI.

Department of Ophthalmology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea.

PURPOSE: To clarify the clinical characteristics of reticular pseudodrusen in Korean patients.

DESIGN: Retrospective, observational, consecutive case series.

METHODS: A total of 255 eyes of 130 patients diagnosed with reticular pseudodrusen were evaluated. Reticular pseudodrusen were diagnosed by characteristic fundus findings using ophthalmoscopy, color fundus photography with blue-channel examination, near-infrared photography, red-free photography, autofluorescence imaging, fluorescein angiography, indocyanine green angiography, and spectral-domain optical coherence tomography. Age-related macular degeneration (AMD) was determined by the International Classification and Grading System.

RESULTS: The mean age was 72.6 ± 9.0 years (range, 43 to 92 years). Most reticular pseudodrusen patients had bilateral disease (97.7%), with a female preponderance (86.2%). All 3 patients who showed unilateral reticular pseudodrusen had neovascular AMD in the eye with no reticular pseudodrusen. AMD was found in 183 eyes (71.8 %), among which early AMD was found in 115 eyes (45.1%), geographic atrophy was found in 41 eyes (16.1%), and neovascular AMD was found in 27 eyes (10.6%). The mean age of patients with AMD and with no AMD was 73.7 ± 9.2 years (range, 58 to 92 years) and 69.9 ± 11.7 years (range, 43 to 90 years), respectively, and there was a statistical difference between these 2 groups ($P < .05$). Classic choroidal neovascularization was found in 13 eyes (48.1%), and occult choroidal neovascularization was found in 14 eyes (51.9%) in the neovascular AMD group.

CONCLUSIONS: Reticular pseudodrusen occurs in Koreans, and clinical manifestations of reticular pseudodrusen in Koreans did not differ significantly from those described in white persons. However, our study demonstrated a higher rate of bilaterality compared with those previously reported, and geographic atrophy was found to be associated more commonly with reticular pseudodrusen than with neovascular AMD. Ethnical differences may be associated with these findings, and further studies are required.

PMID: 21996310 [PubMed - as supplied by publisher]

J Fr Ophtalmol. 2011 Oct 10. [Epub ahead of print]

[Visual impairment in elderly fallers.]

[Article in French]

Tran TH, Nguyen Van Nuoi D, Baiz H, Baglin G, Leduc JJ, Bulkaen H.

Service d'ophtalmologie, hôpital Saint-Vincent-de-Paul, groupe hospitalier de l'institut catholique de Lille, boulevard Belfort, BP 387, 59020 Lille cedex, France.

OBJECTIVE: To study visual impairment and the etiology of visual loss in fallers and non-fallers in older patients.

PATIENTS AND METHOD: Cross-sectional study including two groups of patients: elderly patients admitted for a fall (group1) and elderly individuals who did not report a fall during the 6months before admission (group 2). Visual acuity was measured in both eyes of all participants. Complete ophthalmologic evaluation was performed in the fallers group.

RESULTS: The fallers group included 98 patients (mean age, 83.4±6.3) and the non-fallers group included 106 patients (mean age, 79±6.6). The fallers had lower vision than non-fallers (P<0.001). Visual impairment (visual acuity less than 20/40) was more frequent in the fallers (49.5% vs 15.3%, P<0.001). Causes of visual impairment in fallers were cataract (47.4%), association of cataract and age-related macular degeneration (17.5%), age-related macular degeneration without cataract (13.4%), and optic neuropathy (9.3%). Management of fallers was difficult, and only 17 of 48 eyes (35.4%) with cataract had undergone surgery.

CONCLUSION: Fallers have a higher prevalence of visual impairment and blindness. Vision may improve with surgery in half of these eyes. This study highlights the need for systematic ophthalmologic evaluation in this high-risk population in order to prevent falls.

PMID: 21992994 [PubMed - as supplied by publisher]

Genetics

Mol Ther. 2011 Oct 11. doi: 10.1038/mt.2011.212. [Epub ahead of print]

Short-interfering RNAs Induce Retinal Degeneration via TLR3 and IRF3.

Kleinman ME, Kaneko H, Cho WG, Dridi S, Fowler BJ, Blandford AD, Albuquerque RJ, Hirano Y, Terasaki H, Kondo M, Fujita T, Ambati BK, Tarallo V, Gelfand BD, Bogdanovich S, Baffi JZ, Ambati J.

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Abstract

The discovery of sequence-specific gene silencing by endogenous double-stranded RNAs (dsRNA) has propelled synthetic short-interfering RNAs (siRNAs) to the forefront of targeted pharmaceutical engineering. The first clinical trials utilized 21-nucleotide (nt) siRNAs for the treatment of neovascular age-related macular degeneration (AMD). Surprisingly, these compounds were not formulated for cell permeation, which is required for bona fide RNA interference (RNAi). We showed that these "naked" siRNAs suppress neovascularization in mice not via RNAi but via sequence-independent activation of cell surface Toll-like receptor-3 (TLR3). Here, we demonstrate that noninternalized siRNAs induce retinal degeneration in mice by activating surface TLR3 on retinal pigmented epithelial cells. Cholesterol conjugated siRNAs capable of cell permeation and triggering RNAi also induce the same phenotype. Retinal degeneration was not observed after treatment with siRNAs shorter than 21-nts. Other cytosolic dsRNA sensors are not critical to this response. TLR3 activation triggers caspase-3-mediated apoptotic death of the retinal pigment epithelium (RPE) via nuclear translocation of interferon regulatory factor-3. While this unexpected adverse effect of siRNAs has implications for future clinical trials, these findings also introduce a new preclinical model of geographic atrophy (GA), a late stage of dry AMD that causes blindness in millions worldwide.

PMID: 21988875 [PubMed - as supplied by publisher]

PLoS One. 2011;6(10):e25775. Epub 2011 Oct 6.

Influence of ROBO1 and RORA on Risk of Age-Related Macular Degeneration Reveals Genetically Distinct Phenotypes in Disease Pathophysiology.

Jun G, Nicolaou M, Morrison MA, Buros J, Morgan DJ, Radeke MJ, Yonekawa Y, Tsironi EE, Kotoula MG, Zacharaki F, Mollema N, Yuan Y, Miller JW, Haider NB, Hageman GS, Kim IK, Schaumberg DA, Farrer LA, Deangelis MM.

Medicine (Biomedical Genetics), Boston University Schools of Medicine and Public Health, Boston, Massachusetts, United States of America.

Abstract

ROBO1 is a strong candidate gene for age-related macular degeneration (AMD) based upon its location under a linkage peak on chromosome 3p12, its expression pattern, and its purported function in a pathway that includes RORA, a gene previously associated with risk for neovascular AMD. Previously, we observed that expression of ROBO1 and RORA is down-regulated among wet AMD cases, as compared to their unaffected siblings. Thus, we hypothesized that contribution of association signals in ROBO1, and interaction between these two genes may be important for both wet and dry AMD. We evaluated association of 19 single nucleotide polymorphisms (SNPs) in ROBO1 with wet and dry stages of AMD in a sibling cohort and a Greek case-control cohort containing 491 wet AMD cases, 174 dry AMD cases and 411 controls. Association signals and interaction results were replicated in an independent prospective cohort (1070 controls, 164 wet AMD cases, 293 dry AMD cases). The most significantly associated ROBO1 SNPs were rs1387665 under an additive model (meta P=0.028) for wet AMD and rs9309833 under a recessive model (meta P=6×10(-4)) for dry AMD. Further analyses revealed interaction between ROBO1 rs9309833 and RORA rs8034864 for both wet and dry AMD (interaction P<0.05). These studies were further supported by whole transcriptome expression profile studies from 66 human donor eyes and chromatin immunoprecipitation assays from mouse retinas. These findings suggest that distinct ROBO1 variants may influence the risk of wet and dry AMD, and the effects of ROBO1 on AMD risk may be modulated by RORA variants.

PMID: 21998696 [PubMed - in process]

Eur J Hum Genet. 2011 Oct 12. doi: 10.1038/ejhg.2011.118. [Epub ahead of print]

No evidence of association between complement factor I genetic variant rs10033900 and age-related macular degeneration.

Cipriani V, Matharu BK, Khan JC, Shahid H, Hayward C, Wright AF, Armbrecht AM, Dhillon B, Harding SP, Bishop PN, Bunce C, Clayton DG, Moore AT, Yates JR.

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PMID: 21989362 [PubMed - as supplied by publisher]

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