

Supplementary Information

Reduced glutathione level in the aqueous humor of patients with primary open-angle glaucoma and normal-tension glaucoma

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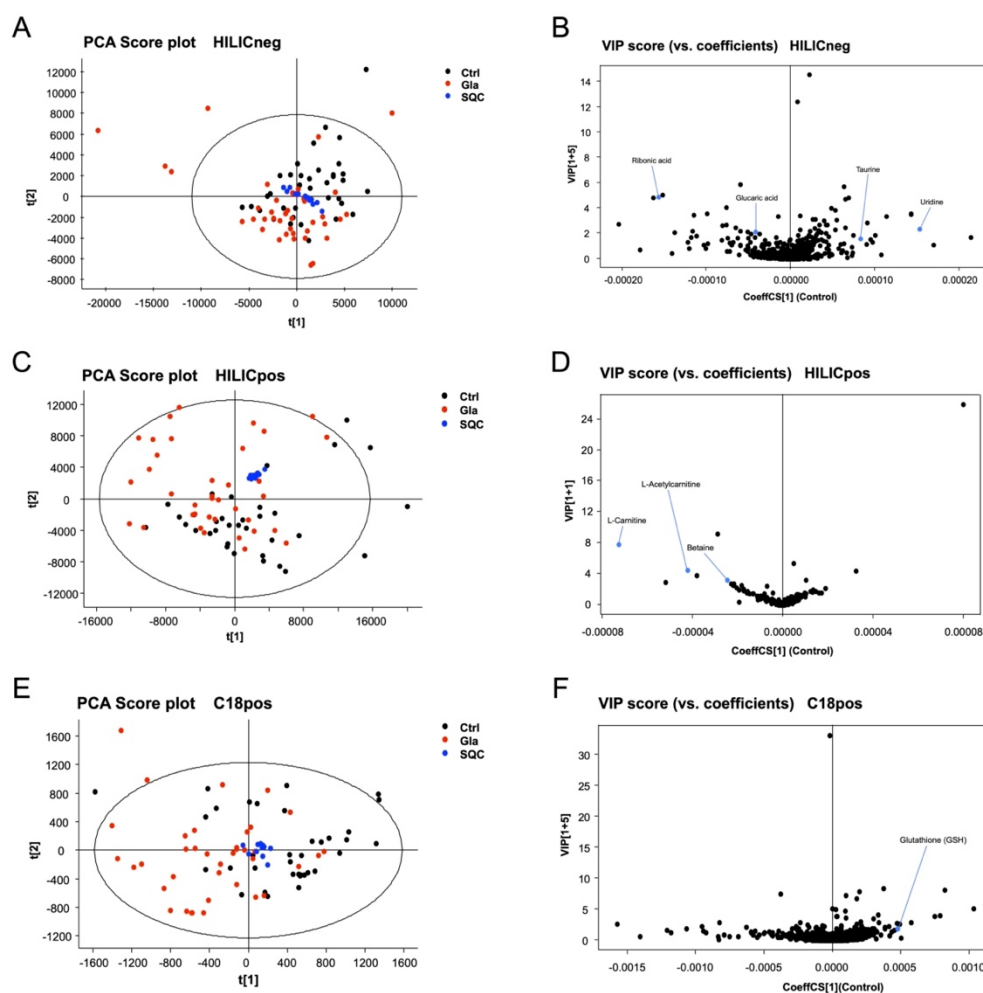
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42 Supplementary Figure 1



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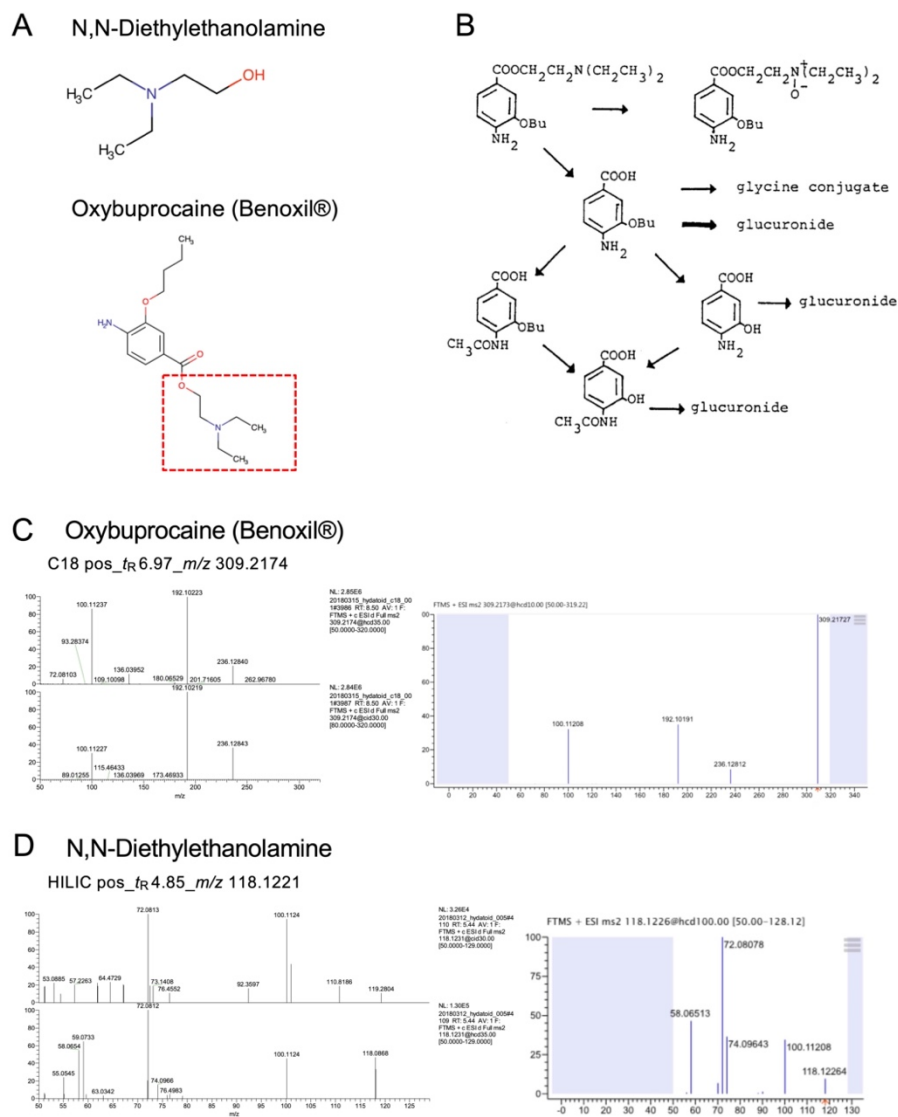
44 Supplementary Figure 1. PCA and VIP analysis with the HILIC negative mode (A, B),

45 HILIC positive mode (C, D) and C18 positive mode (E, F) after removing the eye-drop

46 component.

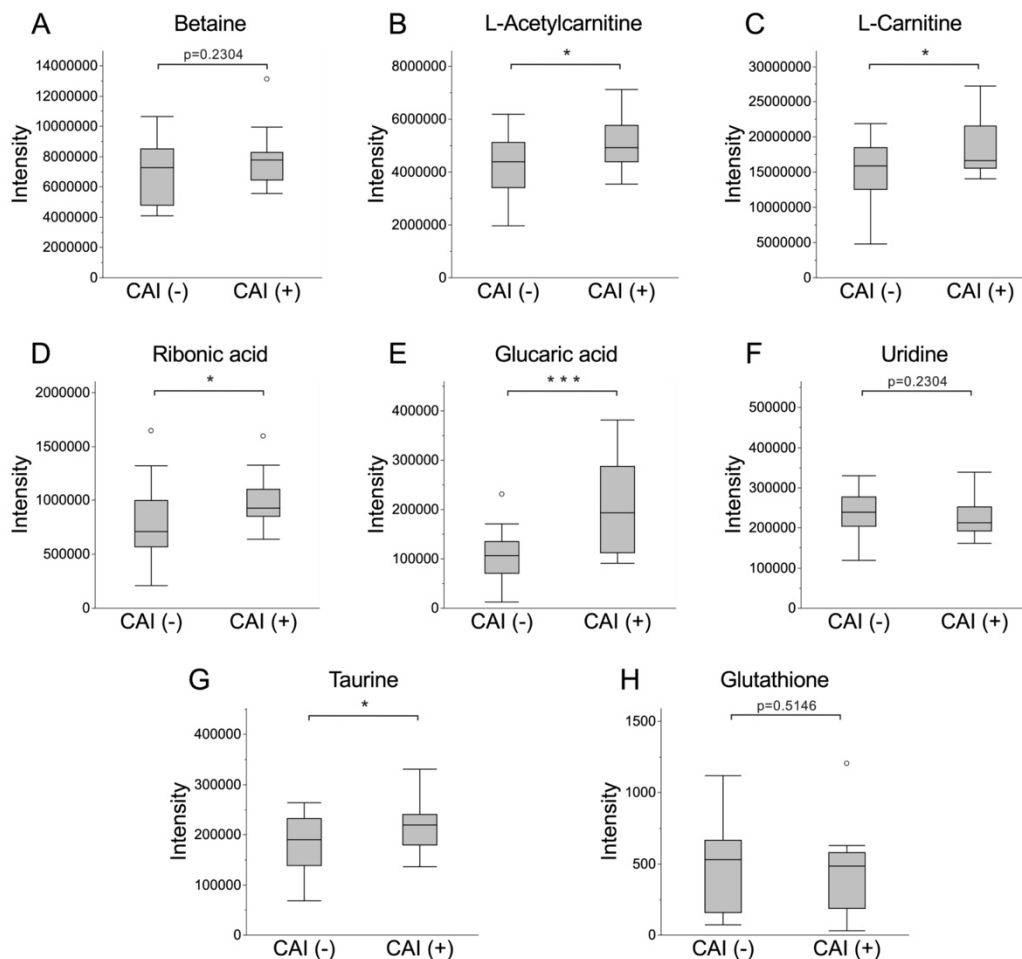
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48 Supplementary Figure 2



49 Supplementary Figure 2. N,N-Diethylethanamine as an intermediate metabolite of
 50 oxybuprocaine. (B) The metabolic pathway of oxybuprocaine is reprinted from Journal
 51 of Pharmaceutical Sciences, 76(4), Kasuya F, Metabolism of Benoxinate in Humans,
 52 303-305, 1987, with permission from Elsevier.

53 Supplementary Figure 3



54 Supplementary Figure 3. Comparison of aqueous humor metabolites with and without

55 acetazolamide in glaucoma patients. Boxplots showing the metabolite intensity of

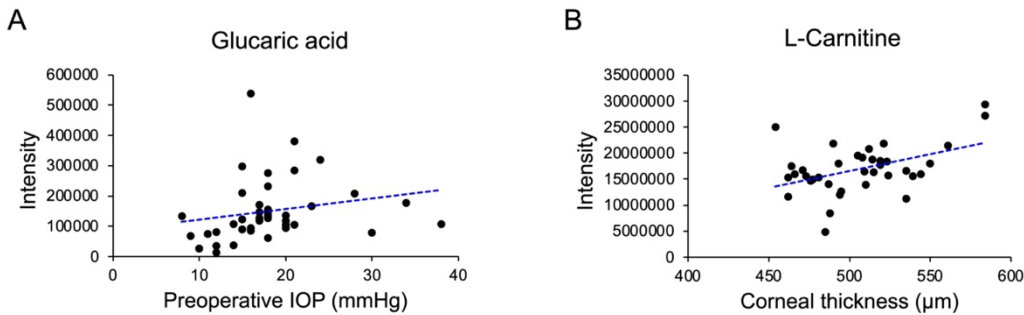
56 betaine (A), L-acetylcarnitine (B), L-carnitine (C), ribonic acid (D), glucaric acid (E),

57 uridine (F), taurine (G), and glutathione (H) compared without acetazolamide (CAI-,

58 n=25) and with acetazolamide (CAI+, n=15). This statistical analysis used the Student t-

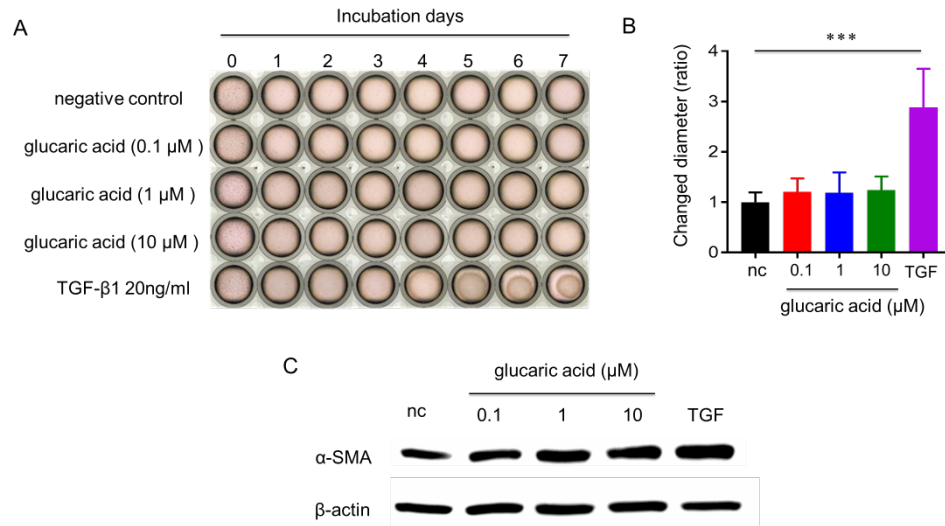
59 test. * $P < 0.05$, *** $P < 0.001$.

Supplementary Figure 4



Supplementary Figure 4. Association of aqueous humor metabolites and clinical parameters in glaucoma patients. (A) Scatterplot showing the correlation of preoperative intraocular pressure and the aqueous humor level of glucaric acid. (B) Scatterplot showing the correlation of central corneal thickness and the aqueous humor level of L-carnitine.

Supplementary Figure 5



Supplementary Figure 5. Effects of glucaric acid on functional and morphological changes in human trabecular meshwork cells (HTMCs). (A) Representative photographs of collagen gel preparations of HTMCs and changes over 7 days. (B) Histogram showing changes in gel diameter, determined by comparing collagen gel surface diameter on day 7 and day 0 for HTMCs treated with glucaric acid, TGF-β1 (20 μg/m) or sterilized distilled water as a negative control (nc). Data are shown as mean ± SD (n=16 in each well) and were analyzed with Dunnett's multiple test. ***P<0.001 vs. the control group. (C) Western blot for αSMA in HTMCs treated with glucaric acid or TGF-β1 (20 ng/ml) 24 hours after treatment. ***P<0.001 vs. the control group.

83	Supplementary Table 1
84	List of compounds in glaucoma eye drops
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86	Supplementary Table 2
87	Extracted feature from OPLS-DA S-plot.
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89	Supplementary Table 3
90	Extracted feature from VIP.
91	
92	Supplementary Table 4
93	Comparison of aqueous humor metabolites in glaucoma patients receiving and not
94	receiving intraocular pressure-lowering drugs.
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96	Supplementary Table 5
97	The list of MRM for targeted compounds by negative ion mode.

