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Review Article

Supplementary Materials

Modulation of microRNAs by natural compounds: A potential new strategy for glaucoma treatment

Eugenio Ragazzi

Studium Patavinum, University of Padova, 35122 Padova, Italy.

Corresponding Author
Prof. Dr. Eugenio Ragazzi
Studium Patavinum, University of Padova, 35122 Padova, Italy.
E-mail: eugenio.ragazzi@unipd.it, Tel: +393491016016

List of material

Table S1. Most relevant miRNA in glaucoma.

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Table S1. Most relevant miRNA in glaucoma.

miRNA	Functions/mechanisms	References	Glaucoma relevance
miR-21-5p	Induced in TM; increases AH outflow; neuroprotective	[1-4]	Possible therapeutical strategy for reducing IOP
miR-29 family (29a, 29b, 29c)	Antifibrotic; blocks ECM production via TGF-β	[5-9]	Strong therapeutic target for TM fibrosis in POAG
miR-122-5p	Associated with PXG and XFG; TGF-β signaling	[4,10,11]	Involved in fibrosis and ECM, overexpressed in AH
miR-125b miR-125b-5p	Involved in TGF-β signaling, TM remodeling, RGC damage	[4,8,11-13]	Appears in AH, TM, tears; therapeutic potential and reproducibility; consistent in 3+ studies
miR-125b-2-5p	Tear and AH biomarker in POAG/OHT	[4,8,12,14]	Non-invasive diagnostic potential
miR-143 miR-143-3p	Regulates apoptosis, TM, ECM, AH outflow	[4,8,13,15]	Therapeutic target; found in AH and TM; consistent in 3+ studies
miR-146b-5p	Tear biomarker in POAG. Upregulated in POAG	[4,13,16]	Possible diagnostic marker
miR-200 family	Regulates TM cell contraction and IOP	[8]	Functional target for IOP reduction; validated *in vivo*
miR-206	Targets BCL2/JUN and CCND1 genes of cell proliferation	[4,17]	Upregulated in POAG; biomarker validated in POAG
miR-302d-3p	Differentially expressed in POAG vs. controls and XFG	[4,11,14]	Potential subtype-specific biomarker ir AH
miR-451a	Associated with POAG; potential biomarker	[11,13]	Biomarker candidate
miR-486 miR-486-5p	Reduces oxidative stress and ECM via TGF-β/SMAD2	[8,13]	Biomarker candidate; TM-targeted therapy potential

Abbreviations: AH: aqueous humor; BCL2: B-cell leukemia/lymphoma 2 gene; CCND1: Cyclin D1 gene**;** ECM: extracellular matrix; IOP: intraocular pressure; JUN: Jun proto-oncogene; OHT: ocular hypertension; POAG: primary open-angle glaucoma; PXG: pseudoexfoliation glaucoma; RGC: retinal ganglion cell; SMAD2: small mother against decapentaplegic 2; TGF-β: transforming growth factor beta; TM: trabecular meshwork; XFG: exfoliated glaucoma.

References

1. Su, W.; Li, Z.; Jia, Y.; Zhu, Y.; Cai, W.; Wan, P.; Zhang, Y.; Zheng, S.G.; Zhuo, Y. microRNA-21a-5p/PDCD4 axis regulates mesenchymal stem cell-induced neuroprotection in acute glaucoma. J. Mol. Cell. Biol. 2017, 9(4), 289-301. https://doi.org/10.1093/jmcb/mjx022. Erratum in: J. Mol. Cell. Biol. 2023, 15(4), mjad028. https://doi.org/10.1093/jmcb/mjad028
2. Tan, C.; Song, M.; Stamer, W.D.; Qiao, Y.; Chen, X.; Sun, X.; Lei, Y.; Chen, J. miR-21-5p: A viable therapeutic strategy for regulating intraocular pressure. Exp. Eye Res. 2020, 200, 108197. https://doi.org/10.1016/j.exer.2020.108197
3. Tan, C.; Jia, F.; Zhang, P.; Sun, X.; Qiao, Y.; Chen, X.; Wang, Y.; Chen, J.; Lei, Y. A miRNA stabilizing polydopamine nano-platform for intraocular delivery of miR-21-5p in glaucoma therapy. J. Mater. Chem. B. 2021, 9(15), 3335-3345. https://doi.org/10.1039/d0tb02881a. Erratum in: J. Mater. Chem. B. 2021, 9(16), 3595. https://doi.org/10.1039/d1tb90052h
4. Dobrzycka, M.; Sulewska, A.; Biecek, P.; Charkiewicz, R.; Karabowicz, P.; Charkiewicz, A.; Golaszewska, K.; Milewska, P.; Michalska-Falkowska, A.; Nowak, K.; Niklinski, J.; Konopińska, J. miRNA studies in glaucoma: a comprehensive review of current knowledge and future perspectives. Int. J. Mol. Sci. 2023, 24(19), 14699. https://doi.org/10.3390/ijms241914699
5. Molasy, M.; Walczak, A.; Szaflik, J.; Szaflik, J.P.; Majsterek, I. MicroRNAs in glaucoma and neurodegenerative diseases. J. Hum. Genet. 2017, 62, 105–112. https://doi.org/10.1038/jhg.2016.91
6. Liu, H.; Xiu, Y.; Zhang, Q.; Xu, Y.; Wan, Q.; Tao, L. Silencing microRNA-29b-3p expression protects human trabecular meshwork cells against oxidative injury via upregulation of RNF138 to activate the ERK pathway. Int. J. Mol. Med. 2021, 47, 101. https://doi.org/10.3892/ijmm.2021.4934

https://doi.org/10.56717/jpp.2025.v04i02.043

7. Dalgaard, L.T.; Sørensen, A.E.; Hardikar, A.A.; Joglekar, M.V. The microRNA-29 family: role in metabolism and metabolic disease. Am. J. Physiol. Cell. Physiol. 2022, 323(2), C367-C377. https://doi.org/10.1152/ajpcell.00051.2022
8. Zhang, R.; Tao, Y.; Huang, J. The application of micrornas in glaucoma research: A bibliometric and visualized analysis. Int. J. Mol. Sci. 2023, 24(20), 15377. https://doi.org/10.3390/ijms242015377
9. Smyth, A.; Callaghan, B.; Willoughby, C. E.; O'Brien, C. The role of miR-29 family in TGF-β driven fibrosis in glaucomatous optic neuropathy. Int. J. Mol. Sci. 2022, 23(18), 10216. https://doi.org/10.3390/ijms231810216
10. Rao, A.; Chakraborty, M.; Roy, A.; Sahay, P.; Pradhan, A.; Raj, N. Differential miRNA expression: Signature for glaucoma in pseudoexfoliation. Clin. Ophthalmol. 2020, 14, 3025–3038. https://doi.org/10.2147/OPTH.S254504
11. Drewry, M.D.; Challa, P.; Kuchtey, J.G.; Navarro, I.; Helwa, I.; Hu, Y.; Mu, H.; Stamer, W.D.; Kuchtey, R.W.; Liu, Y. Differentially expressed microRNAs in the aqueous humor of patients with exfoliation glaucoma or primary open-angle glaucoma. Hum. Mol. Genet. 2018, 27, 1263–1275. https://doi.org/10.1093/hmg/ddy040
12. Raga-Cervera, J.; Bolarin, J.M.; Millan, J.M.; Garcia-Medina, J.J.; Pedrola, L.; Abellán-Abenza, J.; Valero-Vello, M.; Sanz-González, S.M.; O'Connor, J.E.; Galarreta-Mira, D.; Bendala-Tufanisco, E.; Mayordomo-Febrer, A.; Pinazo-Durán, M.D.; Zanón-Moreno, V. miRNAs and genes involved in the interplay between ocular hypertension and primary open-angle glaucoma. Oxidative stress, inflammation, and apoptosis networks. J. Clin. Med. 2021, 10, 2227. https://doi.org/10.3390/jcm10112227
13. Greene, K.M.; Stamer, W.D.; Liu, Y. The role of microRNAs in glaucoma. Exp. Eye Res. 2022, 215, 108909. https://doi.org/10.1016/j.exer.2021.108909
14. Gasińska, K.; Kosior-Jarecka, E.; Żarnowski, T. MicroRNA in the pathogenesis of glaucoma. Ophthatherapy. 2020, 7(4), 277-286. https://doi.org/ 10.24292/01.OT.311220.1
15. Seong, H.; Cho, H.K.; Kee, C.; Song, D.H.; Cho, M.C.; Kang, S.S. Profiles of microRNA in aqueous humor of normal tension glaucoma patients using RNA sequencing. Sci. Rep. 2021, 11, 19024. https://doi.org/10.3390/10.1038/s41598-021-98278-0
16. Tamkovich, S.; Grigor'eva, A.; Eremina, A.; Tupikin, A.; Kabilov, M.; Chernykh, V.; Vlassov, V.; Ryabchikova, E. What information can be obtained from the tears of a patient with primary open angle glaucoma? Clin. Chim. Acta. 2019, 495, 529–537. https://doi.org/10.1016/j.cca.2019.05.028
17. Zhai, R.; Xu, H.; Kong, X.; Wang, J. Differentially expressed microRNAs associated with primary open-angle glaucoma based on bioinformatics analysis of microRNA microarray data. Investig. Ophthalmol. Vis. Sci. 2018, 59, 3520.

https://doi.org/10.56717/jpp.2025.v04i02.043