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MD Research News

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Drug treatment

Br J Ophthalmol. 2011 Dec 15. [Epub ahead of print]

Long-term outcome of subretinal coapplication of rtPA and bevacizumab followed by repeated intravitreal anti-VEGF injections for neovascular AMD with submacular haemorrhage.

Treumer F, Roider J, Hillenkamp J.

University Medical Center Schleswig-Holstein, Kiel, Germany.

Aim: To evaluate short-term and long-term outcomes of subretinal coapplication of recombinant tissue plasminogen activator (rtPA) and bevacizumab followed by intravitreal injections of bevacizumab or ranibizumab for neovascular age-related macular degeneration with submacular haemorrhage (SMH).

Methods: Retrospective, consecutive, interventional case series of 41 eyes of 40 patients. All patients underwent pars plana vitrectomy with subretinal coapplication of rtPA and bevacizumab and intravitreal gas tamponade. Postoperatively, repeated intravitreal injections of bevacizumab or ranibizumab were applied following a flexible, predominantly visual acuity-driven re-treatment regimen.

Results: Mean diameter of SMH was 4.5 disc diameters (range 1.5-12). Complete displacement of SMH was achieved in 35 of 41 eyes. Large and prominent SMH extending beyond the vascular arcades were completely displaced in six of eight eyes. SMH recurred in eight eyes after a mean of 9.1 months (2-19). A mean of 4.5 (2-9) intravitreal anti-vascular endothelial growth factor injections were applied during 12 months postoperatively. Short-term (3 months, n=41), mean best corrected logMAR visual acuity (BCVA) improved significantly from the preoperative value 1.7 (3.0-0.5) to 0.8 (1.6-0.2). 12 eyes had reading ability (≤logMAR 0.4) and 29 eyes had gained ambulatory visual acuity (≤logMAR 1.6). Long-term (mean 17 months (12-32), n=26) BCVA was 0.9 (1.6-0.1). Compared with short-term, BCVA had decreased in 12 of 26 eyes.

Conclusion: The operation effectively displaces small and large SMHs. In the long-term, a predominantly visual acuity-driven re-treatment regimen puts the initial functional improvement at risk. More sensitive re-treatment parameters may help to improve long-term functional outcome.

PMID:22174095 [PubMed - as supplied by publisher]

Eye (Lond). 2011 Dec 16. doi: 10.1038/eye.2011.324. [Epub ahead of print]

Intravitreal bevacizumab and ranibizumab injections for patients with polypoidal choroidal

vasculopathy.

Cho HJ, Kim JW, Lee DW, Cho SW, Kim CG.

Department of Ophthalmology, Kim's Eye Hospital, Konyang University College of Medicine, Seoul, Korea.

Purpose: To compare the effectiveness of intravitreal injection of bevacizumab and ranibizumab in patients with treatment-naïve polypoidal choroidal vasculopathy (PCV).

Methods: A total of 66 and 60 eyes of 121 consecutive patients who received intravitreal bevacizumab (1.25 mg) or ranibizumab (0.5 mg) injection for treatment of PCV were retrospectively reviewed. After initial three loading injections by month, injection was performed as needed. Main outcome measures included best corrected visual acuity (BCVA), foveal center thickness (FCT) as assessed by spectral domain optical coherence tomography (SD-OCT), and change in polypoidal lesion on indocyanine green angiography (ICGA).

Results: At 12 months, average number of injections was 4.72±1.84 in the bevacizumab group and 5.52±1.54 in the ranibizumab group. Mean logarithm of the minimum angle of resolution of BCVA from baseline at 12 months after injection improved by 0.11 in the bevacizumab group (P=0.02) and by 0.14 in the ranibizumab group (P=0.01). Average FCT decreased from 368±62.48 to 298±40.77 μm in the bevacizumab group (P=0.01) and from 371±50.79 to 286±36.93 μm in the ranibizumab group (P=0.01). Polyp regression rate was 24.2% (16 eyes out of 66 eyes) in the bevacizumab group and 23.3% (14 eyes out of 60 eyes) in the ranibizumab group. There was no statistically significant difference in BCVA improvement achieved, FCT improvement achieved, and polyp regression rate between groups.

Conclusion: Intravitreal injections of bevacizumab and ranibizumab have similar effects in stabilization of visual acuity, macular edema, and regression of polypoidal complex with PCV eyes.

Eye advance online publication, 16 December 2011; doi:10.1038/eye.2011.324.

PMID:22173075 [PubMed - as supplied by publisher]

Eye (Lond). 2011 Dec 16. doi: 10.1038/eye.2011.326. [Epub ahead of print]

Environmental Amsler test as a monitoring tool for retreatment with ranibizumab for neovascular age-related macular degeneration.

Mathew R, Sivaprasad S.

Laser and Retinal Research Unit, Department of Ophthalmology, King's College Hospital, London, UK.

Purpose: To assess the ability of patients to predict the need for retreatment with intravitreal ranibizumab in neovascular age-related macular degeneration (NVAMD) based on their perception of visual deterioration or distortion of objects in their everyday environment (environmental Amsler).

Methods: A questionnaire was given to 89 patients undergoing optical coherence tomography (OCT)-guided retreatment with intravitreal ranibizumab for NVAMD following an initial loading regimen of three injections and with at least 12-month follow-up. The patient's opinion on the need for an injection on the current visit, based on their perception of change in environmental Amsler, was recorded. This subjective measure was compared with the objective evaluation of retreatment, based on predefined retreatment criteria comprising of changes in visual acuity and morphological changes on OCT. The patients were then instructed on the technique of environmental Amsler, and this evaluation was repeated. The sensitivity and specificity of patient prediction were analyzed at baseline and after the training.

Results: The ability of patients to predict disease activity at baseline showed a sensitivity of 61% and specificity of 96.6%. The area under the receiver operating characteristic curve was 0.8. The presence of macular fluid correlated well with the patient's perception of an abnormal environmental Amsler. After

training, the sensitivity and specificity improved to 87.5% and 98.5%, respectively.

Conclusion: In real life, most patients are able to predict the reactivation of the disease in NVAMD, after 12-month follow-up, after training to monitor their symptoms using the environmental Amsler test.Eye advance online publication, 16 December 2011; doi:10.1038/eye.2011.326.

PMID:22173073 [PubMed - as supplied by publisher]

J Ophthalmol. 2012;2012:319728. Epub 2011 Nov 19.

Antivascular endothelial growth factor agents for neovascular age-related macular degeneration.

Zampros I, Praidou A, Brazitikos P, Ekonomidis P, Androudi S.

Department of Ophthalmology, Aristotle University, 54124 Thessaloniki, Greece.

Abstract

Age-related macular degeneration (AMD) is the leading cause of severe visual loss and blindness over the age of 50 in developed countries. Vascular endothelial growth factor (VEGF) is considered as a critical molecule in the pathogenesis of choroidal neovascularization (CNV), which characterizes the neovascular AMD. Anti-VEGF agents are considered the most promising way of effectively inhibition of the neovascular AMD process. VEGF is a heparin-binding glycoprotein with potent angiogenic, mitogenic and vascular permeability-enhancing activities specific for endothelial cells. Two anti-VEGF agents have been approved by the US Food and Drug Administration (FDA) for the treatment of neovascular AMD. Pegaptanib sodium, which is an aptamer and ranibizumab, which is a monoclonal antibody fragment. Another humanized monoclonal antibody is currently off-label used, bevacizumab. This paper aims to discuss in details the effectiveness, the efficacy and safety of these three anti-VEGF agents. New anti-VEGF compounds which are recently investigated for their clinical usage (VEGF-trap, small interfering RNA) are also discussed for their promising outcomes.

PMID:22174998[PubMed - in process]

J Ophthalmol. 2012;2012:154659. Epub 2011 Dec 7.

One-year results of photodynamic therapy combined with intravitreal ranibizumab for exudative age -related macular degeneration.

Nakamura T, Miyakoshi A, Fujita K, Yunoki T, Mitarai K, Yanagisawa S, Fuchizawa C, Hayashi A.

Department of Ophthalmology, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, 2630 Sugitani, Toyama 930-0194, Japan.

Purpose. To evaluate the effects of photodynamic therapy (PDT) combined with intravitreal injection of ranibizumab (IVR) for exudative age-related macular degeneration (AMD).

Methods. Retrospective case series. Thirty eight eyes of 38 patients with exudative AMD underwent combined therapy consisting first of IVR, followed by PDT within a week and the second IVR at 1 month. All patients were followed up for more than 12 months. The best corrected visual acuity (BCVA) and central macular thickness (CMT) were examined.

Results. The mean number of IVR and PDT sessions were 2.9 ± 1.3 and 1.1 ± 0.3, respectively. The mean BCVA and CMT were significantly improved to 0.38 logMAR units ($P < 0.01$) and 240 μm ($P < 0.01$) at 12 months, respectively. Thirty-six of 38 eyes (94.8%) improved or maintained BCVA at 12 months.

Conclusion. PDT combined with IVR for exudative AMD was effective at improving visual acuity and CMT with a low recurrence rate for 12 months.

PMID:22174997 [PubMed - in process]

J Ophthalmol. 2011;2011:752543. Epub 2011 Nov 22.

Management of neovascular age-related macular degeneration in clinical practice: initiation, maintenance, and discontinuation of therapy.

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NIHR Biomedical Research Centre for Ophthalmology, Moorfields Eye Hospital NHS Foundation Trust, City Road, London EC1V 2PD, UK.

Abstract

Neovascular age-related macular degeneration (AMD) is a leading cause of irreversible visual loss in elderly populations. In recent years, pharmacological inhibition of vascular endothelial growth factor (VEGF), via intravitreal injection of ranibizumab (Lucentis) or bevacizumab (Avastin), has offered the first opportunity to improve visual outcomes in patients diagnosed with this disorder. In this paper, we provide recommendations on how bevacizumab and ranibizumab may be best applied in current clinical practice, with an emphasis on their underlying pharmacology and efficacy. In addition, we review current guidelines for the initiation, maintenance, and discontinuation of anti-VEGF therapies, as well as emerging treatment strategies and future directions in the field.

PMID:22174995 [PubMed - in process]

J Ophthalmol. 2011;2011:405724. Epub 2011 Nov 28.

One-year outcomes using ranibizumab for neovascular age-related macular degeneration: results of a prospective and retrospective observational multicentre study.

Hjelmqvist L, Lindberg C, Kanulf P, Dahlgren H, Johansson I, Siewert A.

St. Erik's Eye Hospital, Karolinska Institutet, Polhemsgatan 50, 11282 Stockholm, Sweden.

Abstract

The Swedish Lucentis Quality Registry is a 12-month, open-label, observational, prospective, and retrospective study of ranibizumab administration for wet AMD. Visual acuity (VA) was measured with Snellen or ETDRS chart in 370 patients (66.8% women; age range 46-93 years). In total, a mean of 4.7 ± 1.6 injections per patient (range 1-10) was given to month 12. Mean VA score was 58.3 ± 12.2 letters before treatment, 63.3 ± 12.5 after 3 injections (Δ4.9 ± 10.1 letters from baseline), and 59.3 ± 16.2 at 12 months (Δ1.0 ± 13.6). VA score from baseline to month 12 was stable in 74.4% of patients, improved by 15 letters/3 lines or more in 14.7%, and decreased by ≥15 letters/3 lines in 10.9% of patients. With a mean of 4.7 ranibizumab injections per patient per year, mean VA was stabilised but not increased. To maintain the initial gain seen after the first three injections, an average of 1.8 ± 1.5 additional injections does not appear to be adequate.

PMID:22174994 [PubMed - in process]

J Ophthalmol. 2012;2012:861384. Epub 2011 Nov 29.

Bevacizumab injection in patients with age-related macular degeneration associated with poor initial visual acuity.

El Matri L, Bouraoui R, Chebil A, Kort F, Bouladi M, Limaiem R, Landoulsi H.

Department B of Ophthalmology, Hedi Rais Institute of Ophthalmology, Boulevard 9 Avril, Bab Saadoun Tunis 1006, Tunisia.

Purpose: To evaluate functional and anatomic effects of intravitreal bevacizumab in patients with neovascular AMD and initial low visual acuity.

Methods: Retrospective case series of 38 eyes with neovascular AMD and initial visual acuity of 20/200 or less, treated with intravitreal bevacizumab injection.

Results: Mean followup was 14.1 months ± 7.1 (range: 5 to 24 months). Mean logMAR vision at baseline was 1.38 logMAR ± 0.33, at 6 months was 1.14 logMAR ± 0.37 (P = 0.001) and at 12 months was 1.22 logMar ± 0.33 (P = 0.004). Mean baseline central retinal thickness was 431 µm ± 159.7 at 6 months was 293.43 µm ± 122.79 (P = 10(-4)) and at 12 months was 293.1 µm ± 130 (P = 0.004). Visual acuity improved in both patients with or without prior PDT treatment.

Conclusions: Intravitreal bevacizumab injection may increase the chance of visual acuity gain in neovascular AMD even in cases with initial low visual acuity.

PMID:22174999[PubMed - in process]

Clin Ophthalmol. 2011;5:1659-62. Epub 2011 Nov 24.

Acute anterior uveitis following intravitreal bevacizumab but not subsequent ranibizumab.

Antonopoulos C, Stem M, Comer GM.

Department of Ophthalmology, Boston University, Boston, MA, USA.

PURPOSE: Previous reports have identified noninfectious uveitis as a potential sequela following both intravitreal bevacizumab and ranibizumab injections. We present two unique cases of acute anterior uveitis following intravitreal bevacizumab that did not occur with subsequent ranibizumab injections.

METHODS: Case report.

CONCLUSION: These cases may reflect differences in the etiology of anterior uveitis following intravitreal bevacizumab and ranibizumab. Given these differences, it may be reasonable to offer ranibizumab to patients who have experienced presumed bevacizumab-induced anterior uveitis.

PMID:22174573 [PubMed - in process]

Can J Ophthalmol. 2011 Dec;46(6):486-90.

Recurrence of macular edema in retinal vein occlusions after treatment with intravitreal ranibizumab (Lucentis).

Karagiannis DA, Karampelas MD, Soumplis VM, Amariotakis C, Georgalas I, Kandarakis A.

Ophthalmiatrion Eye Hospital of Athens, Athens, Greece.

OBJECTIVE: To evaluate the recurrence of macular edema (ME) in a mixed group of patients with branch (BRVO) and central (CRVO) retinal vein occlusion after early onset treatment with intravitreal injections of ranibizumab.

DESIGN: Nonrandomized, uncontrolled prospective clinical trial.

PARTICIPANTS: Forty patients were enrolled in our study. Twenty-two patients had BRVO and 18 patients had CRVO.

METHODS: All patients had a minimum follow-up of 12 months. All patients had fundus fluorescein angiography (FFA) and optical coherence tomography (OCT) at presentation. The time period between RVO occurrences and initial examination and treatment was <1 month. Every patient was treated with 2 consecutive intravitreal injections of ranibizumab (0.5 mg) 1 month apart. Assessment was carried out on a monthly basis and injection was carried out if necessary, based on OCT findings.

RESULTS: Recurrence of ME occurred in 13 patients (13/22, 59%) in the BRVO group, whereas in the CRVO group occurred in all patients (18/18, 100%). Mean time interval of these recurrences from last injection was 2.4 months and 1.2 months for BRVO and CRVO groups, respectively. Mean period of ME reabsorption was 2.5 months for the BRVO group and 3.5 months for the CRVO group.

CONCLUSIONS: Recurrent ME occurred in 77.5% of our patients. These recurrences occurred sooner, were more prominent and lasted longer in patients with CRVO.

PMID:22153634 [PubMed - in process]

N Engl J Med. 2011 Dec 8;365(23):2237; author reply 2237.

Ranibizumab and bevacizumab for AMD.

Cheung CM, Wong TY.

Comment on

N Engl J Med. 2011 May 19;364(20):1897-908.

PMID:22150050[PubMed - in process] Related citations

Diagnosis and other treatment

J Vis Exp. 2011 Dec 4;(58). pii: 3176. doi: 10.3791/3176.

Multifocal electroretinograms.

Creel DJ.

John A. Moran Eye Center, University of Utah.

Abstract

A limitation of traditional full-field electroretinograms (ERG) for the diagnosis of retinopathy is lack of sensitivity. Generally, ERG results are normal unless more than approximately 20% of the retina is affected. In practical terms, a patient might be legally blind as a result of macular degeneration or other scotomas and still appear normal, according to traditional full field ERG. An important development in ERGs is the multifocal ERG (mfERG). Erich Sutter adapted the mathematical sequences called binary m-sequences enabling the isolation from a single electrical signal an electroretinogram representing less than each square millimeter of retina in response to a visual stimulus(1). Results that are generated by mfERG appear similar to those generated by flash ERG. In contrast to flash ERG, which best generates data appropriate for whole-eye disorders. The basic mfERG result is based on the calculated mathematical average of an approximation of the positive deflection component of traditional ERG response, known as the b-wave(1). Multifocal ERG programs measure electrical activity from more than a hundred retinal areas per eye, in a few minutes. The enhanced spatial resolution enables scotomas and retinal dysfunction to be mapped and quantified. In the protocol below, we describe the recording of mfERGs using a bipolar speculum contact lens. Components of mfERG systems vary between manufacturers. For the presentation of visible stimulus, some suitable CRT monitors are available but most systems have adopted the use of flat-panel liquid

crystal displays (LCD). The visual stimuli depicted here, were produced by a LCD microdisplay subtending 35 - 40 degrees horizontally and 30 - 35 degrees vertically of visual field, and calibrated to produce multifocal flash intensities of 2.7 cd s m(-2). Amplification was 50K. Lower and upper bandpass limits were 10 and 300 Hz. The software packages used were VERIS versions 5 and 6.

PMID:22158462 [PubMed - in process]

Invest Ophthalmol Vis Sci. 2011 Dec 9. [Epub ahead of print]

Multifocal Pupillography identifies Ranibizumab induced changes in retinal function for Exudative Age-related Macular Degeneration.

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

ARC Centre of Excellence in Vision Science and Centre for Visual Sciences, Research School of Biology, The Australian National University, Canberra, ACT, Australia.

Purpose: To investigate the efficacy of multifocal pupillographic objective perimetry (mfPOP) to quantify the effects of intravitreal ranibizumab injection for choroidal neovascularization (CNV) secondary to exudative Age-related macular degeneration (AMD).

Methods: MfPOP visual fields from 20 patients with unilateral exudative AMD treated with intravitreal ranibizumab were measured pre-treatment, and following 3 months treatment, and compared with 30 normal subjects. Two stimulus types consisting of ensembles of 24 or 44 independent stimuli per eye had a mean presentation interval at each region of 1 second. Pupil responses were recorded with video cameras under infrared illumination. Multiple linear models were fitted to contraction amplitudes and delay to peak responses to determine the independent effects of exudative AMD before and after ranibizumab therapy.

Results: After 3 months treatment mean additional response delays compared to normal subjects for the 24 region stimulus improved significantly ($p < 5x10(-9)$) from a mean of 18.82 ± 3.0 ms at baseline to 7.45 ± 3.15 ms. The mean effect of exudative AMD at baseline decreased constriction amplitude by -1.11 ± 0.24 dB ($p < .00001$) with little improvement following ranibizumab therapy. Small pre-treatment elevations of extra-foveal sensitivity were correlated with improvements in central retinal thickness (CRT) post-treatment ($p<.0005$).

Conclusions: Improvements in mfPOP contraction amplitudes and time to peak responses were measured in eyes treated with intravitreal ranibizumab, however response delays appeared to be the most indicative of functional improvement. Confirmation of hypersensitivity in the extra-foveal field in a larger group may support this finding as a prognostic marker for good treatment outcomes.

PMID:22159011 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2011 Dec 8. [Epub ahead of print]

Automated Characterization of Pigment Epithelial Detachment using Optical Coherence Tomography.

Lee SY, Stetson PF, Ruiz-Garcia H, Heussen FM, Sadda SR.

Doheny Image Reading Center, Doheny Eye Institute, Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA.

Purpose:To assess the accuracy of automated classification of pigment epithelial detachments (PED) using a software algorithm applied to spectral-domain optical coherence tomography (SD-OCT) scans.

Methods:Cirrus HD OCT volume scans (512 × 128 cube) were retrospectively collected from 46 eyes of 33 patients with evidence of PEDs in the setting of age-related macular degeneration (AMD, n =28) or central serous chorioretinopathy (CSCR, n=5). From these eyes, 168 PEDs were automatically detected using the Cirrus HD OCT RPE Elevation Analysis tool. Two independent, certified Doheny Image Reading Center (DIRC) OCT graders classified these PEDs into three categories: Serous, Drusenoid or Fibrovascular, via inspection of the B-scans. Manual classification results served as the gold standard for comparisons with automated classification. For automatic classification, inter-individual variation in intensities was normalized in all images. Individual A-scans within the detected PEDs were then automatically classified into one of three categories based upon the mean internal intensity and the standard deviation of the internal intensity (STD): mean intensity <30 (Serous type), mean intensity≥30 but <60 OR mean intensity ≥30 and STD ≥30 (Fibrovascular type), or mean intensity ≥60 & STD< 30 (Drusenoid type). Individual PEDs were then automatically classified into the same three categories based on the predominant type of A-scan within the PED. For mixed PEDs (many A-scans of each type), a Risk Index for neovascularization could be computed based on the percentage of fibrovascular A-scans. In addition, a Confidence Index was computed for each PED based on its mathematical distance to the PED category boundaries.

Results:Among the 168 PEDs, the DIRC graders classified 16 as serous, 88 as fibrovascular, and 64 as drusenoid PEDs. The automated algorithm classified 14 as serous, 96 as fibrovascular and 58 as drusenoid PEDs. The sensitivity and specificity values for automated classification according to type of PED were 88 % sensitivity and 100 % specificity for serous PED, 76 % and 64 % for fibrovascular PED, and 58 % and 81 % for drusenoid PEDs.

Conclusion:Automated classification of PEDs using internal reflectivity characteristics appears to be sensitive for detecting serous and fibrovascular PEDs. Automated classification and quantification of PEDs may be a useful tool in future studies for stratifying PEDs according to risk, and possibly predicting the risk of advanced AMD.

PMID:22159019 [PubMed - as supplied by publisher]

Clin Rehabil. 2011 Dec 14. [Epub ahead of print]

Challenges faced by older adults with vision loss: a qualitative study with implications for rehabilitation.

Cimarolli V, Boerner K, Brennan-Ing M, Reinhardt JP, Horowitz A.

Jewish Home Lifecare, Research Institute on Aging, The Guild Center for Research in Vision and Aging, New York, USA.

Objective: To provide an in-depth assessment of challenges faced by older adults with recent vision loss and to determine changes in the nature of these challenges over time for the purpose of informing the design of vision rehabilitation services.Design: Longitudinal, qualitative study with three time points.

Setting: Vision rehabilitation agency.Subjects: Three hundred and sixty-four older adults aged 65 with significant vision impairment due to age-related macular degeneration.Interventions: In-person interviews conducted at baseline, one year and two years and coded using a qualitative analytical approach.

Main measures: Open-ended questions assessing challenges faced due to vision loss in functional, social and psychological life domains.

Results: Almost all participants reported a wide variety of challenges across all three domains with the most variety in the functional domain. Over a two-year period, functional challenges (e.g. using transportation) increased, social challenges (e.g. recognizing people) remained stable, and psychological challenges (e.g. negative affect) decreased overall.

Conclusions: Although functional challenges are predominant, social and psychological challenges are

quite common and need to be addressed in vision rehabilitation. Rehabilitation planning should also consider that vision-related challenges can change over time.

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Eye (Lond). 2011 Dec 16. doi: 10.1038/eye.2011.302. [Epub ahead of print]

Visual function 5 years or more after macular translocation surgery for myopic choroidal neovascularisation and age-related macular degeneration.

Takeuchi K, Kachi S, Iwata E, Ishikawa K, Terasaki H.

Department of Ophthalmology, Nagoya University Graduate School of Medicine, Nagoya, Japan.

Purpose: To evaluate the changes in the best-corrected visual acuity (BCVA) after 1 year and after ≥5 years after macular translocation for age-related macular degeneration (AMD) or myopic choroidal neovascularisation (mCNV).

Methods: The medical records of 61 consecutive patients who underwent macular translocation with 360° retinotomy for AMD (35 eyes) or mCNV (26 eyes) were reviewed. Overall, 40 patients, 17 mCNV and 23 AMD, were followed for at least 5 years. BCVA and area of the Goldmann visual field (VF) measured before, 12 months after surgery, and at the final visit.

Results: In the 23 AMD eyes followed for ≥5 years, the mean preoperative BCVA was 1.149±0.105 logMAR units, which significantly improved to 0.69±0.06 logMAR units at 1 year (P<0.001). This BCVA was maintained at 0.633±0.083 logMAR units on their final examination. In the 17 eyes with mCNV followed for ≥5 years, the mean preoperative BCVA was 1.083±0.119 logMAR units, which was significantly improved to 0.689±0.121 logMAR units at 1 year (P=0.001). This BCVA was maintained at 0.678±0.142 logMAR units on their final examination. The area of the VF was significantly decreased at 12 months and did not change significantly thereafter.

Conclusions: Our results show that macular translocation surgery significantly improves the BCVA and significantly decreases the VF area of eyes with mCNV or AMD after first 1 year. The BCVA and VF area do not change significantly from the values at 1 year for at least 5 years.Eye advance online publication, 16 December 2011; doi:10.1038/eye.2011.302.

PMID:22173070 [PubMed - as supplied by publisher]

Pathogenesis

Hum Genomics. 2011 Oct 1;5(6):538-68.

Systems biology-based analysis implicates a novel role for vitamin D metabolism in the pathogenesis of age-related macular degeneration.

Morrison MA, Silveira AC, Huynh N, Jun G, Smith SE, Zacharaki F, Sato H, Loomis S, Andreoli MT, Adams SM, Radeke MJ, Jelcick AS, Yuan Y, Tsiloulis AN, Chatzoulis DZ, Silvestri G, Kotoula MG, Tsironi EE, Hollis BW, Chen R, Haider NB, Miller JW, Farrer LA, Hageman GS, Kim IK, Schaumberg DA, Deangelis MM.

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Abstract

Vitamin D has been shown to have anti-angiogenic properties and to play a protective role in several types of cancer, including breast, prostate and cutaneous melanoma. Similarly, vitamin D levels have been shown to be protective for risk of a number of conditions, including cardiovascular disease and chronic kidney disease, as well as numerous autoimmune disorders such as multiple sclerosis, inflammatory bowel diseases and type 1 diabetes mellitus. A study performed by Parekh et al. was the first to suggest a role for vitamin D in age-related macular degeneration (AMD) and showed a correlation between reduced serum vitamin D levels and risk for early AMD. Based on this study and the protective role of vitamin D in diseases with similar pathophysiology to AMD, we examined the role of vitamin D in a family-based cohort of 481 sibling pairs. Using extremely phenotypically discordant sibling pairs, initially we evaluated the association of neovascular AMD and vitamin D/sunlight-related epidemiological factors. After controlling for established AMD risk factors, including polymorphisms of the genes encoding complement factor H (CFH) and age-related maculopathy susceptibility 2/HtrA serine peptidase (ARMS2/HTRA1), and smoking history, we found that ultraviolet irradiance was protective for the development of neovascular AMD (p = 0.001). Although evaluation of serum vitamin D levels (25-hydroxyvitamin D [25(OH)D]) was higher in unaffected individuals than in their affected siblings, this finding did not reach statistical significance. Based on the relationship between ultraviolet irradiance and vitamin D production, we employed a candidate gene approach for evaluating common variation in key vitamin D pathway genes (the genes encoding the vitamin D receptor [VDR]; cytochrome P450, family 27, subfamily B, polypeptide 1 [CYP27B1]; cytochrome P450, family 24, subfamily A, polypeptide 1 [CYP24A1]; and CYP27A1) in this same family-based cohort. Initial findings were then validated and replicated in the extended family cohort, an unrelated case-control cohort from central Greece and a prospective nested case-control population from the Nurse's Health Study and Health Professionals Follow-Up Studies, which included patients with all subtypes of AMD for a total of 2,528 individuals. Single point variants in CYP24A1 (the gene encoding the catabolising enzyme of the vitamin D pathway) were demonstrated to influence AMD risk after controlling for smoking history, sex and age in all populations, both separately and, more importantly, in a meta-analysis. This is the first report demonstrating a genetic association between vitamin D metabolism and AMD risk. These findings were also supplemented with expression data from human donor eyes and human retinal cell lines. These data not only extend previous biological studies in the AMD field, but further emphasise common antecedents between several disorders with an inflammatory/immunogenic component such as cardiovascular disease, cancer and AMD.

PMID:22155603 [PubMed - in process]

Br J Pharmacol. 2011 Dec 13. doi: 10.1111/j.1476-5381.2011.01812.x. [Epub ahead of print]

Concordance of Preclinical and Clinical Pharmacology and Toxicology of Monoclonal Antibodies and Fusion Proteins: 1-Soluble Targets.

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Biologics Toxicology Centocor Research & Development, a division of Johnson & Johnson Pharmaceutical Research & Development, L.L.C.

Abstract

Monoclonal antibodies (mAb) and fusion proteins directed toward soluble targets make an important contribution to the treatment of disease. The purpose of this review was to correlate the clinical and preclinical data on the 14 currently approved mAbs and fusion proteins targeted to soluble targets. The principal sources used to gather data were: the peer reviewed literature; European Medicines Agency (EMA) "Scientific Discussions" and United States Food and Drug Administration (FDA) "Pharmacology/ Toxicology Reviews" and package inserts (USPIs). Data on the following approved biopharmaceuticals were included: adalimumab; anakinra; bevacizumab;; canakinumab; certolizumab pegol; denosumab; eculizumab; etanercept; golimumab; infliximab; omalizumab; ranibizumab; rilonacept and ustekinumab. Some related biopharmaceuticals in late stage development were also included for comparison. Good

concordance with human pharmacodynamics was found for both non-human primates receiving the human biopharmaceutical and mice receiving rodent homologues (surrogates). In contrast, there was limited concordance for human adverse effects in genetically deficient mice, mice receiving surrogates or Non-Human Primates (NHPs) receiving the human pharmaceutical. In summary, the results of this survey show that although both mice and NHPs have good predictive value for human pharmacodynamics, neither species have good predictive value for human adverse effects. No evidence that NHP have superior predictive value was found.

PMID:22168335 [PubMed - as supplied by publisher]

Chembiochem. 2011 Dec 12. doi: 10.1002/cbic.201100648. [Epub ahead of print]

Enzymatic Recognition of 2'-Modified Ribonucleoside 5'-Triphosphates: Towards the Evolution of Versatile Aptamers.

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Abstract

The quest for effective, selective and nontoxic nucleic-acid-based drugs has led to designing modifications of naturally occurring nucleosides. A number of modified nucleic acids have been made in the past decades in the hope that they would prove useful in target-validation studies and therapeutic applications involving antisense, RNAi, aptamer, and ribozyme-based technologies. Since their invention in the early 1990s, aptamers have emerged as a very promising class of therapeutics, with one drug entering the market for the treatment of age-related macular degeneration. To combat the limitations of aptamers containing naturally occurring nucleotides, chemically modified nucleotides have to be used. In order to apply modified nucleotides in aptamer drug development, their enzyme-recognition capabilities must be understood. For this purpose, several modified nucleoside 5'-triphosphates were synthesized and investigated as substrates for various enzymes. Herein, we review studies on the enzyme-recognition of various 2'-sugar-modified NTPs that were carried out with a view to their effective utilization in SELEX processes to generate versatile aptamers.

PMID:22162282 [PubMed - as supplied by publisher]

Clin Experiment Ophthalmol. 2011 Dec 15. doi: 10.1111/j.1442-9071.2011.02747.x. [Epub ahead of print]

Monocyte chemoattractant protein-1 in the aqueous humor of patients with age-related macular degeneration.

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Background: To investigate the role of inflammation in age-related macular degeneration (AMD) by measuring the levels of cytokines in the aqueous humor.

Methods: Samples of aqueous humor were collected from 34 patients with AMD and 16 age-matched control subjects undergoing cataract surgery. AMD stage (AREDS) was determined clinically, before surgery. Levels of cytokines were measured using Luminex X-MAP technology, and positive results were

verified by Western blot.

Results: AMD was moderate in 18 patients and advanced in 16. The advanced-AMD group was further divided into patients with active choroidal neovascularization (CNV) (n = 7), disciform scar (n = 7), or central geographic atrophy (n = 2). Higher-than-normal levels of monocyte chemoattractant protein-1 (MCP-1) in the aqueous humor were associated with advanced AMD (200 ± 140 pg/ml vs 100 ± 61 pg/ml; p = 0.03), especially active CNV (255 ± 155 pg/ml; p = 0.02), Western blot analysis verified the MCP-1 findings. Patients with disciform scar showed a trend of abnormally high levels of IL-12 (p70) (1.7 ± 2.4 pg/ml vs 0.2 ± 1 pg/ml; p = 0.07), tumor necrosis factor (TNF)-α (1.8 ± 2.4 pg/ml vs 0.3 ± 1 pg/ml; p = 0.06), and IL-8 (4.7 ± 6.4 pg/ml vs 1.2 ± 2.1 pg/ml; p = 0.08).

Conclusion: Elevated levels of inflammation-related cytokines in the aqueous humor in various stages of AMD may suggest a pathogenic role of inflammation. MCP-1 may be indicative of the angiogenic phase. Further corroborative studies are required.

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J Neuroinflammation. 2011 Dec 16;8(1):176. [Epub ahead of print]

Neuroprotective response after photodynamic therapy: Role of vascular endothelial growth factor.

Suzuki M, Ozawa Y, Kubota S, Hirasawa M, Miyake S, Noda K, Tsubota K, Kadonosono K, Ishida S.

BACKGROUND: Anti-vascular endothelial growth factor (VEGF) drugs and/or photodynamic therapy (PDT) constitute current treatments targeting pathological vascular tissues in tumors and age-related macular degeneration. Concern that PDT might induce VEGF and exacerbate the disease has led us to current practice of using anti-VEGF drugs with PDT simultaneously. However, the underlying molecular mechanisms of these therapies are not well understood.

METHODS: We assessed VEGF levels after PDT of normal mouse retinal tissue, using a laser duration that did not cause obvious tissue damage. To determine the role of PDT-induced VEGF and its downstream signaling, we intravitreally injected a VEGF inhibitor, VEGFR1 Fc, or a PI3K/Akt inhibitor, LY294002, immediately after PDT. Then, histological and biochemical changes of the retinal tissue were analyzed by immunohistochemistry and immunoblot analyses, respectively.

RESULTS: At both the mRNA and protein levels, VEGF was upregulated immediately and transiently after PDT. VEGF suppression after PDT resulted in apoptotic destruction of the photoreceptor cell layer in only the irradiated area during PDT. Under these conditions, activation of the anti-apoptotic molecule Akt was suppressed in the irradiated area, and levels of the pro-apoptotic protein BAX were increased. Intravitreal injection of a PI3K/Akt inhibitor immediately after PDT increased BAX levels and photoreceptor cell apoptosis.

CONCLUSION: Cytotoxic stress caused by PDT, at levels that do not cause overt tissue damage, induces VEGF and activates Akt to rescue the neural tissue, suppressing BAX. Thus, the immediate and transient induction of VEGF after PDT is neuroprotective.

PMID:22171708 [PubMed - as supplied by publisher] Related citations

Epidemiology

Arch Ophthalmol. 2011 Dec;129(12):1605-6.

Risk assessment models for late age-related macular degeneration.

Klein R, Klein BE, Myers CE.

Department of Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health, 610 N Walnut St, 417 WARF, Madison, WI 53726. kleinr@epi.ophth.wisc.edu.

PMID:22159681[PubMed - in process] Related citations

Arch Ophthalmol. 2011 Dec 12. [Epub ahead of print]

Prevalence of and Risk Factors for Age-Related Macular Degeneration in a Multiethnic Asian Cohort.

Cheung CM, Tai ES, Kawasaki R, Tay WT, Lee JL, Hamzah H, Wong TY.

Singapore National Eye Centre (Drs Cheung and Wong and Mss Tay and Hamzah), and Departments of Medicine (Drs Tai and Wong), Epidemiology and Public Health (Dr Lee), and Ophthalmology (Dr Wong), National University of Singapore, Singapore; and Centre of Eye Research Australia, University of Melbourne, Melbourne (Dr Kawasaki).

OBJECTIVE: To describe the prevalence of and risk factors for age-related macular degeneration (AMD) in a multiethnic Asian cohort of Chinese, Malay, and Indian persons.

METHODS: In this population-based study, 3172 persons of Chinese, Malay, and Indian ethnicities 40 years and older were included. Participants underwent comprehensive systemic and ocular examination, retinal photography, and laboratory investigations. Early and late AMD signs were graded from retinal photographs. Age-standardized prevalence estimates were calculated using the 2010 Singapore adult population as the standard population. Association with a range of systemic risk factors was analyzed.

RESULTS: Of 3172 participants, AMD was present in 211 subjects. Age-standardized prevalence of AMD was 7.0% in persons 40 years and older. The age-standardized prevalence was similar in all 3 Asian ethnic groups: Chinese, 7.3%; Malay, 7.7%; and Indian, 5.7% (P value = .44). The prevalence increased with age and was higher in men. Of the range of risk factors evaluated, only myopic refractive error (<-0.5 D) was significantly associated with a lower risk for AMD (odds ratio, 0.44; P < .001, compared with emmetropia) in Chinese men.

CONCLUSIONS: The prevalence of AMD was similar in the 3 major ethnic groups in Asia and comparable with white populations. Myopic refractive error was associated with reduced risk of AMD in Chinese men.

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Genetics

J Lipid Res. 2011 Dec 9. [Epub ahead of print]

ELOVL4 protein preferentially elongates 20:5n3 to very long chain polyunsaturated fatty acids over 20:4n6 and 22:6n3.

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Abstract

We hypothesized that reduction/loss of very long chain polyunsaturated fatty acids (VLC-PUFA) due to mutations in the Elongation of Very Long Chain Fatty Acids-4 (ELOVL4) protein contributes to retinal degeneration in autosomal dominant Stargardt macular dystrophy (STGD3) and age-related macular degeneration; hence, increasing VLC-PUFA in the retina of these patients could provide some therapeutic

benefits. Thus, we tested the efficiency of elongation of C20-C22 PUFA by the ELOVL4 protein to determine which substrates are the best precursors for biosynthesis of VLC-PUFA. The ELOVL4 protein was expressed in pheochromocytoma cells, while GFP-expressing and non-transduced cells served as controls. The cells were treated with 20:5n3, 22:6n3 and 20:4n6, either individually or in equal combinations. Both transduced and control cells internalized and elongated the supplemented fatty acids to C22-C26 precursors. Only ELOVL4-expressing cells synthesized C28-C38 VLC-PUFA from these precursors. In general, 20:5n3 was more efficiently elongated to VLC-PUFA, regardless of whether it was in combination with 22:6n3 or with 20:4n6 in the ELOVL4-expressing cells. In each fatty acid treatment group, C34 and C36 VLC-PUFA were the predominant VLC-PUFA in the ELOVL4-expressing cells. In summary, 20:5n3, followed by 20:4n6 seems to be the best precursor for boosting the synthesis of VLC-PUFA by ELOVL4 protein.

PMID:22158834 [PubMed - as supplied by publisher]

Can J Ophthalmol. 2011 Dec;46(6):549-51.

Can genetic factors predict response to antivascular endothelial growth factor therapy in age-related macular degeneration?

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PMID:22153646[PubMed - in process]

Pac Symp Biocomput. 2012:363-74.

Mixture model for sub-phenotyping in gwas.

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Abstract

Genome Wide Association (GWA) studies resulted in discovery of genetic variants underlying several complex diseases including Chron's disease and age-related macular degeneration (AMD). Still geneticists find that in majority of studies the size of the effect even if it is significant tends to be very small. There are several factors contributing to this problem such as rare variants, complex relationships among SNPs (epistatic effect), and heterogeneity of the phenotype. In this work we focus on addressing phenotypic heterogeneity. We introduce the problem of identifying, from GWAS data, separate genotypic markers from overlapping mixtures of clinically indistinguishable phenotypes. We propose a generative model for this scenario and derive an expectation-maximization (EM) procedure to fit the model to data, as well as a novel screening procedure designed to identify skew specific to certain phenotypic regimes. We present results on several simulated datasets as well as preliminary findings in applying the model to type 2 diabetes dataset.

PMID:22174291 [PubMed - in process]

PLoS One. 2011;6(12):e28847. Epub 2011 Dec 12.

A Common Complement C3 Variant Is Associated with Protection against Wet Age-Related Macular

Degeneration in a Japanese Population.

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Department of Surgery, Division of Ophthalmology, Kobe University Graduate School of Medicine, Kobe, Japan.

BACKGROUND: Genetic variants in the complement component 3 gene (C3) have been shown to be associated with age-related macular degeneration (AMD) in Caucasian populations of European descent. In particular, a nonsynonymous coding variant, rs2230199 (R102G), is presumed to be the most likely causal variant in the C3 locus based on strong statistical evidence for disease association and mechanistic functional evidence. However, the risk allele is absent or rare (<1%) in Japanese and Chinese populations, and the association of R102G with AMD has not been reported in Asian populations. Genetic heterogeneity of disease-associated variants among different ethnicities is common in complex diseases. Here, we sought to examine whether other common variants in C3 are associated with wet AMD, a common advanced-stage manifestation of AMD, in a Japanese population.

METHODOLOGY/PRINCIPAL FINDINGS: We genotyped 13 tag single nucleotide polymorphisms (SNPs) that capture the majority of common variations in the C3 locus and tested for associations between these SNPs and wet AMD in a Japanese population comprising 420 case subjects and 197 controls. A noncoding variant in C3 (rs2241394) exhibited statistically significant evidence of association (allelic P=8.32×10(-4); odds ratio=0.48 [95% CI=0.31-0.74] for the rs2241394 C allele). Multilocus logistic regression analysis confirmed that the effect of rs2241394 was independent of the previously described loci at ARMS2 and CFH, and that the model including variants in ARMS2 and CFH plus C3 rs2241394 provided a better fit than the model without rs2241394. We found no evidence of epistasis between variants in C3 and CFH, despite the fact that they are involved in the same biological pathway.

CONCLUSIONS: Our study provides evidence that C3 is a common AMD-associated locus that transcends racial boundaries and provides an impetus for more detailed genetic characterization of the C3 locus in Asian populations.

PMID:22174912 [PubMed - in process]

Cell Immunol. 2011 Nov 25. [Epub ahead of print]

Tannic acid suppresses ultraviolet B-induced inflammatory signaling and complement factor B on human retinal pigment epithelial cells.

Chou WW, Wang YS, Chen KC, Wu JM, Liang CL, Juo SH.

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Abstract

Ultraviolet B (UVB) radiation may cause the inflammation of retinal pigment epithelium (RPE) cells and play a role in development of age-related macular degeneration (AMD). The activation of the complement factor B (CFB) gene has been shown to be involved in formation of AMD. Here our results revealed that UVB induces IL-6/STAT3 signaling activation and the UVB-induced STAT3 is able to regulate the CFB expression in ARPE-19 cells. Tannic acid (TA) is a kind of water-soluble polyphenol and may have anti-inflammation effects. We also found that TA attenuates the UVB-induced IL-6 protein production, the STAT3 phosphorylation and the CFB expression. Taken together, these findings suggest UVB-induced inflammation of RPE can be mediated through the IL-6/STAT3/CFB pathway, and TA has a protected effect via the inhibition to the inflammatory response.

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Ophthalmic Genet. 2011 Dec 15. [Epub ahead of print]

Guangzhou , China.

Background: Recently, two genome-wide association studies with large cohorts both identified rs9621532, a new single nucleotide polymorphism (SNP) that is associated with advanced age-related macular degeneration (AMD) and located near the TIMP3 gene. Previous studies have demonstrated that AMD and polypoidal choroidal vasculopathy (PCV) share some common genetic background and that the incidence of PCV is higher in Asian populations than Caucasian populations. In this study, we aimed to investigate whether the rs9621532 SNP is associated with neovascular AMD (nAMD) and PCV in a Chinese Han population.

Methods: We performed a case-control study in a Chinese Han population. The rs9621532 SNP was genotyped in 136 patients with nAMD, 195 patients with PCV, and 181 control individuals using the Multiplex SNaPshot system and the direct DNA sequencing technique. Rs9621532 genotypes and allele frequencies in the nAMD, PCV and control groups were evaluated using PLINK software.

Results: In the nAMD, PCV, and control groups, the minor allele frequencies of the rs9621532 variant were 0.05147, 0.02564, and 0.03039, respectively. The rs9621532 SNP was not significantly associated with susceptibility to nAMD ($p = 0.1773$) or PCV ($p = 0.6933$). None of the p-values for the additive or dominant models were found to be statistically significant in the nAMD or PCV groups. No recessive homozygotes were genotyped in any of the three groups.

Conclusions: No evidence was found to support an association between the rs9621532 variant and susceptibility to either nAMD or PCV in a Chinese Han population.

PMID:22171703 [PubMed - as supplied by publisher]

PLoS One. 2011;6(12):e28560. Epub 2011 Dec 5.

Gene transfer using micellar nanovectors inhibits choroidal neovascularization in vivo.

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PURPOSE: Age-related macular degeneration caused by choroidal neovascularization (CNV) remains difficult to be treated despite the recent advent of several treatment options. In this study, we investigated the in vivo angiogenic control by intravenous injection of polyion complex (PIC) micelle encapsulating plasmid DNA (pDNA) using a mice CNV model.

METHODS: The transfection efficiency of the PIC micelle was investigated using the laser-induced CNV in eight-week-old male C57 BJ/6 mice. Firstly, each mouse received intravenous injection of micelle encapsulating pDNA of Yellow Fluorescent Protein (pYFP) on days 1,3 and 5. The expression of YFP was analyzed using fluorescein microscopy and western blotting analysis. In the next experiments, each mouse received intravenous injection of micelle encapsulating pDNA of soluble Fms-like tyrosine kinase-1 (psFlt-1) 1,3 and 5 days after the induction of CNV and the CNV lesion was analyzed by choroidal flatmounts on day 7.

RESULTS: Fluorescein microscopy and western blotting analysis revealed that the expression of YFP was confirmed in the CNV area after injection of the PIC micelle, but the expression was not detected neither in mice that received naked pDNA nor those without CNV. Furthermore, the CNV area in the mice that received intravenous injection of the psFlt-1-encapsulated PIC micelle was significantly reduced by 65% compared to that in control mice ($p<0.01$).

CONCLUSIONS: Transfection of sFlt-1 with the PIC micelle by intravenous injection to mice CNV models showed significant inhibition of CNV. The current results revealed the significant potential of nonviral gene

therapy for regulation of CNV using the PIC micelle encapsulating pDNA.

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Ophthalmic Genet. 2011 Dec 15. [Epub ahead of print]

Clinical features of a Japanese case with Bothnia dystrophy.

Nojima K, Hosono K, Zhao Y, Toshiba T, Hikoya A, Asai T, Kato M, Kondo M, Minoshima S, Hotta Y.

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Purpose: Bothnia dystrophy is a variant of recessive retinitis punctata albescens (RPA) and is caused by a homozygous R234W mutation in the RLBP1 gene. We report the clinical features of a Japanese patient with the homozygous R234W mutation in the RLBP1 gene.

Methods: An affected woman with RPA has been examined clinically for 25 years. Her DNA was obtained with informed consent, and the exons and surrounding areas of RDH5, rhodopsin, and RLBP1 were amplified by PCR and directly sequenced.

Results: Our patient was first examined in our hospital in 1986 when she was 6 years old. Ophthalmoscopy showed numerous small white dots in the posterior pole of both eyes. Although the a- and b-waves of the single flash ERGs were severely reduced after a standard 30 min of dark-adaptation, the amplitudes of both waves increased markedly after 24 hr of dark-adaptation. The visual disturbances and visual field scotomas became more evident in her twenties, and her BCVAs were 0.2 OD and 0.5 OS when she was 31 years old in 2010. Fundus examinations showed macular degeneration in both eyes. A homozygous R234W mutation was detected in RLBP1, and no mutations were detected in RDH5 and rhodopsin.

Conclusions: The clinical characteristics of a Japanese patient with a homozygous R234W mutation in RLBP1 are very similar to that of Swedish patients with Bothnia dystrophy. The origin of the Japanese R234W mutation is probably not the same as that of the Swedish patients, but more likely due to the high incidence of C to T transitions.

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Diet

Bioresour Technol. 2011 Nov 30. [Epub ahead of print]

Preparation of highly pure zeaxanthin particles from sea water-cultivated microalgae using supercritical anti-solvent recrystallization.

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Abstract

Xanthophylls, including zeaxanthin, are considered dietary supplements with a potentially positive impact on age-related macular degeneration. Using pilot-scale column fractionation coupled with supercritical anti-solvent (SAS) recrystallization, highly pure zeaxanthin particulates were prepared from ultrasonic extracts of the microalgae, Nannochloropsis oculata, grown in sea water. Column partition chromatography

increased the concentration of zeaxanthin from 36.2mg/g of the ultrasonic extracts to 425.6mg/g of the collected column fractions. A response surface methodology was systematically designed for the SAS process by changing feed concentration, CO(2) flow rate and anti-solvent pressure. Zeaxanthin-rich particles with a purity of 84.2% and a recovery of 85.3% were produced using supercritical anti-solvent recrystallization from the column eluate at a feed concentration of 1.5mg/mL, CO(2) flow rate of 48.6g/min and pressure of 135bar.

PMID:22169217 [PubMed - as supplied by publisher]