# Foodomics

*How knowing more about what's in our foods will lead to a new nutrition*

**Emily Hill, PhD, RDN**
University of Colorado Anschutz Medical Campus
Department of Pediatrics – Section of Nutrition

University of Colorado Anschutz Medical Campus

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## Disclosures

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- NIH/NIDDK
- National Center for Research Resources
- National Cattlemen's Beef Association
- National Pork Board
- Colorado Clinical and Translational Sciences Institute (NIH/NCATS)

The funding sources were not involved in the study design; data collection, analysis, or interpretation; or in the presenting of this work.





## Disclosures

This presentation is supported by:
- National Cattlemen's Beef Association, a contractor to the Beef Checkoff
- Indiana Beef Council





## Learning Objectives

After this session, attendees will be able to:

1. List strengths and limitations of current dietary assessment methods
2. Describe the application of metabolomics to nutrition studies for identification of biomarkers of exposure
3. Explain how new approaches to measuring foods can be used for precision nutrition and applied to dietetics practice





Diet → ? → Health

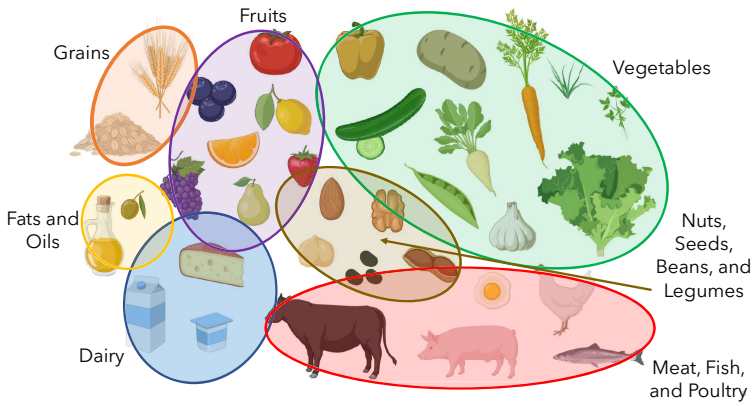




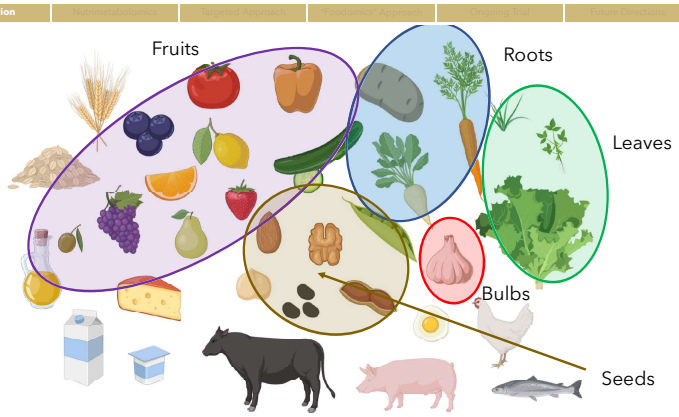
How do we categorize foods in our diets?





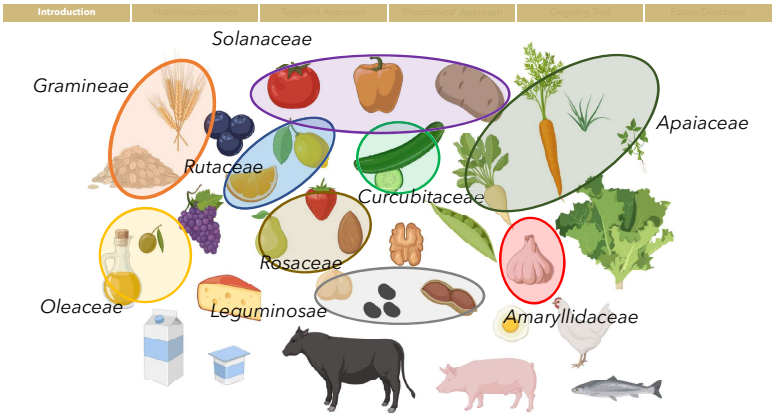


















How do we know what people are eating?

Diet →  → Health





Diet →  → Health





Diet →  → Health





Diet →  → Health



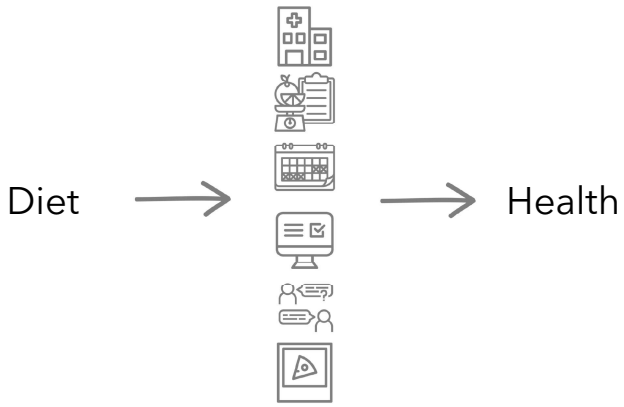


Diet →  → Health



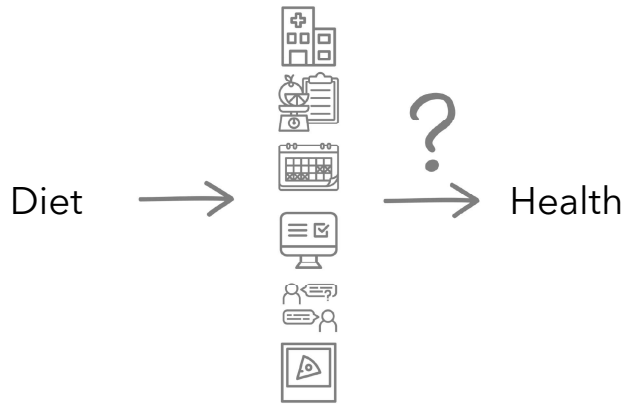


Diet →  → Health












## Nutritional Metabolomics

The application of metabolomics to the analysis of samples derived from human nutritional studies

Ulaszewska et al., *Mol Nutr Food Res*, 2018





**Combining traditional dietary assessment methods with novel metabolomics techniques: present efforts by the Food Biomarker Alliance**

Elske M. Brouwer-Brolsma[1], Lorraine Brennan[2], Christian A. Drevon[3], Henk van Kranen[4], Claudine Manach[5], Lars Ove Dragsted[6], Helen M. Roche[7], Cristina Andres-Lacueva[8,9], Stephan J. L. Bakker[10], Jildau Bouwman[11], Francesco Capozzi[12], Sarah De Saeger[13], Thomas E. Gundersen[14], Marjukka Kolehmainen[15], Sabine E. Kulling[16], Rikard Landberg[17], Jakob Linseisen[18], Fulvio Mattivi[19], Ronald P Mensink[20], Cristina Scaccini[21], Thomas Skurk[22], Inge Tetens[23], Guy Vergeres[24], David S. Wishart[25,*], Augustin Scalbert[26] and Edith J. M. Feskens[1,*]

International Journal of Obesity (2020) 44:2372–2381
https://doi.org/10.1038/s41366-020-0628-1

TECHNICAL REPORT

Techniques and Methods

**Quantifying the human diet in the crosstalk between nutrition and health by multi-targeted metabolomics of food and microbiota-derived metabolites**

Raúl González-Domínguez[1,2] · Olga Jáuregui[2,3] · Pedro Mena[4] · Kati Hanhineva[5] · Francisco José Tinahones[6,7] · Donato Angelino[4] · Cristina Andrés-Lacueva[1,2]

**Nutritional Metabolomics and the Classification of Dietary Biomarker Candidates: A Critical Review**

Talha Rafiq,[1,2] Sandi M Azab,[3,4] Koon K Teo,[3,5,6] Lehana Thabane,[3] Sonia S Anand,[3,5,6] Katherine M Morrison,[7] Russell J de Souza,[3,8] and Philip Britz-McKibbin[1]

[1]Medical Sciences Graduate Program, Faculty of Health Sciences, McMaster University, Hamilton, Canada; [2]Population Health Research Institute, Hamilton Health Sciences, McMaster University, Hamilton, Canada; [3]Department of Chemistry and Chemical Biology, McMaster University, Hamilton, Canada; [4]Department of Pharmacognosy, Alexandria University, Alexandria, Egypt; [5]Department of Health Research Methods, Evidence & Impact, McMaster University, Hamilton, Canada; [6]Department of Medicine, McMaster University, Hamilton, Canada; and [7]Department of Pediatrics, McMaster University, Hamilton, Canada

**Perspective: Dietary Biomarkers of Intake and Exposure—Exploration with Omics Approaches**

Padma Maruvada,[1] Johanna W Lampe,[2,*] David S Wishart,[3] Dinesh Barupal,[3] Deirdra N Chester,[3] Dylan Dodd,[3,4] Yannick Djoumbou-Feunang,[3] Pieter C. Dorrestein,[4,5,6] Lars O Dragsted,[7] John Draper,[8,9] Linda C. Dumke,[10] Johanna T Dwyer,[11,12] Nancy J Emenaker,[13] Oliver Fiehn,[2] Robert E Gerszten,[14] Frank B Hu,[15,16] Robert W Karp,[1] David M Klurfeld,[17] Maren R Laughlin,[1] A Roger Little,[18] Christopher J Lynch,[1] Steven C Moore,[19] Holly L Nicastro,[20] Diane M O'Brien,[21] José M Ordovás,[22] Stavroula K Osganian,[1] Mary Playdon,[23] Ross Prentice,[24] Daniel Raftery,[2,25] Nichole Reisdorph,[26] Helen M Roche,[27] Sharon A Ross,[28] Shengmin Sang,[29] Augustin Scalbert,[30] Pothur R Srinivas,[31] and Steven H Zeisel[32]

*foods*

MDPI

*Review*

**You Are What You Eat: Application of Metabolomics Approaches to Advance Nutrition Research**

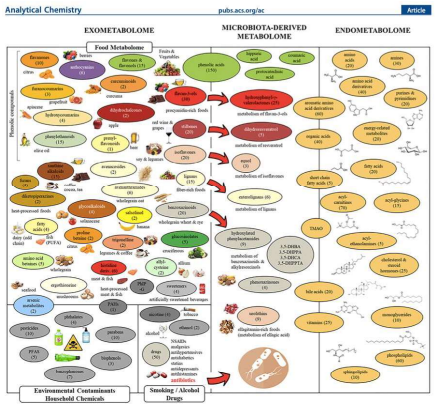
Abdul-Hamid M. Emwas [1], Nahla Al-Rifai [2], Kacper Szczepski [3], Shuruq Alsuhaymi [3], Saleh Rayyan [4], Hanan Almahasheer [5], Mariusz Jaremko [3], Lorraine Brennan [6] and Joanna Izabela Lachowicz [7,*]

**Nutrimetabolomics reveals food-specific compounds in urine of adults consuming a DASH-style diet**

Nichola A. Reisdorph[1*], Audrey E. Hendricks[2], Minghua Tang[3], Katrina A. Doenges[2], Richard M. Reisdorph[1], Brian C. Tooker[2], Kevin Quinn[2], Sarah J. Borrenpause[2], Yasmeen Nkrumah-Elie[2], Daniel N. Frank[4], Wayne W. Campbell[3,4] & Nancy F. Krebs[2,4]








Gonzalez-Dominguez et al., *Anal Chem*, 2020

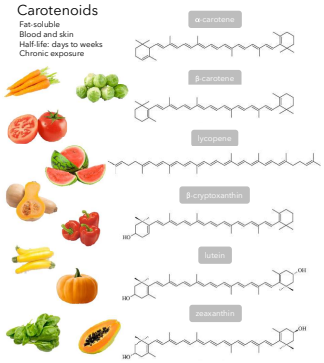




Can assessment of common compounds found in our foods help us measure diet and its effect on health?

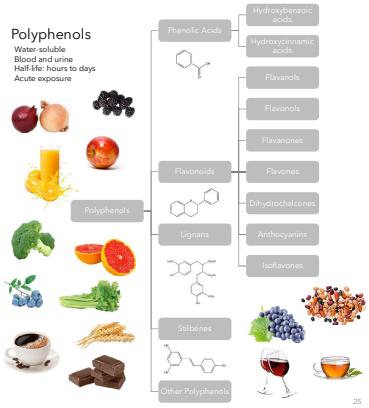
## Carotenoids

Fat-soluble
Blood and skin
Half-life: days to weeks
Chronic exposure




## Polyphenols

Water-soluble
Blood and urine
Half-life: hours to days
Acute exposure

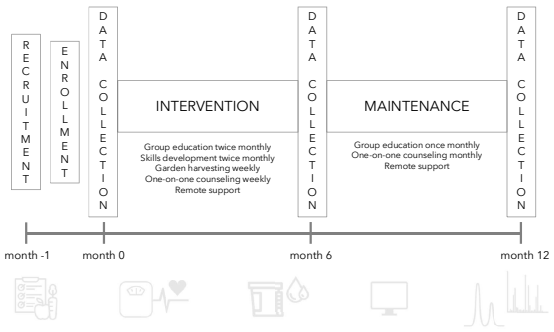



Campbell, et al., 1994; Jahns et al., 2014; Woodward, et al., 2018; Manach et al., 2004; Medina-Remón, et al., 2017





## Nutrition and Exercise Trial (NExT)

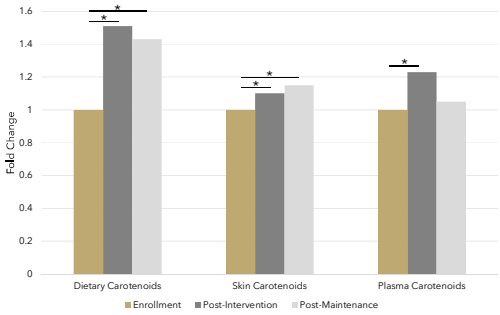







Carotenoids

### Change in Carotenoids Over Intervention and Maintenance




Hill et al., *unpublished data*





Polyphenols

### Correlation between Dietary Patterns and Dietary Polyphenols

| Dietary Polyphenols (mg/1000 kcal/day) | HEI-2015 | aMED | DASH |
|---|---|---|---|
| Phenolic Acids | | | |
| Hydroxybenzoic acids | | | |
| Hydroxycinnamic acids | | | |
| Flavonoids | | | |
| Flavanols | | | |
| Flavonols | | | |
| Flavanones | | | |
| Flavones | | | |
| Dihydrochalcones | | | |
| Isoflavones | | | |
| Lignans | | | |
| Stilbenes | | | |
| Other Polyphenols | | | |
| **Total Dietary Polyphenols** | | | |

### Correlation between Dietary Patterns and Urinary Polyphenols

| Urinary Polyphenols (μmol/day) | HEI-2015 | aMED | DASH |
|---|---|---|---|
| Phenolic Acids | | | |
| Hydroxybenzoic acids | | | |
| Hydroxycinnamic acids | | | |
| Flavonoids | | | |
| Flavanols | | | |
| Flavonols | | | |
| Flavanones | | | |
| Flavones | | | |
| Dihydrochalcones | | | |
| Isoflavones | | | |
| Lignans | | | |
| Stilbenes | | | |
| Other Polyphenols | | | |
| **Total Urinary Polyphenols** | | | |

$r_s$ +1.0 … -1.0

Hill et al., *unpublished data*





Polyphenols

### Correlation between Indicators of Cardiometabolic Health and Dietary Polyphenols

| Dietary Polyphenols (mg/1000 kcal/day) | BMI (kg/m²) | SBP (mmHg) | DBP (mmHg) | HDL (mg/dL) | LDL (mg/dL) | TGL (mg/dL) | hs-CRP (mg/L) | IL-6 (pg/mL) | TNF-α (pg/mL) | C-peptide (ng/L) |
|---|---|---|---|---|---|---|---|---|---|---|
| Phenolic Acids | | | | | | | | | | |
| Hydroxybenzoic acids | | | | | | | | | | |
| Hydroxycinnamic acids | | | | | | | | | | |
| Flavonoids | | | | | | | | | | |
| Flavanols | | | | | | | | | | |
| Flavonols | | | | | | | | | | |
| Flavanones | | | | | | | | | | |
| Flavones | | | | | | | | | | |
| Dihydrochalcones | | | | | | | | | | |
| Isoflavones | | | | | | | | | | |
| Lignans | | | | | | | | | | |
| Stilbenes | | | | | | | | | | |
| Other Polyphenols | | | | | | | | | | |
| **Total Dietary Polyphenols** | | | | | | | | | | |

$r_s$ +1.0 … -1.0

Hill et al., *unpublished data*





- Common compounds (carotenoids and polyphenols) are associated with dietary exposure and metabolism of plant-based foods
- Exposure to these compounds is related to established measures of overall dietary patterns
- Dietary intakes of these compounds may be associated with indicators of cardiometabolic health

What other compounds in our food might be responsible for impacts on health?





- Which foods within "healthy" dietary patterns cause effects? Are there specific compounds in these foods that are responsible?
- What is the role of food-specific compounds? Can they be used as biomarkers of food intake?
- How and why do different people respond to the same dietary intakes in different ways?






## Foodomics Team


NIH/NIDDK 1R01DK113957-01A1 (to Drs. Krebs, Campbell, and Reisdorph)

National Pork Board and USDA (2011-38420-20038) (to Dr. Campbell)

National Cattleman's Beef Association (to Drs. Krebs and Tang)





- Identify food-specific compounds present within foods consumed within healthy dietary patterns
- Evaluate biospecimens (e.g., urine, blood) to determine presence of food-specific compounds
- Evaluate association between food-specific compounds found in plasma and clinical indicators of health
- Design and implement a controlled feeding trial to confirm and validate

Reisdorph et al., *Sci Rep*, 2020





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Reisdorph et al., *Sci Rep*, 2020





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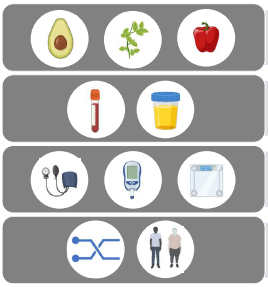
Reisdorph et al., *Sci Rep*, 2020



Identify food-specific compounds present within foods consumed within healthy dietary patterns

Evaluate biospecimens (e.g., urine, blood) to determine presence of food-specific compounds

Evaluate association between food-specific compounds found in plasma and clinical indicators of health

Design and implement a controlled feeding trial to confirm and validate

Reisdorph et al., *Sci Rep*, 2020



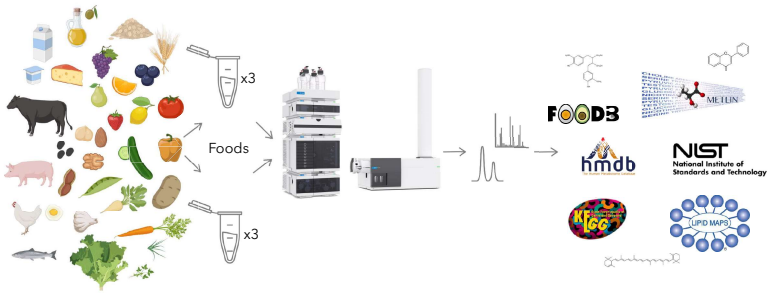


What's in our food?





## Food-centric Metabolomics Approach: Foodomics




Reisdorph et al., *Sci Rep*, 2020



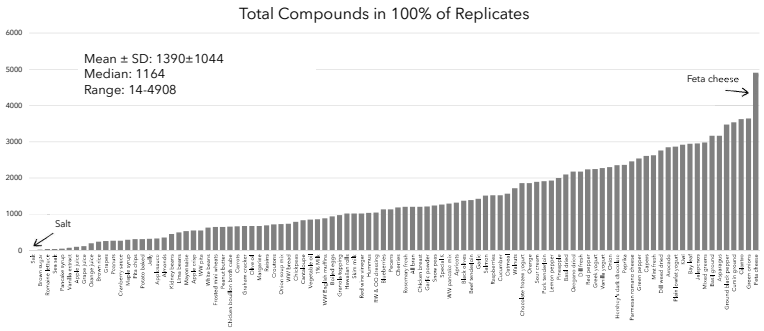


## Foodomics of 100 Foods

| | | | | |
|---|---|---|---|---|
| 1% Milk | Carrot | Graham cracker | Olive oil | Rosemary |
| Bran flakes cereal | Cherry | Granola | Onion | Red wine and olive oil |
| Almond | Chicken broth cube | Grape juice | Onion soup mix | Salmon |
| Apple crisp | Chicken | Grape | Orange | Salt |
| Apple juice | Chickpea | Green onion | Orange juice | Sea salt |
| Applesauce | Chocolate frozen yogurt | Green pepper | Oregano | Skim milk |
| Apricot | Cilantro, dried | Hawaiian roll | Pancake syrup | Snow pea |
| Asparagus | Cilantro, fresh | Hummus | Paprika | Sour cream |
| Avocado | Cranberry sauce | Jalapeno | Parmesan Romano cheese | Vanilla extract |
| Basil, dried | Croutons | Jelly, grape | Peanut butter | Yogurt, Greek, fruited |
| Basil, ground | Cucumber | Kidney bean | Peanut | Yogurt, plain |
| Bay leaf | Cumin, ground | Kiwi | Pecan | Yogurt, vanilla |
| Beef | Dark chocolate | Lemon pepper | Pineapple | Vegetable oil |
| Black olive | Dill, fresh | Lima bean | Pita chip | Walnut |
| Black pepper | Dill, dried | Maple syrup | Pork | White bean |
| Blueberry | Egg | Margarine | Raisin | White potato |
| Brown rice | Feta cheese | Mayonnaise | Raspberry | WW bread |
| Brown sugar | Frosted mini-wheats | Mint | Red pepper | WW English muffins |
| Cantaloupe | Garlic, fresh | Mixed greens | Red wine vinegar | WW pancake mix |
| Capers | Garlic, powder | Oatmeal | Romaine lettuce | WW pita |







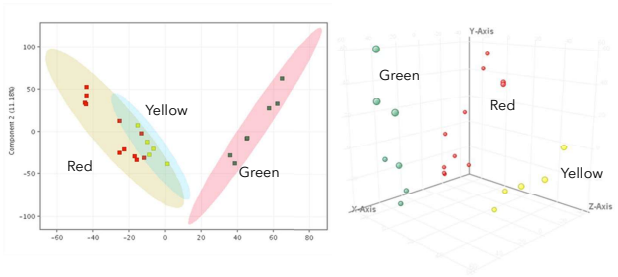

Hill et al., *Curr Dev Nutr*, 2022





How do foods group based on the compounds within them?

## Deeper Dive Example: Bell Peppers

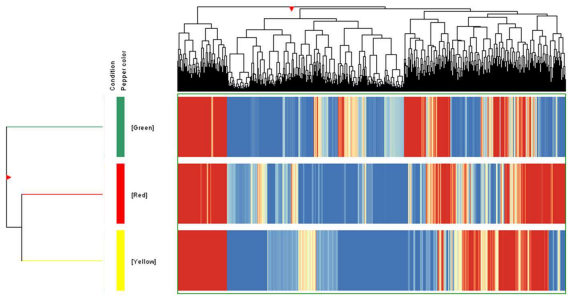



Sutliff et al., *Metabolites*, 2021





## Deeper Dive Example: Bell Peppers



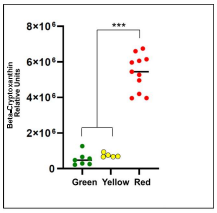

Sutliff et al., *Metabolites*, 2021





## Deeper Dive Example: Bell Peppers

| Compound | P-value | FDR |
|---|---|---|
| Beta-Cryptoxanthin | 5.99E-05 | 0.0080 |
| Sucrose acetate isobutyrate | 4.85E-03 | 0.0560 |
| Leukotriene D4 | 8.67E-03 | 0.0817 |
| Lansiumarin B | 9.36E-03 | 0.0895 |
| Glycidyl oleate | 1.06E-02 | 0.1293 |
| Archaetidylglycerol-myo-inositol | 1.57E-02 | 0.1499 |
| Fusicoplagin A | 3.01E-02 | 0.1026 |
| Oligomycin A | 4.13E-02 | 0.2081 |
| N-(3-(hexadecanoyloxy)-heptadecanoyl)-L-ornithine | 4.74E-02 | 0.3437 |




Sutliff et al., *Metabolites*, 2021





Could these compounds in our food help us better measure diet and its effect on health?





## Mediterranean Diet (MED) Study

| Week | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 11 | 11 | 12 | 13 | 14 | 15 | 16 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Period | Washout | | Dietary intervention | | | | | Washout | | | | Dietary intervention | | | | |
| Diet | Habitual diet | | MED diet #1 | | | | | Habitual diet | | | | MED diet #2 | | | | |

Pre-Diet Plasma and Clinical Indicators | Post-Diet Plasma and Clinical Indicators | Pre-Diet Plasma and Clinical Indicators | Post-Diet Plasma and Clinical Indicators

**Secondary data analysis**

N=41 individuals

Mean age: 46 years ± 2 years
Mean BMI: 30.52 ± 0.6 kg/m$^2$

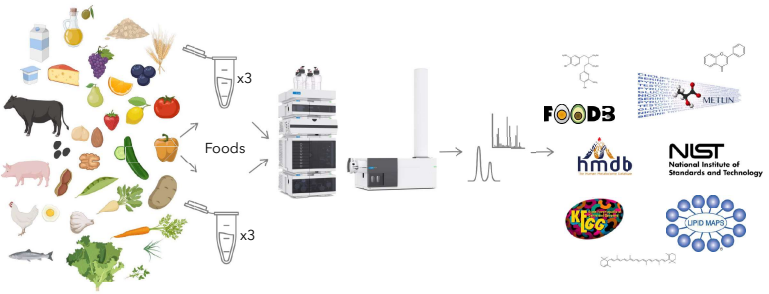
n=13 n=28

O'Connor LE et al., *Am J Clin Nutr*, 2018





Food-specific compound → Presence in biofluids → Association with health



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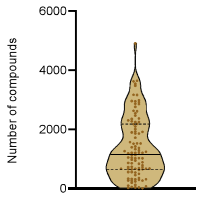
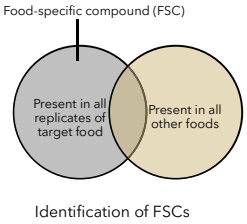


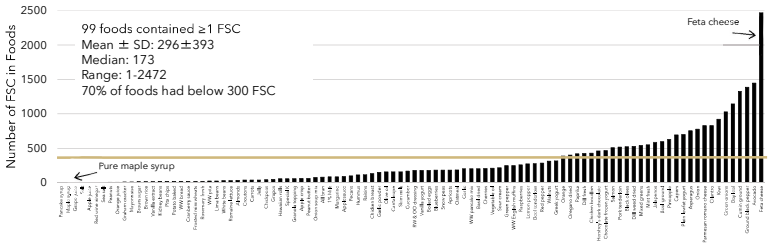

Identification of FSCs

Hill et al., *Curr Dev Nutr*, 2022





## Food-specific compound → Presence in biofluids → Association with health




Hill et al., *Curr Dev Nutr*, 2022

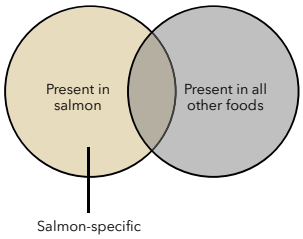




## Food-specific compound → Presence in biofluids → Association with health

780 lipid-soluble compounds
**289 unique to salmon**
132 annotated

738 water-soluble compounds
**219 unique to salmon**
134 annotated

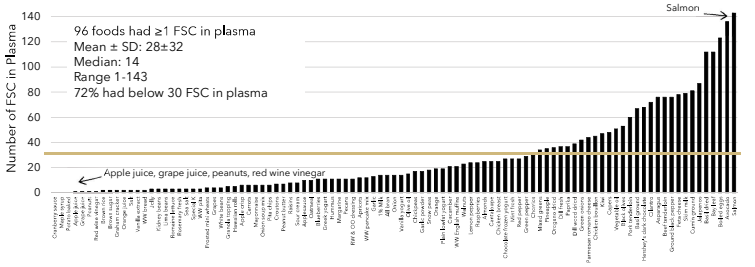



Hill et al., *J Nutr*, 2023





## Food-specific compound → Presence in biofluids → Association with health




Hill et al., *Curr Dev Nutr*, 2022



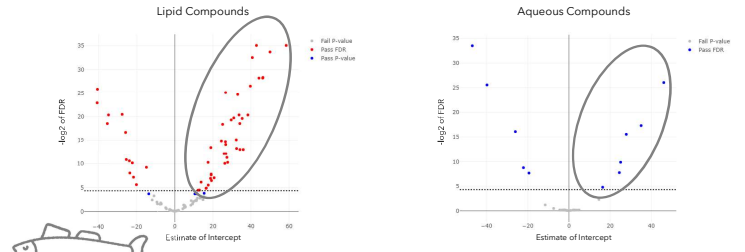


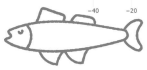
Do the FSCs in plasma change after dietary intervention?





## Food-specific compound → Presence in biofluids → Association with health



107 unique to salmon lipid compounds present in plasma
36 unique to salmon aqueous compounds present in plasma
48 total **increase** significantly (FDR<0.05) after MED

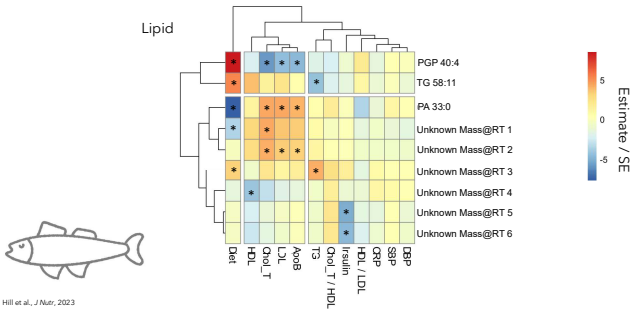
Hill et al., *J Nutr*, 2023

Are the FSCs in plasma associated with health?





Food-specific compound → Presence in biofluids → Association with health

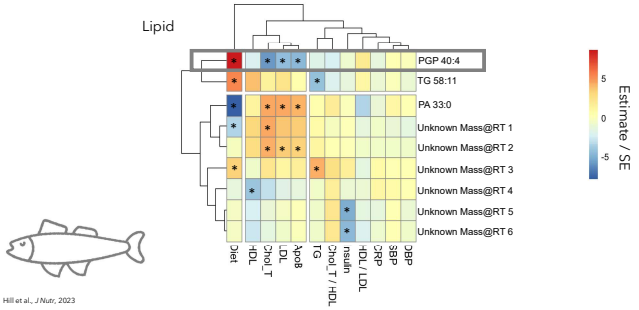



Hill et al., *J Nutr*, 2023





Food-specific compound → Presence in biofluids → Association with health




Hill et al., *J Nutr*, 2023



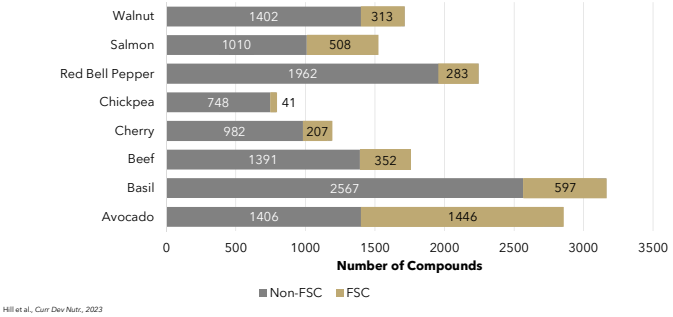


Will we see the same results in a different group of people?





Food-specific compound → Presence in biofluids → Association with health




Hill et al., *Curr Dev Nutr*, 2023





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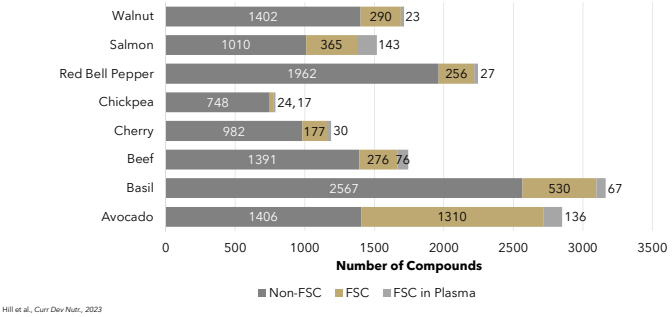


Hill et al., *Curr Dev Nutr*, 2023

## Food-specific compound → Presence in biofluids → Association with health

| Food | Food Group | Lipid FSC Detected | Lipid FSC Increase | Aqueous FSC Detected | Aqueous FSC Increase |
|---|---|---|---|---|---|
| Avocado | Fruit/vegetable; MUFA | 20 | 2 | 116 | 5 |
| Basil | Herb | 7 | 1 | 105 | 2 |
| Beef | Lean meat | 18 | 3 | 58 | 6 |
| Cherries | Fruit | 19 | 5 | 11 | 0 |
| Chickpeas | Legume | 16 | 2 | 5 | 0 |
| Oats | Whole grain | 9 | 0 | 1 | 0 |
| Red bell pepper | Vegetable | 3 | 1 | 24 | 2 |
| Salmon | Fish | 107 | 42 | 36 | 6 |
| Walnuts | Nuts | 11 | 1 | 12 | 0 |

Hill et al., *Curr Dev Nutr., 2023*





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Hill et al., *Curr Dev Nutr., 2023*





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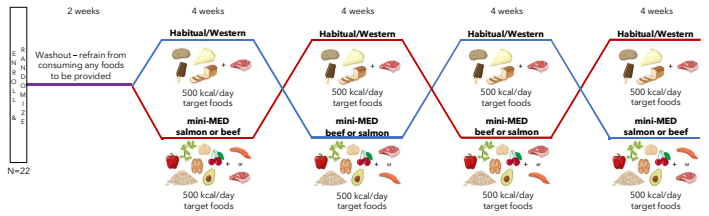
Potential biomarkers??

Hill et al., *Curr Dev Nutr., 2023*





## Prospective Semi-Controlled Feeding Trial




Note: Order for Mini-MED salmon and Mini-MED beef is randomized

Hill et al., *Trials, 2024*



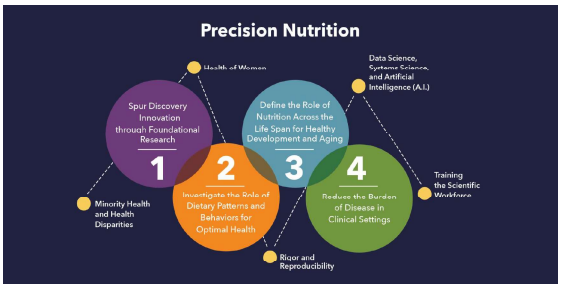


How can this be used for precision nutrition?





## 2020-2030 Strategic Plan for NIH Nutrition Research



One size fits all → personalization

Advances in assessment

Larger, more diverse populations

What impacts response to diet?
- Genes
- Lifestyle
- Health history
- Gut microbiome
- Social determinants of health

All of Us RESEARCH PROGRAM

Nutrition for Precision Health

Nutrition for Precision Health, powered by the All of Research Program

10,000 participants





How does this apply to dietetics practice?





Diet →  → Health





Diet →  → Health





Take Home Point

University of Colorado Anschutz Medical Campus

"Foodomics" allows us to learn more about what's in our foods and how our diet may be linked to health, which will lead to a new nutrition

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NIH T32 (DK007658), PI: Krebs
NIH/NIDDK 1R01DK113957-01A1 (mPI: Krebs, Campbell, and Reisdorph)
National Pork Board and USDA (2011-38420-20038) (PI: Campbell)
National Cattlemen's Beef Association (mPI: Krebs, Tang)

NCBA National Cattlemen's Beef Association

NIH National Institute of Diabetes and Digestive and Kidney Diseases