Poster #11: ENZYMATIC CHANGES IN ENDOGENOUS OXALATE PATHWAY IN OBESE MOUSE MODEL

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Introduction

Increasing body weight/BMI has been associated with increased urinary oxalate excretion. This finding may be secondary to increased endogenous oxalate synthesis. Using an obese mouse model induced by high fat feeding (HFF), we demonstrated increased endogenous oxalate synthesis. Here, we investigated the protein expression of enzymes involved in the endogenous oxalate pathway.

Methods

Wild type (WT) controls (n=6), HFF (n=6) were fed a diet ultra-low in oxalate (<10µg/g diet) and glycolate (<3µg/g diet) and housed in metabolic cages. In the high fat diet, 45% of calories were fat vs 17% in normal diet. Liver tissue was harvested after 12 weeks of feeding. Western blot analysis was performed to assess protein expression of alanine glyoxylate aminotransferase (AGT), glycolate oxidase (GO), and glyoxylate reductase (GR). Mass spectrometry was used for protein measurements in the liver samples to corroborate Western blot results. Data analysis was performed using t-tests.

Results

Significant increase in liver GR was seen in HFF vs WT mice ($p<0.001$). Decreases were seen in GO ($p=0.03$) expression and AGT ($p=0.08$) expression in HFF vs WT. Proteomic results demonstrated a decrease in AGT (2.2 fold, $p=0.004$) and an increase in GO (1.5 fold, $p=0.03$) and GR (1.5 fold, $p=0.004$).

		Control		Hfat				
Protein Name	Acc#	avg	stdev	avg	stdev	SAM	Ttest	Fold(Hfat/C)
Haptoglobin	Q61646	3.2	1.3	12.5	4.4	1.64	0.0013	3.9
Elongation factor G, mitochondrial	Q8K0D5	1.6	0.6	6.0	2.2	1.57	0.0016	3.8
Beta-glucuronidase	P12265	1.9	1.1	6.1	1.9	1.41	0.0008	3.3
Myosin-10	Q61879	3.7	2.7	11.5	6.0	0.90	0.0203	3.1
Ubiquitin-conjugating enzyme E2 variant 2	Q9D2M8	2.2	1.3	6.8	3.1	1.04	0.0071	3.0
Mitochondrial import inner membrane translocase subuni	P62075	2.9	0.5	8.3	1.3	3.00	0.0000	2.9
Acyl-CoA-binding domain-containing protein 5	Q5XG73	3.8	1.7	10.9	4.9	1.08	0.0075	2.9
Ectonucleoside triphosphate diphosphohydrolase 5	Q9WUZ9	2.9	2.4	8.2	3.8	0.86	0.0092	2.8
Translocation protein SEC63 homolog	Q8VHE0	1.6	0.7	4.4	1.9	1.10	0.0120	2.8
Lon protease homolog 2, peroxisomal	Q9DBN5	4.3	1.3	11.9	3.6	1.54	0.0012	2.8
Serine/threonine-protein phosphatase 2A 56 kDa regulat	Q61151	0.9	0.1	2.5	1.1	1.30	0.0185	2.7
Cystatin-B	Q62426	3.5	2.6	9.1	2.4	1.14	0.0026	2.6
Serum paraoxonase/arylesterase 1	P52430	6.5	3.8	17.0	2.2	1.73	0.0002	2.6
Bifunctional UDP-N-acetylglucosamine 2-epimerase/N-a	Q91WG8	2.9	2.0	7.5	1.9	1.17	0.0011	2.6
Fatty acid-binding protein, adipocyte	P04117	4.1	1.6	10.3	1.1	2.29	0.0000	2.5
Signal transducer and activator of transcription 1	P42225	0.9	0.1	2.3	0.9	1.43	0.0125	2.5
Polymeric immunoglobulin receptor	O70570	1.6	0.5	3.8	1.9	0.93	0.0171	2.4
Peroxisomal biogenesis factor 19	Q8VCI5	1.7	0.7	4.0	1.8	0.94	0.0189	2.4
Cytochrome P450 3A13	Q64464	5.2	1.5	12.6	6.0	0.98	0.0143	2.4
Probable D-lactate dehydrogenase, mitochondrial	Q7TNG8	7.2	2.2	16.8	2.9	1.90	0.0000	2.4

Figure 1. Sample proteomic analysis generated a listing of all enzymes that were significantly elevated in the high fat diet mice compared to control mice.

Discussion

Both Western blot and proteomic data demonstrated a decrease in AGT expression and an increase in GR expression. These findings may explain the increased glycolate and oxalate seen in these mice. Further studies are needed to clarify the effects of obesity on the endogenous oxalate pathway.

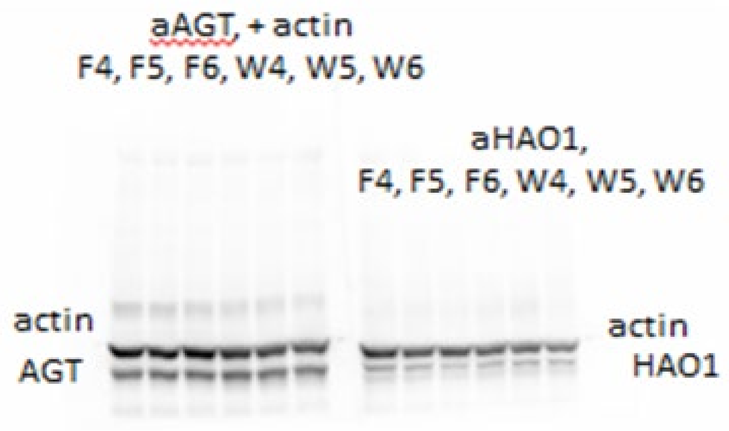

Figure 2. Representation of western blot analysis.

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