Postprandial plasma proteomics in metabolic dysfunction-associated steatotic liver disease

Maria Mironova, MD[1], Paul S. Blank, PhD[2], Regina Umarova, MS[1],
Mary Walter, PhD[3], Yaron Rotman, MD, MSc[1]

[1] Liver Diseases Branch, NIDDK, [2] Section on Integrative Biophysics (HNT4E5), NICHD, and [3] Clinical Laboratory Core, NIDDK, National Institutes of Health, Bethesda, MD, United States.

National Institute of Diabetes and Digestive and Kidney Diseases

Background

- The drivers of progression from steatosis to metabolic dysfunction–associated steatohepatitis (MASH) and subsequent fibrosis in metabolic dysfunction-associated steatotic liver disease (MASLD) are unclear.
- The acute alterations of metabolism after a single caloric load are relatively unstudied.
- We previously identified postprandial alterations in the plasma lipidome in subjects with MASLD.[1]

Aim

Identify postprandial changes in plasma proteome that are unique to MASLD as a tool to explore pathophysiology.

Methods

- A single-center prospective study (NCT02520609).
- Subjects with MASLD and healthy controls were fed a standardized liquid mixed meal (Ensure Plus).
- Plasma and serum samples were obtained at fasting, and 30 min, 1, 2 and 4 hours after the meal.
- The plasma proteome was measured using the SomaScan v3.2 assay.
- Key proteins identified by SomaScan were validated using ELISA.
- Repeated measures ANOVA was used to assess temporal patterns
- KEGG database used for pathway analysis.

Results

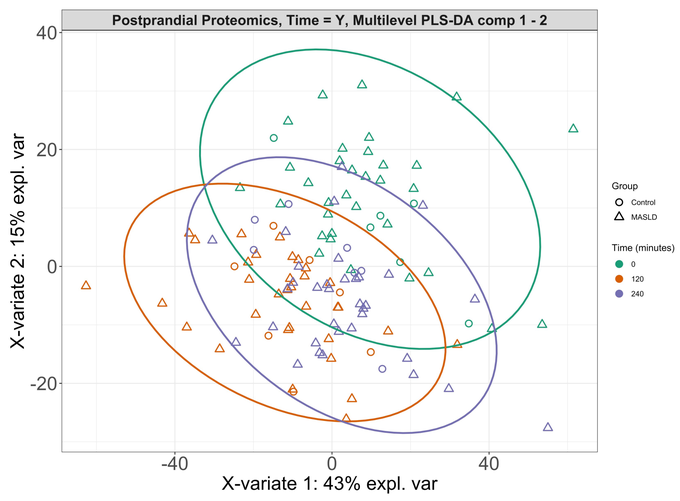
- 37 subjects with MASLD and 10 controls.

Clinical characteristics

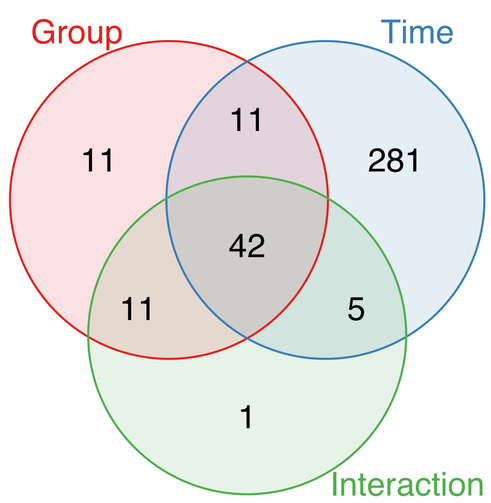
Characteristic	Controls (n=10)[1]	MASLD (n=37)[1]	p-value[2]
Age, years	32 (22-43)	54 (44-60)	<0.001
Female	4 (40%)	20 (54%)	0.5
Ethnicity			0.014
Asian	1 (10%)	2 (5.4%)	
African American	3 (30%)	1 (2.7%)	
Hispanic	0	14 (38%)	
Multiple	1 (10%)	3 (8.1%)	
White	5 (50%)	17 (46%)	
BMI, kg/m^2	22 (21-23)	32 (30-35)	<0.001
Alanine aminotransferase, U/L	15 (11-18)	42 (29-67)	<0.001
Fasting glucose, mg/dL	92 (86-93)	100 (94-115)	<0.001
Fasting insulin, mcU/mL	6 (4-11)	25(19-30)	<0.001
HbA1C, %	5.3 (5.0-5.4)	5.7 (5.3-6.6)	<0.001
Triglycerides, mg/dL	58 (52-74)	156 (129-202)	<0.001
HOMA-IR	1.2 (1.0-2.6)	5.9 (5.0-8.5)	<0.001

- 1317 unique proteins quantified with SomaScan.
- On SomaScan PLS-DA demonstrated postprandial changes in the proteome.
- ***42 plasma proteins*** had different postprandial temporal patterns between MASLD and controls.

Temporal Change in Proteome

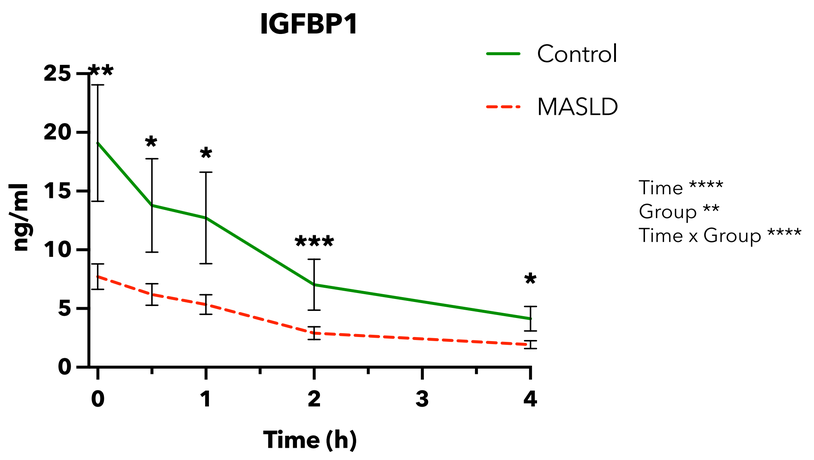


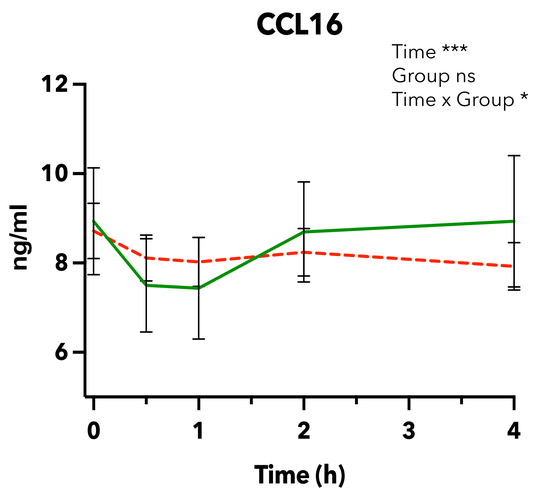
Differentially Affected Proteins

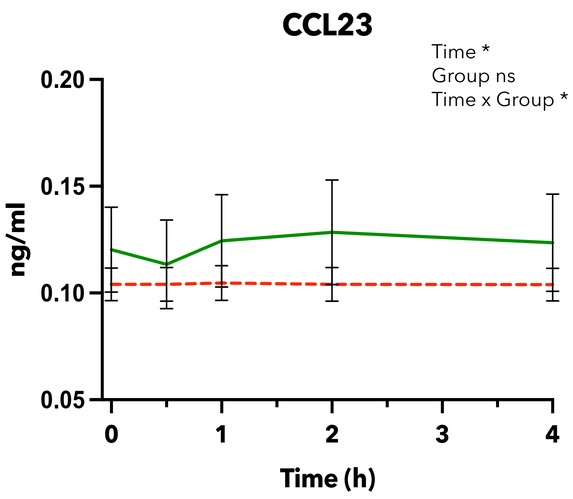


- Pathway analysis: affected pathways in energy metabolism, cytokine signaling, complement cascade and acute phase reaction.
- ELISA: different postprandial behavior of ***IGFBP1***, ***CCL16*** and ***CCL23***. Blunted response in MASLD.

Key Protein Changes







Conclusion

Postprandial blunting in response of IGFBP1 and chemokines CCL16 and CCL23 in MASLD may suggest impaired compensatory mechanisms in MASLD and greater susceptibility to postprandial oxidative stress after a meal.

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1. Velenosi TJ, Ben-Yakov G, Podszun MC, et al. Postprandial Plasma Lipidomics Reveal Specific Alteration of Hepatic-derived Diacylglycerols in Nonalcoholic Fatty Liver Disease. *Gastroenterology*. 2022;162(7):1990-2003.