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MD Research News

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Drug treatment

Biol Ther. 2012 May 29;2:3.

Aflibercept: a Potent Vascular Endothelial Growth Factor Antagonist for Neovascular Age-Related Macular Degeneration and Other Retinal Vascular Diseases.

Sophie R, Akhtar A, Sepah YJ, Ibrahim M, Bittencourt M, Do DV, Nguyen QD.

INTRODUCTION: In the western hemisphere, age-related macular degeneration (AMD) is the leading cause of visual loss in the elderly. Currently approved therapies for AMD include argon laser, photodynamic therapy, and antivascular endothelial growth factor (VEGF) therapy. The index review discusses aflibercept (VEGF Trap-Eye) in the context of current anti-VEGF therapies for neovascular AMD and other retinal vascular diseases. It highlights important differences between VEGF Trap-Eye and currently used anti-VEGF therapies for neovascular AMD; and discusses the efficacy of these treatments utilizing information from landmark clinical trials.

METHODS: A systematic search of literature was conducted on PubMed, Science Direct, and Scopus with no limitations of language or years of publication.

RESULTS: Preclinical studies have shown that VEGF Trap-Eye binds to VEGF-A with a higher affinity than other anti-VEGF molecules; and that it also binds to placental growth factor (PlGF). In clinical trials, VEGF Trap-Eye has been shown to be as effective in the treatment of neovascular AMD as other anti-VEGF therapies and possibly to have a longer duration of drug activity.

CONCLUSION: VEGF Trap-Eye has enhanced the treatment options currently available for the management of neovascular AMD. The comparable efficacy of VEGF Trap-Eye (to other anti-VEGF agents) coupled with its longer dosing interval may decrease the number of annual office visits for patients with AMD and their caregivers.

PMID: 24392297 [PubMed] PMCID: PMC3873045

Am J Ophthalmol. 2013 Dec 31. pii: S0002-9394(13)00808-8. doi: 10.1016/j.ajo.2013.12.018. [Epub ahead of print]

Clinical Utilization of Anti-VEGF Agents and Disease Monitoring in Neovascular Age-Related Macular Degeneration.

Holekamp NM1, Liu Y2, Yeh WS2, Chia Y2, Kiss S3, Almony A4, Kowalski JW2.

PURPOSE: To examine bevacizumab and ranibizumab utilization and disease monitoring patterns in patients with neovascular age-related macular degeneration (neovascular AMD) in clinical practice.

DESIGN: Retrospective medical claims analysis.

METHODS: Patients receiving ≥1 ranibizumab or bevacizumab injection(s) during the 12 months after initial neovascular AMD diagnosis were included. Annual bevacizumab and/or ranibizumab injection utilization was assessed by year of first injection cohorts: 2006 and 2007 (received either agent because of billing code overlap), 2008, 2009, and January to June 2010 (received each agent). Outcome measures were time -to-first injection relative to neovascular AMD diagnosis, and mean numbers of intravitreal injections, ophthalmologist visits, optical coherence tomography (OCT) and fluorescein angiography (FA) examinations in 12 months.

RESULTS: In the 2006 and 2007 cohorts (n=8767), mean annual numbers of bevacizumab or ranibizumab injections were 4.7 and 5.0, respectively. Over 92% of patients in all cohorts received first treatment within 3 months of neovascular AMD diagnosis. In the 2008 to 2010 cohorts (n=10,259), mean annual number of injections remained low (bevacizumab: 4.6, 5.1, and 5.5; ranibizumab: 6.1, 6.6, and 6.9), as did mean numbers of ophthalmologist visits (bevacizumab only) and OCT examinations (both agents), but there was no such trend in FA examinations.

CONCLUSIONS: Compared with treatment paradigms validated by clinical trials published at the time, in clinical practice, patients with neovascular AMD received fewer bevacizumab or ranibizumab injections and less frequent monitoring from 2006 to mid-2011. Factors contributing to this lower injection frequency and visual outcomes associated with reduced utilization need to be researched.

PMID: 24388973 [PubMed - as supplied by publisher]

Biomaterials. 2014 Jan 1. pii: S0142-9612(13)01515-9. doi: 10.1016/j.biomaterials.2013.12.031. [Epub ahead of print]

VEGF-binding aptides and the inhibition of choroidal and retinal neovascularization.

Jo DH1, Kim S2, Kim D2, Kim JH3, Jon S4, Kim JH5.

Abstract: Age-related macular degeneration and diabetic retinopathy are leading causes of blindness. Vascular endothelial growth factor (VEGF) is known to be the main factor that induces pathological angiogenesis in these diseases. In this study, we investigate the therapeutic potential and safety profiles of high-affinity peptides targeting VEGF which are identified using an 'aptide' technology. We show that two VEGF-binding aptides, APTVEGF1 and APTVEGF2, demonstrate high binding affinity and specificity to VEGF. Furthermore, they suppress VEGF-induced activation of VEGF receptor-2, in vitro angiogenesis, and in vivo pathological choroidal and retinal neovascularization. Despite potent anti-angiogenic effects, both VEGF-binding aptides do not induce any definite toxicity at the level of cellular viability, histological integrity, and gene expression. Our data show the therapeutic potential of VEGF-binding peptides for the treatment of choroidal and retinal neovascularization.

PMID: 24388818 [PubMed - as supplied by publisher]

Ophthalmology. 2014 Jan 4. pii: S0161-6420(13)01111-1. doi: 10.1016/j.ophtha.2013.11.029. [Epub ahead of print]

Intraocular Pressure in Eyes Receiving Monthly Ranibizumab in 2 Pivotal Age-Related Macular Degeneration Clinical Trials.

Bakri SJ1, Moshfeghi DM2, Francom S3, Rundle AC3, Reshef DS3, Lee PP4, Schaeffer C3, Rubio RG3,

Lai P3.

PURPOSE: To characterize preinjection intraocular pressure (IOP) in eyes receiving monthly ranibizumab versus sham or verteporfin photodynamic therapy (PDT) for age-related macular degeneration (AMD).

DESIGN: Post hoc analysis of IOP data from 2 phase 3 clinical trials, the Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular AMD (MARINA) and the Anti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in AMD (ANCHOR) trial.

PARTICIPANTS: All safety-evaluable patients who received 1 or more injections of sham or PDT or of ranibizumab and had 1 or more postbaseline IOP measurements recorded for the study eye.

METHODS: Preinjection IOP measurements for study eyes (n = 1125) and fellow eyes in MARINA and ANCHOR at baseline and at each monthly visit through month 24 were analyzed.

MAIN OUTCOME MEASURES: End points evaluated were maximum preinjection IOP during the 24-month treatment period; any occurrence of absolute preinjection IOP of 21 mmHg or more, 25 mmHg or more, or 30 mmHg or more; any occurrence of IOP increase of 6 mmHg or more, 8 mmHg or more, or 10 mmHg or more from baseline; any combination of IOP increase of 6 mmHg or more or 8 mmHg or more from baseline with concurrent absolute preinjection IOP of 21 mmHg or more or 25 mmHg or more; glaucoma-related adverse events; new glaucoma medications used for 45 days or more; and glaucoma filtration or laser surgeries.

RESULTS: Across treatment groups, 60.1% to 70.9% of study eyes had a maximum preinjection IOP of less than 21 mmHg. Comparing ranibizumab 0.5 mg versus sham or PTD treatment, respectively: 39.9% versus 29.1% and 10.9% versus 5.1% had maximum preinjection IOPs of 21 mmHg or more or 25 mmHg or more, respectively; 44.1% versus 29.9% and 24.2% versus 13.6% had IOP increases from baseline of 6 mmHg or more or 8 mmHg or more, respectively; 26.1% versus 13.6% and 16.8% versus 9.0% had 1 or more IOP increase from baseline of 6 mmHg or more or 8 mmHg or more, respectively, with a concurrent IOP of 21 mmHg or more; 9.6% versus 3.7% and 7.5% versus 2.4% had 1 or more IOP increase from baseline of 6 mmHg or more or 8 mmHg or more, respectively, with a concurrent IOP of 25 mmHg or more. No differences were observed in fellow eyes.

CONCLUSIONS: Most ranibizumab-treated eyes did not experience sustained preinjection IOP of 21 mmHg or more (>2 consecutive visits) over 24 months. When evaluating the combined IOP end point, more ranibizumab-treated eyes had 1 or more IOP increase from baseline of 6 mmHg or more or 8 mmHg or more, with concurrent highest IOPs of 21 mmHg or more and 25 mmHg or more versus sham or PDT. Intraocular pressure should be monitored in eyes receiving ranibizumab.

PMID: 24393349 [PubMed - as supplied by publisher]

Ophthalmology. 2014 Jan 7. pii: S0161-6420(13)01043-9. doi: 10.1016/j.ophtha.2013.10.037. [Epub ahead of print]

Cost-Effectiveness of Bevacizumab and Ranibizumab for Newly Diagnosed Neovascular Macular Degeneration.

Stein JD1, Newman-Casey PA2, Mrinalini T3, Lee PP2, Hutton DW3.

PURPOSE: We sought to determine the most cost-effective treatment for patients with newly diagnosed neovascular macular degeneration: monthly or as-needed bevacizumab injections, or monthly or as-needed ranibizumab injections.

DESIGN: Cost-effectiveness analysis.

PARTICIPANTS: Hypothetical cohort of 80-year-old patients with newly diagnosed neovascular macular

degeneration.

METHODS: Using a mathematical model with a 20-year time horizon, we compared the incremental cost-effectiveness of treating a hypothetical cohort of 80-year-old patients with newly diagnosed neovascular macular degeneration using monthly bevacizumab, as-needed bevacizumab, monthly ranibizumab, or as-needed ranibizumab. Data came from the Comparison of Age-related macular degeneration Treatment Trial (CATT), the Medicare Fee Schedule, and the medical literature.

MAIN OUTCOME MEASURES: Costs, quality-adjusted life-years (QALYs), and incremental costs per QALY gained.

RESULTS: Compared with as-needed bevacizumab, the incremental cost-effectiveness ratio of monthly bevacizumab is $242 357/QALY. Monthly ranibizumab gains an additional 0.02 QALYs versus monthly bevacizumab at an incremental cost-effectiveness ratio of >$10 million/QALY. As-needed ranibizumab was dominated by monthly bevacizumab, meaning it was more costly and less effective. In sensitivity analyses assuming a willingness to pay of $100 000/QALY, the annual risk of serious vascular events would have to be ≥2.5 times higher with bevacizumab than that observed in the CATT trial for as-needed ranibizumab to have an incremental cost-effectiveness ratio of <$100 000/QALY. In another sensitivity analysis, even if every patient receiving bevacizumab experienced declining vision by 1 category (e.g., from 20/25-20/40 to 20/50-20/80) after 2 years but every patient receiving ranibizumab retained their vision level, as-needed ranibizumab would have an incremental cost-effectiveness ratio of $97 340/QALY.

CONCLUSIONS: Even after considering the potential for differences in risks of serious adverse events and therapeutic effectiveness, bevacizumab confers considerably greater value than ranibizumab for the treatment of neovascular macular degeneration.

PMID: 24405740 [PubMed - as supplied by publisher]

PLoS One. 2013 Dec 31;8(12):e83759. doi: 10.1371/journal.pone.0083759.

Proof of concept, randomized, placebo-controlled study of the effect of simvastatin on the course of age-related macular degeneration.

Guymer RH1, Baird PN1, Varsamidis M1, Busija L2, Dimitrov PN1, Aung KZ1, Makeyeva GA1, Richardson AJ1, Lim L1, Robman LD1.

BACKGROUND: HMG Co-A reductase inhibitors are ubiquitous in our community yet their potential role in age-related macular degeneration (AMD) remains to be determined.

METHODOLOGY/PRINCIPAL FINDINGS: Objectives: To evaluate the effect of simvastatin on AMD progression and the effect modification by polymorphism in apolipoprotein E (ApoE) and complement factor H (CFH) genes. Design: A proof of concept double-masked randomized controlled study.

PARTICIPANTS: 114 participants aged 53 to 91 years, with either bilateral intermediate AMD or unilateral non-advanced AMD (with advanced AMD in fellow eye), BCVA≥20/60 in at least one eye, and a normal lipid profile. Intervention: Simvastatin 40 mg/day or placebo, allocated 1:1. Main outcome measures: Progression of AMD either to advanced AMD or in severity of non-advanced AMD. Results. The cumulative AMD progression rates were 70% in the placebo and 54% in the simvastatin group. Intent to treat multivariable logistic regression analysis, adjusted for age, sex, smoking and baseline AMD severity, showed a significant 2-fold decrease in the risk of progression in the simvastatin group: OR 0.43 (0.18-0.99), p=0.047. Post-hoc analysis stratified by baseline AMD severity showed no benefit from treatment in those who had advanced AMD in the fellow eye before enrolment: OR 0.97 (0.27-3.52), p=0.96, after adjusting for age, sex and smoking. However, there was a significant reduction in the risk of progression in the bilateral intermediate AMD group compared to placebo [adjusted OR 0.23 (0.07-0.75), p=0.015]. The most prominent effect was observed amongst those who had the CC (Y402H) at risk genotype of the CFH

gene [OR 0.08 (0.02-0.45), p=0.004]. No evidence of harm from simvastatin intervention was detected.

CONCLUSION/SIGNIFICANCE: Simvastatin may slow progression of non-advanced AMD, especially for those with the at risk CFH genotype CC (Y402H). Further exploration of the potential use of statins for AMD, with emphasis on genetic subgroups, is warranted.

PMID: 24391822 [PubMed - in process] PMCID: PMC3877099

Other treatment & diagnosis

Clin Exp Optom. 2013 Nov 13. doi: 10.1111/cxo.12119. [Epub ahead of print]

Australian optometric and ophthalmologic referral pathways for people with age-related macular degeneration, diabetic retinopathy and glaucoma.

Jamous KF, Jalbert I, Kalloniatis M, Boon MY.

BACKGROUND: This study investigated the referral pathways offered to patients with age-related macular degeneration (AMD), diabetic retinopathy (DR) or glaucoma (GL) by ophthalmologists and optometrists.

METHODS: Australian ophthalmologists and optometrists were surveyed regarding referral decisions to other eye-care specialists (inter- or intra-professional), general medical practitioners (GPs), low vision rehabilitation (LVR) and support services. Thematic analysis and concept mapping were applied to highlight current and ideal referral pathways.

RESULTS: The survey was completed by 155 optometrists and 50 ophthalmologists and deemed representative of their respective professions in Australia. Not surprisingly, the vast majority of the participating optometrists (97 to 99 per cent) referred to ophthalmologists regardless of the underlying condition. Clear differences (Chi-square: $p < 0.05$) were observed in the referral patterns of optometrists and ophthalmologists to GPs and support services. General medical practitioner services were almost exclusively used for patients with DR, while AMD triggered a significantly higher referral rate to low vision rehabilitation and support services than the other two disorders.

CONCLUSION: While ophthalmologists predominantly referred patients with AMD, DR or GL to low vision rehabilitation services, optometrists' referrals were highly skewed toward ophthalmology. Referrals to other supporting services by the two groups were not greatly used. The perceived referral pathways by the two eye-care professionals suggested a unidirectional route, potentially highlighting the need for a more collaborative approach that facilitates optimal use of eye health care and allied services.

PMID: 24400653 [PubMed - as supplied by publisher]

Ophthalmic Surg Lasers Imaging Retina. 2014 Jan 1;45(1):32-7. doi: 10.3928/23258160-20131220-04.

Analysis of short-term change in subfoveal choroidal thickness in eyes with age-related macular degeneration using optical coherence tomography.

Fein JG, Branchini LA, Manjunath V, Regatieri CV, Fujimoto JG, Duker JS.

BACKGROUND AND OBJECTIVE: To measure the subfoveal choroidal thickness in patients with age-related macular degeneration (AMD) over 6 months.

PATIENTS AND METHODS: A retrospective, observational study of patients with AMD followed up for 6 months at the New England Eye Center. Baseline and 6-month follow-up subfoveal choroidal thickness was measured using spectral-domain OCT and compared.

RESULTS: For the entire cohort, there was statistically significant thinning of the subfoveal choroidal thickness at 6 months compared to baseline that was driven by the cohort of patients with neovascular AMD (181.2 ± 75 μm to 173.4 ± 63 μm; P = .049).

CONCLUSION: There was a statistically significant decrease in subfoveal choroidal thickness observed in this cohort of patients with AMD over 6 months, but it was driven by the subgroup of patients with neovascular age-related macular degeneration. [Ophthalmic Surg Lasers Imaging Retina. 2014;45:32-37.].

PMID: 24392909 [PubMed - in process]

Biomed Opt Express. 2013 Nov 1;4(12):2729-50. doi: 10.1364/BOE.4.002729.

Semi-automatic geographic atrophy segmentation for SD-OCT images.

Chen Q1, de Sisternes L2, Leng T3, Zheng L3, Kutzscher L3, Rubin DL4.

Abstract: Geographic atrophy (GA) is a condition that is associated with retinal thinning and loss of the retinal pigment epithelium (RPE) layer. It appears in advanced stages of non-exudative age-related macular degeneration (AMD) and can lead to vision loss. We present a semi-automated GA segmentation algorithm for spectral-domain optical coherence tomography (SD-OCT) images. The method first identifies and segments a surface between the RPE and the choroid to generate retinal projection images in which the projection region is restricted to a sub-volume of the retina where the presence of GA can be identified. Subsequently, a geometric active contour model is employed to automatically detect and segment the extent of GA in the projection images. Two image data sets, consisting on 55 SD-OCT scans from twelve eyes in eight patients with GA and 56 SD-OCT scans from 56 eyes in 56 patients with GA, respectively, were utilized to qualitatively and quantitatively evaluate the proposed GA segmentation method. Experimental results suggest that the proposed algorithm can achieve high segmentation accuracy. The mean GA overlap ratios between our proposed method and outlines drawn in the SD-OCT scans, our method and outlines drawn in the fundus auto-fluorescence (FAF) images, and the commercial software (Carl Zeiss Meditec proprietary software, Cirrus version 6.0) and outlines drawn in FAF images were 72.60%, 65.88% and 59.83%, respectively.

PMID: 24409376 [PubMed]

Invest Ophthalmol Vis Sci. 2014 Jan 9. pii: iovs.13-12172v1. doi: 10.1167/iovs.13-12172. [Epub ahead of print]

Differential Vulnerability of Retinal Layers to Early Age-Related Macular Degeneration: Evidence by SD-OCT Segmentation Analysis.

Savastano MC, Minnella AM, Tamburrino A, Giovinco G, Ventre S, Falsini B.

Purpose: To evaluate layer-by-layer retinal thickness in spectral-domain optical coherence tomography (SD -OCT), determined by automated segmentation analysis (ASA) software in healthy and early age-related maculopathy (ARM) eyes.

Methods: Fifty-seven eyes, specifically, 19 healthy eyes under 60 years old, 19 healthy eyes over 60, and 19 ARM eyes, were recruited into this cross-sectional study. The mean ages were 36.78 (SD: ± 13.82), 69.89 (SD: ± 6.14) and 66.10 (SD: ± 8.67) years, respectively, in the three study groups. SD-OCT scans were transferred into a dedicated software program that performed automated segmentation of different retinal layers.

Results: Automated layer segmentation showed clear boundaries between the following layers: Retinal Nerve Fiber Layer (RNFL); Ganglion Cell Layer + Inner Plexiform Layer (GCL + IPL); Inner Nuclear Layer +

Outer Plexiform Layer (INL + OPL); Outer Nuclear Layer (ONL); and Retinal Pigment Epithelium complex (RPE). The thickness of the RNFL, ONL and RPE layers did not show a statistically significant change across the three groups by ANOVA (P= 0.10; P=0.09; P= 0.15, respectively). The thickness of both GCL+IPL and INL+OPL was significantly different across the groups (P< 0.01), being reduced in the ARM eyes compared with healthy eyes, both under and over 60 yo.

Conclusions: The early morphological involvement of the GCL+IPL and INL+OPL layers in ARM eyes, as revealed by the ASA, could be related to early anatomic changes described in the inner retina of ARM eyes. This finding may represent a morphological correlation to the deficits in postreceptoral retinal function in ARM eyes.

PMID: 24408984 [PubMed - as supplied by publisher]

Graefes Arch Clin Exp Ophthalmol. 2014 Jan 10. [Epub ahead of print]

Fundus autofluorescence in patients with retinal pigment epithelial (RPE) tears: an in-vivo evaluation of RPE resurfacing.

Mendis R, Lois N.

AIM: Investigate RPE resurfacing by changes in fundus autofluorescence (AF) in patients with retinal pigment epithelial (RPE) tears secondary to age-related macular degeneration (AMD).

METHODS: A retrospective case series of patients presenting with RPE tears from 1 March 2008 to 1 April 2011. The pattern and area of AF signal distribution in RPE tears were evaluated. The change in the size of the area of debrided RPE over the follow-up period was used as the main outcome measure. A reduction in this area was termed "RPE resurfacing", and an enlargement termed "progression of RPE cell loss".

RESULTS: Thirteen patients (14 eyes) with RPE tears (mean age 82 years) were included in this study. The mean baseline area of reduced AF signal was 4.1 mm2 (range 0.33-14.9, median 0.29). "Resurfacing" of the RPE occurred in ten eyes and "progression of RPE cell loss" in four eyes after a median follow-up of 11.5 months (range, 1-39). The mean area of healing was 2.0 mm2, and progression was 1.78 mm2.

CONCLUSION: A consistent AF pattern was observed in patients with RPE tears. RPE resurfacing over the area of the RPE tear occurred, to a varying degree, in the majority of the cases.

PMID: 24407824 [PubMed - as supplied by publisher]

Retina. 2014 Jan 8. [Epub ahead of print]

SENSITIVITY OF FLUID DETECTION IN PATIENTS WITH NEOVASCULAR AMD USING SPECTRAL DOMAIN OPTICAL COHERENCE TOMOGRAPHY HIGH-DEFINITION LINE SCANS.

De Niro JE, McDonald HR, Johnson RN, Jumper JM, Fu AD, Cunningham ET Jr, Lujan BJ.

PURPOSE: To determine the sensitivity of the Cirrus high-definition (HD) 5-line raster scans for detecting retinal fluid in neovascular age-related macular degeneration when using the spectral domain optical coherence tomography macular cubes as a gold standard.

METHODS: Patients were retrospectively identified from their initial follow-up visit after being newly diagnosed with neovascular age-related macular degeneration in at least one eye. Patients were imaged with Cirrus spectral domain optical coherence tomography using the 512 × 128 macular cube scan and HD 5-line raster scan settings. Patients with other diseases that cause subretinal or intraretinal fluid, or who had an epiretinal membrane causing macular traction were excluded from the analysis. We recorded the presence or absence of subretinal or intraretinal fluid in the macular cube and on the HD 5-line raster

scans.

RESULTS: Seventy-nine patients met the study requirements. Of the 63 patients who had fluid present on the macular cube, 1 did not seem to have fluid on the HD 5-line raster scans. Taking the macular cube as a gold standard, the sensitivity of the HD 5-line raster scans for detecting retinal fluid in this cohort was 98.4%.

CONCLUSION: The Cirrus HD 5-line raster scans have a high sensitivity for detecting fluid in the macular cube in patients with neovascular age-related macular degeneration.

PMID: 24406389 [PubMed - as supplied by publisher]

Case Rep Ophthalmol. 2013 Oct 11;4(3):165-71. doi: 10.1159/000355829.

Retinal pigment epithelium tear after vitrectomy for vitreomacular traction syndrome in an eye with retinal angiomatous proliferation.

Baba T, Uehara J, Kitahashi M, Yokouchi H, Kubota-Taniai M, Oshitari T, Yamamoto S.

Abstract: An 87-year-old Japanese man presented with retinal angiomatous proliferation (RAP) and a retinal pigment epithelium (RPE) detachment in his right eye. His decimal best-corrected visual acuity was 0.15 in the right eye, and optical coherence tomography (OCT) showed a vitreomacular adhesion in the right eye as well. After 3 monthly intravitreal injections of ranibizumab, the size and height of the RPE detachment was significantly reduced. The accumulated intra- and subretinal fluid also disappeared, but the vitreomacular traction remained. Pars plana vitrectomy was performed, and the posterior hyaloid was separated from the retina with a vitrectomy cutter without any intraoperative complications. Two months after the surgery, a large RPE tear was observed over the macular area. His visual acuity decreased to 0.06 and remained unchanged thereafter. We suggest that the small tear led to the larger RPE tear because vitreomacular traction was transmitted to the RPE through the fibrovascular tissue of the RAP during the creation of the hyaloid detachment. Because such an RPE tear has not been reported after vitrectomy for vitreomacular traction, surgeons need to pay special attention to this potential complication in eyes with vitreomacular traction and RAP.

PMID: 24403899 [PubMed]

Invest Ophthalmol Vis Sci. 2014 Jan 7. pii: iovs.13-12912v1. doi: 10.1167/iovs.13-12912. [Epub ahead of print]

THE CLINICAL SPECTRUM OF MICROCYSTIC MACULAR OEDEMA.

Burggraaff MC, Trieu J, de Vries-Knoppert WA, Balk L, Petzold A.

Purpose: Microcystic macular oedema (MMO) defines microcysts in the inner nuclear layer (INL) of the retina. MMO was described in multiple sclerosis (MS), but can be found in numerous disorders. Presence of MMO has important prognostic and therapeutic implications, however, the differential diagnosis is unknown. This study aimed to describe the clinical spectrum of MMO.

Methods: a single-centre, retrospective cohort study. A bootstrap analysis was performed to reduce the 5,865 patients (22,376 scans), who had undergone OCT imaging between January 2010 and February 2013, to a representative dataset. Presence of MMO was rated by independent observers.

Results: The dataset consisted of 1,368 patients (mean age 62, range 4-101 years), 2,589 eyes and 6,449 scans. MMO was present in 133/1,303 (10%) of patients and 0/65 (0%) of healthy controls. The inter-rater agreement for detecting MMO was substantial (0.6) and could be further improved after refining the criteria (0.8). The clinical spectrum included age-related macular degeneration, epiretinal membranes, post-

operative lesions, diabetic retinopathy, vascular occlusion, MS (with/without optic neuritis), optic neuropathy, central serous chorioretinopathy, medication and miscellaneous causes. The longitudinal pattern of MMO was transient in 84% of cases. MMO could be associated with an increase or decrease in INL thickness and was predominantly located nasally (48%) and/or temporally (50%).

Conclusions: This study substantially widened the clinical spectrum of MMO. Diagnostic criteria were refined and validated. The associated phenotype may imply Müller cell dysfunction within the watershed zone. The longitudinal data and evidence from previous studies suggest follow-up of these patients and their visual function.

PMID: 24398089 [PubMed - as supplied by publisher]

Lupus. 2014 Jan 9. [Epub ahead of print]

Polypoidal choroidal vasculopathy and systemic lupus erythematosus.

Chin Y, Bhargava M, Khor C, Cheung C, Wong T.

Abstract: Systemic lupus erythematosus (SLE) associated with antiphospholipid syndrome can have ocular complications. We report a 44-year-old Chinese lady with recurrent relapses of SLE and antiphospholipid syndrome with high disease activity, presenting with visual distortion in her right eye for 2 months. There was subretinal hemorrhage in her right eye, confirmed on investigations to be choroidal neovascularization secondary to a variant of age-related macular degeneration known as polypoidal choroidal vasculopathy (PCV). Anti-vascular endothelial growth factor therapy resolved her eye condition. SLE could be associated with PCV via common mechanisms, including complement pathway activation and vasculitis involving the choroidal circulation.

PMID: 24407425 [PubMed - as supplied by publisher]

Retina. 2014 Jan 6. [Epub ahead of print]

AUTOMATED IMAGE ALIGNMENT AND SEGMENTATION TO FOLLOW PROGRESSION OF GEOGRAPHIC ATROPHY IN AGE-RELATED MACULAR DEGENERATION.

Ramsey DJ, Sunness JS, Malviya P, Applegate C, Hager GD, Handa JT.

PURPOSE: To develop a computer-based image segmentation method for standardizing the quantification of geographic atrophy (GA).

METHODS: The authors present an automated image segmentation method based on the fuzzy c-means clustering algorithm for the detection of GA lesions. The method is evaluated by comparing computerized segmentation against outlines of GA drawn by an expert grader for a longitudinal series of fundus autofluorescence images with paired 30° color fundus photographs for 10 patients.

RESULTS: The automated segmentation method showed excellent agreement with an expert grader for fundus autofluorescence images, achieving a performance level of 94 ± 5% sensitivity and 98 ± 2% specificity on a per-pixel basis for the detection of GA area, but performed less well on color fundus photographs with a sensitivity of 47 ± 26% and specificity of 98 ± 2%. The segmentation algorithm identified 75 ± 16% of the GA border correctly in fundus autofluorescence images compared with just 42 ± 25% for color fundus photographs.

CONCLUSION: The results of this study demonstrate a promising computerized segmentation method that may enhance the reproducibility of GA measurement and provide an objective strategy to assist an expert in the grading of images.

PMID: 24398699 [PubMed - as supplied by publisher]

Med Phys. 2014 Jan;41(1):011707. doi: 10.1118/1.4842455.

Dosimetric properties of a proton beamline dedicated to the treatment of ocular disease.

Slopsema RL1, Mamalui M1, Zhao T2, Yeung D1, Malyapa R1, Li Z1.

Purpose: A commercial proton eyeline has been developed to treat ocular disease. Radiotherapy of intraocular lesions (e.g., uveal melanoma, age-related macular degeneration) requires sharp dose gradients to avoid critical structures like the macula and optic disc. A high dose rate is needed to limit patient gazing times during delivery of large fractional dose. Dose delivery needs to be accurate and predictable, not in the least because current treatment planning algorithms have limited dose modeling capabilities. The purpose of this paper is to determine the dosimetric properties of a new proton eyeline. These properties are compared to those of existing systems and evaluated in the context of the specific clinical requirements of ocular treatments.

Methods: The eyeline is part of a high-energy, cyclotron-based proton therapy system. The energy at the entrance of the eyeline is 105 MeV. A range modulator (RM) wheel generates the spread-out Bragg peak, while a variable range shifter system adjusts the range and spreads the beam laterally. The range can be adjusted from 0.5 up to 3.4 g/cm(2); the modulation width can be varied in steps of 0.3 g/cm(2) or less. Maximum field diameter is 2.5 cm. All fields can be delivered with a dose rate of 30 Gy/min or more. The eyeline is calibrated according to the IAEA TRS-398 protocol using a cylindrical ionization chamber. Depth dose distributions and dose/MU are measured with a parallel-plate ionization chamber; lateral profiles with radiochromic film. The dose/MU is modeled as a function of range, modulation width, and instantaneous MU rate with fit parameters determined per option (RM wheel).

Results: The distal fall-off of the spread-out Bragg peak is 0.3 g/cm(2), larger than for most existing systems. The lateral penumbra varies between 0.9 and 1.4 mm, except for fully modulated fields that have a larger penumbra at skin. The source-to-axis distance is found to be 169 cm. The dose/MU shows a strong dependence on range (up to 4%/mm). A linear increase in dose/MU as a function of instantaneous MU rate is observed. The dose/MU model describes the measurements with an accuracy of ±2%. Neutron dose is found to be 146 ± 102 μSv/Gy at the contralateral eye and 19 ± 13 μSv/Gy at the chest.

Conclusions: Measurements show the proton eyeline meets the requirements to effectively treat ocular disease.

PMID: 24387499 [PubMed - in process]

Pathogenesis

Int J Ophthalmol. 2013 Dec 18;6(6):772-7. doi: 10.3980/j.issn.2222-3959.2013.06.06.

Acetylcholinesterase function in apoptotic retina pigment epithelial cells induced by H2O2.

Cai L1, Liao HF1, Zhang XJ2, Shao Y3, Xu M1, Yi JL1.

AIM: To investigate the acetylcholinesterase (AChE) expression involved in retina pigment epithelial (RPE) apoptosis induced by higher concentrations H2O2.

METHODS: The human retinal pigment epithelium cell line ARPE-19 was from ATCC (Rockville, MD). Cultured ARPE-19 cells were treated with H2O2 at 0, 250, 500, 1 000, 2 000μmol/L and cell viability was measured with MTT assay. AChE expression and DNA fragments were analyzed by immunocytochemistry, TUNEL and PARP-1 Western blotting.

RESULTS: Immunofluorescence detected AChE exist in the normal human retinal tissue. When H2O2 >500μmol/L, AChE expression showed an increase after 2h, and this concentration was selected for the present study. RPE cell was induced with 1 000μmol/L H2O2 for 2h, compared to the control group, cell

activity decline detected by MTT, AChE and PARP-1 protein expression was significantly increased detected by Western blotting. AChE immunofluorescence staining was positive in RPE cell after H2O2 incubate 2h. In addition, pretreatment with 100μmol/L epigallocatechin gallate (EGCG), cell viability increased from 31.20%±3.90% to 70.23%±12.96%.

CONCLUSION: AChE is weakly expressed in normal human RPE cells. Stimulation with H2O2 caused the stable increase of AChE expression in RPE cells, which may indicate that AChE may be an important role in AMD.

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Gene. 2014 Jan 6. pii: S0378-1119(13)01680-6. doi: 10.1016/j.gene.2013.12.019. [Epub ahead of print]

Therapeutic potentials of gene silencing by RNA interference: Principles, challenges, and new strategies.

Deng Y1, Wang CC2, Choy KW1, Du Q3, Chen J2, Wang Q4, Chung TK2, Tang T5.

Abstract: During recent decades there have been remarkable advances in biology, in which one of the most important discoveries is RNA interference (RNAi). RNAi is a specific post-transcriptional regulatory pathway that can result in silencing gene functions. Efforts have been done to translate this new discovery into clinical applications for disease treatment. However, technical difficulties restrict the development of RNAi, including stability, off-target effects, immunostimulation and delivery problems. Researchers have attempted to surmount these barriers and improve the bioavailability and safety of RNAi-based therapeutics by optimizing the chemistry and structure of these molecules. This paper aimed to describe the principles of RNA interference, review the therapeutic potential in various diseases and discuss the new strategies for in vivo delivery of RNAi to overcome the challenges.

PMID: 24406620 [PubMed - as supplied by publisher]

J Proteome Res. 2014 Jan 8. [Epub ahead of print]

Exosomal Proteins in the Aqueous Humor as Novel Biomarkers in Patients with Neovascular Age-related Macular Degeneration.

Kang GY, Bang JY, Choi AJ, Yoon J, Lee WC, Choi S, Yoon S, Kim HC, Baek JH, Park HS, Lim HJ, Chung H.

Abstract: Age-related macular degeneration (AMD) describes the progressive degeneration of the retinal pigment epithelium (RPE), retina, and choriocapillaris and is the leading cause of blindness in people over 50. The molecular mechanisms underlying this multifactorial disease remain largely unknown. To uncover novel secretory biomarkers related to the pathogenesis of AMD, we adopted an integrated approach to compare the proteins identified in the conditioned medium (CM) of cultured RPE cells and the exosomes derived from CM and from the aqueous humor (AH) of AMD patients by LC-ESI-MS/MS. Finally, LC-MRM was performed on the AH from patients and controls, which revealed that cathepsin D, cytokeratin 8 and 4 other proteins increased in the AH of AMD patients. The present study has identified potential biomarkers and therapeutic targets for AMD treatment, such as proteins related to the autophagy-lysosomal pathway and epithelial-mesenchymal transition, and demonstrated a novel and effective approach to identifying AMD-associated proteins that might be secreted by RPE in vivo in the form of exosomes. The proteomics-based characterization of this multifactorial disease could help to match a particular marker to particular target-based therapy in AMD patients with various phenotypes.

PMID: 24400796 [PubMed - as supplied by publisher]

Arch Pharm Res. 2014 Jan 7. [Epub ahead of print]

Allosteric regulation of pathologic angiogenesis: potential application for angiogenesis-related blindness.

Jo DH, Kim JH, Kim KW, Suh YG, Kim JH.

Abstract: Angiogenesis-related blindness (ARB) includes age-related macular degeneration, diabetic retinopathy, and retinopathy of prematurity, all of which are based on pathologic angiogenesis. Current treatment options such as surgery, laser photocoagulation, and steroid have shown limitations because they do not directly resolve the pathologic events in the retina. Furthermore, recently approved and developed therapeutic drugs only focus on direct inhibition of growth factors and suppression of downstream signaling molecules of activated receptor proteins by orthosteric ligands. In this regard, allosteric regulation of receptors and ligands can be a valuable mechanism in the development of novel drugs for ARB. In this review, we briefly address the clinical significance of ARB for further discussion on allosteric regulation of pathologic angiogenesis for ARB. Interestingly, key molecules in the pathogenesis of ARB can be targets for allosteric regulation, sharing characteristics as allosteric proteins. With investigation of allostery by introducing well-established models for allosteric proteins and currently published novel allosteric modulators, we discuss the potential of allosteric regulation for ARB. In conclusion, we hope that allosteric regulation of pathologic angiogenesis in ARB can open new opportunities for drug development.

PMID: 24395531 [PubMed - as supplied by publisher]

Nihon Ganka Gakkai Zasshi. 2013 Nov;117(11):903-10.

[RhoJ signaling pathway in retinal angiogenesis: promising targets for novel anti-angiogenic therapy].[Article in Japanese]

Fukushima Y.

Abstract: In quiescent retinal vessels, adjacent endothelial cells (ECs) form a tightly sealed junction, leading to maintenance of vascular integrity. By contrast, during pathological angiogenesis in diabetic retinopathy and age-related macular degeneration, vascular endothelial growth factor (VEGF) activates intracellular signaling pathways in ECs, resulting in the dissociation of cell-cell adhesions and induction of EC migration. To inhibit undesirable angiogenesis, it would be clinically beneficial to manipulate intracellular signals that control migratory behavior of ECs. Here we show that the small GTPase RhoJ is expressed predominantly in angiogenic ECs, and regulates cell motility through cytoskeletal rearrangement. We also found that Arhgef15, an EC-specific guanine nucleotide exchange factor, inactivates RhoJ downstream of VEGF signals, thereby promoting retinal vascular growth. These signaling molecules can be potential drug targets for novel antiangiogenic therapy.

PMID: 24397187 [PubMed - in process]

Epidemiology

JAMA Ophthalmol. 2014 Jan 2. doi: 10.1001/jamaophthalmol.2013.6636. [Epub ahead of print]

Ten-Year Follow-up of Age-Related Macular Degeneration in the Age-Related Eye Disease Study: AREDS Report No. 36.

Chew EY1, Clemons TE2, Agrón E1, Sperduto RD2, Sangiovanni JP1, Davis MD3, Ferris FL 3rd1; for the Age-Related Eye Disease Study Research Group.

IMPORTANCE: Providing long-term follow-up of the natural history of age-related macular degeneration

(AMD) and associated risk factors will facilitate future epidemiologic studies and clinical trials.

OBJECTIVE: To describe 10-year progression rates to intermediate or advanced AMD.

DESIGN, SETTING, AND PARTICIPANTS: We observed the Age-Related Eye Disease Study (AREDS) participants for an additional 5 years after a randomized clinical trial of antioxidant vitamins and minerals was completed. Observation occurred at 11 clinical sites of medical retinal practices from academic institutions and community medical centers. Participants aged 55 to 80 years with no AMD or AMD of varying severity (n = 4757) were followed up in the AREDS trial for a median duration of 6.5 years. When the trial ended, 3549 of the 4203 surviving participants were followed for 5 additional years.

EXPOSURE: Treatment with antioxidant vitamins and minerals.

MAIN OUTCOMES AND MEASURES: Development of varying stages of AMD and changes in visual acuity. The rates of progression to large drusen and advanced AMD (neovascular AMD or central geographic atrophy) were evaluated using annual fundus photographs assessed centrally. Best-corrected visual acuity was measured at annual study visits.

RESULTS: The risk of progression to advanced AMD increased with increasing age (P = .01) and severity of drusen. Women (P = .005) and current smokers (P < .001) were at increased risk of neovascular AMD. In the oldest participants with the most severe AMD status at baseline, the risks of developing neovascular AMD and central geographic atrophy by 10 years were 48.1% and 26.0%, respectively. Similarly, rates of progression to large drusen increased with increasing severity of drusen at baseline, with 70.9% of participants with bilateral medium drusen progressing to large drusen and 13.8% to advanced AMD in 10 years. Median visual acuity at 10 years in eyes that had large drusen at baseline but never developed advanced AMD was 20/25; eyes that developed advanced AMD had a median visual acuity of 20/200.

CONCLUSIONS AND RELEVANCE: The natural history of AMD demonstrates relentless loss of vision in persons who developed advanced AMD. These progression data and the risk factor analyses may be helpful to investigators conducting research in clinic populations.

PMID: 24385141 [PubMed - as supplied by publisher]

Maturitas. 2013 Dec 14. pii: S0378-5122(13)00373-3. doi: 10.1016/j.maturitas.2013.12.001. [Epub ahead of print]

Age-related macular degeneration and 5-year incidence of impaired activities of daily living.

Gopinath B1, Liew G2, Burlutsky G2, Mitchell P2.

OBJECTIVES: We aimed to assess the prospective association between age-related macular degeneration (AMD) and impaired activities of daily living (ADL) among a large cohort of older adults.

STUDY DESIGN: Functional status was determined by the Older Americans Resources and Services ADL scale from 2002-2004 to 2007-2009 among 761 participants aged 60+ years. AMD was assessed from retinal photographs.

RESULTS: After adjusting for age, sex, living status, self-rated poor health, smoking, body mass index, visual impairment, hypertension, diabetes, hospital admissions in the past year, walking disability, probable depression, mini-mental state examination scores, having any AMD or late AMD increased the risk of incident impaired total ADL 5 years later, odds ratio, OR 2.87 (95% confidence intervals, CI 1.44-5.71) and OR 12.95 (95% CI 3.78-44.35), respectively. Having any AMD increased the risk of developing instrumental ADL disability over the 5 years, multivariable-adjusted OR 2.06 (95% CI 1.11-3.83).

CONCLUSIONS: This study shows that the presence of AMD could independently signal an increased risk of functional disability, particularly in performing instrumental ADL tasks.

PMID: 24388736 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2014 Jan 9. doi: 10.1136/bjophthalmol-2013-304050. [Epub ahead of print]

Prevalence and causes of vision loss in Southeast Asia and Oceania: 1990-2010.

Keeffe J, Taylor HR, Fotis K, Pesudovs K, Flaxman SR, Jonas JB, Leasher J, Naidoo K, Price H, White RA, Wong TY, Resnikoff S, Bourne RR; on behalf of the Vision Loss Expert Group of the Global Burden of Disease Study.

BACKGROUND: To assess prevalence and causes of vision impairment in Southeast Asia and Oceania in 1990 and 2010.

METHODS: Based on a systematic review of medical literature, prevalence of moderate and severe vision impairment (MSVI; presenting visual acuity <6/18 but ≥3/60 in the better eye) and blindness (presenting visual acuity <3/60) was estimated for 1990 and 2010.

RESULTS: In Oceania, the age-standardised prevalence of blindness and MSVI did not decrease significantly (1.3% to 0.8% and 6.6% to 5.1%) respectively, but in Southeast Asia, blindness decreased significantly from 1.4% to 0.8%, a 43% decrease. There were significantly more women blind (2.18 million) compared with men (1.28 million) in the Southeast Asian population in 2010, but no significant gender differences in MSVI in either subregion. Cataract was the most frequent cause of blindness in Southeast Asia and Oceania in 1990 and 2010. Uncorrected refractive error, followed by cataract, macular degeneration, glaucoma and diabetic retinopathy were the most common causes for MSVI in 1990 and 2010. With the increasing size of the older population, there have been relatively small increases in the number of blind (2%), and with MSVI (14%) in Southeast Asia, whereas increases have been greater in Oceania of 14% for blindness and of 31% for MSVI.

CONCLUSIONS: The prevalence of blindness has reduced significantly from 1990 to 2010, with moderate but non-significant lowering of MSVI. Cataract and uncorrected refractive error are the main causes of vision impairment and blindness; cataract continues as the main cause of blindness, but at lower proportions.

PMID: 24407561 [PubMed - as supplied by publisher]

Genetics

Int J Ophthalmol. 2013 Dec 18;6(6):861-7. doi: 10.3980/j.issn.2222-3959.2013.06.21.

Complement factor B polymorphism (rs641153) and susceptibility to age-related macular degeneration: evidence from published studies.

Wang X, Zhang Y, Zhang MN.

AIM: To determine whether single nucleotide polymorphism (SNP) rs641153 is associated with the risk of age-related macular degeneration (AMD), we performed a systematic meta-analysis of 15 eligible studies. SNP in the complement factor B (CFB) gene is considered to have significant association with AMD susceptibility, but there is great discrepancy in these results.

METHODS: The eligible studies were identified by searching the databases of PubMed, EMBASE, and Web of Science. Odds ratios (ORs) with 95% confidence intervals (CIs) were used to assess the association. All data were analyzed using Stata software.

RESULTS: The association between rs641153 and AMD risk was statistically significant under the homozygous model (AA vs GG:OR=0.26, 95%CI=0.15-0.45, P h=0.973, I (2)=0.0%, fixed effects), dominant model (AA+GA vs GG:OR=0.49, 95%CI=0.40-0.59, P h=0.004, I (2)=56.4%, random effects) and recessive model (AA vs GA+GG:OR=0.30, 95%CI=0.17-0.51, P h=0.983, I (2)=0.0%, fixed effects). The same results were also observed in the stratified analyses by ethnicity, source of control and sample size.

CONCLUSION: Our meta-analysis suggests that rs641153 in the CFB gene may play a protective role in AMD susceptibility, the late AMD in particular, both in Caucasians and in Asians.

PMID: 24392338 [PubMed] PMCID: PMC3874529

Ophthalmology. 2014 Jan 3. pii: S0161-6420(13)01049-X. doi: 10.1016/j.ophtha.2013.10.042. [Epub ahead of print]

Genes in the High-Density Lipoprotein Metabolic Pathway in Age-Related Macular Degeneration and Polypoidal Choroidal Vasculopathy.

Liu K1, Chen LJ2, Lai TY1, Tam PO1, Ho M3, Chiang SW1, Liu DT2, Young AL2, Yang Z4, Pang CP5.

PURPOSE: To investigate the associations of genetic variants in the high-density lipoprotein (HDL) metabolism pathway with neovascular age-related macular degeneration (AMD) and polypoidal choroidal vasculopathy (PCV).

DESIGN: Cross-sectional, case-control association study.

PARTICIPANTS: A Chinese case-control group of 200 neovascular AMD patients, 233 PCV patients, and 275 control subjects.

METHODS: Eight single nucleotide polymorphisms (SNPs) from 6 genes of the HDL metabolism pathway and 2 known AMD-associated SNPs, rs800292 (from complement factor H [CFH]) and rs11200638 (from HtrA serine peptidase 1 [HTRA1]), were genotyped in all study subjects using the TaqMan genotyping technology (Applied Biosystems, Foster City, CA).

MAIN OUTCOME MEASURES: Allele and genotypic frequencies of selected SNPs.

RESULTS: The SNP rs3764261 in the cholesteryl ester transfer protein (CETP) gene was associated significantly with neovascular AMD (P = 1.82×10-4; odds ratio [OR], 1.89) and PCV (P = 4.04×10-4; OR, 1.80). The associations remained significant after adjusting for the CFH SNP rs800292 and the HTRA1 SNP rs11200638. A significant interaction between the CETP SNP rs3764261 and the CFH SNP rs800292 existed in both neovascular AMD and PCV, the rs800292 G allele conferring a significantly increased risk of the diseases only in individuals carrying the risk allele T of rs3764261. A borderline association was detected between the ATP-binding cassette, subfamily G, member 1 (ABCG1) gene SNP rs57137919 and PCV (P = 0.03).

CONCLUSIONS: Our results showed that CETP is a susceptibility gene for neovascular AMD and PCV and that ABCG1 a putative gene for PCV. CETP exerts a modifying effect on CFH in the genetic risk. Our data suggest a link of the HDL metabolism pathway with neovascular AMD and PCV.

PMID: 24393350 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2014;8:143-8. doi: 10.2147/OPTH.S56483. Epub 2013 Dec 27.

Retinal angiomatous proliferation associated with risk alleles of ARMS2/HTRA1 gene polymorphisms in Japanese patients.

Ohkuma Y1, Hayashi T1, Sakai T1, Watanabe A1, Yamada H2, Akahori M3, Itabashi T3, Iwata T3, Noda T4, Tsuneoka H1.

BACKGROUND: The purpose of this study was to investigate the association between ARMS2/HTRA1, CFH, and C3 gene polymorphisms and retinal angiomatous proliferation (RAP), an infrequent and severe form of exudative age-related macular degeneration, which is characterized by intraretinal

neovascularization.

METHODS: Diagnosis of RAP was based on fundus photographs, images of fluorescein and indocyanine green angiographies, and optical coherence tomography findings. Six single nucleotide polymorphisms (SNPs), A69S (rs10490924) in ARMS2, rs11200638 in HTRA1, I62V (rs800292) in CFH, Y402H (rs1061170) in CFH, R80G (rs2230199) in C3, and rs2241394 in C3, were genotyped in eight Japanese patients with RAP.

RESULTS: The two SNPs in the ARMS2/HTRA1 were in complete linkage disequilibrium. The frequency of the risk T allele in ARMS2 (the risk A allele in HTRA1) was 93.8% in the RAP patients. The frequency of homozygosity for the risk genotype TT of ARMS2 (the risk genotype AA of HTRA1) was 87.5%. The frequency of the non-risk allele (A) of I62V was 100%. The frequencies of risk alleles of Y402H, R80G, and rs2241394 were 12.5%, 0%, and 18.8%, respectively.

CONCLUSION: Our results suggest that the risk alleles of the ARMS2/HTRA1 SNPs may be associated with development of RAP and play a major role in the pathogenesis of intraretinal angiogenesis.

PMID: 24403817 [PubMed]

Nihon Ganka Gakkai Zasshi. 2013 Nov;117(11):869-77.

[Novel gene transfer using micellar nanovectors inhibits choroidal neovascularization].[Article in Japanese]

Aoki A.

Abstract: The treatment of age-related macular degeneration (AMD) caused by choroidal neovascularization (CNV) is difficult. More effective therapy for regulating CNV is needed. We demonstrated that intravenous nonviral vectors based on the complex of plasmid DNA with synthetic cationic polymers accumulate in choroidal neovascularization (CNV) with high efficiency through an enhanced the permeability and retention (EPR) effect. This review shows the results of in vivo angiogenic control by intravenous injection of a polyplex micelle-encapsulating plasmid vector using a mice CNV model. Polyion complex (PIC) micelles consisting of plasmid DNA and poly (ethylene glycol)-b-poly (N-[N-(2 -aminoethyl)-2-aminoethyl] aspartamidef block copolymers [PEG-b-PAsp (DET)] were used. These show minimal cytotoxicity and high transfection efficiency both in vitro and in vivo, and have been utilized for gene therapy against a mouse corneal neovascularization model by local administration of plasmid-encoding soluble vascular endothelial growth factor receptor 1 (soluble Fms-like tyrosine kinase-1: sFlt-1). Transfection of plasmid-expressing sFlt-1 with PEG-C6-P[Asp (DET)] polyplex micelles by intravenous injection into mice CNV models showed significant inhibition of developing CNV. We found that nonviral gene therapy has significant potential for regulation of CNV using plasmids with PEG-C6-P [Asp (DET)] polyplex micelles.

PMID: 24397183 [PubMed - in process]

Diet & lifestyle

Asia Pac J Clin Nutr. 2000 Sep;9 Suppl 1:S55-9.

Clinicians changing individual food habits.

Wahlqvist ML.

Abstract: There is ample evidence from repeat food surveys that people are actually and passively changing their food habits. Understanding the reasons for this are vital to any efforts by clinicians to enable

individuals to move in an increasing healthful direction with their food intake, and to dispel the pessimism that often prevails about the ability to make a useful contribution to nutritional status by changing food intake. Current success and failure rates are predicated on inadequate methods and inappropriate outcome measures, rather than an inability to achieve outcomes. Factors that allow for or encourage change are food availability, exposure to new food experiences, food memory, pleasure, eating with peers or companions, health interest and changing constructs and beliefs about food. It is possible to change the health impact of food by non-food means like physical activity, stress management, recreational activities, improved relationships, changing the work environment and through adequate sleep (including siesta). Yet another consideration is that the full consequences of food choice are not appreciated with more and more food-health relationships being defined (e.g. with cataract, macular degeneration, in depression and cognitive function). These various approaches require a management strategy that underpins the field of behavioural therapy. In this approach it is possible to make progress through small but consequential changes, like climbing the stairs, or increasing intake of particular foods like fish or drinking more water; and exploring and contracting ways to do these things.

PMID: 24398279 [PubMed]