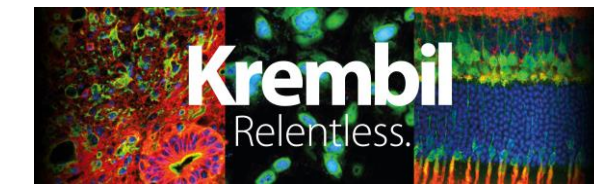


Aqueous Humor Lipidomic Profile in Primary Open Angle Glaucoma Patients



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Introduction

- Lipoxins A₄ (LXA₄) and B₄ (LXB₄) are decreased in inner retinal injury models
- Supplementation of LXA₄ and LXB₄ conferred neuroprotection.
- Lipoxins have not yet been studied in clinical glaucoma.

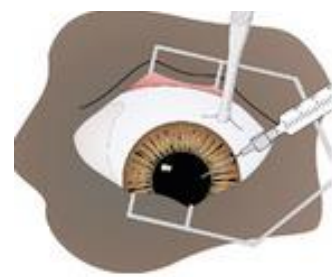
Purpose

To identify the aqueous humor (AH) profile of lipid mediators in primary open angle glaucoma (POAG) eyes compared to those without glaucoma

- Prospective comparative study

Methods

- AH samples from eyes with and without glaucoma underwent lipidomic analyses using liquid chromatography-mass spectrometry (LC-MS).
- Glaucoma samples: 60-80-year-old POAG patients undergoing a glaucoma surgery with or without cataract surgery
- Control samples: Age-matched patients without glaucoma undergoing routine cataract surgery.
- Exclusion criteria: Diabetes mellitus, systemic inflammatory disease, uveitis, retinopathy, age-related macular degeneration and patients on Aspirin



Sample collection:

- 100 µL of AH
- Collected using a 30 Gauge needle mounted on a 1-mL syringe, introduced into the anterior chamber anterior to the limbus, prior to any surgical intraocular entry.
- The samples were immediately snap frozen on dry ice and stored at -80C until analyses.
- Lipidomic analyses of a panel of 40 polyunsaturated fatty acids (PUFA), metabolites and lipid mediators.
- All participating patients signed an informed consent form
- This study was approved by the University Health Network and Kensington Eye Institute Research and Ethics Boards.

Methods (Cont'd)

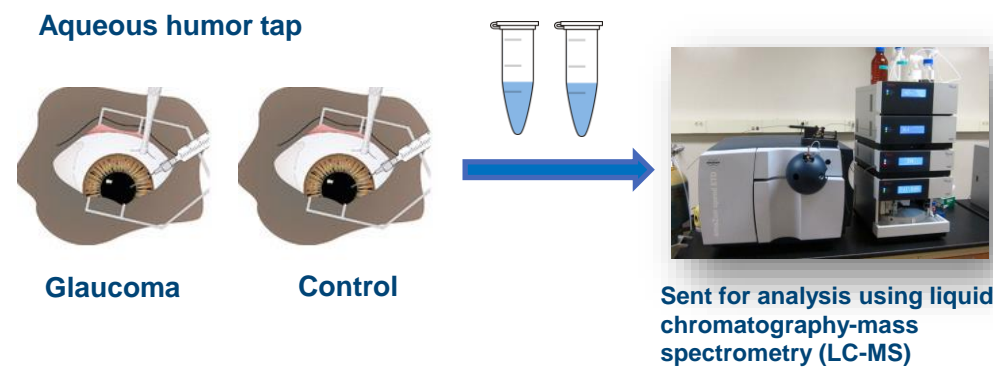


Figure 1. Schematic representation the study.

Results

	Glaucoma	Control	p value
n	16	18	--
Age	68.7 ± 6.4 years	71.0 ± 4.7 years	0.25
IOP	14.1 ± 3.1 mmHg	15.2 ± 1.6 mmHg	0.24
CDR	0.9 ± 0.1	0.3 ± 0.1	<0.001

Table 1. Demographics and baseline characteristics.

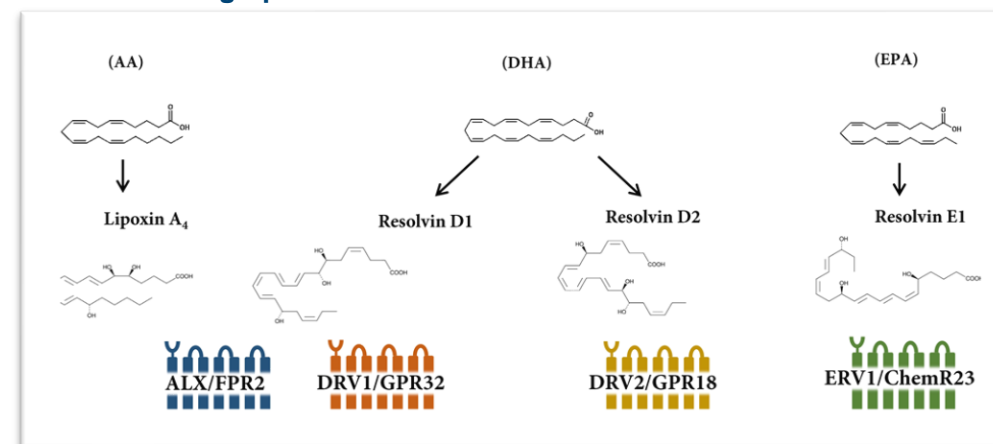


Figure 2. Overview of three substrates in the lipidomic pathway.

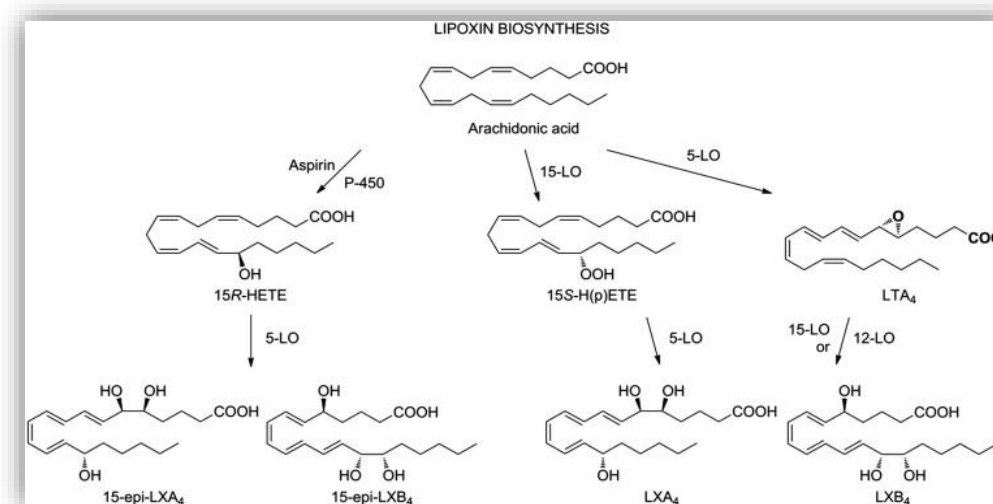


Figure 3. Arachidonic acid pathway culminating in lipoxins.

Results (Cont'd)

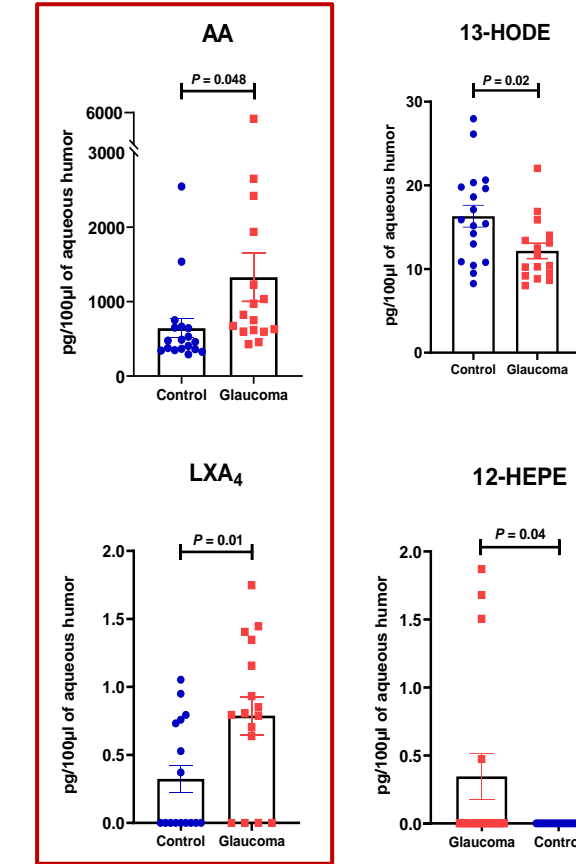


Figure 4. Analytes that showed a significant difference between control and glaucoma samples.

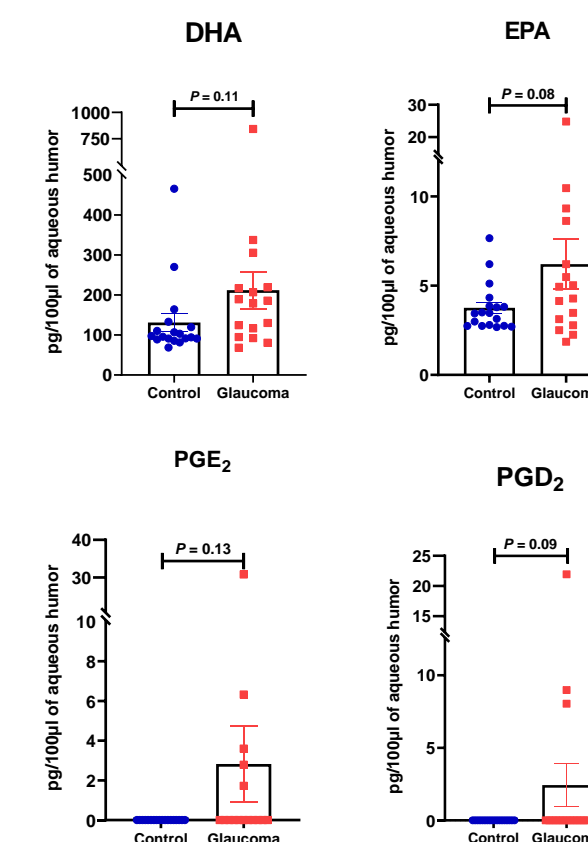


Figure 5. Analytes that were within the detection threshold but did not show a significant difference.

Results (Cont'd)

Analyte	Glaucoma	Control	Analyte	Glaucoma	Control
AA	1328.04 ± 312.43	643.07 ± 127.15	15-deoxy PGJ ₂	ND	ND
DHA	212.03 ± 185.33	131.09 ± 21.76	LXA ₄	1.05 ± 0.36	0.74 ± 0.08
EPA	6.21 ± 5.59	3.76 ± 0.31	LXB ₄	ND	ND
5-HETE	ND	ND	LTB ₄	ND	ND
12-HETE	ND	ND	6-trans-LTB ₄	ND	ND
15-HETE	ND	ND	20-hydroxy-LTB ₄	ND	ND
20-HETE	ND	ND	20-carboxy LTB ₄	ND	ND
5-oxo-EETE	ND	ND	LTB ₆	ND	ND
4-HDHA	ND	ND	LTC ₄	ND	ND
7-HDHA	ND	ND	LTD ₄	ND	ND
14-HDHA	ND	ND	LTE ₄	ND	ND
17-HDHA	ND	ND	RvD ₁	ND	ND
12-HEPE	1.38 ± 0.62	ND	RvD ₂	ND	ND
15-HEPE	ND	ND	RvD ₃	ND	ND
18-HEPE	ND	ND	RvD ₅	ND	ND
13-HODE	12.17 ± 3.71	16.32 ± 1.27	RvE ₁	ND	ND
PGE ₂	9.05 ± 12.28	ND	TXB ₂	ND	ND
PGD ₂	12.98 ± 7.77	ND	NPD ₁	ND	ND
PGF _{2a}	ND	ND	Maresin-1	ND	ND
6-keto-PGF _{1a}	ND	ND	Maresin-2	ND	ND

Table 2. List of 40 polyunsaturated fatty acids (PUFA), metabolites and lipid mediators and their levels in glaucomatous and non-glaucomatous aqueous humor. ND, not detected. Levels are in pg/100µL of aqueous humor.

Conclusions

- Increased levels of lipid mediators are present in glaucomatous eyes.
- Out of a total of 40 analytes, the arachidonic acid-lipoxin pathway was upregulated in glaucomatous eyes.
- Arachidonic acid metabolites may play a role in glaucoma pathogenesis.

References

- Livne-Bar I, Wei J, Liu H-H, et al. Astrocyte-derived lipoxins A4 and B4 promote neuroprotection from acute and chronic injury. J Clin Invest 2017;127:4403-4414.

Acknowledgements

- Sivak Lab members



No Disclosures