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Drug treatment

Case Rep Ophthalmol. 2015 Feb 10;6(1):44-50.

Evaluation of the Response to Ranibizumab Therapy following Bevacizumab Treatment Failure in Eyes with Diabetic Macular Edema.

Hanhart J, Chowers I.

BACKGROUND/AIMS: Bevacizumab and ranibizumab are routinely used to treat diabetic macular edema (DME). We aim to evaluate the usefulness of switching to ranibizumab therapy following bevacizumab treatment failure in eyes with DME.

METHODS: We performed a retrospective analysis of a consecutive group of patients with DME who received ranibizumab injections following the failure of bevacizumab injections. The injections were delivered following a pro re nata protocol every 4-6 weeks. The data collected included demographics, systemic and ophthalmic findings, as well as the central subfield thickness according to spectral-domain OCT.

RESULTS: Eight eyes (5 patients) were included in the study. The median number of bevacizumab injections prior to the switch to ranibizumab was 4, and the median number of ranibizumab injections during the study was 2. The mean follow-up period was 541 ± 258 days. The mean central retinal thickness (CRT) ($\pm$ SEM) was 539 ± 75 μ m before the initiation of bevacizumab treatment, and 524 ± 43 μ m after the last bevacizumab injection ($p = 0.7$). It reduced to 325 ± 26 μ m following the ranibizumab injections ($p = 0.0063$). The best-corrected visual acuity (BCVA) improved in 4 eyes and remained stable in 4 eyes following the ranibizumab injections.

CONCLUSION: A ranibizumab therapy was effective in reducing the CRT in eyes that failed bevacizumab therapy. A BCVA improvement can also occur in these eyes. Switching between anti-vascular endothelial growth factor compounds may be beneficial in eyes with DME.

PMID: 25802504 [PubMed] PMCID: PMC4357677

J Ophthalmol. 2015;2015:138070.

Future therapies of wet age-related macular degeneration.

Ishikawa M, Jin D, Sawada Y, Abe S, Yoshitomi T.

Abstract: Age-related macular degeneration (AMD) is the leading cause of blindness in the elderly

population, and the prevalence of the disease increases exponentially with every decade after the age of 50 years. While VEGF inhibitors are promising drugs for treating patients with ocular neovascularization, there are limitations to their potential for improving vision in AMD patients. Thus, future therapies are required to have the potential to improve visual outcomes. This paper will summarize the future strategies and therapeutic targets that are aimed at enhancing the efficacy and duration of effect of antiangiogenic strategies.

PMID: 25802751 [PubMed] PMCID: PMC4354726

Case Rep Ophthalmol. 2015 Feb 10;6(1):51-5.

Peripapillary Choroidal Neovascularization Associated with Optic Nerve Head Drusen Treated with Anti-VEGF Agents.

Saffra NA, Reinherz BJ.

Abstract: Optic nerve head drusen can be associated with peripapillary choroidal neovascularization, in both the pediatric and adult population. These membranes can involve the macula, causing significant visual loss. Herein, we present a case that required treatment with an anti-VEGF agent. The patient failed to respond to the initial agent, but subsequently responded to a change of agent. Adult patients with macular degeneration involving peripapillary choroidal neovascularization associated with optic nerve head drusen may require individualized treatment plans.

PMID: 25802505 [PubMed] PMCID: PMC4357672

Nurs Older People. 2015 Mar 26;27(3):6.

Nurse-led eye clinic opens to meet demand in Wales.

[No authors listed]

THE UNIVERSITY Hospital of Wales is the first in the country to offer a service where nurses give injections into patients' eyes. The three nurses in the eye clinic are carrying out the service to treat patients with age-related macular degeneration, which causes gradual loss of central vision.

PMID: 25809030 [PubMed - in process]

JAMA Ophthalmol. 2015 Mar 26. [Epub ahead of print]

Analyses Comparing Visual Acuity Between Ranibizumab and Bevacizumab in the Comparison of Age-Related Macular Degeneration Treatments Trials.— Comment & response

Ying GS, Maguire MG.

PMID: 25811288 [PubMed - as supplied by publisher]

Acta Ophthalmol. 2015 Mar 23. [Epub ahead of print]

Circulating anti-retinal antibodies in response to anti-angiogenic therapy in exudative age-related macular degeneration-reply.

Achiron A.

PMID: 25809013 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Br J Ophthalmol. 2015 Mar 20. [Epub ahead of print]

Reticular drusen in eyes with high-risk characteristics for progression to late-stage age-related macular degeneration.

Steinberg JS, Göbel AP, Fleckenstein M, Holz FG, Schmitz-Valckenberg S.

BACKGROUND/AIMS: To analyse appearance, development over 2 years and characteristic patterns of reticular drusen (RDR) in eyes with high-risk characteristics for progression to late-stage age-related macular degeneration (AMD) (age-related eye disease study stages 3 and 4).

METHODS: 98 eyes of 98 patients (median age 73.4 years, IQR [69-78]) participating in the Molecular Diagnostic of Age-related Macular Degeneration study were included. Simultaneous combined confocal scanning laser ophthalmoscopy (cSLO) and spectral-domain optical coherence tomography (SD-OCT) imaging as well as colour-fundus imaging was performed at baseline and at 24 months. Two independent graders determined the presence of different RDR phenotypes (cSLO modalities: 'dot', 'target', 'ribbon'; SD-OCT: 'spike' and 'wave') at both visits.

RESULTS: At baseline, RDR were detected in 44% (κ 0.96). They were always visible in near-infrared reflectance images. Detection rate was 42% using fundus autofluorescence (FAF), 39% on SD-OCT (waves: 100%; spikes: 90%) and 26% on blue reflectance (BR). 'Dots' were more frequently detected in all imaging compared with 'targets'. The 'ribbon' pattern was most frequently observed in colour images, BR images and FAF images. In 8 of the 48 eyes with no signs of RDR in any imaging modality at baseline, the development of RDR lesions was observed at 24 months (16.6%, κ 0.42).

CONCLUSIONS: Careful and meticulous analysis using three-dimensional in vivo imaging reveals distinct characteristic RDR patterns underlying detectable dynamic changes over a period of 2 years. RDR in eyes with early or intermediate AMD are a common observation but appear to be overall less common compared with eyes with geographic atrophy.

PMID: 25795913 [PubMed - as supplied by publisher]

Ophthalmology. 2015 Mar 17. [Epub ahead of print]

Spectral-Domain Optical Coherence Tomography Angiography of Choroidal Neovascularization.

de Carlo TE, Bonini Filho MA, Chin AT, Adhi M, Ferrara D, Bauman CR, Witkin AJ, Reichel E, Duker JS, Waheed NK.

PURPOSE: To describe the characteristics as well as the sensitivity and specificity of detection of choroidal neovascularization (CNV) on optical coherence tomography angiography (OCTA) using spectral-domain optical coherence tomography.

DESIGN: Observational, retrospective study.

PARTICIPANTS: Seventy-two eyes of 61 subjects (48 eyes of 43 subjects with CNV, 24 eyes of 18 subjects without CNV).

METHODS: Patients imaged using the prototype AngioVue OCTA system (Optovue, Inc, Fremont, CA) between August 2014 and October 2014 at New England Eye Center were assessed. Patients in whom CNV was identified on OCTA were evaluated to define characteristics of CNV on OCTA: size using greatest linear dimension (small, <1 mm; medium, 1-2 mm; large, >2 mm), appearance (well-circumscribed, poorly circumscribed), and presence of subretinal and intraretinal fluid. Concurrently, an overlapping second cohort of patients who underwent same-day OCTA and fluorescein angiography (FA) for suspected CNV was evaluated to estimate sensitivity and specificity of OCTA in detecting CNV using FA as ground truth.

MAIN OUTCOME MEASURES: Choroidal neovascularization appearance, CNV size, and presence of subretinal and intraretinal fluid.

RESULTS: In 48 eyes, CNV was visualized on OCTA. Thirty-one eyes had CNV associated with neovascular age-related macular degeneration. Size of CNV was small in 23% (7/31), medium in 42% (13/31), and large in 35% (11/31). Poorly circumscribed vessels, subretinal fluid, and intraretinal fluid each were seen in 71% (22/31). Seven eyes had CNV associated with central serous chorioretinopathy. Size of CNV was small in 71% (5/7) and large in 29% (2/7). Seventy-one percent (5/7) had well-circumscribed vessels, 86% (6/7) had subretinal fluid, and 14% (1/7) had intraretinal fluid. Thirty eyes with OCTA and same-day FA were evaluated to determine sensitivity and specificity of CNV detection on OCTA. Sensitivity was 50% (4/8) and specificity was 91% (20/22).

CONCLUSIONS: Using OCTA allows the clinician to visualize CNV noninvasively and may provide a method for identifying and guiding treatment of CNV. The specificity of CNV detection on OCTA compared with FA seems to be high. Future studies with larger sample sizes are needed to elaborate better on the sensitivity and specificity of CNV detection and to illustrate clinical usefulness.

PMID: 25795476 [PubMed - as supplied by publisher]

Curr Eye Res. 2015 Mar 24:1-7.

Comparison of Visual Function in Older Eyes in the Earliest Stages of Age-related Macular Degeneration to Those in Normal Macular Health.

Owsley C, Huisinigh C, Clark ME, Jackson GR, McGwin G Jr.

PURPOSE: To compare the ability of several visual functional tests in terms of the strength of their associations with the earliest phases of age-related macular degeneration (AMD), which bears on their potential to serve as functional endpoints in evaluating treatments for early AMD and prevention strategies.

MATERIALS AND METHODS: Eyes from adults ≥ 60 years old were identified as being in normal macular health or in the earliest stages of AMD (steps 2, 3 or 4) through grading of color stereo-fundus photos by an experienced grader masked to all other study variables who used the 9-step Age-Related Eye Disease Study (AREDS) classification system for AMD severity. Visual function was assessed using the following tests: best-corrected visual acuity, low luminance visual acuity, spatial contrast sensitivity, macular cone-mediated light sensitivity and rod-mediated dark adaptation.

RESULTS: A total of 1260 eyes were tested from 640 participants; 1007 eyes were in normal macular health (defined as step 1 in AREDS system) and 253 eyes had early AMD (defined as steps 2, 3 or 4). Adjusting for age and gender, early AMD eyes had two times the odds of having delayed rod-mediated dark adaptation than eyes in normal macular health ($p = 0.0019$). Visual acuity, low luminance acuity, spatial contrast sensitivity and macular light sensitivity did not differ between normal eyes and early AMD eyes.

CONCLUSIONS: Eyes in the earliest phases of AMD were two times more likely to have delayed rod-mediated dark adaptation, as assessed by the rod-intercept, as compared to older eyes in normal macular health, whereas there was no difference in early AMD versus normal eyes in tests of visual acuity, low luminance acuity, macular light sensitivity and spatial contrast sensitivity.

PMID: 25802989 [PubMed - as supplied by publisher]

JAMA Ophthalmol. 2015 Mar 26. [Epub ahead of print]

Scotopic and Photopic Microperimetry in Patients With Reticular Drusen and Age-Related Macular Degeneration.

Steinberg JS, Fitzke FW, Fimmers R, Fleckenstein M, Holz FG, Schmitz-Valckenberg S.

Importance: Clinical observations suggest that patients with age-related macular degeneration (AMD) have vision problems, particularly in dim light conditions. Previous studies on structural-functional analysis in patients with AMD with reticular drusen (RDR) have focused on photopic sensitivity testing but have not specifically assessed scotopic function.

Objective: To evaluate retinal function by scotopic and photopic microperimetry in patients with AMD and a well-demarcated area of RDR.

Design, Setting, and Participants: Prospective case series in a referral center of 22 eyes from 18 patients (mean age, 74.7 years; range, 62-87 years). The study was conducted from June 1, 2014, to October 31, 2014.

Interventions: With the use of combined confocal scanning laser ophthalmoscopy and spectral-domain optical coherence tomography imaging, retinal areas with RDR (category 1) and no visible pathologic alterations (category 2) were identified in each eye. Scotopic and photopic microperimetry (MP-1S; Nidek Technologies) was performed using a grid with 56 stimulus points.

Main Outcomes and Measures: Comparison of mean threshold sensitivities for each category for scotopic and photopic microperimetry.

Results: In all eyes, areas of category 1 showed a relative and sharply demarcated reduction of scotopic threshold values compared with areas of category 2, but only less-pronounced differences were seen for photopic testing. Statistical analysis in the 18 eyes in which the 1.0-log unit neutral density filter was applied revealed a difference of scotopic threshold values in areas of category 1 (mean, 13.5 dB [95% CI, 12.1-15.0]) vs category 2 (mean, 18.3 dB; [95% CI, 17.4-19.3] ($P \leq .001$)). For photopic testing, the mean threshold values were 16.8 dB (95% CI, 15.5-18.2) in category 1 and 18.4 dB (95% CI, 17.1-19.6) in category 2 ($P = .03$).

Conclusions and Relevance: The results of this study suggest that rod function is more severely affected than cone function in retinal areas with RDR. This differential structural-functional correlation underscores the functional relevance of RDR in patients with AMD.

PMID: 25811917 [PubMed - as supplied by publisher]

Stem Cells. 2015 Mar 24. [Epub ahead of print]

Making Stem Cells Retinal: Methods for Deriving Retinal Pigment Epithelium and Implications for Patients with Ocular Disease.

Leach LL, Clegg DO.

Abstract: Stem cells provide a potentially unlimited source of cells for treating a plethora of human diseases. Regenerative therapies for retinal degenerative diseases are at the forefront of translation to the clinic, with stem cell-derived retinal pigment epithelium (RPE)-based treatments for age-related macular degeneration (AMD) already showing promise in human patients. Despite our expanding knowledge of stem cell biology, methods for deriving cells, including RPE have remained inefficient. Thus, there has been a push in recent years to develop more directed approaches to deriving cells for therapy. In this concise review, we summarize recent efforts that have been successful in improving RPE derivation efficiency by directing differentiation from human pluripotent stem cells using developmental cues important for normal RPE specification and maturation in vivo. In addition, potential obstacles for clinical translation are discussed. Finally, we review how derivation of RPE from human induced pluripotent stem cells (hiPSCs) provides in vitro models for studying mechanisms of retinal disease and discovering new avenues for treatment. This article is protected by copyright. All rights reserved.

PMID: 25809736 [PubMed - as supplied by publisher]

Pathogenesis

J Biol Chem. 2015 Mar 23.

Iron-induced Local Complement Component 3 (C3) Up-regulation via Non-Canonical TGF- β Signaling in the Retinal Pigment Epithelium.

Li Y, Song D, Song Y, Zhao L, Wolkow N, Tobias JW, Song W, Dunaief JL.

Abstract: Dysregulation of iron homeostasis may be a pathogenic factor in age-related macular degeneration (AMD). Meanwhile, the formation of complement-containing deposits under the retinal pigment epithelial (RPE) cell layer is a pathognomonic feature of AMD. In this study, we investigated the molecular mechanisms by which C3, a central protein in the complement cascade, is up-regulated by iron in RPE cells. Modulation of TGF- β signaling, involving ERK1/2, SMAD3, and CCAAT/enhancer-binding protein- δ (C/EBP- δ), is responsible for iron-induced C3 expression. The differential effects of spatially distinct SMAD3 phosphorylation sites at the linker region and at the C-terminus determined the up-regulation of C3. Pharmacologic inhibition of either ERK1/2 or SMAD3 phosphorylation decreased iron-induced C3 expression levels. Knockdown of SMAD3 blocked the iron-induced up-regulation and nuclear accumulation of C/EBP- δ , a transcription factor that has been shown previously to bind the basic Leucine Zipper 1 (bZIP1) domain in the C3 promoter. We show herein that mutation of this domain reduced iron-induced C3 promoter activity. In vivo studies support our in vitro finding of iron-induced C3 up-regulation. Mice with a mosaic pattern of RPE-specific iron overload demonstrated co-localization of iron-induced ferritin and C3d deposits. Humans with aceruloplasminemia causing RPE iron overload had increased RPE C3d deposition. The molecular events in the iron-C3 pathway represent therapeutic targets for AMD or other diseases exacerbated by iron-induced local complement dysregulation.

PMID: 25802332 [PubMed - as supplied by publisher]

Mol Cell Biol. 2015 Mar 23.

Gossypol Acetic Acid prevents oxidative stress-induced RPE necrosis by regulating FoxO3/SESTRIN2 pathway.

Hanus J, Zhang H, Chen DH, Zhou Q, Jin P, Liu Q, Wang S.

Abstract: The late stage of dry Age-related macular degeneration (AMD), or geographic atrophy (GA), is characterized by extensive retinal pigment epithelial (RPE) cell death and the cure is not available currently. We have recently demonstrated that RPE cells die from necrosis in response to oxidative stress, providing a potential novel mechanism for RPE death in AMD. In this study, we screened FDA-approved natural compounds and identified Gossypol Acetic Acid (GAA) as a potent inhibitor of oxidative stress-induced RPE cell death. GAA induces anti-oxidative response and inhibits accumulation of excessive reactive oxygen species (ROS) in cells, through which it prevents the activation of intrinsic necrotic pathway in response to oxidative stress. Sestrin2 (SESN2) gene is found to be sufficient and necessary for mediating GAA function in anti-oxidative response and RPE survival upon oxidative stress. Moreover, FoxO3 is further found to be required for GAA mediated SESN2 expression and RPE survival. Mechanistically, GAA promotes FoxO3 nuclear translocation and binding to the SESN2 enhancer, which in turn increases its transcriptional activity. Taken together, we have identified GAA as a potent inhibitor of oxidative stress-induced RPE necrosis by regulating FoxO3/SESN2 pathway. This study may have significant implication in the therapeutics of age-related diseases, especially GA.

PMID: 25802279 [PubMed - as supplied by publisher]

PLoS One. 2015 Mar 25;10(3):e0120587.

Attenuation of choroidal neovascularization by histone deacetylase inhibitor.

Chan N, He S, Spee CK, Ishikawa K, Hinton DR.

Abstract: Choroidal neovascularization (CNV) is a blinding complication of age-related macular degeneration that manifests as the growth of immature choroidal blood vessels through Bruch's membrane, where they can leak fluid or hemorrhage under the retina. Here, we demonstrate that the histone deacetylase inhibitor (HDACi) trichostatin A (TSA) can down-regulate the pro-angiogenic hypoxia-inducible factor-1 α and vascular endothelial growth factor (VEGF), and up-regulate the anti-angiogenic and neuro-protective pigment epithelium derived factor in human retinal pigment epithelial (RPE) cells. Most strikingly, TSA markedly down-regulates the expression of VEGF receptor-2 in human vascular endothelial cells and, thus, can knock down pro-angiogenic cell signaling. Additionally, TSA suppresses CNV-associated wound healing response and RPE epithelial-mesenchymal transdifferentiation. In the laser-induced model of CNV using C57Bl/6 mice, systemic administration of TSA significantly reduces fluorescein leakage and the size of CNV lesions at post-laser days 7 and 14 as well as the immunohistochemical expression of VEGF, VEGFR2, and smooth muscle actin in CNV lesions at post-laser day 7. This report suggests that TSA, and possibly HDACi's in general, should be further evaluated for their therapeutic potential for the treatment of CNV.

PMID: 25807249 [PubMed - in process]

Mol Immunol. 2015 Mar 21. [Epub ahead of print]

Age-related macular degeneration and the role of the complement system.

McHarg S, Clark SJ, Day AJ, Bishop PN.

Abstract: Age-related macular degeneration (AMD) is a leading cause of visual impairment. It is characterised by damage to a tissue complex composed of the retinal pigment epithelium, Bruch's membrane and choriocapillaris. In early AMD extracellular debris including drusen accumulates in Bruch's membrane and then in late AMD geographic atrophy and/or neovascularisation develop. Variants in genes encoding components of the alternative pathway of the complement cascade have a major influence on AMD risk, especially at the RCA locus on chromosome 1, which contains CFH and the CFHR genes. Immunohistochemical studies have demonstrated complement components in unaffected and AMD macular tissue. Whilst other factors, including oxidative stress, play important roles in AMD pathogenesis, evidence for the central role played by complement dysregulation is discussed in this review.

PMID: 25804937 [PubMed - as supplied by publisher]

PLoS One. 2015 Mar 24;10(3):e0121185.

IKK2 Inhibition Using TPCA-1-Loaded PLGA Microparticles Attenuates Laser-Induced Choroidal Neovascularization and Macrophage Recruitment.

Gaddipati S, Lu Q, Kasetti RB, Miller MC, Lu Q, Trent JO, Kaplan HJ, Li Q.

Abstract: The inhibition of NF- κ B by genetic deletion or pharmacological inhibition of IKK2 significantly reduces laser-induced choroid neovascularization (CNV). To achieve a sustained and controlled intraocular release of a selective and potent IKK2 inhibitor, 2-[(aminocarbonyl)amino]-5-(4-fluorophenyl)-3-thiophenecarboxamide (TPCA-1) (MW: 279.29), we developed a biodegradable poly-lactide-co-glycolide (PLGA) polymer-delivery system to further investigate the anti-neovascularization effects of IKK2 inhibition and in vivo biosafety using laser-induced CNV mouse model. The solvent-evaporation method produced spherical TPCA-1-loaded PLGA microparticles characterized with a mean diameter of 2.4 μ m and loading efficiency of 80%. Retrobulbar administration of the TPCA-1-loaded PLGA microparticles maintained a sustained drug level in the retina during the study period. No detectable TPCA-1 level was observed in the untreated contralateral eye. The anti-CNV effect of retrobulbar administrated TPCA-1-loaded PLGA microparticles was assessed by retinal fluorescein leakage and isolectin staining methods, showing

significantly reduced CNV development on day 7 after laser injury. Macrophage infiltration into the laser lesion was attenuated as assayed by choroid/RPE flat-mount staining with anti-F4/80 antibody. Consistently, laser induced expressions of Vegfa and Ccl2 were inhibited by the TPCA-1-loaded PLGA treatment. This TPCA-1 delivery system did not cause any noticeable cellular or functional toxicity to the treated eyes as evaluated by histology and optokinetic reflex (OKR) tests; and no systemic toxicity was observed. We conclude that retrobulbar injection of the small-molecule IKK2 inhibitor TPCA-1, delivered by biodegradable PLGA microparticles, can achieve a sustained and controllable drug release into choroid/retina and attenuate laser-induced CNV development without causing apparent systemic toxicity. Our results suggest a potential clinical application of TPCA-1 delivered by microparticles in treatment of CNV in the patients with age-related macular degeneration and other retinal neovascularization diseases.

PMID: 25803615 [PubMed - in process]

Epidemiology

Sci Rep. 2015 Mar 24;5:9424.

Ethnic differences in the association of SERPING1 with age-related macular degeneration and polypoidal choroidal vasculopathy.

Liu K, Lai TY, Ma L, Lai FH, Young AL, Brelén ME, Tam PO, Pang CP, Chen LJ.

Abstract: Neovascular age-related macular degeneration (AMD) and polypoidal choroidal vasculopathy (PCV) are leading causes of irreversible blindness in developed countries. In this study, we investigated the association of single nucleotide polymorphisms (SNPs) in the serpin peptidase inhibitor, clade G, member 1 (SERPING1) gene with neovascular AMD and PCV. Two haplotype-tagging SNPs, rs1005510 and rs11603020, of SERPING1 were genotyped in 708 unrelated Chinese individuals: 200 neovascular AMD, 233 PCV and 275 controls. A meta-analysis was also performed for all reported associations of SERPING1 SNPs with AMD and PCV. None of the tagging SNPs had a significant association with neovascular AMD or PCV ($P > 0.05$) in our study cohort. The meta-analyses showed that the most-studied SNP rs2511989 was not significantly associated with all forms of AMD, neovascular AMD, or PCV in East Asians ($P = 0.98$, 0.93 and 0.30 , respectively) but was associated with AMD in Caucasians ($P = 0.04$ for all AMD and 0.004 for neovascular AMD). Therefore, the results of our study and meta-analysis suggest that SERPING1 is not a major genetic component of AMD or PCV in East Asians but is a genetic risk factor for AMD in Caucasians, providing evidence for an ethnic diversity in the genetic etiology of AMD.

PMID: 25800435 [PubMed - in process]

Genetics

Klin Monbl Augenheilkd. 2015 Mar;232(3):266-74.

[Genotype-Phenotype Correlation in Patients with PRPH2-Mutations].[Article in German]

Maertz J, Gloeckle N, Nentwich MM, Rudolph G.

BACKGROUND: The peripherin-2 (PRPH2) gene encodes a photoreceptor-specific transmembrane-protein called peripherin-2 which is critical for the formation and maintenance of rod and cone outer segments. Over 90 different disease-causing mutations in PRPH2 have been identified which cause a variety of forms of macular degeneration and also retinopathia pigmentosa.

PATIENTS/MATERIAL AND METHODS: This study is a retrospective observational study of 3 patients ascertained over a 5 month period in the ophthalmogenetic consultation of the university ophthalmic clinic. So far, the patients were followed for 8 months at least. Data examined included clinical history, pedigree analysis, ophthalmological examination, fundus photography, autofluorescence imaging, optical coherence

tomography, Arden colour test, Goldmann perimetry and detailed electrophysiological assessment. Blood samples were taken for DNA extraction and mutation analysis of PRPH2 and ABCA4, BEST1, C1QTNF5, CDH3, CNGB3, ELOVL4, FSCN2, PROM1, RDH12, RP1L1, RPGR, TIMP3 was performed.

RESULTS: All patients had presented with clinically evident maculopathy and visual acuities in the range of 1/50 Metervisus to 0.8 p [dec.]. All had specific electroretinogrammes. All PRPH2 mutations were autosomal dominant. One family was heterozygous for a previously reported missense mutation in the PRPH2 gene c.514C>T, p.R172W. The other patient was heterozygous for a so far non-described PRPH2 deletion and frameshift mutation c.74_77delGGTT, p.W25SfsX12 leading most likely to a truncated, dysfunctional protein. All patients showed a significant, inter-individual phenotypical variability.

CONCLUSION: The data add to the documented phenotypical variability of PRPH2 mutations and describe the c.74_77delGGTT, p.W25SfsX12 mutation within PRPH2 for the first time. FAF, OCT and electrophysiological exams are helpful tools for diagnosis and evaluation of macular disease due to PRPH2 mutations.

PMID: 25803555 [PubMed - in process]

Clin Chem Lab Med. 2015 Mar 26. [Epub ahead of print]

Novel association of FCGR2A polymorphism with age-related macular degeneration (AMD) and development of a novel CFH real-time genotyping method.

Velissari A, Skalidakis I, Oliveira SC, Koutsandrea C, Kitsos G, Petersen MB, Kroupis C.

BACKGROUND: Age-related macular degeneration (AMD) is a degenerative ocular disease, which may lead to loss of central vision. In Caucasian populations, a strong correlation has been established with polymorphism Y402H (rs1061170) in the complement factor H gene (CFH). The H131R polymorphism (rs1801274) in the FCGR2A gene has been associated with many inflammatory diseases, but has not been investigated in relation to AMD. The goal of our study was the development of a novel method for Y402H (g.43097C>T) genotyping, the confirmation of its association with AMD in the Greek population and the investigation of the H131R polymorphism in AMD.

METHODS: DNAs were extracted from blood samples of 120 patients with the severe wet form of AMD and 103 age- and sex-matched controls, all of whom were clinically evaluated. A real-time PCR and melting curve analysis method for Y402H genotyping was developed in the LightCycler platform, after in silico design of appropriate primers and probes. Genotyping for H131R was performed using a real-time PCR method previously described by our group.

RESULTS: The novel genotyping method for Y402H in the CFH gene is fast, reproducible (Efficiency=1.79, reproducibility CVCq=3.33%, Tm C allele 53.36 °C and T allele 61.91 °C, ΔTm=8.55) and accurate as results were confirmed with the gold standard DNA Sequencing method.

CONCLUSIONS: The present study confirmed the association between CFH Y402H SNP and wet AMD in the Greek population (OR=1.77, p=0.002). FCGR2A H131R polymorphism was investigated for the first time in this present study for possible correlation with wet AMD and a statistically significant association was detected (OR=1.74, p=0.006), that awaits further confirmation in a larger set of samples.

PMID: 25811666 [PubMed - as supplied by publisher]

Low vision, nutrition & lifestyle

Biomed Opt Express. 2015 Feb 25;6(3):1010-20.

An aspheric intraocular telescope for age-related macular degeneration patients.

Tabernero J, Qureshi MA, Robbie SJ, Artal P.

Abstract: We have designed an intraocular telescope for the posterior chamber of the human eye of patients with age related macular degeneration. The basic design is composed of two decentered high optical power lenses (+ 66D and -66D) inducing a 3° prismatic effect to project a magnified central field of view into a healthier location off the central fovea. Aspheric surfaces were used to ensure a compromise between good optical quality and high tolerance to the final axial position of both lenses after surgery. With this particular design, the telescope affords an extended range of depth of focus, high tolerance to different axial lengths of the eye and robustness against typical values of astigmatism and higher order aberrations. The final design has been manufactured in a foldable material and is compact enough to facilitate surgical implantation. This telescope is a simple but promising intraocular visual aid for AMD patients.

PMID: 25798322 [PubMed] PMCID: PMC4361417

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