Metabolomics reveals differences in aqueous humor composition between patients with and without pseudoexfoliation syndrome

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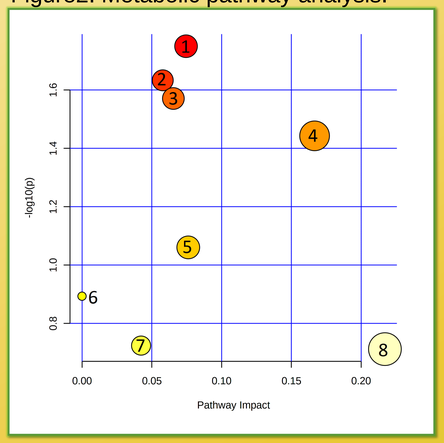
Background and aim

Pseudoexfoliation (PEX) is a stress-induced elastosis accompanied by excessive production of microfibrils, and their deposition in the anterior segment of the eye. The pathogenesis of PEX has not been fully elucidated yet. To evaluate the actual biochemical status of the eye and reveal metabolic pathways dysregulated by an ocular disease, aqueous humor (AH) can be analyzed. AH is a transparent fluid that fills the anterior and posterior chambers of the eye. Determination of metabolites in AH characteristic to PEX may provide valuable information about the molecular mechanisms behind this ocular disorder. Consequently, this study aimed to compare the metabolic composition of aqueous humor between the patients with and without PEX undergoing cataract surgery.

Materials and Methods

AH samples obtained from 34 patients (15 with and 19 without PEX) were analyzed using liquid chromatography coupled to a Quadrupole Time-of-Flight mass spectrometer (LC-QTOF-MS). To increase metabolome coverage, samples were analyzed using reversed-phase and HILIC chromatography to detect non-polar and polar metabolites, respectively.

Figure2. Metabolic pathway analysis.



Metabolic pathway analysis was performed with MetaboAnalyst 4.0. All pathways are marked with the numbers:
1.cysteine and methionine metabolism
2.arginine and proline metabolism
3.tryptophan metabolism
4.aminoacyl-tRNA biosynthesis
5.arginine biosynthesis
6.sphingolipid metabolism
7.glyoxylate and dicarboxylate metabolism
8.glycine, serine and threonine metabolism

Conclusions

Obtained results indicate that PEX can be associated with oxidative stress and inflammation, as well as disturbances in the processes of cellular respiration and energy production in the mitochondria. Implementation of non-targeted metabolomics provided a better insight into the still not fully-understood pathogenesis of PEX.

Results

Eleven statistically significant metabolites were identified. In patients with PEX, a decrease of amino acids and their derivatives was observed. As an example, arginine or homo-arginine can be mentioned. A decreased level of two acylcarnitines: hydroxybutyrylcarnitine and decatrienoylcarnitine were also observed. Contrary, indoleactaldehyde was increased in AH of patients with PEX. Among other significant metabolites, two known antioxidants ascorbic acid and hydroxyanthranilic acid as well as possessing anti-inflammatory activity S-adenosylmethionine can be mentioned. Detailed results are shown in Table1 and Figure1. To give an overview of the metabolic pathways to which identified metabolites belong, a pathway analysis was performed using MetaboAnalyst 4.0. In total, these metabolites could be assigned to 8 metabolic pathways with cysteine and methionine metabolism, arginine and proline metabolism, tryptophan metabolism, and aminoacyl-tRNA biosynthesis being the most represented. Detailed results are shown in Figure 2.

Figure1. Metabolites discriminated AH samples from patients with and without PEX.

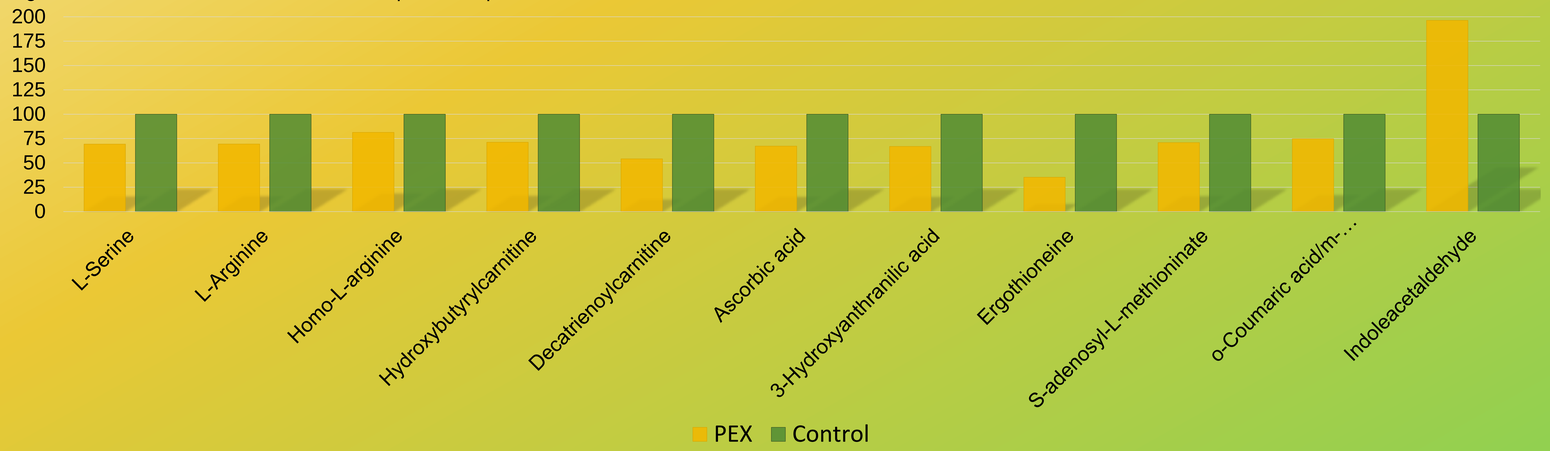


Table1. Metabolites discriminated AH samples from patients with and without PEX.

	L-Serine	L-Arginine	Homo-L-arginine	Hydroxybutyrylcarnitine	Decatrienoylcarnitine	Ascorbic acid	3-Hydroxyanthranilic acid	Ergothioneine	S-adenosyl-L-methioninate	o-Coumaric acid /m-Coumaric acid	Indoleacetaldehyde
change	-30.76	-30.68	-18.72	-28.86	-45.83	-32.81	-33.1	-64.76	-29.15	-25.24	+96.36
VIP	1.01	2.38	1.38	1.24	1.89	2.11	2.25	2.48	1.93	1.23	2.64
p(corr)	-0.44	-0.59	-0.41	-0.46	-0.45	-0.5	-0.5	-0.44	-0.59	-0.51	0.64

Direction of change indicates increased (+) or decreased (-) abundance of metabolite in AH patients with and widhout PEX.