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Review Article

Neuroprotection and/or Neurogenesis: Effect of an Alpha7 nAChR Agonist in the Adult Mammalian Retina

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Abstract

Acetylcholine (ACh) has been investigated as a neuroprotective agent in the brain for several neurodegenerative diseases. Here, the neuroprotective and neurogenesis capability of an ACh receptor agonist in the adult vertebrate retina is discussed. In this review, the neuroprotective potential of ACh released from displaced starburst amacrine cells onto retinal ganglion cells is considered to be a novel function of ACh in adult mammalian retina. Evidence has been provided that starburst amacrine cells and ACh from displaced amacrine cells is compromised under glaucoma conditions, leading to a loss of neuroprotection and contributes to the death of retinal ganglion cells associated with this disease. Surprisingly, evidence has also been provided to indicate that the alpha7 nicotinic acetylcholine receptor (α7nAChR) agonist, PNU-282987, can induce neurogenesis in adult mammalian retinas after artificial stimulation of α7nAChRs on retinal pigment epithelium. A hypothesis is presented that the retinal pigment epithelium release a signaling molecule (or molecules) in response to PNU-282987 to cause cell cycle reentry in adult Muller glia to trigger of retinal progenitor cells that differentiate into mature new neurons. The implications of the endogenous neuroprotective ability of ACh in the adult retina and the induced neurogenesis of new mature neurons from Muller glia are discussed in this review.

Keywords: Neurogenesis; Neuroprotection; Retina; Acetylcholine; PNU-282987; Alpha7nAChR; BrdU

Abbreviations

ACh: Acetylcholine; α7nAChR: Alpha7 Nicotinic Acetylcholine Receptor; MLA: methyllycaconitine; RGC: Retinal Ganglion Cells; ELISA: Enzyme-Linked Immunosorbent Assay; PI3: Phosphoinositide 3; Akt, protein kinase B; Bcl-2: B-Cell Lymphoma 2; IOP: Intraocular Pressure; BrdU: Bromodeoxy Uridine; PBS: Phosphate Buffered Saline; DNA: Deoxyribo Nucleic Acid; RPE: Retinal Pigment Epithelium; RPC: Retinal Progenitor Cell; PAX6: Paired Box Protein; ChaT: Cholineacetyl Transferase; MAPk: Map Kinase; NMDA: N-Methyl-D-Aspartate

Review

Neuroprotection in the nervous system involves any intervention that results in preservation of neuronal structure and function. Neuroprotection can be achieved by direct effects on neurons or indirectly by interfering with the process that typically leads to cell death. Neurogenesis, on the other hand, is a process used by many lower organisms to form new neurons in response to cell loss or damage in order to recover function that has been lost. These two processes; neuroprotection and neurogenesis, are both involved in maintaining neuronal functional stability in an animal. However, although lower organisms possess extensive capacity for neural regeneration, evolutionarily higher organisms that include mammals, are limited in their ability to regenerate nerve cells and do not typically recover function from many neurodegenerative diseases [1]. In this article, the neuroprotection and neurogenic capabilities of an alpha7nAChR agonist, PNU-282987, in the retina of adult mammals is discussed.

PNU-282987 is a potent alpha7 nAChR agonist [2,3]. In binding studies using rat chimera cells, methyllycaconitine (MLA), a specific α7 nAChR antagonist, competitively bound to α7 nAChRs. In electrophysiology studies using rat hippocampal neurons, PNU-282987 evoked a rapidly desensitizing inward whole-cell current associated with the opening of the α7 nAChR channel allowing influx of sodium and calcium ions. This current was eliminated if MLA was introduced before PNU-282987 [2].

Why use an α7 nAChR agonist to study retinal neuroprotection and neurogenesis? Activation of α7 nAChRs in the brain has been linked to neuroprotection in several neurodegenerative diseases. There is strong evidence that α7 nAChRs are neuroprotective, reducing β-amyloid induced toxicity in Alzheimer's disease [4,5] and that the α7 nAChR plays a role in the pathophysiology of schizophrenia [6,7]. In the retina, RGCs, some cone bipolar cells and glycinergic amacrine cells express α7 nAChRs [8-10]. However, RGCs containing α7nAChRs [11-14] receive cholinergic input from a well-described population of starburst amacrine cells [15], which are the only source of ACh in the vertebrate retina.

Initial studies from Dr. Linn's lab demonstrated that activation of α7 nAChRs in the retina with ACh, nicotine or PNU-282987 provided neuroprotection against excitotoxic conditions in vitro, using primary cultures of isolated vertebrate RGCs. (Figure 1A-C) [16,17]. ELISA studies on isolated adult vertebrate RGCs confirmed that activation of α7 nAChR$_s$ on RGCs initiated the PI3-Akt-Bcl2 cell

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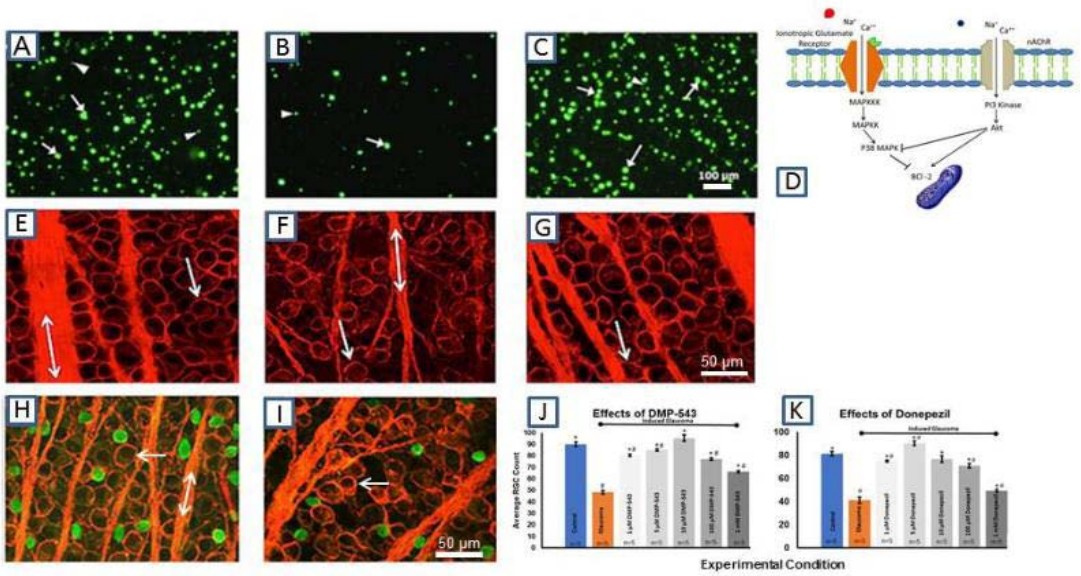

Figure 1: ACh-induced neuroprotection in the adult mammalian retina. Figure 1A-C represent isolated cultured pig RGCs labeled with calcein after cultured for 3 days. RGCs were isolated from all other retinal tissue using a two-step panning technique. Cells were plated at the same density in the three culture dishes. Isolated RGCs in Figure 1A were left untreated, cells in Figure 1B were treated with excessive glutamate (500 µM), while cells in Figure 1C were treated with 100 nM PNU-282987 for an hour before addition of excessive glutamate. PNU-282987 prevented the loss of isolated RGCs. Arrows representing large RGCs while arrowheads represent small RGCs. Figure 1D illustrates a schematic of the pathways involved in glutamate induced excitotoxicity in isolated RGCs as well as in the PNU-282987 induced cell survival pathway resulting from a series of ELISA and pharmacological studies. Figure. 1E-G represents 3 confocal images demonstrating RGCs labeled with antibodies against Thy 1.1. Figure 1E represents a typical confocal image obtained under control untreated conditons, while Figure 1F represents an image obtained from the contralateral eye from the same animal, from the same retinal location, 1 month after hypertonic saline injection. Loss of RGCs and defasciculation of axon bundles is apparent. Figure 1G represents the neuroprotective effect that occurs if 100 nM PNU-28987 is intravitreally injected into the vitreal chamber before performing the procedure to induce glaucoma. The image shown was obtained one month after the procedure was performed. Arrows point to RGC bodies, while double ended arrows represent axon bundles. Figure 1H-I represent double-labeled cells in the RGC layer in a flat-mounted retina. The red fluorescence represents RGCs labeled with antibodies against Thy 1.1. The green fluorescence represents displaced starburst amacrine cells that were labeled with antibodies against ChaT. One month after inducing glaucoma in one eye of an adult Long Evans rat, there is a corresponding loss of RGCs, defasciculation of RGC axon bundles and loss of displaced SACs (Figure. 1I) compared to its internal control (Figure. 1H). Figure 1J-K represent summarized experiments that count RGC survival after inducing glaucoma in the presence of various concentrations of the acetylcholinesterase inhibitor, Donepezil (Figure 1K), or in the presence of various concentrations of DMP-543 (Figure. 1J) to enhance the release of ACh from starburst amacrine cells. Donepezil and DMP-543 produced a dose-dependent neuroprotective effect in glaucoma-induced retinas. * represents a significant difference from the induced glaucoma effect, while # represents significance from the internal control. Significance = $P<0.05$.

survival pathway to prevent cell loss against excessive glutamate [18] after calcium ion influx through α7 nAChR channels (Figure 1D) [19] and inhibited the glutamate-induced apoptosis pathway (Figure 1D).

To determine if the neuroprotective effect of ACh shown in isolated primary cultured cells was also a physiological phenomenon, later studies provided evidence of neuroprotection using an *in vivo* rat glaucoma model. Hypertonic saline injections into the episcleral veins of adult rats, led to a significant increase of Intraocular Pressure (IOP) due to scarring and blockage of the trabecular meshwork [20] as well as a corresponding significant loss of RGCs one month after the procedure to induce glaucoma-like conditions [21,22]. Neuroprotective studies provided evidence that intravitreal injection of PNU-28297 before the procedure to induce glaucoma prevented any loss of RGCs [21] (Figure 1E-G). Further studies provided evidence that displaced starburst amacrine cells, which also reside in the RGC layer and synapse onto RGCs, were also compromised under glaucoma like conditions. The procedure to induce glaucoma resulted in a significant loss of displaced starburst amacrine cells (Figure 1H-I), led to a reduction of ACh content in the retina and a reduction of alpha7 nAChRs in the retina weeks before the loss of RGCs [23]. However, if the efficiency of the remaining ACh was enhanced in glaucoma induced retinas using the acetylcholinesterase inhibitor, Donepezil, or if DMP-543 was used to enhance ACh release from the remaining starburst amacrine cells, the typical loss of RGCs due to glaucoma was eliminated [23] (Figure 1J). These studies provided evidence that ACh released from starburst amacrine cells can provide endogenous neuroprotection to RGCs in the adult vertebrate retina, representing a previously undescribed function for ACh in the mature retina.

As intravitreal injections are invasive, further experiments were performed by directly applying PNU-282987 as eye drops to the adult vertebrate eyes in rats and mice. Eye drop application of the α7 nAChR agonist was also found to prevent the loss of RGCs after the procedure to induce glaucoma [22]. Interestingly, eye drop application of some concentrations of PNU-282987significantly increased the number of RGCs in the adult mammalian retina compared to internal controls from the untreated contralateral retina in the same animal [24,25] (Figure 2A-C), supporting the notion that neurogenesis of new cells in the RGC layer occurred. To investigate this possibility, the thymidine analog, bromodeoxyuridine (BrdU), was added to PBS eye drops containing PNU-282987 to label cells actively synthesizing DNA in mitotically active cells. In time course studies, BrdU positive

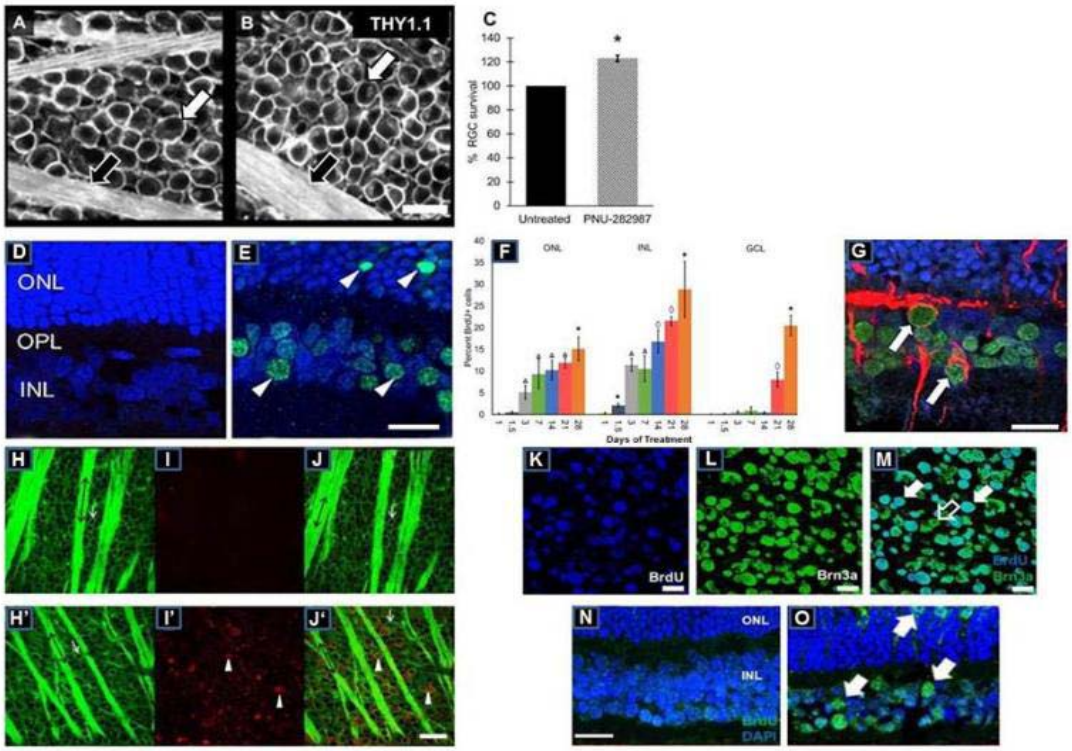

Figure 2: PNU-282987-induced neurogenesis in the adult mammalian retina. Topical application of 1 mM PNU-282987 to adult Long Evans rats increased the number of RGCs (Figure. 2A-C). Figure 2A and B represent flat-mounted confocal images of RGCs immunostained with antibodies against Thy 1.1 after daily eye drop treatments. Figure 2A represents an image obtained from an untreated eye, while the image in Figure. 2B represents an image obtained from the other eye of the same animal, from the same retinal region after topical treatment with eyedrops containing PBS and 1 mM PNU-282987. Eye drops were applied for two weeks. The animals were sacrificed and retinas were analyzed 2 weeks after the termination of the eye drop treatment. The bar graphs in Figure 2C demonstrate that application of PNU-282987 to the eye significantly increased RGC number. * represents a significant difference from internal untreated control eyes (N=12; P<0.05). Figure 2D-E represent retinal slices showing BrdU positive (green) in the inner nuclear layer (INL) and the outer nuclear layer (ONL) under untreated conditions (Figure. 2D) and 1 week after topical eye drop application of PBS containing 1 mM PNU-282987 and 1mg/ml BrdU to an adult rat eye (Figure. 2E). The retinal sections were labeled with DAPI to stain cell nuclei. The bar graphs shown in Figure. 2F summarize where and when BrdU positive cells emerge when eyes are treated with 1 mM PNU-282987 for various amounts of time. BrdU positive cells first emerge in the INL and do not appear in the ganglion cell layer (GCL) for 21 days. Figure 2G demonstrate several BrdU positive cells (green) emerging from labeled Muller glia (red). An adult Long Evans rat eye was treated with 1 mM PNU-282987 and 1mg/ml BrdU in PBS eye drops for 1 week before immunostaining the fixed retina with antibodies against vimentin to label Muller glia and against BrdU to label BrdU positive cells. Cell nuclei were stained with DAPI. Figures H-J' demonstrate how prolonged treatment with PNU-282987 and BrdU leads to BrdU positive RGCs in the RGC layer. The double stained confocal images shown in Figure H-J' illustrate an image of the GCL in a flat mounted retina under control untreated conditions and after topical application of PBS containing PNU-282987 and BrdU control untreated retinas stained with antibodies against Thy 1.1 (green), but fail to label any BrdU positive cells (2I). Figure 2J represents the merged image 2H and 2I. However, if the retinas were given eye drops containing PNU-282987 and BrdU for two weeks and were then removed and immunocytochemically processed at 4 weeks, the retina stained both with antibodies against Thy 1.1 (green, arrows and double-ended arrows, Figure. 2H') and with antibodies against BrdU (red, arrowheads, Figure. 2I'). The merged image (Figure. 2J') illustrate several BrdU positive RGCs (arrowheads). BrdU positive RGCs are also seen in flat-mounted retinal images shown in Figure 2K-M. After treating an adult rodent eye with eye drops containing 1 mM PNU-282987 and 1mg/ml BrdU for two weeks, the animal was sacrificed 4 weeks after beginning treatment and the retina was processed with antibodies against Brn3a (transcription factor for RGCs) and BrdU. Figure 2K show an image of the BrdU positive cells taken from the GCL. Figure 2L show an image of the Brn3a positive RGCs from the same image, while Figure 2M illustrates the merged image. Many Brn3a positive RGCs co-label with antibodies against BrdU. The confocal retinal sections shown in Figure 2N-O were obtained when supernatant from PNU-282987 treated retinal pigment epithelial cells was injected into the vitreal chamber of adult mice eyes. A rat RPE cell line was cultured to confluency before they were treated with 100 nM PNU-28297 for 24 hours. After the 24 hours, the PNU was extensively washed away and the remaining supernatant was collected and injected into an adult mouse eye (Figure 2N) that was then treated with eye drops containing BrdU for 2 weeks. Under these control conditions, after 2 weeks, no BrdU positive cells emerged in the animal. However, if the PNU-282987 treated RPE cells were extensively washed and then cultured for 3 days, collected RPE supernatant under this condition induced the image in Figure 2O when injected into adult mice that were only treated with BrdU.

cells first emerged from the inner nuclear layer, where the cell bodies for Müller glia are located. Immunocytochemistry studies determined that the first BrdU positive cells emerged from vimentin labeled Müller glia (Figure 2D-G), which also labeled with retinal progenitor cell markers, such as PAX6 and nestin, to suggest that proliferation of BrdU positive cells were initiated from Müller glia after treatment with PNU-282987/BrdU. Longer treatments with PNU-282987/BrdU resulted in BrdU-positive RGCs (Figure 2H-M), BrdU-positive cholineacetyltransferase (Chat)-positive starburst amacrine cells and BrdU-positive rhodopsin-positive photoreceptors double stained in the RGC layer, INL and ONL respectively [26]. Based on these results, we provided evidence that the α7 nAChR agonist, PNU-282987, stimulates proliferation of Müller glia in the adult rat retina, resulting in generation of new retinal neurons [25,26]. In other experiments, antibodies against PCNA (proliferating cell nuclear antigen), was used to support this hypothesis [26]. The effect of PNU-282987

occurs without injury, without inducing apoptosis, in the absence of exogenous specific growth factor stimulation and is eliminated if eye drops also contain the α7 nAChR antagonist, MLA [25].

The molecular and cellular mechanisms underlying the α7 nAChR agonist mediated neurogenic response are currently being examined to address what α7 nAChRs in the eye are involved in PNU-282987's effect and how does activation of these receptors trigger proliferation of new retinal neurons. Intriguingly, PNU-282987 cannot act on Müller glia directly, as they lack α7 nAChRs [28-30] [26]. In the retina, α7 nAChRs are found on RGCs, on bipolar cells and a subset of amacrine cells [8-10]. However, these retinal receptors cannot be responsible for proliferation of BrdU positive cells from Muller glia in adult rodents, as ACh is normally released from starburst amacrine cells onto RGCs without triggering neurogenesis. Instead, although retinal stem and progenitor cells have been identified from the ciliary marginal zone [31], the likely target for PNU-282987's effects are α7 nAChRs on retinal pigment epithelium in the eye. RPE cells have been found to have many important functions, such as phagocytic uptake and breakdown of shedded photoreceptor membranes, uptake, processing, transport and release of vitamin A (retinol), setting up the ion gradients within the interphotoreceptor matrix, building up the blood-retina barrier, and providing all transport from blood to the retina and back [32-34]. It may be that a signaling molecule (or molecules) that trigger neurogenesis from Müller glia is released from RPE when exposed to PNU-282987. Conditioned media collected from PNU-282987 treated, cultured RPE cells, can induce BrdU positive cells in the retina when injected into adult rats or mice eyes [26] (Figure 2N-O). Further studies are needed to substantiate this finding, to identify the molecule or molecules that can initiate proliferation and to determine the molecular pathways that lead to neurogenesis.

We have documented BrdU positive retinal neurons in all adult retinal nuclear layers in rats and mice after treatment with PNU-282987. As a result, activation of α7 nAChRs in the eye may be able to reverse the loss of neurons associated with any neurogenerative disease of the retina. Furthermore, if activation of α7 nAChRs in the eye leads to replacement of lost retinal neurons, many other neurodegenerative diseases in the central nervous system that are associated with α7 nAChRs could be explored. These results could lead to transformative treatments that reverse the loss of neurons associated with neurodegenerative disease, traumatic injury +/or age.

Conclusion

It is clear that acetylcholine release from starburst amacrine cells onto α7 nAChRs in the retina does not normally induce neurogenesis in adult mammals. We propose that *in vivo*, acetylcholine released from starburst amacrine cells in response to light has a neuroprotective function, as previously described now in several studies [21,22,35]. However, if RPE cells are stimulated with an exogenous α7 nAChR agonist, it is believed that a signaling molecule (or molecules) is released from RPE cells that stimulate Müller glial cell proliferation. Current work is targeting this issue. *In vivo*, PNU-282987 may be absorbed through the sclera at the back of the eye or enter the choroid circulation to reach the RPE cells [21]. It is not likely that stimulation of the α7 nChRs on RPE cells from endogenous retinal sources would occur under normal physiological conditions. Rather, α7 nAChR-induced neurogenesis is likely to be triggered by pharmacological stimulation of the RPE cells, whereas neuroprotection is more likely mediated directly at the starburst amacrine cell-retinal ganglion cell synapse under physiological conditions.

References

1. Gao Y, Yang Z, Li X. Regeneration strategies after the adult mammalian central nervous system injury. Regen Biomat. 2016; 3: 115-122.
2. Bodnar AL, Cortes-Burgos LA, Cook KK, Dinh DM, Groppi VE, Hajos M, et al. Discovery and structure-activity relationship of quinuclidinebenzamides as agonists of alpha7 nicotinic acetylcholine receptors. J Med Chem. 2005; 48: 905-908.
3. Walker DP, Wishka DG, Piotrowski DW, Jia S, Reitz SC, Yates KM, et al. Design, synthesis, structure-activity relationship and *in vivo* activity of azabicyclic aryl amides as alpha7 nicotinic acetylcholine receptor agonists. Biorg Med Chem. 2006; 14: 8219-8248.
4. Kawamata J, Shimohama S. Stimulating nicotinic receptors trigger multiple pathways attenuating cytotoxicity in models of Alzheimer's and Parkinson's diseases. J Alzheimer's Dis. 2011; 24: 95-109.
5. Oz M, Lorke DE, Yang KH, Petroianu G. On the interaction of β-amyloid peptides and α7-nicotinicacetylcholine receptors in Alzheimer's disease. Curr Alzheimer Res. 2013; 10: 618-630.
6. Winterer G, Gallinat J, Brinkmeyer J, Musso F, Kornhuber J, Thuerauf N, et al. Allosteric alpha-7 nicotinic receptor modulation and P50 sensory gating in schizophrenia: a proof-of-mechanism study. Neuropharmacology. 2013; 64: 197-204.
7. Young JW, Geyer MA. Evaluating the role of the alpha-7 nicotinic acetylcholine receptor in the pathophysiology and treatment of schizophrenia. Biochem Pharmacol. 2013; 86: 1122-1132.
8. Dmitrieva NA, Strang CE, Keyser KT. Expression of alpha 7 nicotinic acetylcholine receptors by bipolar, amacrine, and ganglion cells of the rabbit retina. J Histochem Cytochem. 2007; 55: 461-476.
9. Maneu V, Gerona G, Fernandez L, Cuenca N, Lax P. Evidence of alpha 7 nicotinic acetylcholine receptor expression in retinal pigment epithelial cells. Vis Neurosci. 2010; 27: 139-147.
10. Matsumoto H, Shibasaki K, Uchigashima M, Koizumi A, Kurachi M, Moriwaki Y, et al. Localization of acetylcholine-related molecules in the retina: implication of the communication from photoreceptor to retinal pigment epithelium. PLoS One. 2012; 7: e42841.
11. Keyser KT, Hughes TE, Whiting PJ, Lindstrom JM, Karten HJ. Cholinoceptive neuronsin the retina of the chick: an immunohistochemical study of the nicotinic acetylcholine receptors. Vis Neurosci. 1988; 1: 349-366.
12. Whiting PJ, Schoepfer R, Conroy WG, Gore MJ, Keyser KT, Shimasaki S, et al. Expression of nicotinic acetylcholine receptor subtypes in brain and retina. Mol Brain Res. 1991; 10: 61-70.
13. Keyser KT, Britto LGR, Schoepfer R, Whiting P, Cooper J, Conroy W, et al. Three subtypes of α-Bgt-sensitive nicotinic ACh receptors areexpressed in chick retina. J Neurosci. 1993; 13: 442-454.
14. Kaneda M, Hashimoto M, Kaneko A. Neuronal nicotinic acetylcholine receptors of ganglion cells in the cat retina. Jpn J Physiol. 1995; 45: 491-508.
15. Massey SC, Redburn DA. Transmitter circuits in the vertebrate retina. Prog Neurobiol. 1987; 28: 55-96.
16. Wehrwein E, Thompson SA, Coulibaly SF, Linn DM, Linn CL. Acetylcholine protection of adult pig retinal ganglion cells from glutamate-induced excitotoxicity. Invest Ophthalmol Vis Sci. 2004; 45: 1531-1543.
17. Iwamoto K, Mata D, Linn DM, Linn CL. Neuroprotection of rat retinal ganglion cells mediated through alpha7 nicotinic acetylcholine receptors. Neuroscience. 2013; 237: 184-198.
18. Asomugha C, Linn DM, Linn CL. ACh receptors link two signaling pathways to neuroprotection against glutamate-induced excitotoxicity in isolated pig RGCs. J Neurochem. 2010; 112: 214-226.

19. Brandt SK, Weatherly ME, Ware L, Linn DM, Linn CL. Calcium preconditioning triggers neuroprotection in retinal ganglion cells. Neuroscience. 2011; 172: 387-397.

20. Morrison JC, Moore CG, Deppimeier LM, Gold BG, Meshul CK, Johnson EC. A rat model of chronic pressure-induced optic nerve damage. Exp Eye Res. 1997; 64: 85-96.

21. Iwamoto K, Birkholtz P, Schipper A, Mata D, Linn DM, Linn CL. A nicotinic acetylcholinereceptor agonist prevents loss of retinal ganglion cells in a glaucoma model. Invest Ophthalmol Vis Sci. 2014; 55: 1078-1087.

22. Mata D, Linn DM, Linn CL. Retinal ganglion cell neuroprotection induced by activation of alpha7 nicotinic acetylcholine receptors. Neuropharmacology. 2015; 99: 337-346.

23. Cooley-Themm CA, Ameel Q, Linn DM, Linn CL. Loss of displaced starburst amacrine cells in a rat glaucoma model. Sci Pages of Ophthal. 2017; 1: 28-38.

24. Birkholz PJ, Gossman CA, Webster MK, Linn DM, Linn CL. Prevention of glaucoma induced retinal ganglion cell loss using alpha7 nAChR agonists. J Ophthal Vis Sci. 2016; 1: 1003.

25. Webster MK, Cooley-Themm CA, Barnett JD, Bach HB, Vannier JM, Webster SE, Linn CL. Evidence of BrdU positive retinal neurons after application of an alpha7 nAChR agonist. Neuroscience. 2017; 346: 437-446.

26. Linn C, Webster S, Webster M. Adult mammalian retinal regeneration. 2018.

27. Webster MK, Stanchfield M, Cooley-Themm CA, Webster S, Linn CL. Proliferation and neurogenic activation of Muller glia by an alpha7 nAChR agonist in the adult mammalian retina acts via retinal pigmented epithelium. 2018.

28. Wakakura M, Utsunomiya-Kawasaki I, Ishikawa S. Rapid increase in cytosolic calcium ion concentration mediated by acetylcholine receptors in cultured retinal neurons and Müller cells. Graefes Arch Clin Exp Ophthalmol. 1998; 236: 934-939.

29. Das AV, Edakkot S, Thoreson WB, James J, Bhattacharya S, Ahmad I. Membrane properties of retinal stem cells/progenitors. Prog Retin Eye Res. 2005; 24: 663-681.

30. Beckers S, Singhal S, Jones MF, Eastlake K, Cottrill PB, Jayaran H, et al. Acquisition of RGC phenotype in human Muller glia with stem cell characteristics is accompanied by upregulation of functional nicotinic ACh receptors. Mol Vis. 2013; 19: 1925-1936.

31. Miyake A, Araki M. Retinal stem/progenitor cells in the ciliary marginal zone complete retinal regeneration: a study of retinal regeneration in a novel animal model. Dev Neurobiol. 2014; 74: 739-756.

32. Luz-Madrigal A, Grajales-Esquivel E, McCorkle A, DiLorenzo AM, Barbosa-Sabanero K, Tsonis PA, et al. Reprogramming of the chick retinal pigmented epithelium after retinal injury. BMC Biol. 2014; 12: 28.

33. Schraermeyer U, Heimann K. Current understanding on the role of retinal pigment epithelium and its pigmentation. Pigment Cell Res.1999; 12: 219-236.

34. Nguyen-Ba-Charvet KT, Chedotal A. Development of retinal layers. C R Biol. 2014; 337: 153-159.

35. Zhou X, Cheng Y, Zhang R, Li G, Yang B, Zhang S, et al. Alpha7 nicotinic acetylcholine receptor agonist promotes retinal ganglion cell function via modulating GABAergic presynaptic activity in a chronic glaucomatous model. Sci Rep. 2017; 7: 1734.

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