Demir et al., Int J Ophthalmic Pathol 2012, 1:2
http://dx.doi.org/10.4172/2324-8599.1000104

International Journal of Ophthalmic Pathology

Research Article

A SCITECHNOL JOURNAL

Interleukin-11: A Novel Agent in Retinal Ischemia-Reperfusion Injury

Tamer Demir[1], Azat Alinak[1], Ahmet Godekmerdan[2], Burak Turgut[1]* and Nesrin Demir[2]

Abstract

Objective: To investigate the protective effect of recombinant human IL-11 (rhIL-11) administered in a systemic manner on retina tissue during ischemia/reperfusion (I/R) injury in a guinea pig model.

Study design/materials and methods: An experimental study in retinal I/R. Placebo, ischemia/sham, ischemia/rhIL-11 groups including five animals in each were formed from male albino guinea pigs. Retinal ischemia was induced by cannulating the anterior chambers and lifting the bottle to a height of 205 cm for 90 Min in the sham and ischemia/rhIL-11 groups. The ischemia/sham and ischemia/rhIL-11 groups received 0.1 cc of a saline solution and 5 µg/kg/day rhIL-11 intraperitoneally one hour before the ischemic insult and during two days of reperfusion, respectively. The guinea pigs were sacrificed for biochemical analysis and the levels of tumor necrosis factor alpha (TNF-α), transforming growth factor beta (TGF-β) and interleukin-6 (IL-6) in retina were analyzed with ELISA. Mann–Whitney-U and Kruskal–Wallis tests were used for statistical analysis.

Results: The mean TNF-α level of the sham group was statistically significantly higher than that of the placebo group (p=0.008). The mean TNF-α levels of the placebo and ischemia/rHIL-11 groups were significantly different (p=0.008). The mean retinal TNF-α level of the ischemia/rHIL-11 group was statistically significantly lower than that of the sham group (p=0.008). The mean retinal TGF-β level of the sham group was statistically significantly higher than that of the placebo group (p=0.008). However, the mean retinal TGF-β levels of the placebo and ischemia/rHIL-11 groups were not statistically significantly different (p=0.690). The mean retinal TGF-β level of the ischemia/rHIL-11 group was statistically significantly lower than that of the sham group (p=0.032). The mean retinal IL-6 level of the sham group was significantly higher than that of the placebo group (p=0.008), while there was no statistically significant difference between the placebo group and ischemia/rHIL-11 group for retinal IL-6 levels (p=1.00). The mean retinal IL-6 level of the ischemia/rHIL-11 group was significantly lower than that of the sham group (p=0.008).

Conclusion: rhIL-11 treatment reduces the levels of TNF-α, IL-6 and TGF-β in the retina of the ischemia/reperfusion-injured guinea pig retinas.

Keywords: Retinal ischemia/reperfusion injury; Recombinant human IL-11; TNF-α; IL-6; TGF-β

***Corresponding author:** Burak Turgut, Associate Professor of Ophthalmology, Fırat University School of Medicine, Department of Ophthalmology, Elazığ, Turkey, Tel: +904242333555; Fax: +904242388096; E-mail: drburakturgut@gmail.com

Received: October 31, 2012 **Accepted:** December 07, 2012 **Published:** December 14, 2012

Abbreviations: rhIL-11: Recombinant Human Interleukin-11; TNF-α: Tumor Necrosis Factor-α; TGF-β: Transforming Growth Factor-β; IL-6: Interleukin-6

Introduction

The retina is highly sensitive to ischemic injury and reperfusion, both of which inevitably result in cellular damage and death. Reperfusion induces the synthesis of inflammatory mediators, oxygen derived free radicals and lipid mediators, and activation of the bone-marrow born cells [1]. It has been known that the glial cells exposed to ischemia hasten the death of the retinal ganglion cells by TNF-α synthesis [2]. In ischemia-reperfusion damage, the level of IL-6 in the retina has been shown to significantly increase and TGF-β has been shown to be protective [3,4].

Recombinant human IL-11 (rhIL-11) is a mediator that plays a role in hematopoiesis and hemopoiesis and consists of 199 amino acids. The molecular weight of rhIL-11 is 23 kDs. It was first described by Paul et al in 1990 [5]. Recombinant human (rh) IL-11 is produced by recombinant DNA technology in E coli bacteria (Oprelvekin, Neumega, Wyeth, USA). It has been used in the patients with non-myeloid malignancies receiving immunosuppressive chemotherapy over bone marrow and requiring thrombocyte infusion [6].

Moreland et al. have reported that rhIL-11 reduces the production of the proinflammatory cytokines and nitric oxide levels [7]. rhIL-11 shows its protective effect by down regulating the expression of TNF-α and IL-1β, inhibiting the synthesis of nitric oxide, and stimulating cellular proliferation and differentiation [6]. It has also been shown to act via reducing oxidative stress and up-regulating Heat Shock Protein 25 [8]. Another study has shown that it acts by reducing the levels of mRNA of pro inflammatory cytokines such as IFN- γ [9].

The present study aimed to investigate the protective effect of rhIL-11 administered in a systemic manner on retina tissue during ischemia/reperfusion (I/R) injury in a guinea pig model.

Materials and Methods

Experimental protocol

Fifteen male albino guinea pigs with a mean weight of 500 g (range: 470–640g) were used in the study. All the procedures involving animals were conducted in accordance with the guidelines of Association for Research in Vision and Ophthalmology Resolution on the use of Animals in Research. All the animals were housed in individual cages and maintained under standard conditions at the Experimental Research Center of Fırat University. The study protocol was approved by the Institutional Animal Care and Use Committee of Fırat University.

Groups

Three groups of guinea pigs were established randomly, with five animals in each.

The first group was determined as the placebo group. In this group, no ischemia or reperfusion was induced, and the animals

(n=5) were administered 0.1 cc of a saline solution intraperitoneally as placebo.

The second group was determined as the sham group. In this group, ischemia and reperfusion were induced, and the animals (n=5) were administered a saline solution intraperitoneally as placebo (n=5).

The third group was determined as the ischemia/rhIL-11 group. In this group, ischemia and reperfusion were induced, and the animals (n=5) were administered rhIL-11 were administered intraperitoneally.

Anesthesia technique

All the animals were anaesthetized with 50 mg/kg ketamine HCl and 5mg/kg xylazine HCl intramuscularly. Topical anesthetic consisting of 0.005% proparacaine HCl was administered to both eyes of each animal.

Induction of ischemia and reperfusion

Both eyes of all the animals were included in study. However, only one eye of the animals in each group was used for biochemical assay.

Pressure-induced retinal ischemia was achieved by cannulating both anterior chambers with a 27-gauge needle connected to a bottle of normal saline and lifting the bottle rapidly to a height of 205 cm in order to raise the intraocular pressure to 150 mm Hg. This lasted for 90 min, and reperfusion was established by lowering the saline bottle to the eye level. Then, the eyes were decannulated. The reperfusion period after ischemia lasted 24hours [10].

In the placebo group, which was not inflicted ischemia and reperfusion, 0.1 cc/day saline solutions was given intraperitoneally for two days. In the sham group, 0.1 cc of a saline solution was given intraperitoneally one hour before the ischemic insult and during two days of reperfusion period. In the ischemia/rhIL-11 group, 5 µg/kg/day Recombinant IL-11 was given intraperitoneally one hour before the ischemic insult and during two days of reperfusion period.

At the end of the second day of the experiment, all the animals were re-anesthetized, and both eyes of all the animals were rapidly enucleated and then, the animals were sacrificed using intracardiac thiopental sodium (50 mg/kg).

Biochemical assay

The enucleated eyes were immediately placed on the ice slices. They were then dissected coronally through the pars plana for biochemical assay. After removing the vitreous, the retinal tissue was gently peeled off from the choroidea and cut off from the optic disc with fine forceps and scissors under an operating microscope and washed with phosphate-buffered saline (pH 7.4, 0.2 M). The retina was frozen, smashed, and homogenized in phosphate-buffered saline at a dilution of 1/20. The retinal tissue was homogenized at a rate of 16.000 cycles/minute Ultra Turrax T25 Basic homogenizator (IKA Labortechnik, Germany). The supernatants were collected by centrifugation at 3500 rpm at +4°C for 45 Min, covered in aluminum foil and stored at –80°C until the biochemical assay.

The levels of TNF-α (pg/ml), IL-6 (pg/ml) and TGF-β (pg/ml) in the retina were analyzed with Biosource Rat TNF-α immunoassay kit (Cat. No: KRC3012, USA), Biosource Rat IL-6 ELISA kit (Cat. No: KRC0061, USA), and Biosource Rat TGF-β ELİSA kit (Cat. No: KAC1688, USA) in Triturus Grifols (Spain) full-automatic ELISA device.

Statistical analysis

Statistical analysis was performed using SPSS version 13.0 (SPSS Inc, Chicago, Illinois, USA). Mann–Whitney-U test was used to evaluate the differences between the groups. Kruskal–Wallis test was used to evaluate the intragroup differences. The data were expressed as mean ± SD. A p value less than 0.05 was considered statistically significant.

Results

The mean retinal TNF-α level of the placebo, sham, and ischemia/rHIL-11 groups were 222.80 ± 19.14, 787.80 ± 191.13, 321.60 ± 26.26 pg/ml, respectively. The mean retinal TNF-α level of the sham group was statistically significantly higher than that of the placebo group (p=0.008). The mean retinal TNF-α levels of the placebo and ischemia/rHIL-11 groups were also statistically significantly different (p=0.008). The mean retinal TNF-α level of the ischemia/rHIL-11 group was statistically significantly lower than that of the sham group (p=0.008) (Table 1 and Figure 1).

The mean retinal TGF-β levels of the placebo, sham and ischemia/rHIL-11 groups were 4640.0 ± 385.12, 7048.0 ± 1201.46, 4944.0 ± 784.14 pg/ml, respectively. The mean retinal TGF-β level of the sham group was significantly higher than that of the placebo group

Table 1: The levels of retinal TNF-α, TGF-β and IL-6 in the study groups.

Groups	TNF-α (pg/ml) Mean ± SD (Range)	TGF-β (pg/ml) Mean ± SD (Range)	IL-6 (pg/ml) Mean ± SD (Range)
Placebo	222.80 ± 19.14[1] *(194-247)*	4640.0 ± 385.12[a] *(4640- 5600)*	37.90 ± 7.62* *(29.6-48.4)*
Sham	787.80 ± 191.13[2] *(467-980)*	7048.0 ± 1201.46[b] *(6000-8960)*	148.70 ± 38.99** *(86.9-194)*
Ischemia/ rhIL-11	321.60 ± 26.26[3] *(289-361)*	4944.0 ± 784.14[c] *(4160-6240)*	43.46 ± 19.78*** *(27.1-69.4)*

Notes:

[1]p=0.008 for the sham group vs the placebo group; [2]p=0.008 for the ischemia/rHIL-11 group vs the sham group (p=0.008); [3]p=0.008 for the placebo vs the ischemia/rHIL-11 group.

[a]p=0.008 for the sham group vs the placebo group; [b]p=0.032 for the ischemia/rHIL-11 group vs the sham group; [c]p=0.690 for the placebo group vs ischemia/rHIL-11 group.

*p=0.008 for the sham group vs the placebo group; **p=0.008 for the ischemia/rHIL-11 group vs the sham group; ***p=1.00 for placebo vs ischemia/rHIL-11 group.

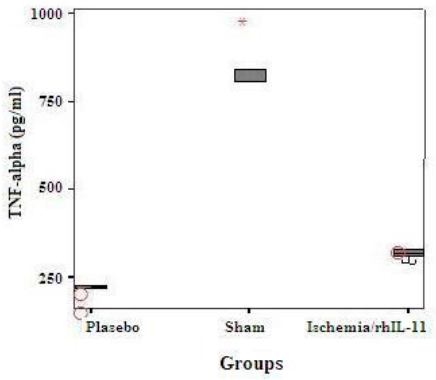

Figure 1: The comparison of the retinal TNF-α levels among the study groups* p<0.05, statistically significant difference.

(p=0.008). However, there was no statistically significant difference between the placebo group and ischemia/rHIL-11 group for retinal TGF-β level (p=0.690). The mean retinal TGF-β level of the ischemia/rHIL-11 group was statistically significantly lower than that of the sham group (p=0.032) (Table 1 and Figure 2).

The mean retinal IL-6 levels of the placebo, sham, and ischemia/rHIL-11 groups were 37.90 ± 7.62, 148.70 ± 38.99, 43.46 ± 19.78 pg/ml, respectively. The mean retinal IL-6 level of the sham group was significantly higher than that of the placebo group (p=0.008), while the mean retinal IL-6 levels of the placebo and ischemia/rHIL-11 groups were not statistically significantly different (p=1.00). The mean retinal IL-6 level of the ischemia/rHIL-11 group was statistically significantly lower than that of the sham group (p=0.008) (Table 1 and Figure 3).

Discussion

Retinal ischemia is one of the most common causes of loss of vision and blindness. Ischemia plays a crucial role in vaso-occlusive and vaso-proliferative diseases of the retina. Diabetes mellitus, retinal artery occlusion, retinal vein occlusion, retinopathy of prematurity, sickle cell anemia, and ocular inflammatory disorders commonly cause the ischemic injury in the retina [11].

Numerous studies have demonstrated that free radicals play a role in retinal ischemic injury [1,2,12]. They cause tissue injury through lipid peroxidation in the cell membranes, alteration in the structure of the proteins, carbohydrates, nucleic acids, and DNA, disturbance of calcium balance and stimulation of the release of excitatory amino acids like aspartate and glutamate [12,13]. Yoneda et al. have determined that IL-1β plays a role in ischemia-reperfusion injury in a rat model and that receptor antagonists of IL-1β prevent ischemic injury [14]. Additionally, the levels of IL-1β, TNF-α, IFN-γ, TGF-β and IL-6 have been reported to increase in IR injury and that IL-1β mediates the degeneration in the inner retinal layers [15].

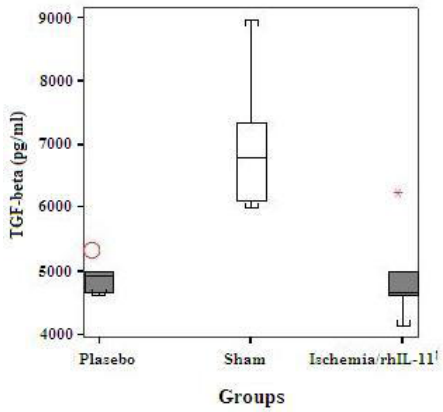

Figure 2: The comparison of the retinal TGF-β levels among the study groups* p<0.05, statistically significant difference.

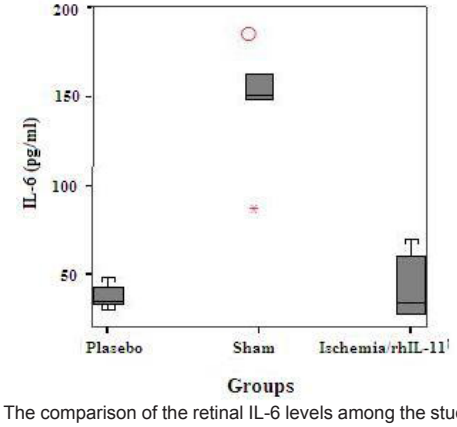

Figure 3: The comparison of the retinal IL-6 levels among the study groups* p<0.05, statistically significant difference.

TNF-α is a messenger inducing the apoptosis in retinal ganglion cells. Although TNF-α at picogram levels is considered non-cytotoxic, it induces cell death by ceasing the survival signals during neurodegeneration. Additionally, it has been known that TNF-α is also responsible for the glial changes and axonal degeneration in the optic nerve, which is observed in patients with AIDS [16]. TNF-α increases the production of the nitric oxide via induction of nitric oxide synthetase in astrocytes. Nitric oxide causes lipid peroxidation in the cell membrane by interacting with O_2^- radical and peroxy nitrite in IRI [17]. Fontaine et al. have found that the activation of TNF-α receptor 1 promotes the cell death and that the activation of TNF-α receptor 2 has neuro protective effects when mouse retina is exposed to IRI [18]. In our study, after IRI of the retina, it was found that the levels of TNF-α in the sham group were significantly higher than those of the placebo group (p=0.008). TNF-α is known to be a potent inflammatory cytokine following ischemic retinal injury. It is released by reactive macrophages, astrocytes, microglias and retinal glial cells during the inflammatory process. Following the injury in IR, the release of TNF-α stimulates nitric oxide and excitotoxins and consequently plays a role in ischemic injury [2,19]. TNF-α increases the production of nitric oxide by inducing nitric oxide synthetase. Nitric oxide interacts with superoxide and peroxy nitrite radicals, and thus disrupts the structure of the cell membrane by lipid peroxidation, thereby causing ischemic injury [20].

In another study evaluating the astrocyte cell culture in human lamina cribrosa, Yu et al were the first to find that the levels of αB-crystalline, TGF-β1 and TGF-β2 were elevated in the ischemia reperfusion process. Additionally, they demonstrated that the usage of TGF-β neutralizing antibodies down regulates the levels of αB-crystalline and protects the cells from IRI [21]. Welge-Lussen et al. demonstrated that the levels of αB-crystalline were increased via the stimulation by TGF-β in the cells of trabecular meshwork and ciliary muscle. Thus, it has been considered that TGF-β1 and TGF-β2 are potent inducers of αB-crystalline, a heat shock protein, all of which may be responsible for IRI [22]. In our study, TGF-β levels of the sham group were significantly higher than those of the placebo group. In a recent study, it has been demonstrated that the levels of αβ-crystalline were increased following the period of cerebral ischemia-reperfusion [21]. In another study, an increase in the synthesis of mRNA and protein of αβ-crystalline has been observed in the astrocytes of the optic nerve head during reperfusion process. This molecule is a heat shock protein that generates after ischemia [22]. In the glial cells and neurons in the central nerve system, HSP70 and HSP27 molecules provide the expression of mRNA and protein and consequently, the expression of TGF-β1 during the period of ischemia and reperfusion. TGF-β contributes to IRI process by increasing the production of reactive oxygen radicals. Additionally, it was determined that other factors mediating IR also increased the intensity of ischemic injury in the optic nerve head by increasing the expression of TGF-β [21]. Decreasing in the TGF-β levels by rhIL-11 might reduce the levels of

αB-crystalline and other heat shock proteins and might protect the cells from IRI.

It has been shown that the protein and mRNA of Endogenic IL-6 increase following IR. These data support that increase in the endogenic IL-6 is a defense mechanism of inner retinal layers including retinal ganglion cells after IRI. In addition, microglial-phagositic cells play an important role in this mechanism [3].

Fischer et al. have demonstrated that IL-6 might augment the ischemic injury [23]. In our study, it was determined that the mean IL-6 level of the sham group was significantly higher than that of the placebo group (0.008). Sappington et al. showed that the expression of Bax and Bcl-2 proteins inducing apoptosis increased in the retinal ganglion cells during ischemic injury. The increase in the Bax and Bcl-2 proteins play a role in injury to retinal ganglion cells that is induced by high-pressure [24]. Previous studies have shown that nitric oxide and TNF-α released by glial cells accelerate the death of the retinal ganglion cells [25]. IL-6 has been shown to affect the lifetime of the ganglion cells by regulating the Bax and Bcl-2 gene expressions [26].

An earlier study evaluating rhIL-11 demonstrated that the levels of TNF-α, IL-6 and IL-1β increased following intestinal ischemia and that the levels of these cytokines were reduced by rhIL-11. A possible mechanism of this condition has been suggested as increased MHC Class I and II antigen presenting cells in intestinal diseases, and it has also been suggested that these cells may be inhibited by IL-11. Another possible mechanism is the modulation of IFN-γ gene expression by NFκB, thereby suppressing the levels of the inflammatory cytokines such as TNF-α, IL-1β, IL-6 [27]. In another study, it was reported that the levels of TGF-β reduced and the levels of IFN-γ decreased via the increase in the levels of IL-11. Similarly, it was emphasized that IL-11 decreases the levels of GM-CSF [28].

In our study, while the levels of TNF-α of the ischemia/rhIL-11 group were significantly higher those of the placebo group, no statistically significant difference was determined between the TGF-β and IL-6 levels. The levels of TNF-α, TGF-β and IL-6 of the ischemia/rhIL-11 group were significantly lower than those of the sham group. RhIL-11 also inhibits the release of IFN-γ and IL-2 by activate T cells [29]. In an earlier study, it was demonstrated that IL-11 suppressed inflammation and reduced the levels of IFN-γ, TNF-α, IL-1β, IL-6, which are pro inflammatory the cytokines, and inducible nitric oxide synthetase in the colons of the rats with chronic colitis [29].

In conclusion, although the small sample size is a limitation in our study, we believe that IL-11, an anti-inflammatory cytokine, has an important role in IRI and that rh-IL is an agent that can be used in the treatment of ischemic retinal diseases because this drug reduces the levels of TNF-α, TGF-β and IL-6 significantly in ischemic retinal injury. However, further clinical and experimental studies are need for the use of rhIL-11 in clinical practice in patients with retinal disease.

Acknowledgements

Those involved in conducting the study would like to thank those who assisted with the collection of data, typing, editing of manuscript, its preparation, for review, and approval of the final manuscript. The authors report no conflicts of interest in this work.

References

1. Conger JD, Weil JV (1995) Abnormal vascular function following ischemia-reperfusion injury. J Investig Med 43: 431-442.
2. Tezel G, Wax MB (2000) Increased production of tumor necrosis factor-alpha by glial cells exposed to simulated ischemia or elevated hydrostatic pressure induces apoptosis in cocultured retinal ganglion cells. J Neurosci 20: 8693-8700.
3. Sanchez RN, Chan CK, Garg S, Kwong JM, Wong MJ, et al. (2003) Interleukin-6 in retinal ischemia reperfusion injury in rats. Invest Ophthalmol Vis Sci 44: 4006-4011.
4. Ahn KS, Sethi G, Aggarwal BB (2007) Simvastatin potentiates TNFalpha-induced apoptosis through the down-regulation of NFkappa B-dependent antiapoptotic gene products: Role of I kapa B alpha kinase and TGF-beta-activated kinase-1. J Immunol 178: 2507–2516.
5. Paul SR, Bennett F, Calvetti JA, Kelleher K, Wood CR, et al. (1990) Molecular cloning of a cDNA encoding interleukin 11, a stromal cell derived lymphopoietic and hematopoietic cytokine. Proc Natl Acad Sci USA 87: 7512–7516.
6. Cotreau MM, Stonis L, Strahs A, Schwertschlag US (2004) A multiple-dose, safety, tolerability, pharmacokinetics and pharmacodynamic study of oral recombinant human interleukin-11 (oprelvekin). Biopharm Drug Dispos 25: 291-296.
7. Moreland L, Gugliotti R, King K, Chase W, Weisman M, et al. (2001) Results of a phase-I/II randomized, masked, placebo-controlled trial of recombinant human interleukin-11 (rhIL-11) in the treatment of subjects with active rheumatoid arthritis. Arthritis Res 3: 247-252.
8. Ropeleski MJ, Tang J, Walsh-Reitz MM, Musch MW, Chang EB (2003) Interleukin-11-induced heat shock protein 25 confers intestinal epithelial-specific cytoprotection from oxidant stress. Gastroenterology 124: 1358-1368.
9. Peterson RL, Wang L, Albert L, Keith JC Jr, Dorner AJ (1998) Molecular effects of recombinant human interleukin-11 in the HLA-B27 rat model of inflammatory bowel disease. Lab Invest 78: 1503-1512.
10. Hughes WF (1991) Quantification of ischemic damage in the rat retina. Exp Eye Res 53: 573–582.
11. Peachey NS, Green DJ, Ripps H (1993) Ocular ischemia and the effects of allopurinol on functional recovery in the retina of the arterially perfused cat eye. Invest Ophthalmol Vis Sci 34: 58-65.
12. Kwon B, Youn BS, Kwon BS (1999) Functions of newly identified members of the tumor necrosis factor receptor/ligand superfamilies in lymphocytes. Curr Opin Immunol 11: 340-345.
13. Schmidt M, Giessl A, Laufs T, Hankeln T, Wolfrum U, et al. (2003) How does the eye breathe? Evidence for neuroglobin-mediated oxygen supply in the mammalian retina. J Biol Chem 278: 1932-1935.
14. Yoneda S, Tanihara H, Kido N, Honda Y, Goto W, et al. (2001) Interleukin-1beta mediates ischemic injury in the rat retina. Exp Eye Res 73: 661-667.
15. Hangai M, Yoshimura N, Honda Y (1996) Increased cytokine gene expression in rat retina following transient ischemia. Ophthalmic Res 28: 248-254.
16. Pfeffer K (2003) Biological functions of tumor necrosis factor cytokines and their receptors. Cytokine Growth Factor Rev 14: 185-191.
17. Hamby ME, Gragnolati AR, Hewett SJ, Hewett JA (2008) TGF beta 1 and TNF alpha potentiate nitric oxide production in astrocyte cultures by recruiting distinct subpopulations of cells to express NOS-2. Neurochem Int 52: 962-971.
18. Fontaine V, Mohand-Said S, Hanoteau N, Fuchs C, Pfizenmaier K, et al. (2002) Neurodegenerative and neuroprotective effects of tumor necrosis factor (TNF) in retinal ischemia: opposite roles of TNF receptor 1 and receptor 2. J Neurosci 22: RC216.
19. McGeer PL, Kawamata T, Walker DG, Akiyama H, Tooyama I, et al. (1993) Microglia in degenerative neurological disease. Glia 7: 84-92.
20. Geyer O, Almog J, Lupu-Meiri M, Lazar M, Oron Y (1995) Nitric oxide synthase inhibitors protect rat retina against ischemic injury. FEBS Lett 374: 399-402.
21. Yu AL, Fuchshofer R, Bikre M, Priglingera SG, Eibl KH, et al. (2007) Hypoxia/reoxygenation and TGF-β increase αB-crystallin expression in human optic nerve head astrocytes. Exp Eye Res 84: 694-706.
22. Welge-Lüssen U, May CA, Eichhorn M, Bloemendal H, Lütjen-Drecoll

E (1999) Alpha B-crystallin in the trabecular meshwork is inducible by transforming growth factor-beta. Invest Ophthalmol Vis Sci 40: 2235-2241.

23. Fisher J, Mizrahi T, Schori H, Yoles E, Levkovitch-Verbin H, et al. (2001) Increased post-traumatic survival of neurons in IL-6-knockout mice on a background of EAE susceptibility. J Neuroimmunol 119: 1–9.

24. Sappington RM, Chan M, Calkins DJ (2006) Interleukin-6 protects retinal ganglion cells from pressure-induced death. Invest Ophthalmol Vis Sci 47: 2932-2942.

25. Yuan L, Neufeld AH (2000) Tumor necrosis factor-α: a potentially neurodestructive cytokine produced by glia in the human glaucomatous optic nerve head. Glia 32: 42-50.

26. Sarup V, Patil K, Sharma SC (2004) Ciliary neurotrophic factor and its receptors are differentially expressed in the optic nerve transected adult rat retina. Brain Res 1013: 152-158.

27. Tsujikawa A, Ogura Y, Hiroshiba N, Miyamoto K, Kiryu J, et al. (1999) Retinal ischemia-reperfusion injury attenuated by blocking of adhesion molecules of vascular endothelium. Invest Ophthalmol Vis Sci 40: 1183-1190.

28. Wei R, Jonakait GM (1999) Neurotrophins and the anti-inflammatory agents interleukin-4 (IL-4), IL-10, IL-11 and transforming growth factor-beta1 (TGF-beta1) down-regulate T cell costimulatory molecules B7 and CD40 on cultured rat microglia. J Neuroimmunol 95: 8-18.

29. Trepicchio WL, Bozza M, Pedneault G, Dorner AJ (1996) Recombinant human IL-11 attenuates the inflammatory response through down-regulation of proinflammatory cytokine release and nitric oxide production. J Immunol 157: 3627-3634.

Author Affiliations

Top

[1]*Fırat University School of Medicine, Department of Ophthalmology, Elazığ, Turkey*
[2]*Fırat University School of Medicine, Department of Immunology, Elazığ, Turkey*