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Drug treatment

Case Report Ophthalmol. 2011 Apr 22;2(1):129-33.

Peripapillary Neovascular Membrane in a Young Pregnant Woman and Prompt Response to Ranibizumab Injections following Uneventful Delivery.

Anastasilakis K, Symeonidis C, Kaprinis K, Mataftsi A, Tzamalis A, Dimitrakos SA.

2nd Department of Ophthalmology, Aristotle University of Thessaloniki, Thessaloniki, Macedonia, Greece.

PURPOSE: Occurrence of choroidal neovascularization (CNV) during pregnancy has been reported as a complication of presumed ocular histoplasmosis syndrome or punctuate inner chorioretinopathy. To our knowledge, idiopathic CNV (ICNV) during pregnancy has only been reported once in the relevant literature. Bevacizumab has been used for the treatment of ICNV in small case series. However, there is limited experience regarding the use of ranibizumab for the management of ICNV.

CASE REPORT: A 31-year-old woman in the eighth month of her second pregnancy was diagnosed with mild macular and papillary edema. She was followed up using biomicroscopy, fluorescein angiography (FA), and optical coherence tomography (OCT). After 3 months, visual acuity further deteriorated and funduscopy, FA and OCT findings revealed a juxtapapillary choroidal neovascular membrane (CNVM). After two ranibizumab injections, best-corrected visual acuity increased significantly, physiological macular anatomy was restored and no subretinal fluid was observed.

DISCUSSION:In this case report, we present a young pregnant patient with peripapillary ICNV and neurosensory detachment involving the macula, and treatment of the eye with intravitreal ranibizumab following uneventful delivery. Increased angiogenic factor levels associated with pregnancy may contribute to the onset of CNV although this relationship has to be investigated experimentally. The rapid response to ranibizumab suggests that this anti-VEGF agent may be an alternative treatment option in the management of peripapillary ICNV.

PMID: 21589847 [PubMed - in process]

PMCID: PMC3094578

Eye (Lond). 2011 May 20. [Epub ahead of print]

One-year outcome after intravitreal ranibizumab for large, serous pigment epithelial detachment secondary to age-related macular degeneration.

Arora S, McKibbin M.

Eye Department, Eye Clinic, St James's University Hospital, Leeds, UK.

Aim: To report the effects of intravitreal ranibizumab therapy for large, serous pigment epithelial detachment (PED), secondary to age-related macular degeneration, and occupying more than 50% of the total lesion area.

Materials and methods: In a retrospective case series, visual acuity, ocular coherence tomography (OCT), and safety data were collected for 19 eyes of 19 patients, with serous PED and evidence of disease progression. Intravitreal ranibizumab of 0.5 mg was given with a loading phase of three consecutive monthly injections, followed by monthly review with further treatment, as indicated according to visual acuity and OCT findings. The change in visual acuity and maximum PED height from baseline to month 12 was determined.

Results: Moderate visual loss was avoided in 18/19 eyes (95%) at the 12-month examination. In all, 12 eyes (63%) had an increase in ETDRS letter score from baseline, and five eyes (26%) had a gain of 15 or more letters. Although there was a trend for the PED height to reduce with treatment, in none of the cases was the PED seen to resolve completely. There was no difference in functional or anatomical outcome between the avascular and vascularised serous PED. A single eye developed a retinal pigment epithelium rip, complicated by extensive sub-retinal haemorrhage, during the study period.

Conclusions: Visual acuity outcomes of intravitreal ranibizumab for large serous PED are comparable to those seen in multicentre, phase 3 trials of other lesion types, and were obtained without the need for either monthly, fixed treatment, or for continued treatment until the PED resolves.Eye advance online publication, 20 May 2011; doi:10.1038/eye.2011.115.

PMID: 21597485 [PubMed - as supplied by publisher]

Clin Ophthalmol. 2011;5:459-63. Epub 2011 Apr 13.

Subretinal recombinant tissue plasminogen activator and pneumatic displacement for the management of subretinal hemorrhage occurring after anti-VEGF injections for wet AMD.

Tognetto D, Skiadaresi E, Cecchini P, Ravalico G.

Eye Clinic, University of Trieste, Trieste, Italy.

Abstract

We describe three cases of submacular hemorrhage that occurred two to four days after anti-VEGF intravitreal injection for occult choroidal neovascularisation in age-related macular degeneration and their management with 25 gauge pars plana vitrectomy with injection of subretinal recombinant tissue plasminogen activator (rTPA) followed by fluid-air exchange and postoperative prone position. Vitrectomy, subretinal rTPA injection and fluid-gas exchange apply as a safe and effective treatment in these cases. Functional results seem to be positive especially if surgical treatment is promptly performed.

PMID: 21573092 [PubMed - in process]

PMCID: PMC3090299

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

Cystoid Macular Degeneration in Exudative Age-Related Macular Degeneration.

Querques G, Coscas F, Forte R, Massamba N, Sterkers M, Souied EH.

Department of Ophthalmology, Centre Hospitalier Intercommunal de Creteil, University of Paris XII, Creteil, France.

PURPOSE: To investigate the prevalence and clinical significance of cystoid macular degeneration in eyes that underwent intravitreal ranibizumab injections for exudative age-related macular degeneration.

DESIGN: Retrospective, interventional case series.

METHODS: We reviewed the charts of 52 consecutive patients (19 male, 37 female; mean age ± standard deviation, 80.81 ± 4.8 years) with exudative age-related macular degeneration who received the last intravitreal ranibizumab injection at least 6 months before and were judged to have a fibroatrophic scar without signs of progression by fluorescein angiography or spectral-domain optical coherence tomography. Main outcome measures were the estimated prevalence and clinical significance of cystoid macular degeneration.

RESULTS: Twenty-two eyes showed various combinations of degenerative pseudocysts, whereas 34 eyes did not show any pseudocysts. The 95% confidence interval for the prevalence estimate was 36.98% to 41.02%. Degenerative pseudocysts appeared square-shaped, did not change their overall appearance over time, and were located just below the internal limiting membrane in 11 eyes (50%), in the inner nuclear layer in 16 eyes (72.7%), in the outer nuclear layer in 8 eyes (36.3%), and in all the retinal layers in 6 eyes (27.2%). Best-corrected visual acuity improved in eyes without degenerative pseudocysts and decreased significantly in eyes with degenerative pseudocysts (P = .03). Mean central macular thickness decreased significantly (P < .001) to 324.1 µm and to 328.2 µm in eyes and without degenerative pseudocysts, respectively.

CONCLUSIONS: Cystoid macular degeneration represents a well-distinguished clinical entity that may be detected in exudative age-related macular degeneration eyes showing a posttreatment fibroatrophic scar and should not be considered as a manifestation of choroidal neovascularization activity.

PMID: 21570056 [PubMed - as supplied by publisher]

Indian J Ophthalmol. 2011 May-Jun;59(3):242-6.

Photodynamic monotherapy or combination treatment with intravitreal triamcinolone acetonide, bevacizumab or ranibizumab for choroidal neovascularization associated with pathological myopia.

Rishi P, Rishi E, Venkataraman A, Gopal L, Sharma T, Bhende M, Ratra D, Sen PR, Sen P.

Shri Bhagwan Mahavir Vitreo Retinal Services, Sankara Nethralaya, 18 College Road, Chennai - 600 006, Tamil Nadu, India.

Abstract

This retrospective, interventional case series analyses treatment outcomes in eyes with choroidal neovascularization (CNV) secondary to pathological myopia, managed with photodynamic therapy, (PDT), (Group 1, N = 11), PDT and intravitreal triamcinolone acetonide (4 mg/0.1ml) (Group 2, N = 3), PDT and intravitreal anti-vascular endothelial growth factor (anti-VEGF) bevacizumab 1.25 mg/0.05 ml, ranibizumab 0.5 mg/0.05 ml and reduced-fluence PDT and intravitreal ranibizumab 0.5 mg/0.05 ml (Group 3, N=12). All the patients underwent PDT. Intravitreal injections were repeated as required. SPSS 14 software was used to evaluate the data. Wilcoxon signed ranks test was used to evaluate pre- and post-treatment vision. The Kruskal-Wallis test was used for comparison between the groups. All the groups were statistically comparable. All the eyes showed complete regression of CNV, with a minimum follow-up of six months. All groups had visual improvement; significantly in Group 3 (p = 0.003). Combination PDT with anti-VEGF agents appeared to be efficacious in eyes with myopic CNV. However, a larger study with a longer follow-up is required to validate these results.

PMID: 21586852 [PubMed - in process]

Indian J Ophthalmol. 2011 May-Jun;59(3):191-6.

Comparative role of intravitreal ranibizumab versus bevacizumab in choroidal neovascular membrane in age-related macular degeneration.

Biswas P, Sengupta S, Choudhary R, Home S, Paul A, Sinha S.

B. B. Eye Foundation, 2/5, Sarat Bose Road, Kolkata - 700 020, India.

Context: Ranibizumab and bevacizumab are used widely for treating patients with choroidal neovascular membrane (CNVM) secondary to age-related macular degeneration (AMD).

Aims: To determine and compare the efficacy and safety of intravitreal ranibizumab and bevacizumab in treatment of CNVM due to AMD.

Settings and Design: Prospective comparative case series carried out in an eye institute and eye department of a hospital in Kolkata, India.

Materials and Methods: One hundred and four eyes with CNVM due to AMD were randomized into two groups. Group A (n=54; 24 occult) received monthly intravitreal ranibizumab injections (0.5 mg in 0.05 ml) and Group B (n=50; 22 occult) received monthly bevacizumab injections (1.25 mg in 0.05 ml) for 3 consecutive months and then as per study criteria. Data analysis done using SPSS software. P-value of <0.05 was considered statistically significant.

Results: The mean best corrected visual acuity (BCVA) in the ranibizumab group increased from 58.19 Early Treatment Diabetic Retinopathy Study (ETDRS) letters at baseline to 64 ETDRS letters at month 3 (P<0.001). In bevacizumab group mean BCVA increased from 56.80 to 61.72 ETDRS letters at month 3 (P<0.001). At the end of 18 months, there was no statistically significant difference between groups A and B with respect to change in BCVA (P=0.563) or central macular thickness (CMT; P=0.281), as measured by optical coherence tomography (Stratus OCT 3000). No significant sight-threatening complications developed.

Conclusions: Ranibizumab and bevacizumab are equally safe and efficacious in treating CNVM due to AMD.

PMID: 21586838 [PubMed - in process]

Arq Bras Endocrinol Metabol. 2011 Mar;55(2):106-113.

[The role of vascular endothelial growth factor in angiogenesis and diabetic retinopathy.]

[Article in Portuguese]

Valiatti FB, Crispim D, Benfica C, Valiatti BB, Kramer CK, Canani LH.

Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brasil.

Abstract

Diabetic retinopathy (DR), a DM microvascular complication, is the leading cause of blindness. Angiogenic factors such as vascular endothelial growth factor (VEGF) are involved in the pathogenesis of DR. VEGF-A is a potent, multifunctional cytokine that acts through the receptors VEGFR-1 and VEGFR-2 expressed in the vascular endothelium and causing increased vascular permeability and neovascularization stimulation in both physiological and pathological processes. The expression of VEGFR-1 is upregulated by hypoxia and is less responsive to VEGF compared to VEGFR-2 which is the main mediator mitogenic, angiogenic, and increased vascular permeability. VEGF polymorphisms have been studied in DR susceptibility and progression. Significant association between the polymorphism 634C / G and the presence of RD is reported

mainly in relation to allele C. The homozygous CC is associated to proliferative RD and to increased vitreous and serum levels of VEGF suggesting that the presence of the C allele is an independent risk factor for RD. The knowledgement of VEGF lead to the development of anti-VEGF drugs (pegaptanib, ranibizumab and bevacizumab) aiming to prevent pathological neovascularization. The anti-VEGF therapy is a reality in practice medical treatment of DR.

PMID: 21584427 [PubMed - as supplied by publisher]

Other treatment & diagnosis

Eye (Lond). 2011 May 13. [Epub ahead of print]

Colour photographs for screening in neovascular age-related macular degeneration: are they necessary?

Hibbs SP, Smith A, Chow LP, Downes SM.

Medical Sciences Division, Oxford University, Oxford, UK.

Aims: To investigate whether optical coherence tomography (OCT) with associated infra-red images provide enough information to determine treatment decisions in the management of neovascular age-related macular degeneration (nAMD), or whether retinal colour photography is also necessary.

Methods: In all, 87 OCT scans of 82 eyes with nAMD undergoing monitoring post ranibizumab treatment were taken using the Zeiss Stratus (Carl Zeiss Meditec, Jena, Germany; n=87) together with their corresponding infra-red images. Fundus colour photographs were also taken. These images were reviewed by an experienced assessor, and a ranibizumab treatment decision was made during a multidisciplinary team retinal image review meeting.

Results: In all, 30 OCT scans (34.5%) showed intraretinal or subretinal oedema. A total of 24 colour photographs (19.5%) demonstrated retinal haemorrhage. Corresponding OCT infra-red images gave poor sensitivity in detecting haemorrhages (0.176). In 16.7% of decisions to treat, haemorrhage alone was the deciding factor. Signs of disease activity seen only on colour photography were the deciding factor in clinical decisions for 8% of scans assessed.

Conclusions: The presence or increase of intra-retinal oedema is an important sign of activity triggering ranibizumab retreatment, but some eyes show signs of retinal haemorrhage without coexisting oedema. These haemorrhages are often only seen on either colour imaging or fundoscopy and are unclear or invisible on OCT scans and infra-red images. Therefore, although retinal colour photography creates additional expense, it is indispensable for making informed retreatment decisions, if patients are monitored using retinal imaging alone.Eye advance online publication, 13 May 2011; doi:10.1038/eye.2011.90.

PMID: 21587273 [PubMed - as supplied by publisher]

Invest Ophthalmol Vis Sci. 2011 May 19. [Epub ahead of print]

Assessment of Reading Behaviour with an Infrared Eyetracker following 360 Degree Macular Translocation for Age Related Macular Degeneration.

Uppal G, Feely M, Crossland M, Membrey L, Lee J, da Cruz L, Rubin GS.

Moorfields Eye Hospital, London.

Purpose: Macular translocation (MT360) is complex surgery used to restore reading in exudative age related macular degeneration (AMD). MT360 involves retinal rotation and subsequent oculomotor globe

counter-rotation and is not without significant surgical risk. This study attempts to gauge the optimal potential of MT360 in restoring reading ability and describe the quality and extent of this recovery.

Methods: We observed the 6 best outcomes from a consecutive series of 23 MT360 cases. Reading behaviour and fixation characteristics were examined with an infrared eyetracker. Results were compared to age matched normal subjects and patients with untreated exudative and non-exudative AMD. Retinal sensitivity was examined with microperimetry to establish threshold visual function.

Results: MT360 produced significant improvements in visual function over untreated disease and approximated normal function for reading speed and fixation quality. Relative to the comparative groups, eyetracking revealed the MT360 cohort generated a greater number of horizontal and vertical saccades, of longer latency and reduced velocity. In contrast saccadic behaviour when reading (forward and regressive saccades) closely matched normal function. Microperimetry revealed a reduction in the central scotoma with 3 patients recovering normal foveal sensitivity.

Discussion: Near normal reading function is recovered despite profound surgical disruption to anatomy (retinal/oculomotor). MT360 restores foveal function sufficient to produce a single stable locus of fixation, with marked reduction of the central scotoma. Despite the limitations on saccadic function, the quality of reading saccadic behaviour is maintained with good reading ability. Oculomotor surgery appears not to limit reading ability and retinal surgery approximates towards normal macular function.

PMID: 21596822[PubMed - as supplied by publisher]

Epidemiology & pathogenesis

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

Retinal Arteriolar Wall Signs and Early Age-Related Macular Degeneration: The Singapore Malay Eye Study.

Cheung CM, Cheung CY, Yang EL, Mitchell P, Wang JJ, Wong TY.

Singapore National Eye Centre, Singapore; Singapore Eye Research Institute, Singapore.

PURPOSE: To determine whether retinal arteriolar wall signs are associated with early age-related macular degeneration (AMD).

DESIGN: Population-based cross-sectional study.

METHODS: The Singapore Malay Eye Study (SiMES) is a population-based eye survey including 3280 (78.7% response) persons aged 40 to 80 years. Retinal arteriolar wall signs and AMD were assessed from photographs by trained technicians, according to standardized protocols. Data on major cardiovascular risk factors and blood pressure were collected.

RESULTS: Of the 3280 participants, 2541 had photographs that were gradable for both AMD and retinal arteriolar wall signs. Early AMD was present in 76 subjects. There were no significant associations of any retinal arteriolar wall signs with early AMD. For specific AMD signs, retinal arteriolar wall opacification was associated with presence of soft distinct drusen (odds ratio [OR] 1.58, 95% confidence interval [CI]: 1.06, 2.35). This association was most significant among non-statin users (OR 1.90, 95% CI: 1.23, 2.93). Focal arteriolar narrowing was associated with retinal hypopigmentation (OR 1.67, 95% CI: 1.02, 2.73). Arteriovenous nicking was not associated with soft drusen (OR 0.89, 95% CI: 0.51, 1.57), hyperpigmentation (OR 0.49, 95% CI: 0.22, 1.08), or hypopigmentation (OR 0.86, 95% CI: 0.46, 1.61).

CONCLUSIONS: Retinal arteriolar wall signs are not consistently associated with early AMD. We report a new association of retinal arteriolar wall opacification and the presence of soft drusen. This finding could support the hypothesis of a link between lipids and drusen formation.

PMID: 21570050 [PubMed - as supplied by publisher]

Eye (Lond). 2011 May 20. [Epub ahead of print]

Sub-lytic C5b-9 induces functional changes in retinal pigment epithelial cells consistent with age-related macular degeneration.

Lueck K, Wasmuth S, Williams J, Hughes TR, Morgan BP, Lommatzsch A, Greenwood J, Moss SE, Pauleikhoff D.

Ophtha-Lab at Department of Ophthalmology, St Franziskus Hospital, Muenster, Germany.

Purpose: There is evidence for complement dysfunction in age-related macular degeneration (AMD). Complement activation leads to formation of the membrane attack complex (MAC), known to assemble on retinal pigment epithelial (RPE) cells. Therefore, the effect of sub-lytic MAC on RPE cells was examined with regard to pro-inflammatory or pro-angiogenic mediators relevant in AMD.

Methods: For sub-lytic MAC induction, RPE cells were incubated with an antiserum to complement regulatory protein CD59, followed by normal human serum (NHS) to induce 5% cell death, measured by a viability assay. MAC formation was evaluated by immunofluorescence and FACS analysis. Interleukin (IL)-6, -8, monocytic chemoattractant protein-1 (MCP-1), and vascular endothelial growth factor (VEGF) were quantified by enzyme-linked immunosorbent assay (ELISA). Intracellular MCP-1 was analysed by immunofluorescence, vitronectin by western blotting, and gelatinolytic matrix metalloproteinases (MMPs) by zymography.

Results: Incubation of RPE cells with the CD59 antiserum followed by 5% NHS induced sub-lytic amounts of MAC, verified by FACS and immunofluorescence. This treatment stimulated the cells to release IL-6, -8, MCP-1, and VEGF. MCP-1 staining, production of vitronectin, and gelatinolytic MMPs were also elevated in response to sub-lytic MAC.

Conclusions: MAC assembly on RPE cells increases the IL-6, -8, and MCP-1 production. Therefore, sub-lytic MAC might have a significant role in generating a pro-inflammatory microenvironment, contributing to the development of AMD. Enhanced vitronectin might be a protective mechanism against MAC deposition. In addition, the increased expression of gelatinolytic MMPs and pro-angiogenic VEGF may be associated with neovascular processes and late AMD.Eye advance online publication, 20 May 2011; doi:10.1038/eye.2011.109.

PMID: 21597483[PubMed - as supplied by publisher]

Genetics

Am J Epidemiol. 2011 May 16. [Epub ahead of print]

Systematic Review and Meta-Analysis of the Association Between Complement Component 3 and Age-related Macular Degeneration: A HuGE Review and Meta-Analysis.

Thakkinstian A, McKay GJ, McEvoy M, Chakravarthy U, Chakrabarti S, Silvestri G, Kaur I, Li X, Attia J.

Abstract

The authors performed a meta-analysis to estimate the magnitude of polymorphism effects for the complement component C3 gene (C3) and their possible mode of action on age-related macular degeneration (AMD). The meta-analysis included 16 and 7 studies for rs2230199 and rs1047286, respectively. Data extraction and risk of bias assessments were performed in duplicate, and heterogeneity and publication bias were explored. There was moderate evidence for association between both polymorphisms and AMD in Caucasians. For rs2230199, patients with CG and GG genotypes were 1.44 (95% confidence interval (CI): 1.33, 1.56) and 1.88 (95% CI: 1.59, 2.23) times more likely to have AMD than patients with the CC genotype. For rs1047286, GA and AA genotypes had 1.27 (95% CI: 1.15, 1.41) and 1.70 (95% CI: 1.27, 2.11) times higher risk of AMD than did GG genotypes. These gene effects suggested an additive model. The

population attributable risks for the GG/GC and AA/GA genotypes are approximately 5%-10%. Subgroup analysis by ethnicity indicates that these variants are very infrequent in Asians and that the observed gene effects are based largely on the high frequency within Caucasian populations. This meta-analysis supports the association between C3 and AMD and provides a robust estimate of the genetic risk.

PMID: 21576320 [PubMed - as supplied by publisher]

Brain. 2011 May 15. [Epub ahead of print]

Fibulin-5 mutations link inherited neuropathies, age-related macular degeneration and hyperelastic skin.

Auer-Grumbach M, Weger M, Fink-Puches R, Papic L, Fröhlich E, Auer-Grumbach P, El Shabrawi-Caelen L, Schabhüttl M, Windpassinger C, Senderek J, Budka H, Trajanoski S, Janecke AR, Haas A, Metze D, Pieber TR, Guelly C.

1 Department of Internal Medicine, Division of Endocrinology and Metabolism, Medical University Graz, Graz, 8036, Austria.

Abstract

To identify the disease-causing gene responsible for an autosomal dominantly inherited Charcot-Marie-Tooth neuropathy subtype in a family excluded for mutations in the common Charcot-Marie-Tooth genes, we used array-based sequence capture to simultaneously analyse the disease-linked protein coding exome at chromosome 14q32. A missense mutation in fibulin-5, encoding a widely expressed constituent of the extracellular matrix that has an essential role in elastic fibre assembly and has been shown to cause cutis laxa, was detected as the only novel non-synonymous sequence variant within the disease interval. Screening of 112 index probands with unclassified Charcot-Marie-Tooth neuropathies detected two further fibulin-5 missense mutations in two families with Charcot-Marie-Tooth disease and hyperextensible skin. Since fibulin-5 mutations have been described in patients with age-related macular degeneration, an additional 300 probands with exudative age-related macular degeneration were included in this study. Two further fibulin-5 missense mutations were identified in six patients. A mild to severe peripheral neuropathy was detected in the majority of patients with age-related macular degeneration carrying mutations in fibulin-5. This study identifies fibulin-5 as a gene involved in Charcot-Marie-Tooth neuropathies and reveals heterozygous fibulin-5 mutations in 2% of our patients with age-related macular degeneration. Furthermore, it adumbrates a new syndrome by linking concurrent pathologic alterations affecting peripheral nerves, eyes and skin to mutations in the fibulin-5 gene.

PMID: 21576112 [PubMed - as supplied by publisher]

Pre-clinical

J Neural Eng. 2011 May 18;8(3):035003. [Epub ahead of print]

Retinal ganglion cell responses to voltage and current stimulation in wild-type and rd1 mouse retinas.

Goo YS, Ye JH, Lee S, Nam Y, Ryu SB, Kim KH.

Department of Physiology, Chungbuk National University School of Medicine, Cheongju 361-763, Korea.

Abstract

Retinal prostheses are being developed to restore vision for those with retinal diseases such as retinitis

pigmentosa or age-related macular degeneration. Since neural prostheses depend upon electrical stimulation to control neural activity, optimal stimulation parameters for successful encoding of visual information are one of the most important requirements to enable visual perception. In this paper, we focused on retinal ganglion cell (RGC) responses to different stimulation parameters and compared threshold charge densities in wild-type and rd1 mice. For this purpose, we used in vitro retinal preparations of wild-type and rd1 mice. When the neural network was stimulated with voltage- and current-controlled pulses, RGCs from both wild-type and rd1 mice responded; however the temporal pattern of RGC response is very different. In wild-type RGCs, a single peak within 100 ms appears, while multiple peaks (approximately four peaks) with ~10 Hz rhythm within 400 ms appear in RGCs in the degenerated retina of rd1 mice. We find that an anodic phase-first biphasic voltage-controlled pulse is more efficient for stimulation than a biphasic current-controlled pulse based on lower threshold charge density. The threshold charge densities for activation of RGCs both with voltage- and current-controlled pulses are overall more elevated for the rd1 mouse than the wild-type mouse. Here, we propose the stimulus range for wild-type and rd1 retinas when the optimal modulation of a RGC response is possible.

PMID: 21593549 [PubMed - as supplied by publisher]

Ann Biomed Eng. 2011 May 18. [Epub ahead of print]

Angiogenesis-Associated Crosstalk Between Collagens, CXC Chemokines, and Thrombospondin Domain-Containing Proteins.

Rivera CG, Bader JS, Popel AS.

Department of Biomedical Engineering, School of Medicine, Johns Hopkins University, 720 Rutland Avenue, 613 Traylor Bldg, Baltimore, MD, 21205, USA, cgrivera@jhu.edu.

Abstract

Excessive vascularization is a hallmark of many diseases including cancer, rheumatoid arthritis, diabetic nephropathy, pathologic obesity, age-related macular degeneration, and asthma. Compounds that inhibit angiogenesis represent potential therapeutics for many diseases. Karagiannis and Popel [Proc. Natl. Acad. Sci. USA 105(37):13775-13780, 2008] used a bioinformatics approach to identify more than 100 peptides with sequence homology to known angiogenesis inhibitors. The peptides could be grouped into families by the conserved domain of the proteins they were derived from. The families included type IV collagen fibrils, CXC chemokine ligands, and type I thrombospondin domain-containing proteins. The relationships between these families have received relatively little attention. To investigate these relationships, we approached the problem by placing the families of proteins in the context of the human interactome including >120,000 physical interactions among proteins, genes, and transcripts. We built on a graph theoretic approach to identify proteins that may represent conduits of crosstalk between protein families. We validated these findings by statistical analysis and analysis of a time series gene expression data set taken during angiogenesis. We identified six proteins at the center of the angiogenesis-associated network including three syndecans, MMP9, CD44, and versican. These findings shed light on the complex signaling networks that govern angiogenesis phenomena.

PMID: 21590489 [PubMed - as supplied by publisher]