International Journal of Ophthalmology & Visual Science
2023; 8(3): 39-43
http://www.sciencepublishinggroup.com/j/ijovs
doi: 10.11648/j.ijovs.20230803.11
ISSN: 2637-384X (Print); ISSN: 2637-3858 (Online)

Lipid Biogenic Gene Pathways as Biomarkers to Identify Elevated Intraocular Eye Pressure

Rakshith Srinivasan, Padmanabhan P. Pattabiraman

Marilyn Eye Glick Institute, Indiana University Purdue University Indianapolis, Indiana, United States

Email address:
rakshith.srinivasan24@gmail.com (Rakshith Srinivasan)

To cite this article:
Rakshith Srinivasan, Padmanabhan P. Pattabiraman. Lipid Biogenic Gene Pathways as Biomarkers to Identify Elevated Intraocular Eye Pressure. *International Journal of Ophthalmology & Visual Science*. Vol. 8, No. 3, 2023, pp. 39-43. doi: 10.11648/j.ijovs.20230803.11

Received: September 7, 2023; **Accepted**: September 25, 2023; **Published**: September 27, 2023

Abstract: Glaucoma is the leading cause of irreversible blindness, and around 2.7 million cases of Glaucoma are diagnosed every year. Glaucoma is when excess aqueous humor fluid in the eye causes high intraocular eye pressure within the eye, which damages the optic nerve overtime. In a healthy eye, the aqueous humor is drained by the trabecular meshwork, a specialized tissue located in the drainage angle of the eye. The trabecular meshwork allows aqueous humor to flow out of the eye through a network of channels and spaces, which helps to maintain the balance of the production and drainage of the fluid, regulating the intraocular eye pressure. When the trabecular meshwork is damaged, it leads to a buildup of the fluid which leads to increase in intraocular eye pressure. Early stages of glaucoma have limited symptoms and it is diagnosed by measuring intraocular eye pressure which has many limitations and difficulties. Therefore, an alternative method, such as looking at a biomarker, would prove more efficient and valuable. Since glaucoma inflicts optic nerve damage and retinal ganglion cell loss overtime, treatments are reactive as opposed to preventive. Using a biomarker to predict when glaucoma will occur can be a game changer in curing the disease more effectively. This research paper looks at lipid biogenic as a biomarker for high intraocular eye pressure, a key sign and effect of glaucoma. Understanding the expression and regulation of lipids in the Trabecular meshwork of the eye is integral in diagnosing glaucoma early in patients, so that treatment can start sooner. Trabecular meshwork cells were taken from a mouse, goat, and pig sample, and lipid expression was analyzed while these cells were under different levels of stress. The hypothesis is that if the TM cell is under more stress, the lipid levels will be under expressed, because lipids are an important factor in regulating intraocular pressure homeostasis, along with aqueous humor drainage. Therefore, a lower expression of lipids in TM cells points towards the patient having abnormally high intraocular eye pressure, effectively having glaucoma. In conclusion, the data points towards lipids being a biomarker towards identifying high intraocular eye pressure. There is a clear correlation between decreased lipid biogenic pathway expression and overstressed trabecular meshwork cells. This research was conducted at the Marilyn Eye Glick Institute in Indiana University under the supervision of Dr. Pattabiraman.

Keywords: Glaucoma, Lipids, Lipid Pathways, Trabecular Meshwork, Interocular Eye Pressure, Lipids in Eye

1. Introduction

Glaucoma, a multifactorial and progressive ocular disorder, remains a significant global public health concern due to its reputation as the leading cause of irreversible blindness. Characterized by the gradual degeneration of the optic nerve and retinal ganglion cells, glaucoma is often associated with elevated intraocular eye pressure (IOP), [9] which ultimately results in optic nerve damage. The delicate balance between the production and drainage of aqueous humor, a vital fluid that nourishes the eye's tissues, plays a pivotal role in maintaining the IOP within a physiological range. The primary drainage route for aqueous humor is the trabecular meshwork (TM), a specialized tissue situated at the anterior chamber angle of the eye. [6] Consequently, disruptions in the functional integrity of the TM can lead to inadequate aqueous humor drainage and the onset of elevated IOP.

Despite its pervasive impact on vision, glaucoma's initial stages often manifest with subtle or absent symptoms, rendering early diagnosis and intervention a challenging endeavor. [9] Currently, IOP measurement remains the primary method for glaucoma diagnosis. However, this approach has limitations, and its utility in predicting the onset of glaucoma is suboptimal. An imperative shift toward predictive and preventative strategies is imperative to revolutionize the landscape of glaucoma management. As such, the exploration of potential biomarkers capable of heralding the advent of elevated IOP and, consequently, glaucoma, presents an avenue of promising research.

This research paper delves into the realm of lipid biogenics as a potential biomarker for high IOP – a cardinal sign and consequential factor in the pathogenesis of glaucoma. [9] Lipids, essential components of cellular membranes and bioactive molecules, exert a multifaceted influence on various cellular processes, including those pertinent to IOP regulation. Given their intricate role in maintaining the structural integrity of the TM and their potential involvement in IOP homeostasis, lipids hold promise as discernible markers for the early detection of glaucoma.

Crucially, this study places emphasis on understanding the nuanced expression and regulation of lipids within the TM, as alterations in lipid profiles could signify the existence of elevated IOP even before overt symptoms emerge. [1] To address this, the investigation employs an experimental approach, utilizing TM cells from diverse species – mouse, goat, and pig – to explore lipid expression patterns under varying degrees of cellular stress. The underlying hypothesis posits that heightened cellular stress leads to a downregulation of lipid expression within TM cells. This hypothesized lipid dysregulation, in turn, could serve as an indicator of elevated IOP and impending glaucomatous changes.

The trabecular meshwork is a dynamic tissue comprising TM cells and extracellular matrix components. TM cells play a vital role in regulating aqueous humor drainage, which is essential for maintaining IOP within a physiological range. When IOP increases, TM cells sense the pressure changes and respond accordingly to facilitate aqueous humor outflow. [6] Dysfunctional TM cells can compromise the drainage system, leading to elevated IOP and glaucoma development.

Lipids are essential components of cellular membranes and serve as signaling molecules in various cellular processes. [5] Recent research has indicated that changes in IOP can influence the expression of lipid biogenic genes in TM cells. Alterations in the levels of lipid-related genes can affect lipid metabolism and composition within the cells, impacting their structural integrity and function. [10] Understanding how lipid biogenic genes respond to pressure changes could shed light on the molecular mechanisms underlying IOP regulation. Given the connection between changes in pressure on TM cells and lipid biogenic gene expression, it is reasonable to hypothesize that alterations in these genes may be associated with elevated intraocular eye pressure and glaucoma. Measuring lipid biogenic gene expression levels in trabecular meshwork cells could potentially serve as a non-invasive biomarker for high intraocular eye pressure and ultimately glaucoma risk. Developing a reliable biomarker for glaucoma could improve early detection and aid in the initiation of timely therapeutic interventions to prevent irreversible vision loss.

By elucidating the intricate interplay between lipid metabolism, trabecular meshwork function, and IOP regulation, this study aspires to establish a foundation for novel diagnostic paradigms in glaucoma. [7] This research's potential to discern early signs of glaucoma, enabling timely intervention and a shift from reactive treatment strategies to proactive preventative measures, holds promise for reshaping the landscape of glaucoma management. Ultimately, the knowledge gained from this study could pave the way for more effective therapeutic approaches, mitigating the burden of irreversible vision loss associated with glaucoma.

2. Purpose

Since glaucoma inflicts optic nerve damage and retinal ganglion cell loss overtime, treatments are reactive as opposed to preventive. [8] Using a biomarker to predict when glaucoma will occur can be a game changer in curing the disease more effectively. This research paper looks at lipid biogenics as a biomarker for high intraocular eye pressure, a key sign and effect of glaucoma. [9] Understanding the expression and regulation of lipids in the Trabecular meshwork of the eye is integral in diagnosing glaucoma early in patients, so that treatment can start sooner. Trabecular meshwork cells were taken from a mouse, goat, and pig sample, and lipid expression was analyzed while these cells were under different levels of stress. The hypothesis is that if the TM cell is under more stress, the lipid levels will be underexpressed, because lipids are an important factor in regulating intraocular pressure homeostasis, along with aqueous humor drainage. Therefore, a lower expression of lipids in TM cells points towards the patient having abnormally high intraocular eye pressure, effectively having glaucoma. [2]

3. Methods

The foundation of this study was built upon the development of primers targeting lipid biogenic genes within the genomes of three distinct species: Mice, Pig, and Goat. Codon sequences for the requisite enzymes were extracted from the UCSC and NCBI nucleotide databases, forming the basis for subsequent experimental steps. Trabecular Meshwork (TM) cells were then meticulously cultured from samples obtained from Mice, Pig, and Goat specimens. This initial cell culture phase laid the groundwork for subsequent investigations into lipid biogenic gene expression under varying conditions of cellular stress. To achieve this, cells were subjected to stress induction through viral vectors and cell transfection, as outlined in detail in the procedures documented.

The heart of this research was the execution of Western blot analysis and gel electrophoresis techniques, which provided insights into the temporal dynamics of lipid biogenic gene expression in TM cells under stress. The primers developed earlier were instrumental in detecting and quantifying the expression of these genes. Western blotting enabled the visualization of protein expression, while gel electrophoresis allowed for the separation and characterization of nucleic acids. The investigative focus extended to observing the cellular responses and morphological changes that ensued following stress induction. Microscope imaging played a crucial role in capturing the effects of viral vectors and cell transfection on the TM cells, shedding light on potential alterations in cellular structure, phenotype, and behavior. [1]

The results were analyzed through the lens of Western blot data and gel electrophoresis outcomes, offering a comprehensive overview of the lipid biogenic gene expression profiles across different time points of cellular stress. Western blot analyses were conducted for each sample – Mice, Pig, and Goat – providing a comparative analysis of lipid biogenic protein expression patterns. [7]

In tandem with the molecular analyses, microscope images enriched the interpretation of results by showcasing the morphological responses of TM cells to viral vectors and transfection, underlining the cellular dynamics resulting from stress induction. [6]

The assimilation of data from these diverse experimental techniques has the potential to elucidate the intricate interplay between lipid biogenesis and cellular stress within the TM. This endeavor underscores the broader objective of this research – to unravel the implications of lipid expression alterations in the context of elevated intraocular eye pressure, offering new avenues for the early detection and potential management of glaucoma. The subsequent sections of this paper delve into the detailed presentation and interpretation of these findings, coupled with insightful discussions on their implications for glaucoma diagnosis and treatment strategies.

4. Results and Discussion

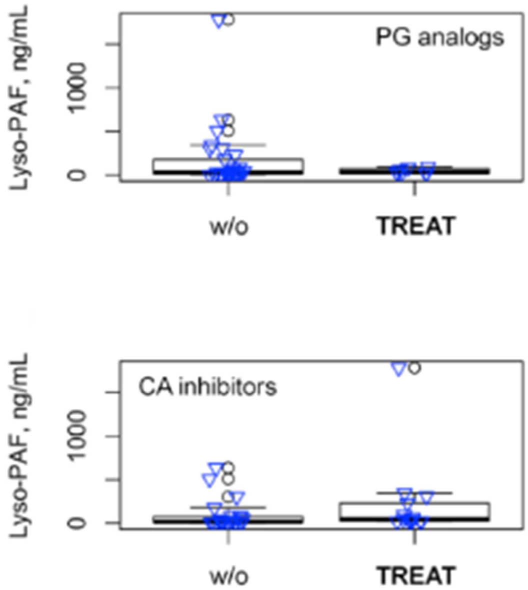

Figure 1. *Pathway Expression of Lipid in Control + Stressed TMCell.*

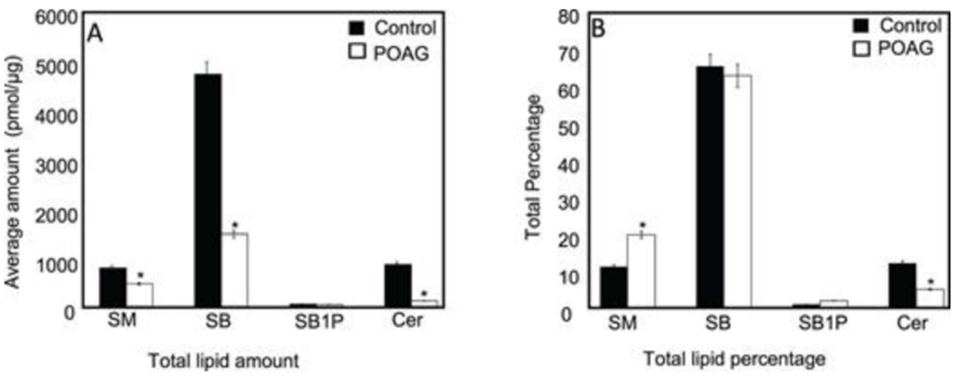

Figure 2. *Lipid Levels in Control vs Simulated Primary Open Angle Glaucoma in Mice, Pig, Goat.*

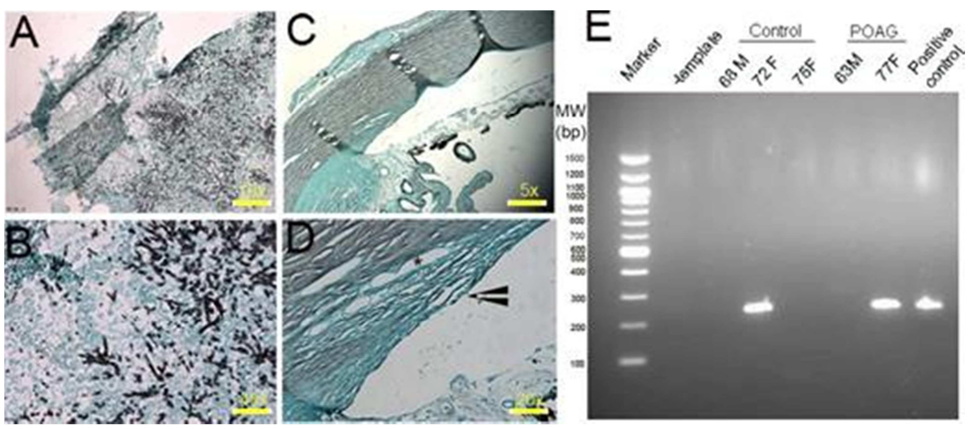

Figure 3. *Western Blot Scan of Control vs Simulated Primary Open Angle Glaucoma.*

Figure 1 references the pathway expression of lipids, data collected through western blots for each sample type. [3] Outlier data points are not taken into consideration when creating conclusions. After analyzing the data, lipid biogenic gene pathways can be used as a biomarker for assessing the presence of glaucoma in a patient sample, given by the underexpressed levels in stressed TM cells. [4] Figure 2 measures Lipid levels in the simulated glaucoma samples, with a decrease being noted amongst all 3 sample types. Notable in that this points towards stress being a driver towards decreased lipid pathway expression, as seen in figure 1. Likewise, we can see in the western blot for trabecular meshwork cells of Sus Scrofa, lipid expression was lower in higher intraocular pressure levels. The significance of our research lies in its potential to transform the landscape of glaucoma diagnosis and treatment. By elucidating the relationship between lipid biogenesis, TM function, and IOP regulation, we have paved the way for the development of novel diagnostic paradigms in glaucoma. The ability to identify early signs of glaucoma, even before overt symptoms emerge, facilitates timely intervention and a shift from reactive treatment strategies to proactive preventative measures [3]. Ultimately, this knowledge holds promise for the development of more effective therapeutic approaches, alleviating the burden of irreversible vision loss associated with glaucoma.

5. Conclusion

This study has focused on understanding the expression and regulation of lipids within the trabecular meshwork (TM), a critical component of the eye responsible for maintaining IOP within a physiological range. Disruptions in the functional integrity of the TM can lead to inadequate aqueous humor drainage and elevated IOP, which is a key factor in glaucoma pathogenesis. Through a comprehensive experimental approach involving TM cells from mouse, goat, and pig samples, this research has provided valuable insights into the relationship between lipid expression and cellular stress in the TM. The results indicate that heightened cellular stress is associated with a downregulation of lipid expression within TM cells. This finding suggests that alterations in lipid profiles could serve as an indicator of elevated IOP and impending glaucomatous changes, even before overt symptoms emerge. Furthermore, the development of primers targeting lipid biogenic genes and the use of Western blot analysis and gel electrophoresis techniques have allowed for the quantification and visualization of lipid biogenic gene expression in TM cells under varying conditions of cellular stress. Microscope imaging has also contributed to our understanding by revealing potential alterations in cellular structure and behavior. The results are promising, as they suggest that lipid biogenic gene expression levels in trabecular meshwork cells could potentially serve as a non-invasive biomarker for high intraocular eye pressure and, ultimately, glaucoma risk. This research has the potential to revolutionize the landscape of glaucoma management by enabling earlier detection and a shift from reactive treatment strategies to proactive preventative measures. Future research in this field could build upon these findings by conducting longitudinal studies to confirm the predictive power of lipid biogenic gene expression as a biomarker for glaucoma. Additionally, investigations into the development of non-invasive diagnostic techniques for measuring lipid biogenic gene expression in clinical settings could be pursued. This could lead to the development of a reliable and widely applicable diagnostic tool for glaucoma. The medical applications of this research are significant. If lipid biogenic gene expression can indeed serve as a reliable biomarker for high IOP and glaucoma risk, it could lead to earlier detection and intervention, potentially preventing irreversible vision loss in countless individuals. Additionally, the insights gained from this study could contribute to the development of more effective therapeutic approaches for glaucoma treatment. This research has provided a foundation for novel diagnostic paradigms in glaucoma and holds the promise of reshaping the management of this sight-threatening disease. By understanding the intricate interplay between lipid metabolism, trabecular meshwork function, and IOP regulation, we move closer to a future where glaucoma can be detected and treated proactively, reducing the burden of irreversible vision loss associated with this condition.

References

[1] Mount. “Patients with Specific Types of Lipids May Be at Higher Risk of Developing Blinding Eye Disease.” Mount Sinai Health System, Mount Sinai Health System, 13 June 2023, www.mountsinai.org/about/newsroom/2023/patients-with-specific-types-of-lipids-may-be-at-higher-risk-of-developing-blinding-eye-disease#:~:text=More%20specifically%2C%20the%20dysregulation%20of,in%20four%20different%20study%20groups.

[2] Wang, Ting, and Padmanabhan P. Pattabiraman. “Analysis of Lipid Contents in Human Trabecular Meshwork Cells by Multiple Reaction Monitoring (MRM) Profiling Lipidomics.” Springer EBooks, Jan. 2023, pp. 291–98, https://doi.org/10.1007/978-1-0716-2966-6_24.

[3] Azbukina, Nadezhda V., et al. “Targeted Lipidomic Analysis of Aqueous Humor Reveals Signaling Lipid-Mediated Pathways in Primary Open-Angle Glaucoma.” Biology, vol. 10, no. 7, Multidisciplinary Digital Publishing Institute, July 2021, pp. 658–58, https://doi.org/10.3390/biology10070658.

[4] Shiming Wang, Xianyi Bao; Hyperlipidemia, Blood Lipid Level, and the Risk of Glaucoma: A Meta-Analysis. Invest. Ophthalmol. Vis. Sci. 2019; 60 (4): 1028-1043. https://doi.org/10.1167/iovs.18-25845.

[5] Xu, Mingxin, et al. “Plasma Lipid Levels and Risk of Primary Open Angle Glaucoma: A Genetic Study Using Mendelian Randomization.” BMC Ophthalmology, vol. 20, no. 1, BioMed Central, Oct. 2020, https://doi.org/10.1186/s12886-020-01661-0.

[6] Ayman J. Aljohani, Genea Edwards, Yenifer Guerra, Sander Dubovy, Darlene Miller, Richard K. Lee, Sanjoy K. Bhattacharya; Human Trabecular Meshwork Sphingolipid and Ceramide Profiles and Potential Latent Fungal Commensalism. Invest. Ophthalmol. Vis. Sci. 2014; 55 (6): 3413-3422. https://doi.org/10.1167/iovs.13-13570.

[7] "Sus Scrofa NAD (P) Dependent Steroid Dehydrogenase-like (NSDHL), MRNA - Nucleotide - NCBI." Nih.gov, 2023, www.ncbi.nlm.nih.gov/nuccore/NM_001167636.1?from=1&to=1086&report=fasta.

[8] Suzana Pavljašević, and Mensura Asccerić. "Primary Open-Angle Glaucoma and Serum Lipids." Bosnian Journal of Basic Medical Sciences, vol. 9, no. 1, Association of Basic Medical Sciences of Federation of Bosnia and Herzegovina, Feb. 2009, pp. 85–88, https://doi.org/10.17305/bjbms.2009.2863.

[9] "Glaucoma | National Eye Institute." Nih.gov, 2022, www.nei.nih.gov/learn-about-eye-health/eye-conditions-and-diseases/glaucoma#:~:text=What%20is%20glaucoma%3F,a%20comprehensive%20dilated%20eye%20exam.

[10] Kian Madjedi, et al. "The Association between Serum Lipids and Intraocular Pressure in 2 Large United Kingdom Cohorts." Ophthalmology, vol. 129, no. 9, Elsevier BV, Sept. 2022, pp. 986–96, https://doi.org/10.1016/j.ophtha.2022.04.023.