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Drug Treatment

Graefes Arch Clin Exp Ophthalmol. 2011 Sep 8. [Epub ahead of print]

Subjective perception versus objective outcome after intravitreal ranibizumab for exudative AMD.

Koch KR, Muether PS, Hermann MM, Hoerster R, Kirchhof B, Fauser S.

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BACKGROUND: The efficacy of ranibizumab in preserving visual acuity in exudative age-related macular degeneration (AMD) has been widely demonstrated. However, statistically significant improvements in outcome measures such as best-corrected visual acuity (BCVA) may not necessarily be clinically relevant. Clinical relevance can be assumed when the treatment success is perceivable for the patient. We therefore investigated the relation between subjective perception of the treatment success and the objective outcome after intravitreal ranibizumab treatment.

METHODS: In this prospective interventional case series, patients received three monthly ranibizumab injections for exudative AMD. To assess the subjective study outcome (SSO) 4 weeks after the third injection, patients had to grade the overall trend of visual quality in the treated eye since baseline. Objective changes of functional (BCVA measured with ETDRS reading charts; reading visual acuity (RVA) and reading speed measured with Radner reading charts) and morphological parameters (central retinal thickness measured with OCT) were evaluated. Agreement between SSO and objective parameters was assessed with non-parametric statistical tests.

RESULTS: Seventy-four eyes of 74 patients were analyzed. Mean BCVA increased from 55 (SD ±13) ETDRS letters by +3.16 letters (SD ±11.99, $p = 0.03$). Mean RVA (measured as logRAD score) increased by -0.067 (SD ±0.294, $p = 0.052$). Fifty patients (68%) perceived a subjective improvement, 16 (21%) no change, and eight (11%) a worsening in the study eye (SSO). SSO was independent of whether treating the better- or worse-seeing eye ($p = 0.83$). SSO was significantly correlated with BCVA, RVA, and reading speed (as assessed using the critical print size (CPS)) changes ($p = 0.002$, $p < 0.001$, and $p = 0.002$), but showed no correlation to central retinal thickness changes ($p = 0.783$). Patients gaining ≥ +5 ETDRS letters had a significantly better SSO ($p = 0.001$). The rate of subjective improvement increased distinctly to >80% among patients gaining ≥ +7 letters.

CONCLUSIONS: In this study, 2/3 of patients reported a subjective improvement from ranibizumab injections. Patients' perception was significantly correlated with objective changes in BCVA and reading visual acuity. Our data indicate that the mean threshold for perceived improvement is a +5 to +7 letter gain, which might accordingly be considered clinically meaningful and relevant. Patients' perception was independent of whether the better- or worse-seeing eye was treated.

PMID: 21901296 [PubMed - as supplied by publisher]

Br J Ophthalmol. 2011 Sep 2. [Epub ahead of print]

Predictive factors of resolved retinal fluid after intravitreal ranibizumab for polypoidal choroidal vasculopathy.

Koizumi H, Yamagishi T, Yamazaki T, Kinoshita S.

Kyoto Prefectural University of Medicine, Kyoto, Japan.

Background/aims: To investigate the predictive factors for the resolution of retinal fluid after intravitreal injections of ranibizumab (IVRs) for polypoidal choroidal vasculopathy (PCV).

Methods: Forty-seven eyes of 45 patients with symptomatic PCV received 0.5 mg of IVR monthly for 3 months. One month after the third IVR, the presence of dry macula, defined as absence of retinal fluid as detected by the use of optical coherence tomography, was retrospectively evaluated and correlated with clinical characteristics at baseline. Most of the eyes were followed for over 6 months.

Results: Of the 47 eyes, 31 eyes (66%) achieved the dry macula along with increased best-corrected visual acuity (BCVA) (0.64 to 0.46 logarithm of the minimum angle of resolution units, p<0.0001), while the other 16 eyes without dry macula showed no significant change of BCVA. Univariate analyses of the baseline characteristics identified the smaller size of the largest polyp (p=0.0008) and the absence of serous or haemorrhagic pigment epithelial detachment (p=0.045) as predictive factors for the dry macula. Multivariate logistic regression found the independent predictor for the dry macula to be the smaller size of the largest polyp (p=0.001). No severe systemic or ocular adverse events were observed.

Conclusions: IVR may be helpful for resolution of retinal fluid and increased BCVA in the short term, but larger polyps and pigment epithelial detachments at baseline may be negative prognostic factors for a therapeutic response. Further studies are needed to clarify the long-term efficacy of IVR for PCV.

PMID: 21890787 [PubMed - as supplied by publisher]

Ophthalmologica. 2011 Sep 1. [Epub ahead of print]

Two-Year Results of Photodynamic Therapy Combined with Intravitreal Anti-Vascular Endothelial Growth Factor for Polypoidal Choroidal Vasculopathy.

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Background/Aims: To evaluate the 2-year efficacy of photodynamic therapy (PDT) combined with intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF) in patients with polypoidal choroidal vasculopathy (PCV).

Methods: Twenty-two eyes of 22 patients with PCV followed up for ≥24 months after PDT and anti-VEGF combination therapy were retrospectively reviewed. The patients received intravitreal anti-VEGF (1.25 mg bevacizumab or 0.5 mg ranibizumab) within 7 days after PDT. Eyes were retreated with PDT and anti-VEGF injection, or with only anti-VEGF injection, when indicated. Main outcome measures were best-corrected visual acuity (BCVA) and central foveal thickness (CFT).

Results: The mean baseline BCVA (0.43 ± 0.33 logarithm of the minimum angle of resolution, logMAR) was 0.28 ± 0.24 at 12 months (p < 0.05 vs. baseline) and 0.39 ± 0.28 at 24 months (not significant). At 24 months, BCVA improved by ≥0.3 logMAR in 27.3% of the eyes, did not significantly decrease in 59.1%, and decreased by ≥0.3 logMAR in 13.6%. The mean CFT was 269.4 ± 134.5 μm at baseline and significantly decreased to 139.6 ± 45.8 μm (12 months) and 199.6 ± 72.9 μm (24 months). PDT was administered 1.45 ± 0.86 times and anti-VEGF injected 4.45 ± 1.36 times over the 24-month period.

Conclusion: Combined PDT and anti-VEGF injection were effective for 2 years in PCV patients. Visual acuity significantly improved during year 1, but the benefit diminished in year 2. Further investigations are required to determine how to prolong the therapeutic effect of combination therapy for PCV.

PMID: 21893965 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Ophthalmic Surg Lasers Imaging. 2011 Sep 1;42(5):369-75. doi: 10.3928/15428877-20110812-01.

Analysis of the relationship between drusen size and drusen area in eyes with age-related macular degeneration.

Friberg TR, Bilonick RA, Brennen PM.

BACKGROUND AND OBJECTIVE: To examine the relationship between drusen counts and drusen area in eyes with age-related macular degeneration, and to correlate drusen areas between fellow eyes.

PATIENTS AND METHODS: Digital images from 378 patients (756 eyes) were analyzed using a validated drusen detection algorithm. Total drusen area and the number of drusen of various sizes (small: < 62 microns, intermediate: 63-124 microns, large: 125-249 microns, etc) were recorded for the central 1,000- and 3,000-micron diameter macular regions. Correlations were assessed using structural equation models.

RESULTS: For the 1,000-micron region, the number of intermediate drusen was more highly correlated to total drusen area than the number of large drusen (R = 0.91 vs 0.82); this difference was statistically significant. The correlation coefficients for drusen area between fellow eyes was 0.73.

CONCLUSION: The number of large drusen does not correlate better with total drusen area than drusen of other sizes. The number of large drusen is not necessarily a good surrogate for total drusen area.

PMID: 21899243 [PubMed - in process]

Neurotherapeutics. 2011 Sep 9. [Epub ahead of print]

Cell-Based Therapy for Neural Disorders - Anticipating Challenges.

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Abstract

Neurological syndromes, such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, Huntington's disease, amyotrophic lateral sclerosis, and lysosomal storage disorders, such as Battens disease, are devastating because they result in increasing loss of cognitive and physical function. Sadly, no drugs are currently available to halt their progression. The relative paucity of curative approaches for these and other conditions of the nervous system have led to a widespread evaluation of alternative treatment modalities including cell-based interventions. Several cell types have been tested successfully in animal models where safety and efficacy have been demonstrated. Early clinical trials have also been initiated in humans, and some have shown a degree of success albeit on a more limited scale than in animal experiments. Recent demonstrations that pluripotent stem cells, such as embryonic stem cells and induced pluripotent stem cells, can differentiate into a variety of specific neural phenotypes has stimulated worldwide enthusiasm for developing cell-based intervention of neurological disease. Indeed, several groups are preparing investigational new drug applications to treat disorders as diverse as macular degeneration, lysosomal storage diseases, and Parkinson's disease. It is noteworthy that cell replacement therapies for neurological conditions

face key challenges, some of which are unique, because of the development and organization of the nervous system, its metabolism, and connectivity. Choice of the cell (or cells), the process of manufacturing them, defining the delivery pathway, developing and testing in an appropriate preclinical model, selecting a patient population, and visualizing and following or monitoring patients all pose specific issues as related to the central and peripheral nervous systems. In this review, we address a myriad of challenges that are solvable, but require careful planning and attention to the special demands of the human nervous system.

PMID: 21901585 [PubMed - as supplied by publisher]

Oftalmologia. 2011;55(2):60-9.

[Correlations between fluorescein angiography and optical coherence tomography in age-related macular degeneration diagnosis].

[Article in Romanian]

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SpitaluL Clinic de Urgenţe Oftalmologice, Bucureşti.

Abstract

Diagnostic tools for macular disease have developped over the last years due both to the elaboration of new methods of approach and to the improvement of the already existing ones. Fluorescein angiography (FA) is a minimally invasive procedure that involves photographic surveillance of the blood circulation of the retina and choroid, thus offering data on fundus pathology In eyes with AMD (Age Related Macular Degeneration) the assessment through FA is necessary in order to confirm the presence of CNV (Choroidal Neovascular Membrane). Beside that, FA offers details about the size, location and type (occult or classic) of CNV and it is useful in the followup after treatment. OCT (Optical Coherence Tomography) is a modern imagistic method, that is non-invasive, easily repetable and lacks complications. It acquires in vivo images that represent cross-sections of the retina. In the last years it has become an ever more popular diagnostic tool. OCT imaging is able to detect the presence of CNV and of sub- and intraretinal fluid accumulation. During the last decade, the management of neovascular AMD has changed, as anti-VEGF therapy has become the treatment of choice for all subfoveal CNV lesions types (occult and classic). Some clinicians tend to overlook the importance of FA assessment and rely only on visual acuity and OCT imaging for establishing both diagnosis and indication of treatment. Experts in the field say that these two investigations provide complementary information. They agree that the anatomical data offered by OCT imaging should be supported by the proof that an active exudation exists, which can only be provided by FA. At this moment the management of AMD includes both FA and OCT scanning. Several studies have tried to determine which OCT parameters corelate best with the activity of CNV as it appears on FA photographs. Further on, we shall present a few clinical cases that we consider representative for the topic.

PMID: 21888071 [PubMed - in process]

Oftalmologia. 2011;55(2):54-9.

[Therapeutic attitude in patients with age-related macular degeneration and cataract].

[Article in Romanian]

Tomi A, Moldoveanu A, Marin I.

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Abstract

Management of the patient with coexisting cataract and AMD presents unique challenges to the cataract surgeon, the retina specialist, and the patient. A common clinical scenario is the patient in whom both the cataract and macular pathology appear to be contributing to decreased visual acuity. As with any surgery, the expectations from cataract removal must be evaluated thoroughly and understood clearly by both the patient and the cataract surgeon. Most patients with AMD who undergo cataract surgery feel that the surgery is worthwhile, and they report improvement of visual function and quality of life. In patients with mild AMD, improvement in central visual acuity and attainment of driving vision are realistic and achievable goals. In an eye with central disciform scarring or geographic atrophy there may be potential for improvement in color discrimination, contrast, or clarity of peripheral vision. In cases of dense cataract obscuring macular detail, cataract removal may be necessary to allow for adequate biomicroscopy and angiography, especially in an eye that may be at high risk for the development of choroidal neovascularization. It is often challenging to estimate the relative impact on visual impairment made by the lens opacities and the macular changes and the benefits and risks of cataract surgery in eyes with AMD should be carefully evaluated. Is cataract surgery justified in these patients? Does cataract surgery aggravate AMD in some patients?

PMID: 21888070 [PubMed - in process]

Pathogenesis

Br J Ophthalmol. 2011 Sep 2. [Epub ahead of print]

The oil spill in ageing Bruch membrane.

Curcio CA, Johnson M, Rudolf M, Huang JD.

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Abstract

Ageing is the largest risk factor for age-related macular degeneration (AMD), and soft drusen and basal linear deposits are lipid-rich extracellular lesions specific to AMD. Oil red O binding neutral lipid represents a major age-related deposition in the Bruch membrane (BrM) and the first identified druse component. Decades after these seminal observations, a natural history of neutral lipid deposition has been articulated and a biochemical model proposed. Results obtained with multiple biochemical, histochemical, and ultrastructural methods, and supported indirectly by epidemiology, suggest that the RPE secretes apolipoprotein B (apoB)-lipoprotein particles of unusual composition into BrM, where they accumulate with age eventually forming a lipid wall, a precursor of basal linear deposit. The authors propose that constituents of these lesions interact with reactive oxygen species to form pro-inflammatory peroxidised lipids that elicit neovascularisation. Here, the authors summarise key evidence supporting both accumulation of BrM lipoproteins leading to lesion formation and lipoprotein production by the RPE. The authors update their model with genetic associations between AMD and genes historically associated with plasma HDL metabolism, and suggest future directions for research and therapeutic strategies based on an oil-spill analogy.

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Curr Opin Ophthalmol. 2011 Sep 3. [Epub ahead of print]

Effects of smoking on ocular health.

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PURPOSE OF REVIEW: To review recent data on the effects of smoking on ocular health.

RECENT FINDINGS: Smoking has been associated with a myriad of negative ocular health effects including age-related macular degeneration (ARMD) and cataract. Most recently, several papers have demonstrated a connection between smoking and ocular inflammation. Smokers are both more likely to develop ocular inflammation and to have more severe disease as manifested by poorer presenting vision and a higher risk of recurrent disease compared to nonsmokers. Smoking has also been shown to enhance the effect of genetic susceptibility with regards to the presence and development of ARMD. Finally, the negative effects of smoking on ocular disease have been increasingly documented in nonwhite populations outside of the USA. However, despite the abundance of data, public awareness on the adverse consequences of smoking on vision is lacking in the USA. In contrast, Australia improved public knowledge by launching a successful antitobacco health campaign highlighting the effects of smoking on ocular health.

SUMMARY: These findings suggest that eye care professionals should discuss and offer options for smoking cessation as part of the management of patients with ocular diseases, especially in those with ocular inflammation, ARMD, lens opacities/cataract, and thyroid-associated orbitopathy. Health campaigns using existing medical data can improve public awareness on the connection between tobacco and visual impairment.

PMID: 21897240 [PubMed - as supplied by publisher]

Inflammation. 2011 Sep 6. [Epub ahead of print]

IL-33 Is Induced by Amyloid-β Stimulation and Regulates Inflammatory Cytokine Production in Retinal Pigment Epithelium Cells.

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Abstract

Age-related macular degeneration (AMD) is the predominant cause of irreversible blindness in the elderly population. Despite intensive basic and clinical research, its pathogenesis remains unclear. However, evidence suggests that immunological and inflammatory factors contribute to the pathogenesis of AMD. A newly identified cytokine, IL-33, appears to be an important pro-inflammatory cytokine promoting tissue inflammation. In this study, IL-33 was increased through amyloid-beta(1-40) (Aβ(1-40)) stimulation and regulated inflammatory cytokines including IL-6, IL-8, IL-1β, and TNF-α secretion using different signaling pathways in retinal pigment epithelium (RPE) cells. Furthermore, ST2L, the important component of the IL-33 receptor, was significantly increased following recombinant human IL-33 stimulation in RPE cells. These findings suggest that IL-33-mediated inflammatory responses in RPE cells are involved in the pathogenesis of AMD. Greater understanding of the inflammatory effect of IL-33 and its role in RPE cells should aid the development of future clinical therapeutics and enable novel pharmacological approaches towards the prevention of AMD.

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Genetics

Nat Nanotechnol. 2011 Sep 4. doi: 10.1038/nnano.2011.141. [Epub ahead of print]

Gold nanoparticles for high-throughput genotyping of long-range haplotypes.

Chen P, Pan D, Fan C, Chen J, Huang K, Wang D, Zhang H, Li Y, Feng G, Liang P, He L, Shi Y.

1] Key Laboratory for the Genetics of Developmental and Neuropsychiatric Disorders (Ministry of Education), Bio-X Institutes, Shanghai Jiao Tong University, Shanghai 200030, China [2].

Abstract

Completion of the Human Genome Project and the HapMap Project has led to increasing demands for mapping complex traits in humans to understand the aetiology of diseases. Identifying variations in the DNA sequence, which affect how we develop disease and respond to pathogens and drugs, is important for this purpose, but it is difficult to identify these variations in large sample sets. Here we show that through a combination of capillary sequencing and polymerase chain reaction assisted by gold nanoparticles, it is possible to identify several DNA variations that are associated with age-related macular degeneration and psoriasis on significant regions of human genomic DNA. Our method is accurate and promising for large-scale and high-throughput genetic analysis of susceptibility towards disease and drug resistance.

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Invest Ophthalmol Vis Sci. 2011 Sep 6. [Epub ahead of print]

Associations of Complement Factor H and ARMS2 Genotypes with Subtypes of Polypoidal Choroidal Vasculopathy.

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Purpose: To clarify whether complement factor H (CFH) and age-related maculopathy susceptibility 2 (ARMS2) genotypes are associated with subtypes of polypoidal choroidal vasculopathy (PCV), such as polypoidal choroidal neovascularization (CNV) and typical PCV.

Methods: We categorized 287 patients as having polypoidal CNV (85 patients) or typical PCV (202) based on indocyanine green angiographic findings. In total, 277 subjects without age-related macular degeneration, i.e. free of PCV and CNV, served as controls. I62V (rs800292) in the CFH gene and A69S (rs10490924) in the ARMS2 gene were genotyped, and case-control studies were performed in subjects with these PCV subtypes.

Results: The polypoidal CNV group included no subjects homozygous for the A/A genotype of rs800292, while 7% of the typical PCV group had this genotype. Case-control studies of polypoidal CNV and typical PCV showed significant differences in all distributions of rs10490924 between these two groups. In contrast, the distributions of rs10490924 did not differ between the typical PCV and control groups. Logistic regression analysis with adjustment for confounding factors showed the distributions of rs10490924 to differ highly significantly between the controls and polypoidal CNV cases (p=2.1 × 10(-10), OR: 10.87). The T/T genotype was significantly more common in the polypoidal CNV than in the typical PCV group (p=3.6 × 10(-14), OR: 19.61).

Conclusions: PCV might be genetically divisible into polypoidal CNV and typical PCV. The rs800292 variant of the CFH gene is a potential marker for typical CNV. The rs10490924 variant of the ARMS2 gene was shown to be associated with polypoidal CNV. Typical PCV was not associated with this variant.

PMID: 21896867 [PubMed - as supplied by publisher]

Biomaterials. 2011 Sep 2. [Epub ahead of print]

Delivery of Oct4 and SirT1 with cationic polyurethanes-short branch PEI to aged retinal pigment epithelium.

Peng CH, Cherng JY, Chiou GY, Chen YC, Chien CH, Kao CL, Chang YL, Chien Y, Chen LK, Liu JH, Chen SJ, Chiou SH.

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Abstract

Cationic polyurethane, a biodegradable non-viral vector, protects DNA from nuclease degradation and helps to deliver genes efficiently. Oct4, a POU-domain transcription factor, is highly expressed in maintaining pluripotency and cellular reprogramming process in stem cells. SirT1, a NAD-dependent histone deacetylase, is an essential mediator of cellular longevity. Herein we demonstrated that both Oct4 and SirT1 (Oct4/SirT1) expression was decreased in an age-dependent manner in retina with aged-related macular degeneration and retinal pigment epithelium cells (RPEs). To investigate the possible rescuing role of Oct4/SirT1, polyurethane-short branch polyethylenimine (PU-PEI) was used to deliver Oct4/SirT1 into aged RPEs (aRPEs) or light-injured rat retinas. Oct4/SirT1 overexpression increased the expression of several progenitor-related genes and the self-renewal ability of aRPEs. Moreover, Oct4/SirT1 overexpression resulted in the demethylation of the Oct4 promoter and enhanced the expression of antioxidant enzymes, which was accompanied by a decrease in intracellular ROS production and hydrogen peroxide-induced oxidative stress. Importantly, PU-PEI-mediated Oct4/SirT1 gene transfer rescued retinal cell loss and improved electroretinographic responses in light-injured rat retinas. In summary, these data suggest that PU-PEI-mediated delivery of Oct4/SirT1 reprograms aRPEs into a more primitive state and results in cytoprotection by regulating the antioxidative capabilities of these cells.

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Invest Ophthalmol Vis Sci. 2011 Sep 6. [Epub ahead of print]

Association of Genetic Variation on Chromosome 9p21 with Polypoidal Choroidal Vasculopathy and Neovascular Age-Related Macular Degeneration.

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Purpose: Polypoidal choroidal vasculopathy (PCV) contains aneurismal morphologic and histopathologic feature and it is considered to be a possible distinct entity from neovascular age-related macular degeneration (AMD). In this study, we investigated the association of identified risk variants for intracranial aneurysm on chromosome 9p21 with PCV and neovascular AMD in a Chinese Han population.

Methods: We genotyped rs1333040 and rs10757278 on 9p21 in 177 PCV patients, 131 neovascular AMD patients and 182 controls using the Multiplex SNaPshot system and direct DNA sequencing. Allele and genotypes frequencies in the PCV and neovascular AMD groups were compared to controls using PLINK software and binary logistic regression analysis.

Results: Rs1333040 was not associated with PCV or neovascular AMD. Rs10757278 was significantly associated with PCV [risk allele: A, p(allelic)=0.014, OR=1.44 (95%CI: 1.08-1.94)], but not associated with neovascular AMD. After adjusting for gender, age, smoking status, history of hypertension, type 2 diabetes and coronary artery disease, the odds ratio for homozygous carriers of rs10757278-A was 2.10 (95% CI: 1.14-3.85) for PCV.

Conclusions: The rs10757278 on chromosome 9p21 is significantly associated with the risk of PCV but not with neovascular AMD in the Chinese Han population.

PMID: 21896860 [PubMed - as supplied by publisher]

Methods Mol Biol. 2011;787:121-36.

Combined Lentiviral and RNAi Technologies for the Delivery and Permanent Silencing of the hsp25 Gene.

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Abstract

Elevated heat shock protein 27 (Hsp27) expression has been found in a number of tumors, including breast, prostate, gastric, uterine, ovarian, head and neck, and tumor arising from the nervous system and urinary system, and determined to be a predictor of poor clinical outcome. Although the mechanism of action of Hsp27 has been well documented, there are currently no available inhibitors of Hsp27 in clinical trials. RNA interference (RNAi) has the potential to offer more specificity and flexibility than traditional drugs to silence gene expression. Not surprisingly, RNAi has become a major focus for biotechnology and pharmaceutical companies, which are now in the early stages of developing RNAi therapeutics, mostly based on short interfering RNA (siRNAs), to target viral infection, cancer, hypercholesterolemia, cardiovascular disease, macular degeneration, and neurodegenerative diseases. However, the critical issues associated with RNAi as a therapeutic are delivery, specificity, and stability of the RNAi reagents. To date, the delivery is currently considered the biggest hurdle, as the introduction of siRNAs systemically into body fluids can result in their degradation, off-target effects, and immune detection. In this chapter, we discuss a method of combined lentiviral and RNAi-based technology for the delivery and permanent silencing of the hsp25 gene.

PMID: 21898232 [PubMed - in process]

Immunobiology. 2011 Jul 26. [Epub ahead of print]

Complement polymorphisms: Geographical distribution and relevance to disease.

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Abstract

The evolution of man has been characterised by recurrent episodes of migration and settlement with infectious disease a constant threat. This long history of demographic change, together with the action of evolutionary forces such as natural selection and genetic drift, has shaped human genetic diversity. In particular, the interaction between humans, pathogens and the environment has played a crucial role in generating patterns of human genetic variation. The complement system plays a crucial role in the early protective immune response after exposure to a pathogen. Pathogens, over time, have developed mechanisms to circumvent the effects of complement which in turn has led to development of a more complex complement system. During the evolution of the complement system genes coding complement proteins have evolved polymorphisms, some of which have a functional effect, and this may reflect human-pathogen interaction and geographical origin. An example is the polymorphism Ile62Val (rs800292 (A>G)) in the complement regulator Factor H gene which alters the susceptibility to age-related macular degeneration (AMD), with the Ile62 polymorphism protecting against AMD. When sub-Saharan African and European populations are compared, the frequency of this polymorphism shows a very marked geographical distribution. Polymorphisms in other complement genes such as complement factor B show similar trends. This paper describes the geographical variation present in complement genes and discusses the implications of these observations. The analysis of genetic variation in complement genes is a promising tool to unravel mechanisms of host-pathogen interaction and can provide new insights into the evolution of the human immune system.

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Diet

Br J Nutr. 2011 Sep 8:1-10. [Epub ahead of print]

Lutein and zeaxanthin intake and the risk of age-related macular degeneration: a systematic review and meta-analysis.

Ma L, Dou HL, Wu YQ, Huang YM, Huang YB, Xu XR, Zou ZY, Lin XM.

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Abstract

Lutein and zeaxanthin are thought to decrease the incidence of age-related macular degeneration (AMD); however, findings have been inconsistent. We conducted a systematic literature review and meta-analysis to evaluate the relationship between dietary intake of lutein and zeaxanthin and AMD risk. Relevant studies were identified by searching five databases up to April 2010. Reference lists of articles were retrieved, and experts were contacted. Literature search, data extraction and study quality assessment were performed independently by two reviewers and results were pooled quantitatively using meta-analysis methods. The potential sources of heterogeneity and publication bias were also estimated. The search yielded six longitudinal cohort studies. The pooled relative risk (RR) for early AMD, comparing the highest with the lowest category of lutein and zeaxanthin intake, was 0·96 (95 % CI 0·78, 1·17). Dietary intake of these carotenoids was significantly related with a reduction in risk of late AMD (RR 0·74; 95 % CI 0·57, 0·97); and a statistically significant inverse association was observed between lutein and zeaxanthin intake and neovascular AMD risk (RR 0·68; 95 % CI 0·51, 0·92). The results were essentially consistent among subgroups stratified by participant characteristics. The findings of the present meta-analysis indicate that dietary lutein and zeaxanthin is not significantly associated with a reduced risk of early AMD, whereas an increase in the intake of these carotenoids may be protective against late AMD. However, additional studies are needed to confirm these relationships.

PMID: 21899805 [PubMed - as supplied by publisher]