

# Quantitation of 55 Common Human Plasma Proteins in Healthy Young Adults and Correlation with Body Mass Index and Dietary Patterns

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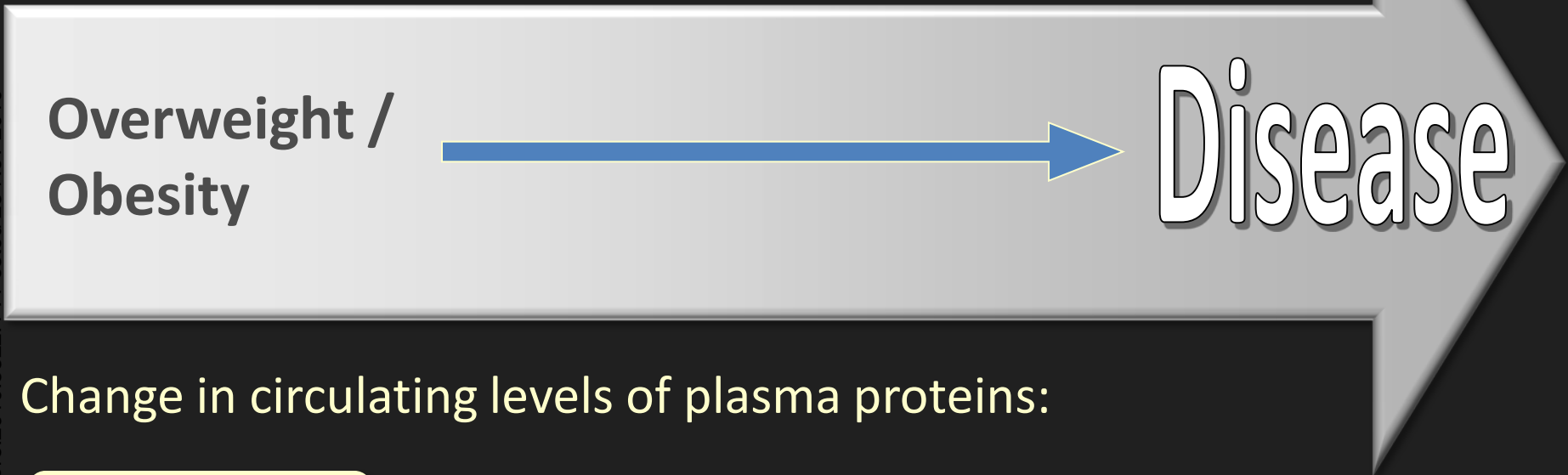
**Overweight =  
Body Mass Index  $\geq 25$  kg/m<sup>2</sup>**



**Unhealthy  
Dietary  
Patterns**

**BMI  $\geq 25$**

**Chronic  
Disease**



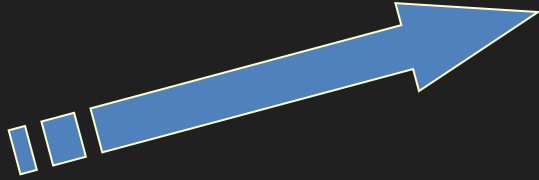
Change in circulating levels of plasma proteins:

**Inflammation**

**Endothelial dysfunction**

**Lipid metabolism**

**DIETARY PATTERNS**

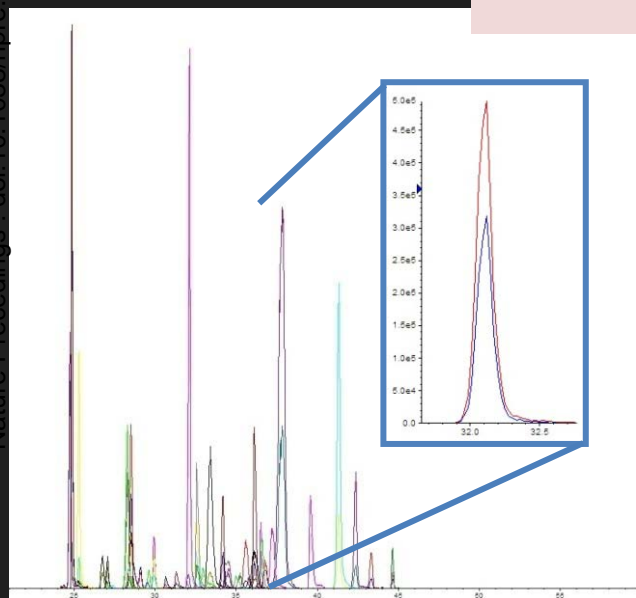


# Multiple Reaction Monitoring-based, Multiplexed, Absolute Quantitation of 45 Proteins in Human Plasma\*

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and Christopher M. Murphy<sup>¶||</sup>

63

73



Synthetic internal standards added  
Concentration balanced to match  
natural abundance

LC-MS/MS-based

*Mol Cell Proteomics* 2009 8(8):1860-77

Adiponectin	Apolipoprotein L1	Gelsolin, isoform 1
Afamin	Aspartate aminotransferase, mitochondrial (m-type)	Glial fibrillary acidic protein (GFAP)
Albumin	Beta-2-glycoprotein I	Haptoglobin beta chain
Aldolase C	CD105-endoglin	Hemopexin
Alpha-1-acid glycoprotein 1	Ceruloplasmin	Heparin cofactor II
Alpha-1-antichymotrypsin	Clusterin	Histidine-rich glycoprotein
Alpha-1-Anti-trypsin	Coagulation factor XIIIa HC	Inter-alpha-trypsin inhibitor HC
Alpha-1B-glycoprotein	Coagulation Factor XIII (a chain)	Kininogen-1
Alpha-2-antiplasmin	Complement C1 inactivator	L-selectin
Alpha-2-HS-glycoprotein	Complement C3	Plasma retinol-binding protein
Alpha-2-macroglobulin	Complement C4 beta chain	Plasminogen
Angiotensinogen	Complement C4 gamma chain	Prothrombin
Antithrombin-III	Complement C9	Serum amyloid P-component
Apolipoprotein A-I	Complement factor B	Thrombospondin-1
Apolipoprotein A-II precursor	Complement factor H	Transferrin
Apolipoprotein A-IV	CRP	Transthyretin
Apolipoprotein B-100	Fibrinogen alpha chain	Tropomyosin 1 alpha chain
Apolipoprotein C-I	Fibrinogen beta chain	Vitamin D-binding protein
Apolipoprotein C-III	Fibrinogen gamma chain	Vitronectin
Apolipoprotein D	Fibrinopeptide A	von Willebrand Factor
Apolipoprotein E	Fibronectin	Zinc-alpha-2-glycoprotein

# Objective

To determine whether a panel of plasma proteins is associated with specific dietary patterns and overweight / obesity

# Subjects

Toronto Nutrigenomics and Health (TNH) study

n = 1088

Men and women

Multi-ethnocultural population

Age 20 – 29 years

Exclusion criteria

Pregnant or breastfeeding

No blood sample provided

# Data collection

196-item semi-quantitative food frequency questionnaire

- 179 items after exclusion of dietary supplements

General health and lifestyle questionnaire

Fasting blood sample

- Plasma for MRM analysis



# Statistical analysis

## Principal Components Analysis (PCA)

- Patterns of food intake
- Proteomic biomarker profiles

## T-test

- Differences in proteomic profile scores between BMI groups

## Linear regression

- Association between dietary pattern scores and proteomic profile scores

# Dietary patterns in the TNH population



## ‘Western’:

Processed, high salt and sugary foods, enriched white flour products, high sugar/energy beverages



## ‘Prudent’:

Fruits and vegetables, nuts, dried beans, whole grains, water



## ‘Eastern’:

Seafood, vegetables, rice, organ meats

Brenner et al (submitted)

# Protein panel – reproducibility between runs

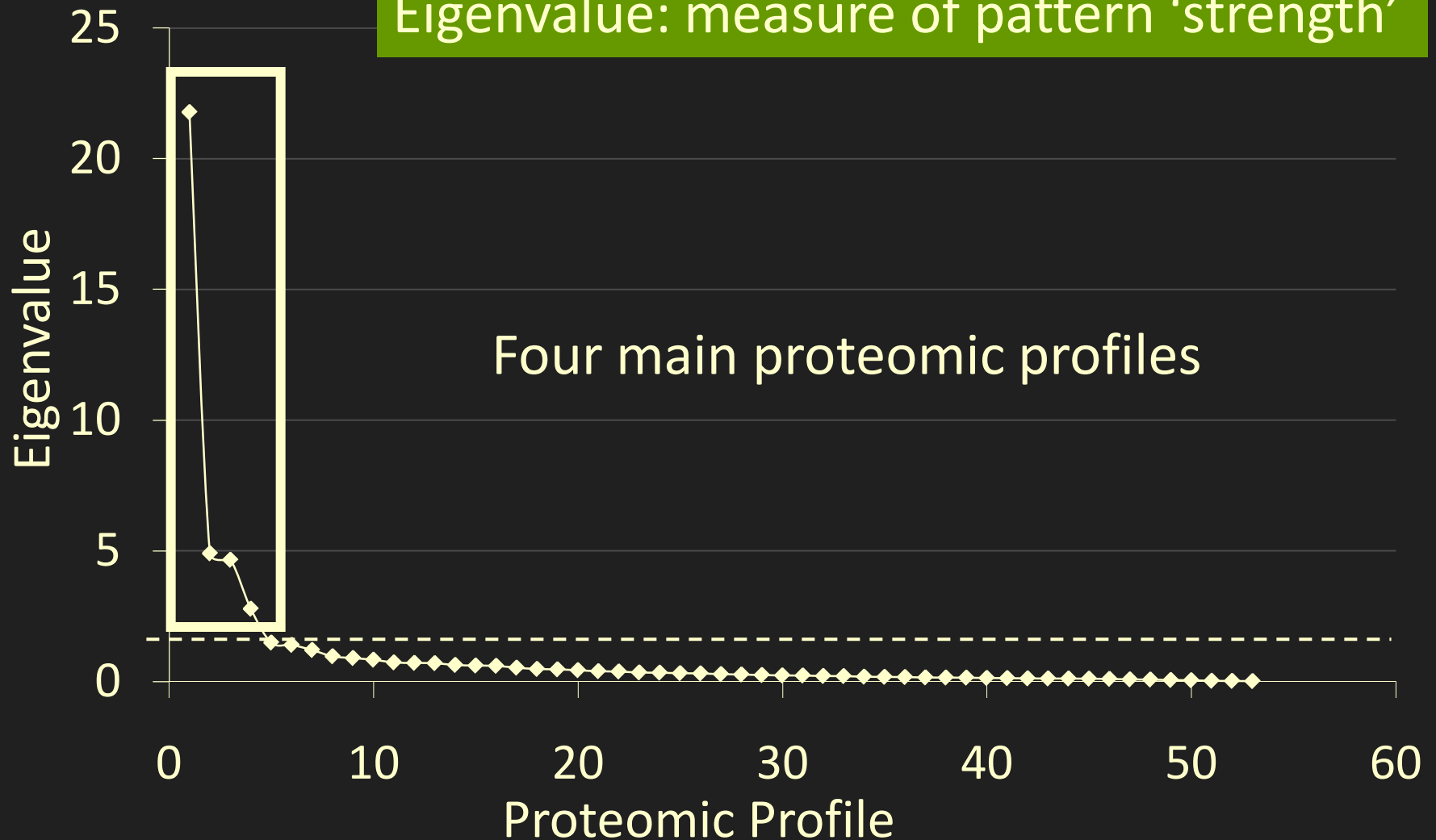
## Coefficient of Variation (CV)

	Total	<10%	10 – 15 %	20%	>20%	Not Detected
No. Proteins	63	50	4	1	2	6

55 proteins included in analyses

# PCA – Protein panel

Eigenvalue: measure of pattern 'strength'



## Proteomic Profile 1

Angiotensinogen  
Kininogen-1  
Ceruloplasmin  
Vitamin D-binding protein  
Vitronectin  
Plasminogen  
Apolipoprotein A-II precursor  
Alpha-1-Anti-trypsin  
Plasma retinol-binding protein  
Heparin cofactor II  
Apolipoprotein L1  
Coagulation factor XIIIa HC  
Transferrin  
Apolipoprotein A-I  
Apolipoprotein C-III  
Alpha-2-HS-glycoprotein  
Afamin  
Hemopexin  
Inter-alpha-trypsin inhibitor HC  
Clusterin  
Prothrombin  
Apolipoprotein B-100  
Alpha-2-antiplasmin  
Apolipoprotein C-I  
Complement C3

## Proteomic Profile 2

Albumin  
Antithrombin-III  
Gelsolin, isoform 1  
Complement C1 inactivator  
Alpha-2-antiplasmin  
Histidine-rich glycoprotein  
Apolipoprotein A-IV  
Beta-2-glycoprotein I  
Apolipoprotein E  
Transthyretin  
Apolipoprotein C-I  
L-selectin  
Alpha-2-macroglobulin  
Clusterin

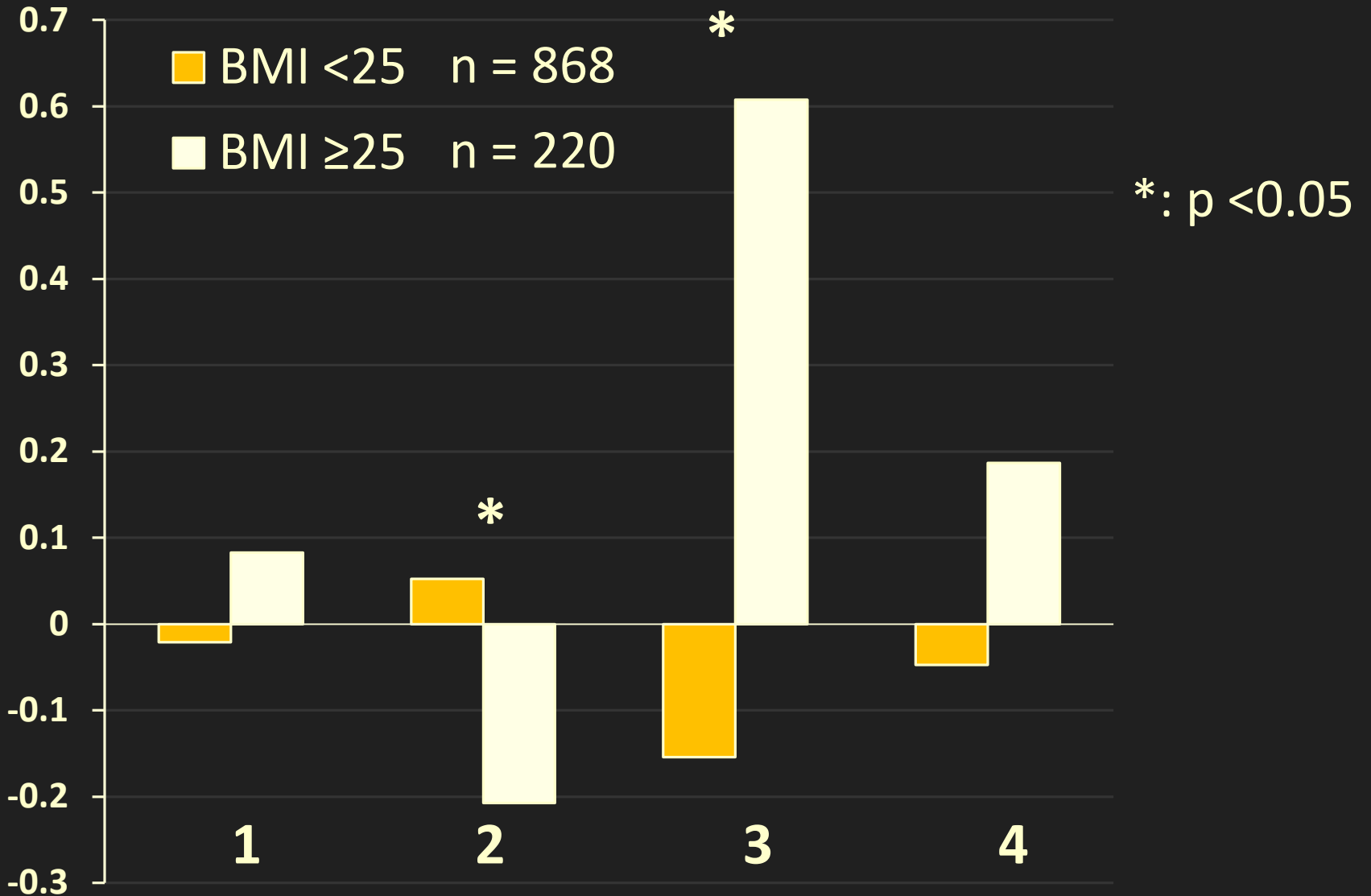
## Proteomic Profile 3

Complement C4 beta chain  
Complement C4 gamma chain  
Alpha-1-acid glycoprotein 1  
Complement factor B  
Haptoglobin beta chain  
**'Inflammatory'**  
Complement C5  
Alpha-1-antichymotrypsin  
Complement factor H  
Complement C3  
Serum amyloid P-component  
Complement C1 inactivator

## Proteomic Profile 4

Fibrinogen alpha chain  
Fibrinogen beta chain  
Fibrinopeptide A  
Fibrinogen gamma chain  
Fibronectin

# Average Protein Score



## Proteomic profile scores stratified by BMI status

# Association between dietary pattern scores and proteomic profile scores

Dietary Pattern

Proteomic Profile

		1	2	3	4
<b>Western</b>	$\beta$	0.144 <b>+</b>	-0.007	0.122 <b>+</b>	0.032
	p	<0.01	0.885	<0.05	0.506
<b>Prudent</b>	$\beta$	0.053	0.018	0.032	-0.025
	p	0.146	0.647	0.409	0.519
<b>Eastern</b>	$\beta$	-0.207 <b>-</b>	0.093 <b>+</b>	-0.010	-0.017
	p	<.0001	<0.01	0.756	0.624

Models adjusted for age, sex, ethnocultural group and physical activity

# Summary

Four main proteomic profiles identified

Average protein loading scores differ by BMI

→ Profile 3 scores higher in BMI  $\geq 25$

Positive association between Western diet and profile 3

## Profile 3:

Complement C4 beta chain  
Complement C4 gamma chain  
Alpha-1-acid glycoprotein 1  
Complement factor B  
Haptoglobin beta chain  
Complement C9  
Alpha-1-antichymotrypsin  
Complement factor H  
Complement C3  
Serum amyloid P-component  
Complement C1 inactivator

**Proteomic profile 3 → Biomarker of poor diet and overweight/obesity**



# Acknowledgements

## University of Toronto

Ahmed El-Sohemy

Christine Asik

Joanne Brathwaite

Darren Brenner

Leah Cahill

Cristina Cuda

Laura Da Costa

Erica Day-Tasevski

Andre Dias

Karen Eny

Francesca Garofalo

Hyeon-Joo Lee

Lilli Mauer

Daiva Nielsen

Lola Oseni

## University of Victoria –

## Genome BC Proteomics Centre

Christoph Borchers

Jun Han

Derek Smith

## Public Health Agency of Canada – Office of Biotechnology, Genomics and Population Health

Alaa Badawi

Mohamed Karmali

## Funding



Public Health  
Agency of Canada

Agence de la santé  
publique du Canada

