UC Davis Education: Dynamic New Trends & Benefits from Food Fermentation, Probiotics, & Prebiotics

In Partnership with Southern California Institute of Food Technologists Section

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45 YEARS Natural Products EXPO WEST

UC Davis Education: Dynamic New Trends & Benefits from Food Fermentation, Probiotics, & Prebiotics

David Mills, Ph.D.
Distinguished Professor & Peter J. Shields Chair in Dairy Food Science
University of California at Davis

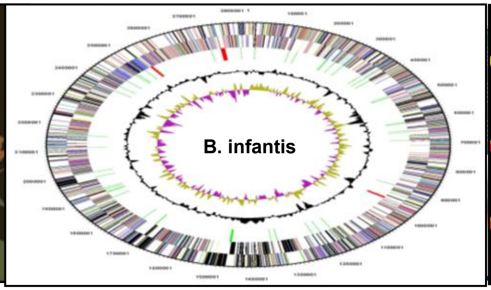
Maria Marco, Ph.D.
Professor & Chair of the Food Science Graduate Group
University of California at Davis

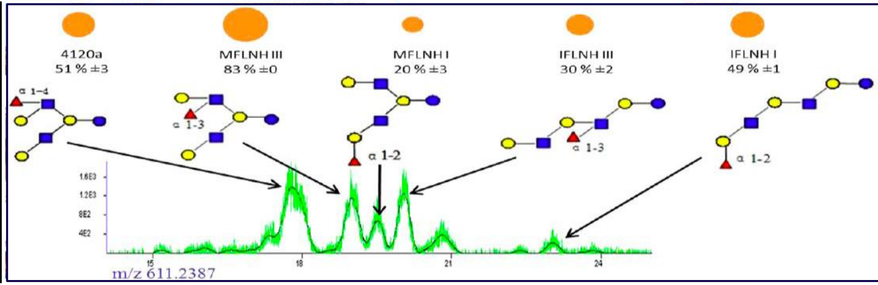
Carolyn Slupsky, Ph.D.
Professor Food Science, Technology, & Nutrition | Endowed Chair in Food, Nutrition, & Health
University of California at Davis

In Partnership with Southern California Institute of Food Technologists Section

Milk in Smart! Gut Microbe Metabolism of Milk Glycans Influences Brain Health

David Mills, Ph.D.
Distinguished Professor & Peter J. Shields Chair in Dairy Food Science
University of California at Davis





Milk is Smart! Gut Microbe Metabolism of Milk Glycans Influences Brain Health and More

David A. Mills
Distinguished Professor, UC Davis
Peter J. Shields Endowed Chair in Dairy Food Science
mills.ucdavis.edu

UC DAVIS FOOD SCIENCE AND TECHNOLOGY

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UC Davis Milk Bioactives Group

- >23 yrs of interdisciplinary collaboration (chemists, microbiologists, neonatologists, physiologists, engineers, data scientists & more)
- >$50M in research funding (federal, many companies, foundations)
- Hundreds of collaborative publications and numerous patents
- Spun off several start up companies

Faculty

Bruce German
Carlito Lebrilla
Mark Underwood
Helen Raybould
David Mills
Daniella Barile
Danielle Lemay
Juliana de Moura Bell
Carolyn Slupsky
Xi Chen
Ameer Taha

Infinant HEALTH™ one·bio MATRUBIALS Proof GOODVICE™ N1853

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Many are seeking to implant microbes in the gut for prophylactic and therapeutic purposes

Rebiotix® Microbiota Restoration Therapy — A FERRING COMPANY

enterome

FINCH

METABOGEN

SERES THERAPEUTICS — Leading the Microbiome Revolution

thryve

AXIAL THERAPEUTICS

Siolta Therapeutics

OptiBiotix® HEALTH PLC

VEDANTA BIOSCIENCES

synlogic

YSOPIA bioscience — Unleashing microbiome-based therapies

A-Mansia BIOTECH

EnteroBiotix

SCIBAC

Are their natural models bacterial enrichment in animals via natural processes?

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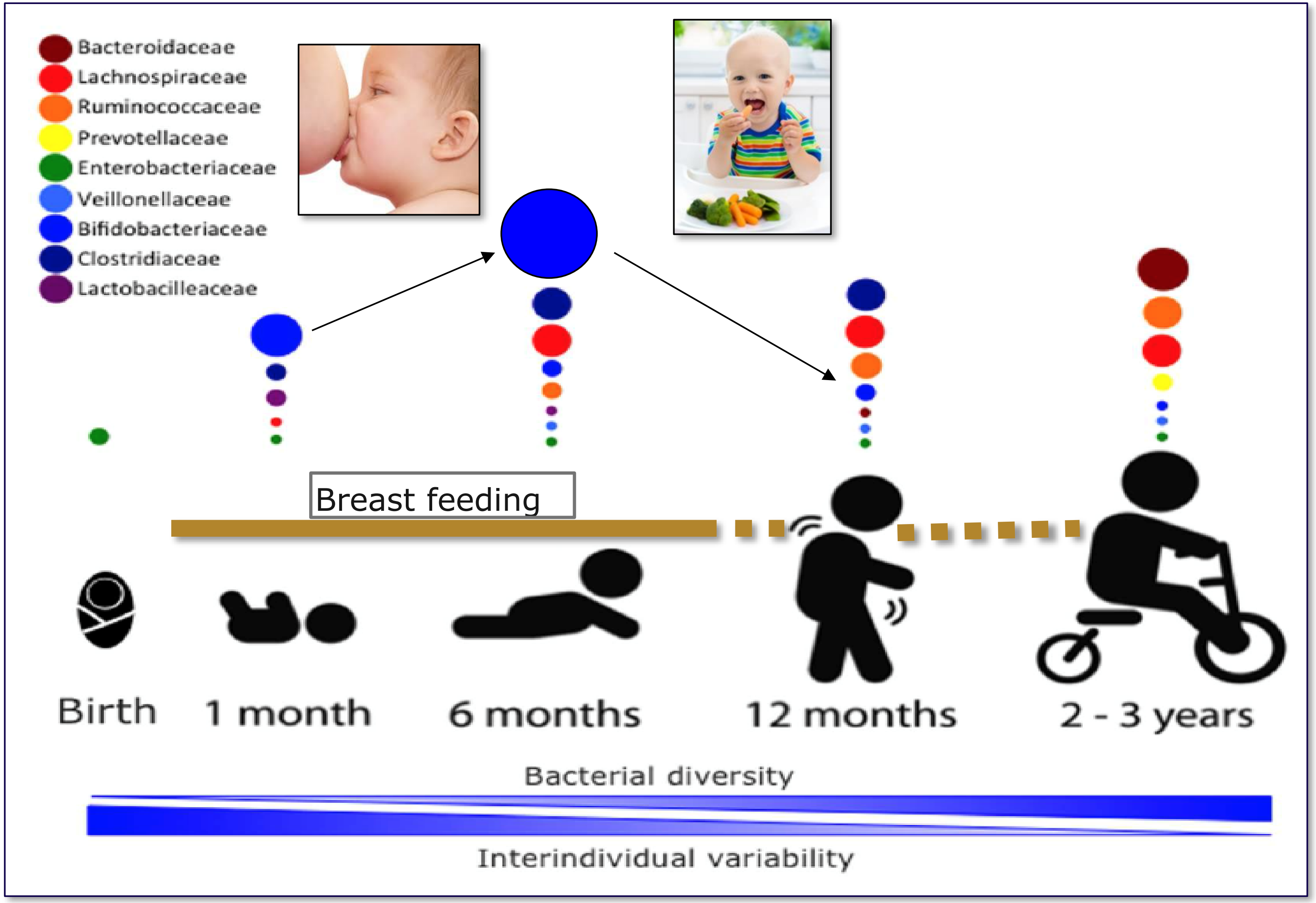
How does a gut microbiome grow?



- **Bloom of *Bifidobacterium* driven (in part) by human milk oligosaccharides & glycoconjugates**
- **Persistence and function of *Bifidobacterium* is associated with beneficial health impacts**
- **Regional differences in level of *Bifidobacterium* (↓industrialized vs↑ non-industrialized)**

Arrieta et al Front Immunol 2014, 427

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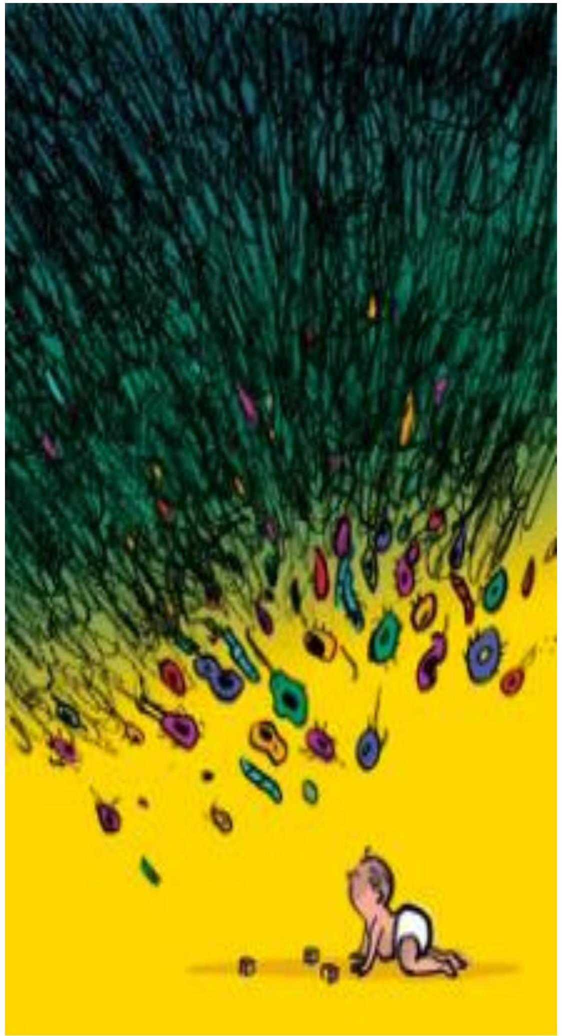

What milk components are influencing the infant gut microbiota?

Do these components promote some microbes and restrict others?

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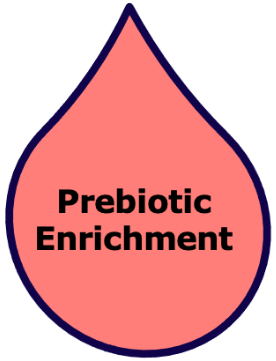
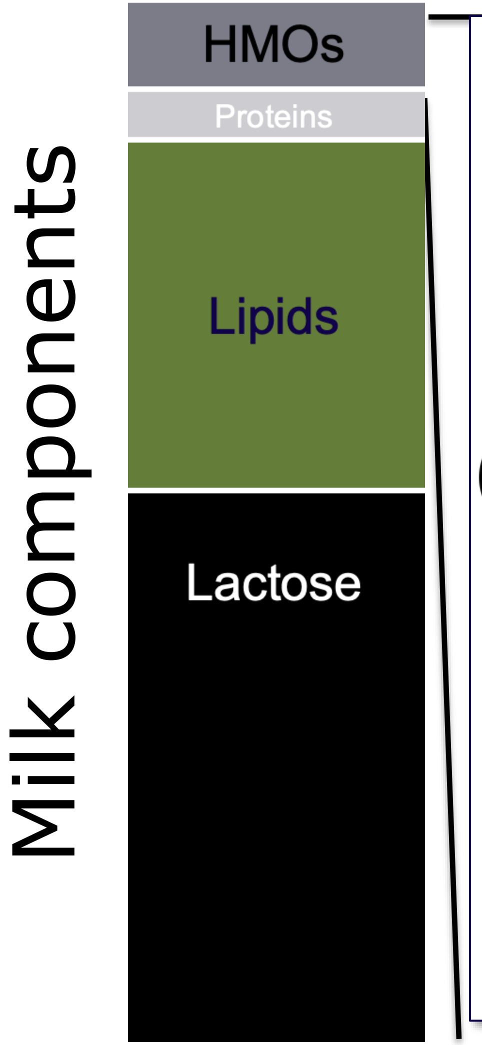
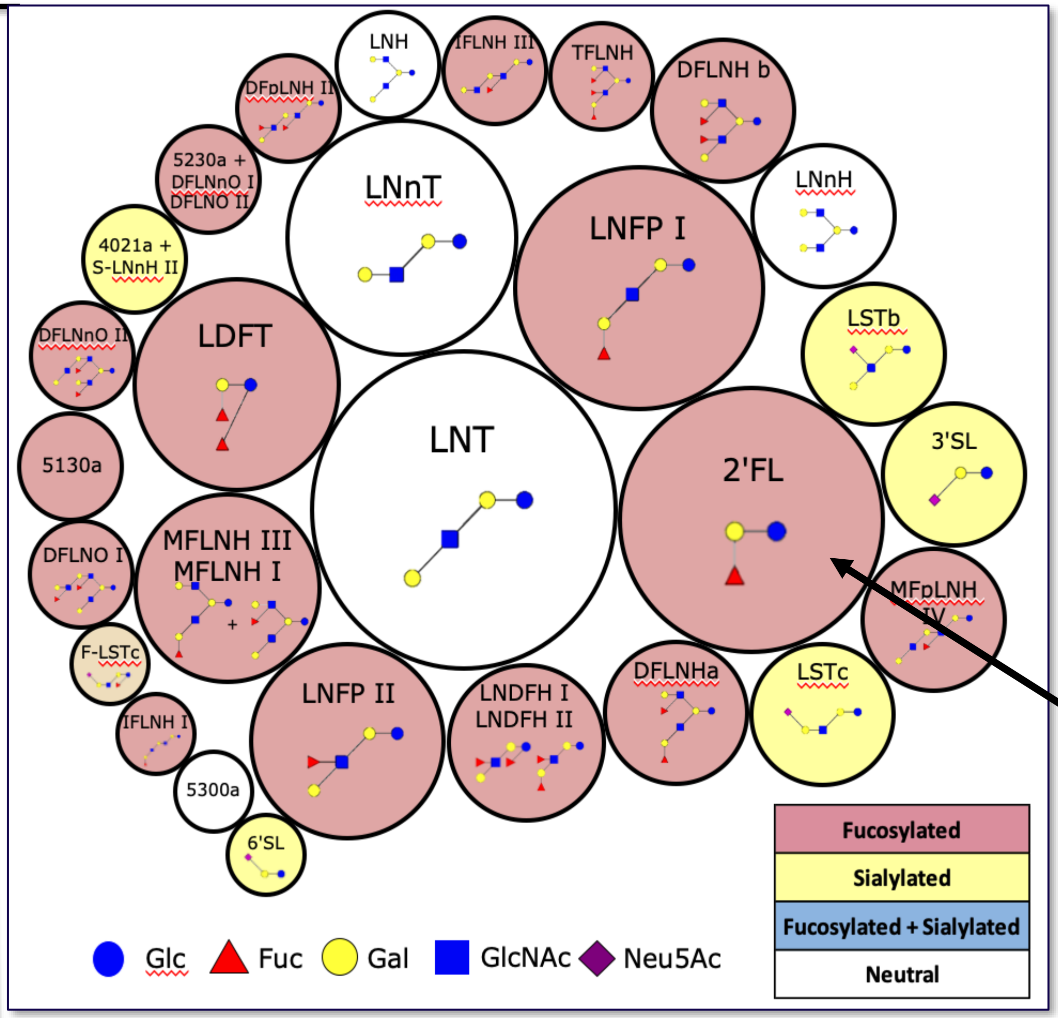
Human milk oligosaccharides



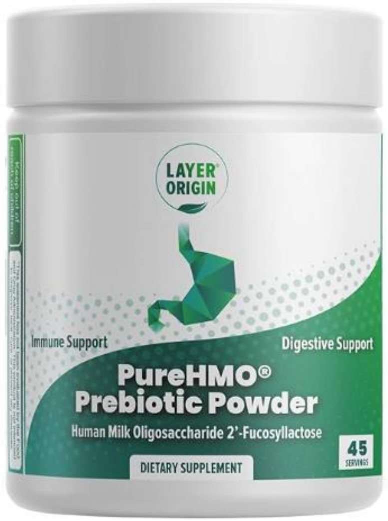




Over 160 species

6 or so are made commercially

- Increasing use in formula
- Increasing use for adult gut dysbiosis (IBS etc.)



Do breast milk oligosaccharides enrich all, or select, bifidobacteria?

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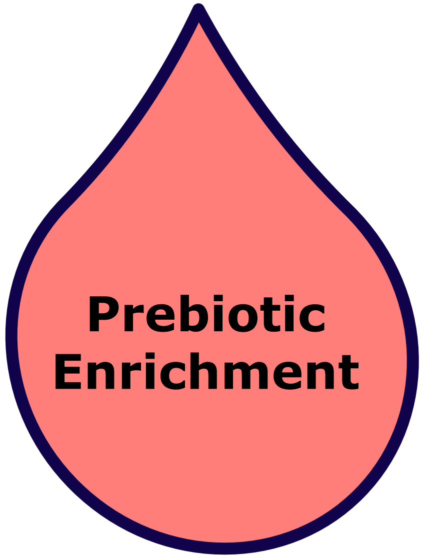
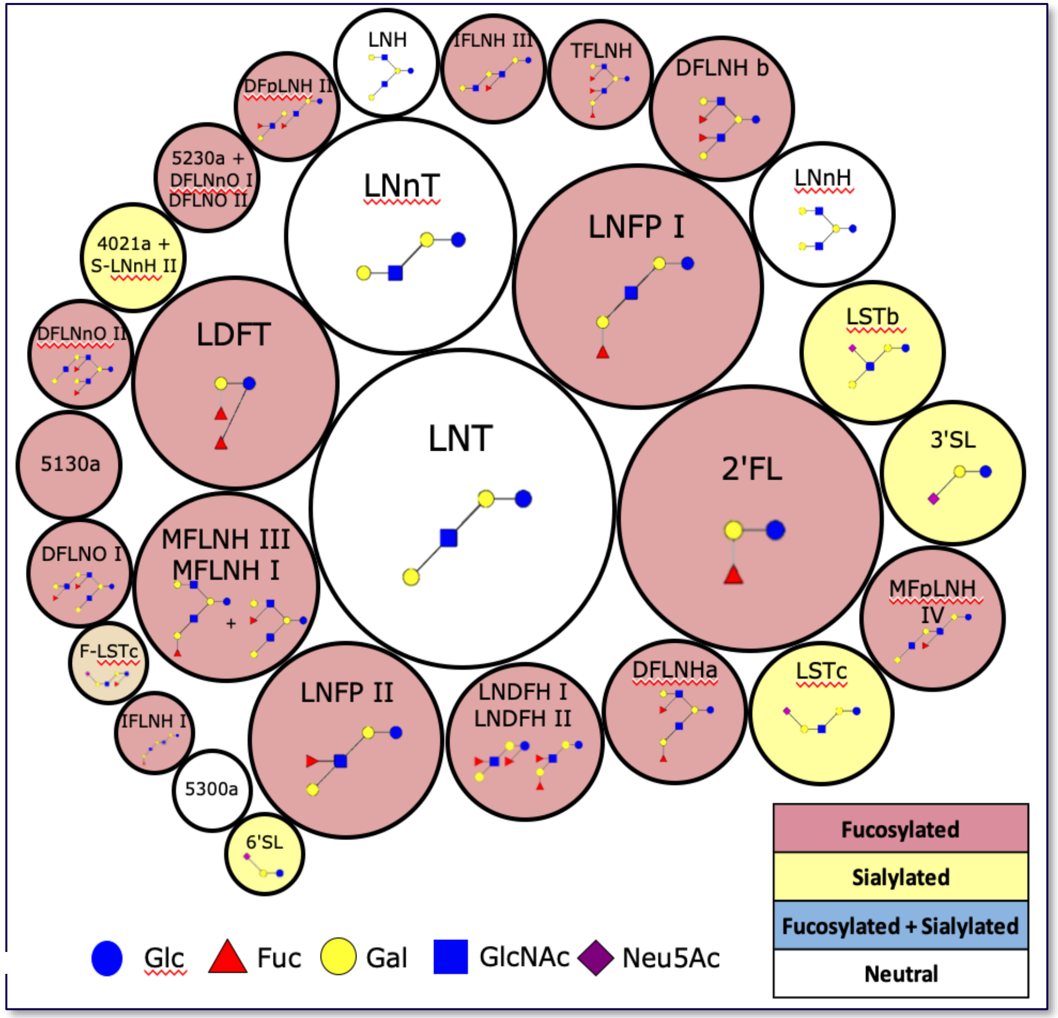
Consumption of HMOs by *Bifidobacterium* species

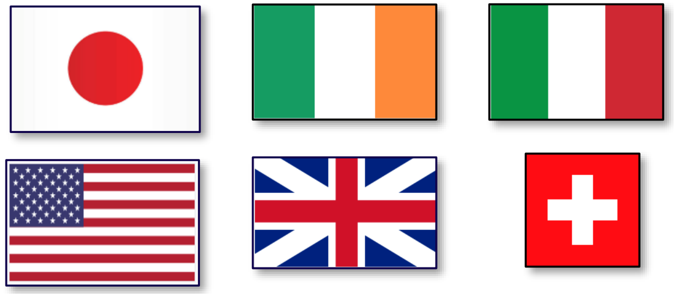




HMO consumed by isolates of:

- *B. longum* subsp. *infantis*
- *B. bifidum*
- *B. longum* subsp. *longum*
- *B. breve*
- *B. pseudocatenulatum*
- *B. kashiwanohense*

Research from various countries



Takane Katayama

Kyoto University

Nutrients 2020, 12, 71; doi:10.3390/nu12010071

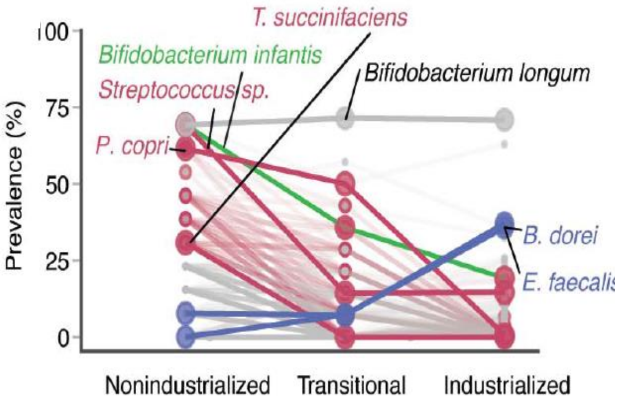
B. longum subsp. *infantis* is being lost in industrialized settings

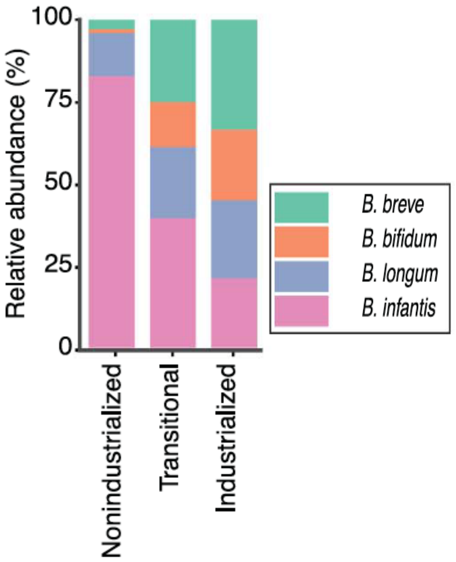
MICROBIOME

Science 2022

Robust variation in infant gut microbiome assembly across a spectrum of lifestyles

Matthew R. Olm[1]†, Dylan Dahan[1]†, Matthew M. Carter[1], Bryan D. Merrill[1], Feiqiao B. Yu[2], Sunit Jain[2], Xiandong Meng[3], Surya Tripathi[4], Hannah Wastyk[1], Norma Neff[2], Susan Holmes[1,5], Erica D. Sonnenburg[1], Aashish R. Jha[6], Justin L. Sonnenburg[1,2]*





J. Sonnenburg
Stanford

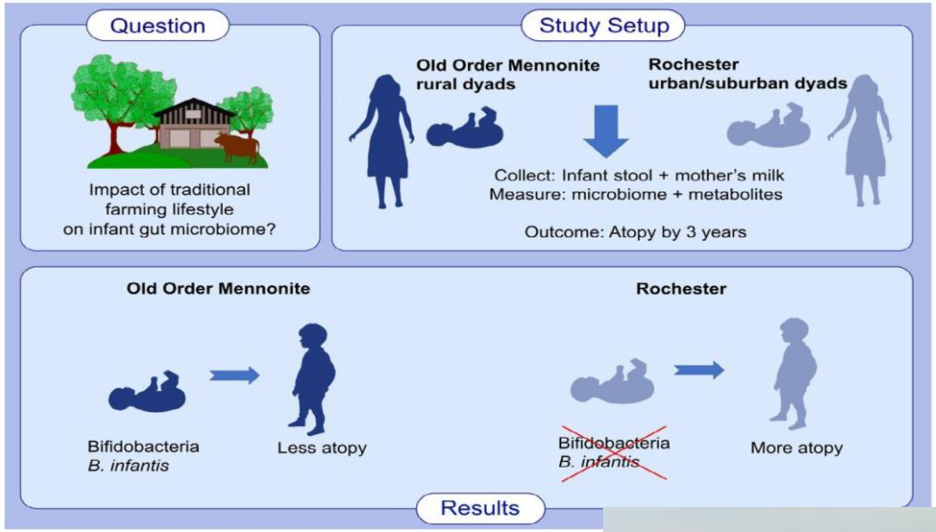
Received: 8 December 2020 | Revised: 16 March 2021 | Accepted: 24 March 2021
DOI: 10.1111/all.14877

ORIGINAL ARTICLE

Seppo et al 2021

Allergy WILEY
Food Allergy and Gastrointestinal Disease

Infant gut microbiome is enriched with *Bifidobacterium longum ssp. infantis* in Old Order Mennonites with traditional farming lifestyle



K. Jarvinen-Seppo
U. Rochester

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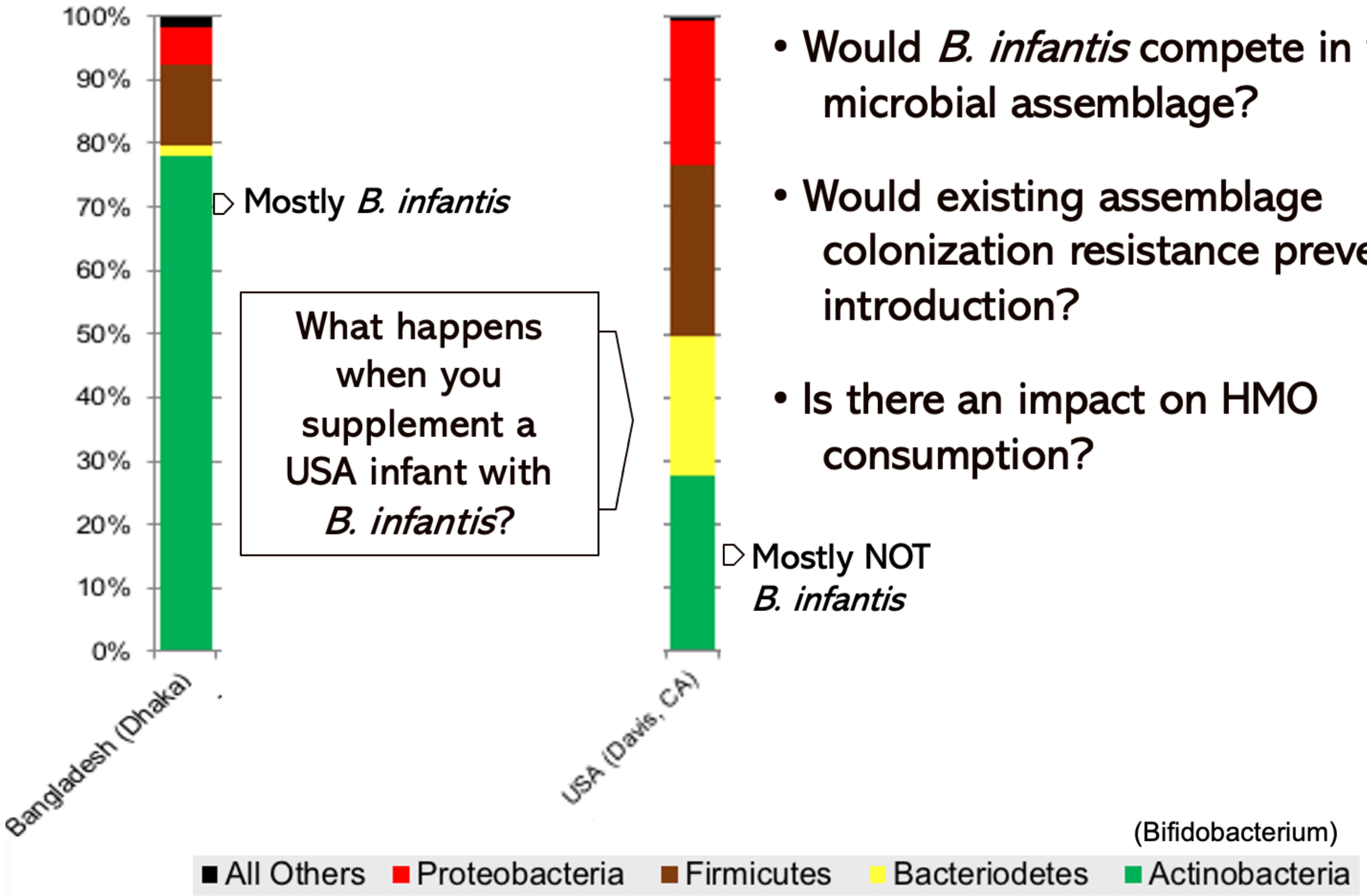
Is supplemented *B. longum* subsp. *infantis* competitive *in situ*?

Can we established bifidobacterial populations in human milk-fed baby by probiotic supplementation?



- Would *B. infantis* compete in this microbial assemblage?
- Would existing assemblage colonization resistance prevent introduction?
- Is there an impact on HMO consumption?

H. Tissier

Not a new idea. In 1906 Tissier proposed putting bifidobacteria from infants who were "colonized" into infants who were not (i.e. "dysbiotic")

Tissier H. 1906. C.R. Soc. Biol. 60:359–361

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Supplemented *B. infantis* dominates and colonizes breast-fed infants

THE JOURNAL OF PEDIATRICS • www.jpeds.com 2013 ORIGINAL ARTICLES

A Comparison of Two Probiotic Strains of Bifidobacteria in Premature Infants

Mark A. Underwood, MD, MAS[1,2], Karen M. Kalanetra, PhD[2,3], Nicholas A. Bokulich, MS[2,3], Zachery T. Lewis, BS[2,3], Majid Mirmiran, MD, PhD[1], Daniel J. Tancredi, PhD[1], and David A. Mills, PhD[2,3]

AMERICAN SOCIETY FOR MICROBIOLOGY | mSphere 2017

Persistence of Supplemented *Bifidobacterium longum* subsp. *infantis* EVC001 in Breastfed Infants

Steven A. Frese,[a] Andra A. Hutton,[a] Lindsey N. Contreras,[a] Claire A. Shaw,[a] Michelle C. Palumbo,[a*] Giorgio Casaburi,[a] Gege Xu,[b] Jasmine C. C. Davis,[b] Carlito B. Lebrilla,[b,c] Bethany M. Henrick,[c,d] Samara L. Freeman,[a] Daniela Barile,[c,d] J. Bruce German,[c,d] David A. Mills,[c,d,e] Jennifer T. Smilowitz,[c,d] Mark A. Underwood[c,f]

- Dramatic domination and **persistence** of *B. infantis* with breast feeding
- Dramatic reduction in Enterobacteriaceae and Bacteriodaceae
- Reduction in endotoxin (LPS), pro-inflammatory cytokines & calprotectin

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Is there a clinical health benefit to *B. infantis* supplementation?

ORIGINAL ARTICLES 2022 www.jpeds.com • THE JOURNAL OF PEDIATRICS

Check for updates

Bifidobacterium longum subsp. *infantis* EVC001 Administration Is Associated with a Significant Reduction in the Incidence of Necrotizing Enterocolitis in Very Low Birth Weight Infants

Joseph Tobias, MD, MA[1], Amy Olyaei, BS[2], Bryan Laraway, MS[3], Brian K. Jordan, MD, PhD[2], Stephanie L. Dickinson, MS[4], Lilian Golzarri-Arroyo, MS[4], Elizabeth Fialkowski, MD[1], Arthur Owora, MPH, PhD[4], and Brian Scottoline, MD, PhD[2]

Journal of Perinatology 2024 www.nature.com/jp

ARTICLE OPEN

Check for updates

Bifidobacterium longum subsp *infantis* (EVC001) is associated with reduced incidence of necrotizing enterocolitis stage ≥2 and bloody stools in premature babies

Kristin Sohn[1,2]✉, Victoria Palacios[3] and Reese Clark[4]

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE 2022

GUT MICROBIOTA

Bifidobacterium infantis treatment promotes weight gain in Bangladeshi infants with severe acute malnutrition

Michael J. Barratt[1,2,3]§, Sharika Nuzhat[4]§, Kazi Ahsan[1,2]§, Steven A. Frese[5,6]†, Aleksandr A. Arzamasov[7], Shafiqul Alam Sarker[4], M. Munirul Islam[4], Parag Palit[4], Md Ridwan Islam[4], Matthew C. Hibberd[1,2,3], Swetha Nakshatri[1,2], Carrie A. Cowardin[1,2]||, Janaki L. Guruge[1,2], Alexandra E. Byrne[1,2], Siddarth Venkatesh[1,2,3], Vinaik Sundaresan[1,2], Bethany Henrick[5,6], Rebbeca M. Duar[5], Ryan D. Mitchell[5], Giorgio Casaburi[5], Johann Prambs[5], Robin Flannery[5], Mustafa Mahfuz[4], Dmitry A. Rodionov[7,8], Andrei L. Osterman[7], David Kyle[5], Tahmeed Ahmed[4]‡, Jeffrey I. Gordon[1,2,3]*‡

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HMO-consuming bifidobacteria are more routinely included in probiotic formulations for infants/premies receiving human milk

GUT MICROBES
2023, VOL. 15, NO. 1, 2192458
https://doi.org/10.1080/19490976.2023.2192458

Taylor & Francis
Taylor & Francis Group

REVIEW

OPEN ACCESS | Check for updates

Translating neonatal microbiome science into commercial innovation: metabolism of human milk oligosaccharides as a basis for probiotic efficacy in breast-fed infants

David A. Mills[a,b,c], J. Bruce German[a,c], Carlito B. Lebrilla[c,d,e], and Mark A. Underwood[c,f]

[a]Department of Food Science and Technology, University of California-Davis, Davis, CA, United States; [b]Department of Viticulture and Enology, University of California-Davis, Davis, CA, United States; [c]Foods for Health Institute, University of California-Davis, Davis, CA, United States; [d]Department of Chemistry, University of California-Davis, Davis, CA, United States; [e]Department of Biochemistry and Molecular Medicine, University of California-Davis, Davis, CA, United States; [f]Division of Neonatology, Department of Pediatrics, University of California-Davis, Sacramento, CA, United States

Gut Microbes 15 (1), 2192458 (2023)

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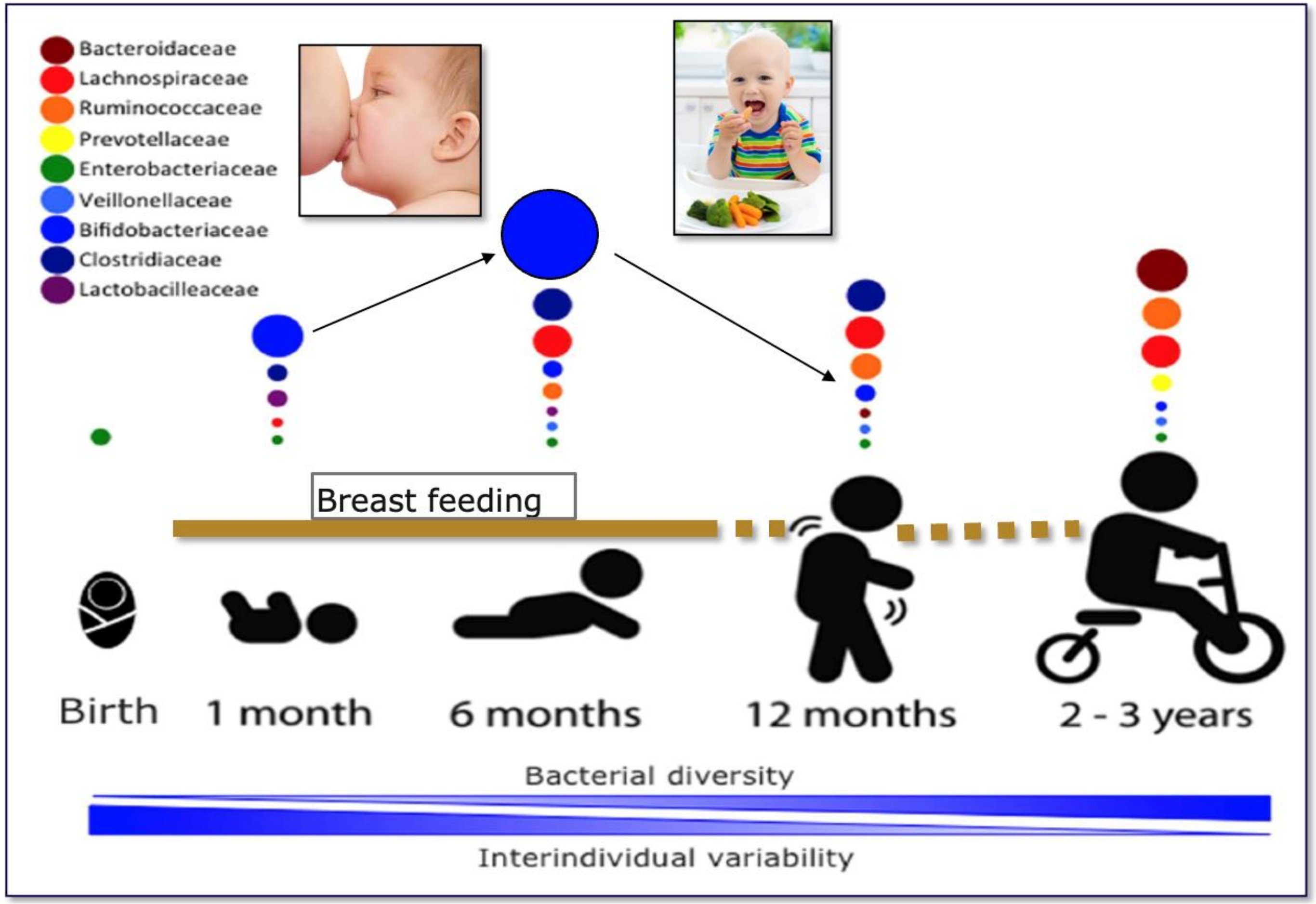
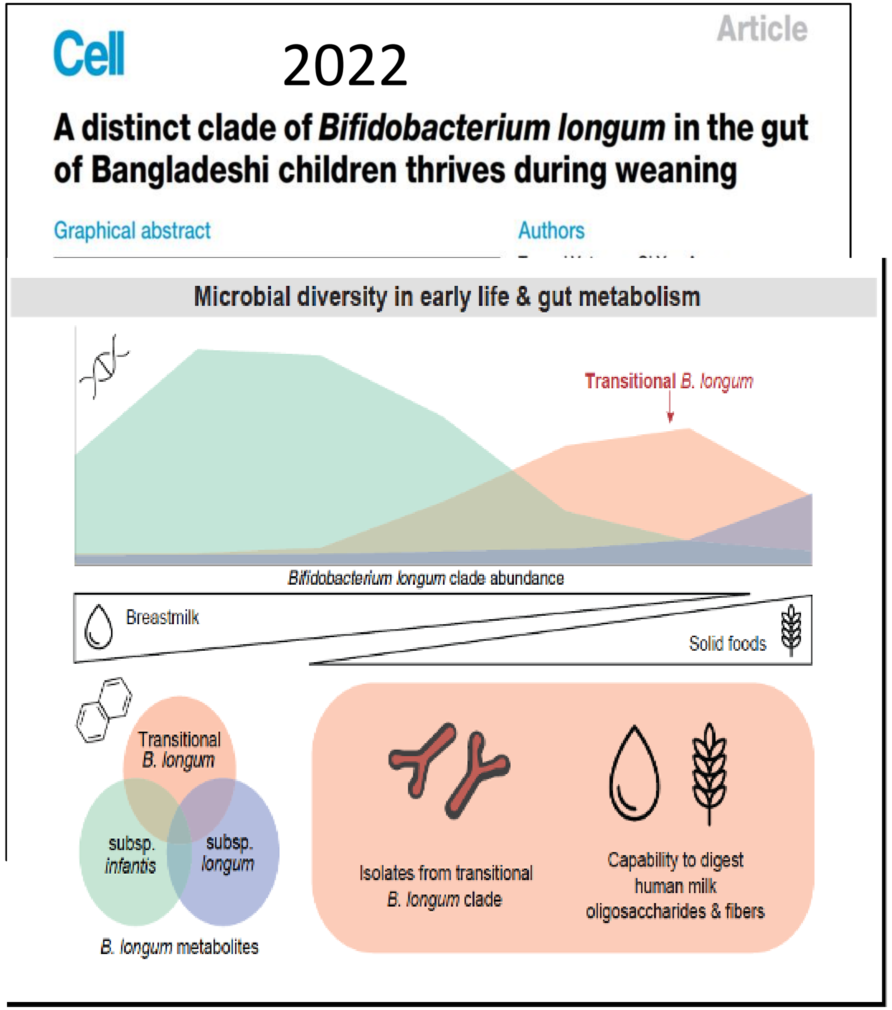
What about weaning?

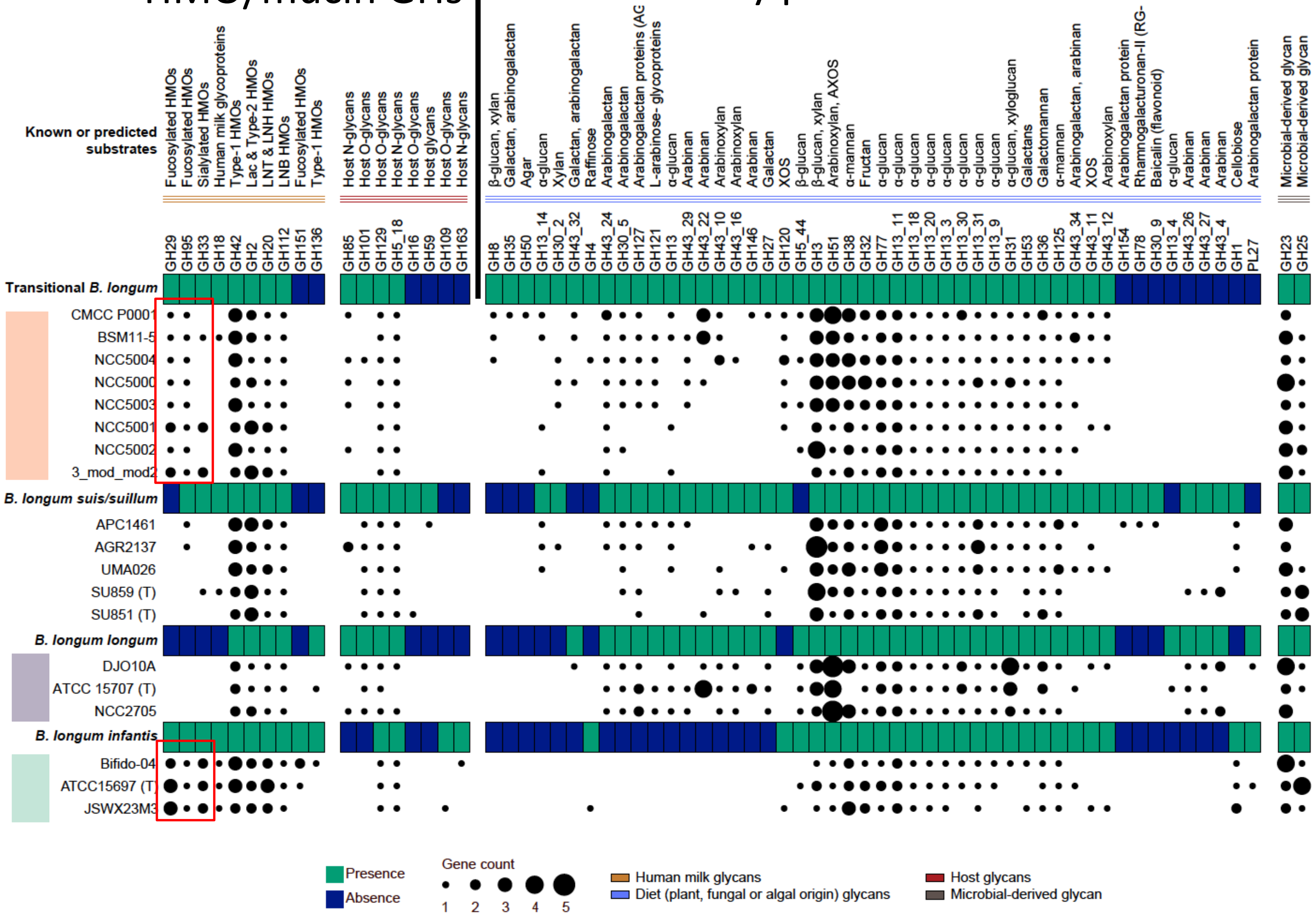


Arrieta et al Front Immunol 2014, 427



HMO/mucin GHs

Mostly plant fiber GHs



GH = glycosyl hydrolase

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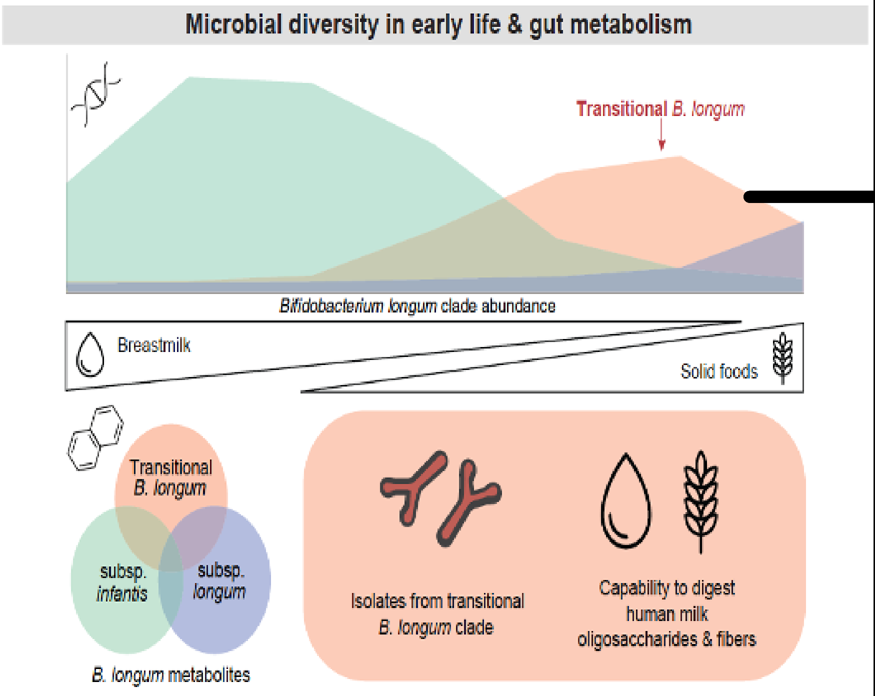
Cell 2022 Article

A distinct clade of *Bifidobacterium longum* in the gut of Bangladeshi children thrives during weaning

Graphical abstract

Authors



SCIENTIFIC REPORTS

OPEN

Received: 24 May 2016
Accepted: 15 September 2016
Published: 19 October 2016

A novel gene cluster allows preferential utilization of fucosylated milk oligosaccharides in *Bifidobacterium longum* subsp. *longum* SC596

Daniel Garrido[1,2,3], Santiago Ruiz-Moyano[1,2,†], Nina Kirmiz[1,2], Jasmine C. Davis[2,4], Sarah M. Totten[2,4], Danielle G. Lemay[2,5], Juan A. Ugalde[6], J. Bruce German[2,7], Carlito B. Lebrilla[2,4] & David A. Mills[1,2,7]

AEM Journals.ASM.org

Variation in Consumption of Human Milk Oligosaccharides by Infant Gut-Associated Strains of *Bifidobacterium breve*

Santiago Ruiz-Moyano,[a,d] Sarah M. Totten,[b,d] Daniel A. Garrido,[a,d]* Jennifer T. Smilowitz,[c,d] J. Bruce German,[c,d] Carlito B. Lebrilla,[b,d] David A. Mills[a,c,d]

Departments of Viticulture and Enology,[a] Chemistry,[b] and Food Science and Technology[c] and Foods for Health Institute,[d] University of California, Davis, Davis, California, USA

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FOOD MICROBIOLOGY
January 2022 Volume 88 Issue 2 e01707-21
https://doi.org/10.1128/AEM.01707-21

Fucosylated Human Milk Oligosaccharide Foraging within the Species *Bifidobacterium pseudocatenulatum* Is Driven by Glycosyl Hydrolase Content and Specificity

Guy Shani[a,*], Jennifer L. Hoeflinger[a,§], Britta E. Heiss[a,◊], Chad F. Masarweh[a], Jules A. Larke[b], Nick M. Jensen[a], Saumya Wickramasinghe[a], Jasmine C. Davis[c], Elisha Goonatilleke[c], Amr El-Hawiet[d,e], Linh Nguyen[e], John S. Klassen[e], Carolyn M. Slupsky[b,f], Carlito B. Lebrilla[c,f], David A. Mills[a,f,g]

Katayama

Van Sinderen

Hall

Schwab
Lecroix

GH = glycosyl hydrolase

Prolonged breastfeeding enabling persistence of bifidobacterial populations is associated with health outcomes

Resource
Cell Host & Microbe 2015

Dynamics and Stabilization of the Human Gut Microbiome during the First Year of Life

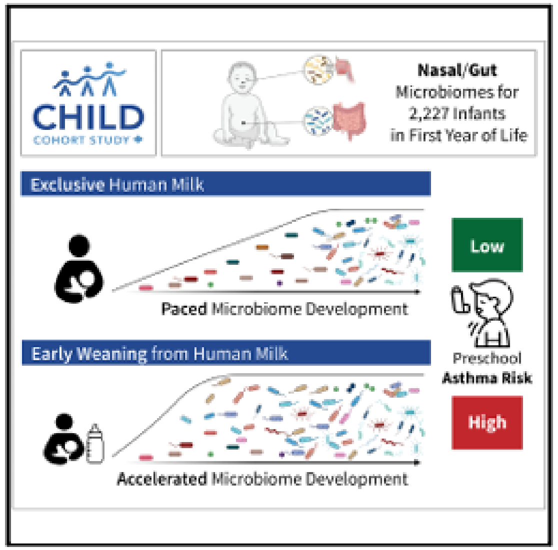
Authors
Fredrik Bäckhed, Josefine Roswall, ..., Jovanna Dahlgren, Jun Wang

"…cessation of breast-feeding, rather than introduction of solid food, being required for maturation into an adult-like microbiota."

Cell 2024 Article

Microbial colonization programs are structured by breastfeeding and guide healthy respiratory development

Graphical abstract



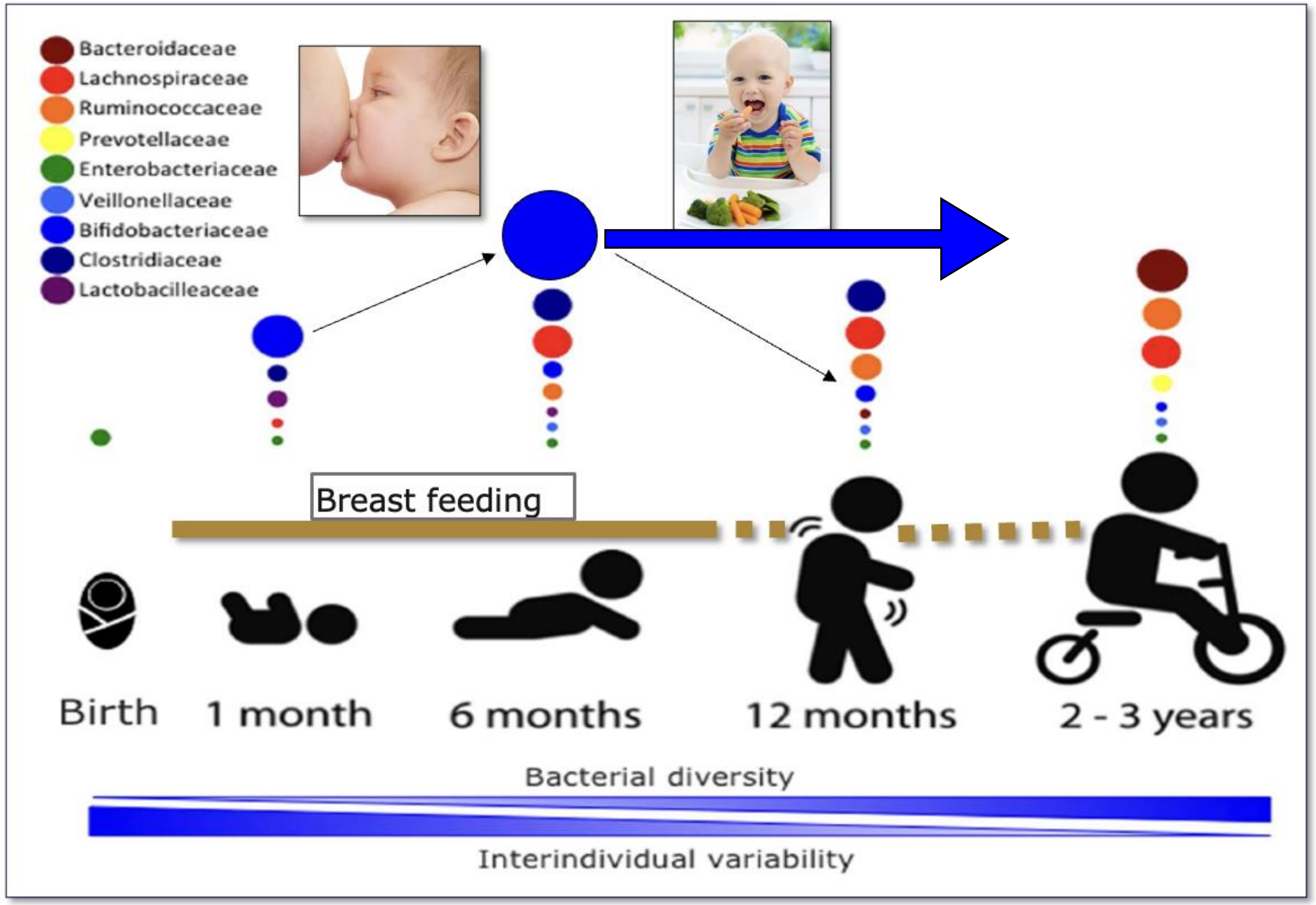
Authors
Liat Shenhav, Kelsey Fehr, Myrtha E. Reyna, ..., Padmaja Subbarao, Michael G. Surette, Meghan B. Azad

Correspondence
liat.shenhav@nyulangone.org (L.S.), padmaja.subbarao@sickkids.ca (P.S.), surette@mcmaster.ca (M.G.S.), meghan.azad@umanitoba.ca (M.B.A.)

In brief
Human milk serves as a "pacemaker," indirectly protecting against asthma by regulating nasal and gut microbiome development during the first year of life.

Human milk serves as a "pacemaker," indirectly protecting against asthma by regulating nasal and gut microbiome development during the first year of life

Can we extend bifidobacteria more into weaning?



Arrieta et al Front Immunol 2014, 427

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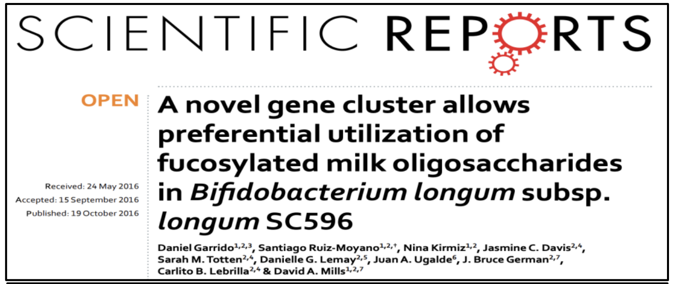
Synbiotic HMO+bifidobacterial strain overcomes colonization resistance in a healthy adult mouse



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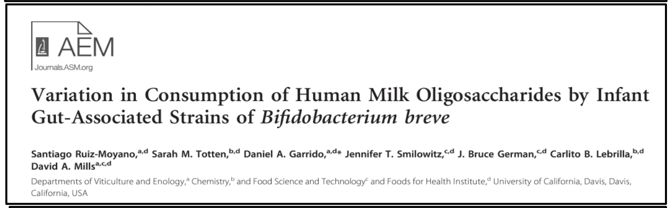

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Departments of Viticulture and Enology,[a] Chemistry,[b] and Food Science and Technology[c] and Foods for Health Institute,[d] University of California, Davis, Davis, California, USA

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FOOD MICROBIOLOGY
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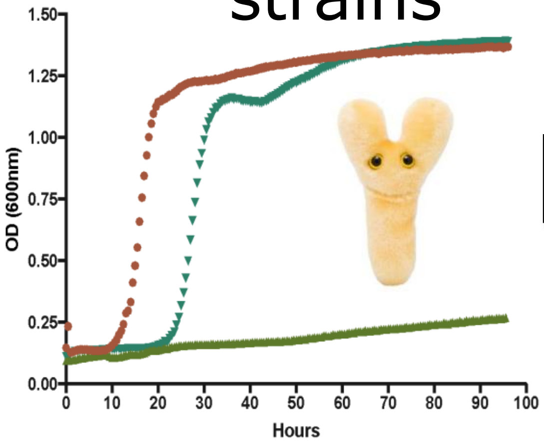
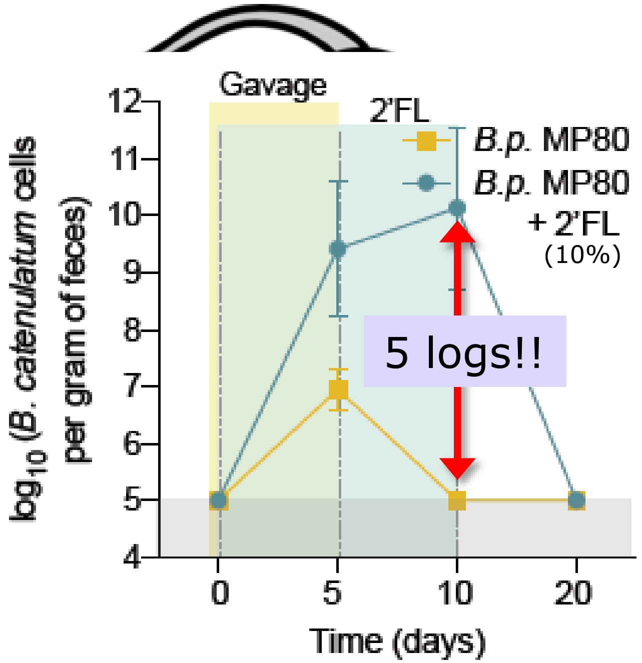
Bifidobacterial strains





WT mouse

Fed mice normal chow

Helen Raybould

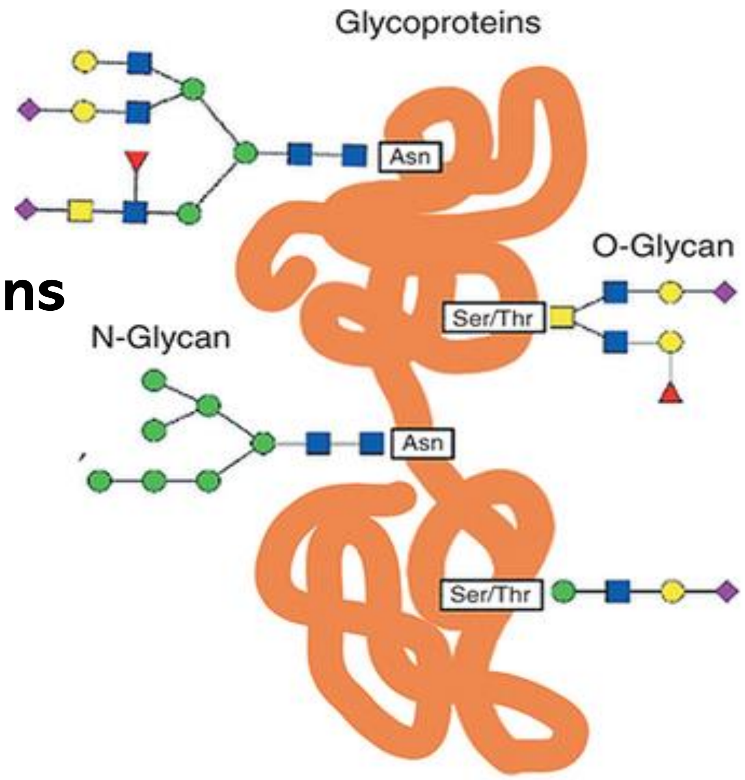
Britta Heiss

Amy Ehrlich

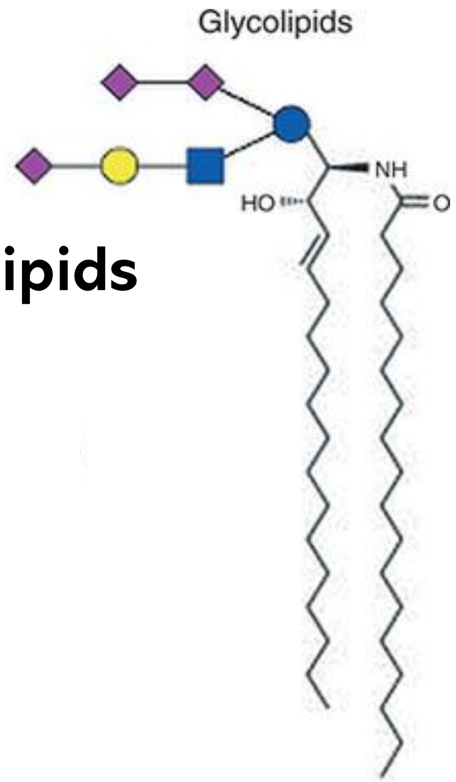
Gut Microbes 13:1986666 (2021)

Can we promote a better weaning with a better understanding of milk glycoconjugates to facilitate greater persistance of bifidobacterial species

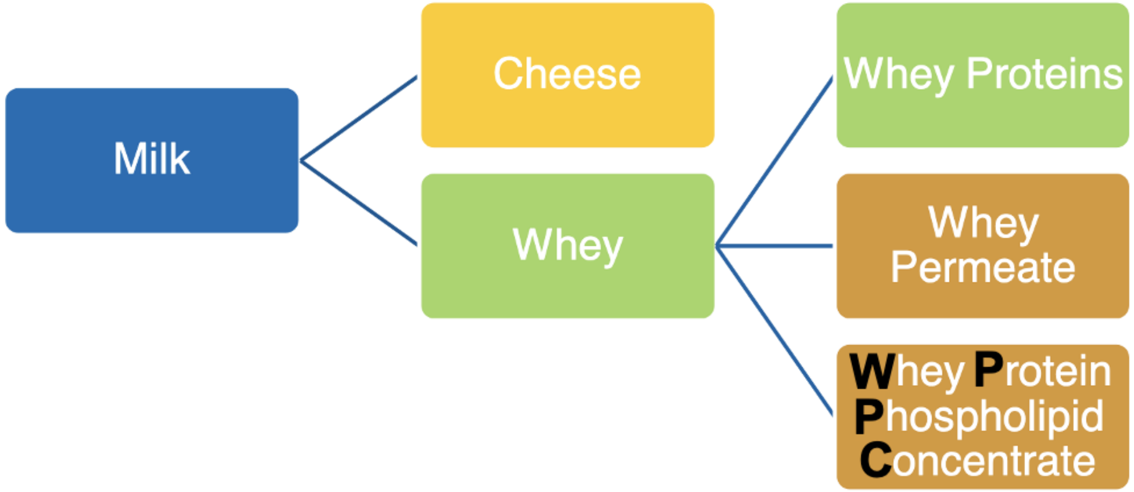
Glycoproteins



Glycolipids

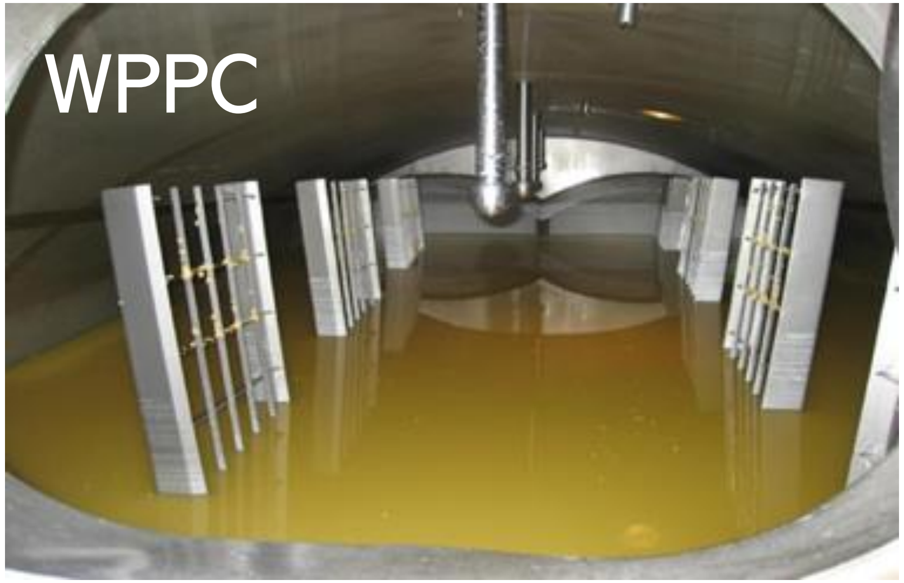


Can we improve weaning by enriching more bifidobacterial fermentation of milk glycoconjugates?



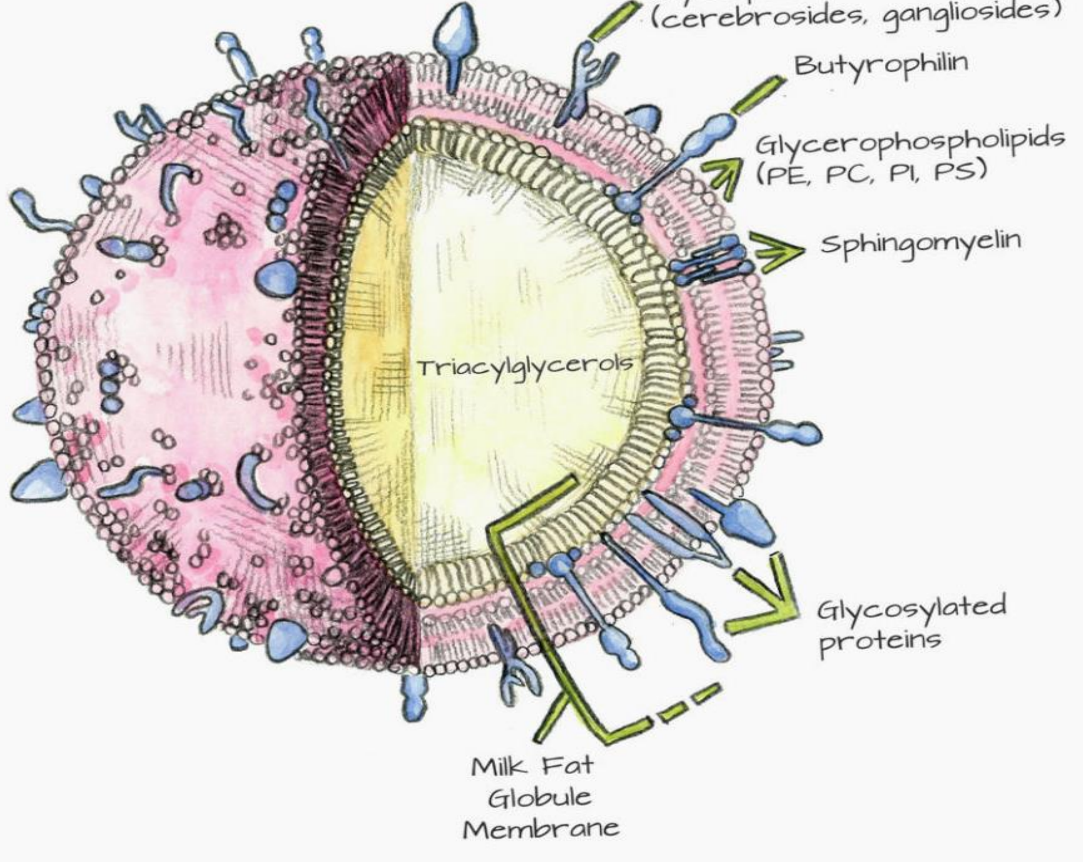
"Procream"

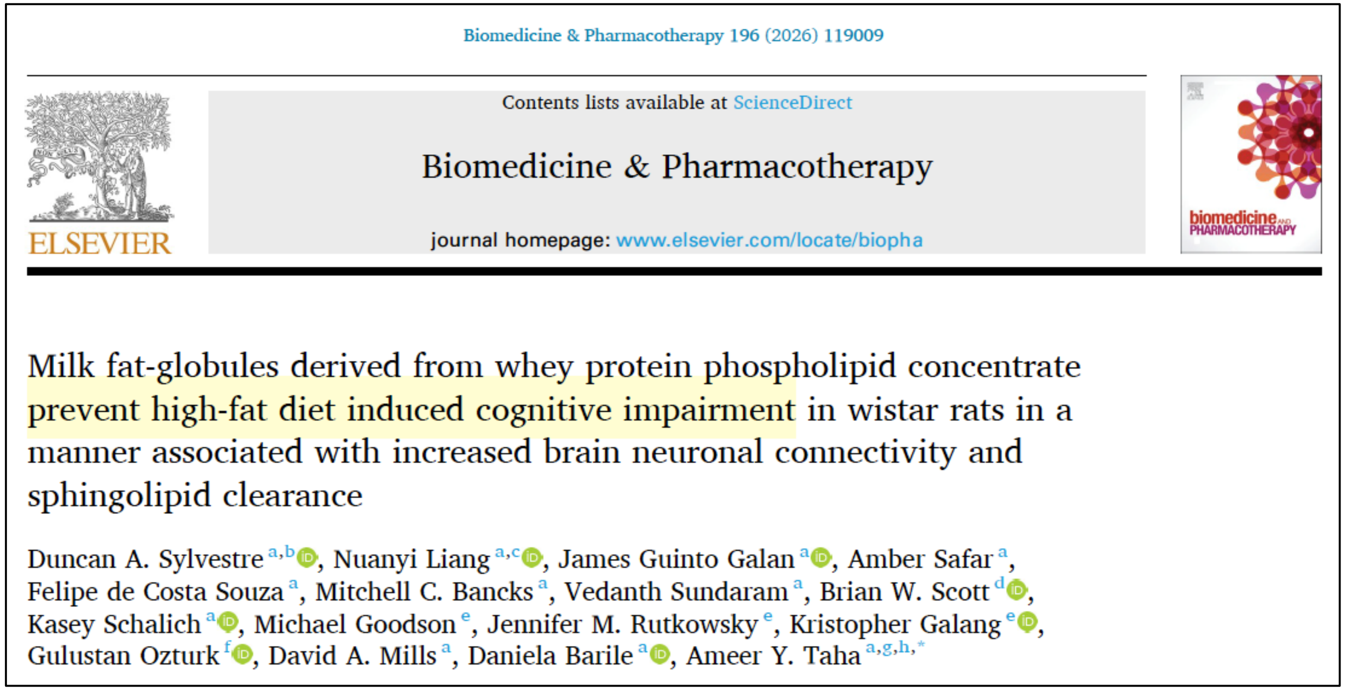
- >30M tons/year worldwide
- Current Uses: Animal feed, Ingredients for processed foods



WPPC contains milk fat globule membrane (MFGM) fraction from bovine milk

Milk Fat Globule Membrane




Biomedicine & Pharmacotherapy 196 (2026) 119009

Contents lists available at ScienceDirect

Biomedicine & Pharmacotherapy

journal homepage: www.elsevier.com/locate/biopha

ELSEVIER

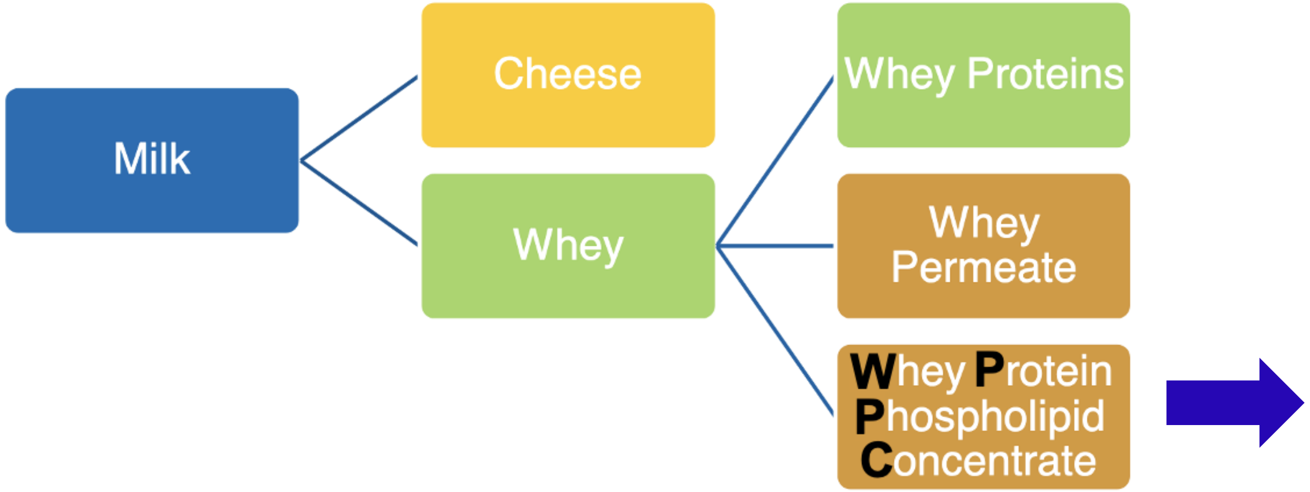
Milk fat-globules derived from whey protein phospholipid concentrate prevent high-fat diet induced cognitive impairment in wistar rats in a manner associated with increased brain neuronal connectivity and sphingolipid clearance

Duncan A. Sylvestre [a,b], Nuanyi Liang [a,c], James Guinto Galan [a], Amber Safar [a], Felipe de Costa Souza [a], Mitchell C. Bancks [a], Vedanth Sundaram [a], Brian W. Scott [d], Kasey Schalich [a], Michael Goodson [e], Jennifer M. Rutkowsky [e], Kristopher Galang [e], Gulustan Ozturk [f], David A. Mills [a], Daniela Barile [a], Ameer Y. Taha [a,g,h,*]

➢ Promote cognitive function in aging (Calvo, et

n, et

Do Bifidobacteria grow on WPPC?

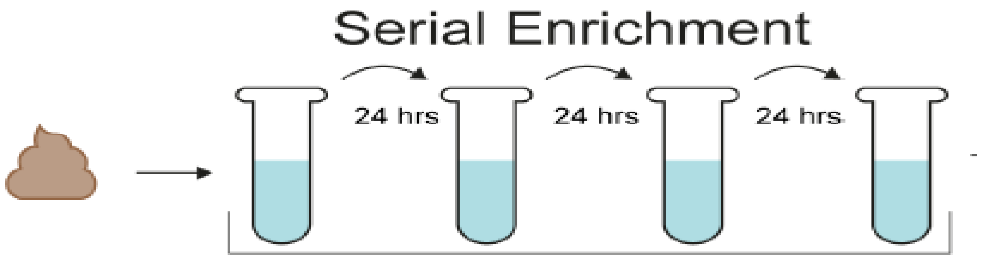


"Procream"

Do bifidobacteria use the glycans on WPPC for a carbon source for growth?

Bifidobacterial fecal enrichments using WPPC

Dr. You-Tae Kim



1% WPPC

Bifidobacterial selective media

<u>Isolates</u>

B. bifidum

B. longum subsp. longum

B. breve

J. Dairy Sci. 108:3366-3381 (2025)

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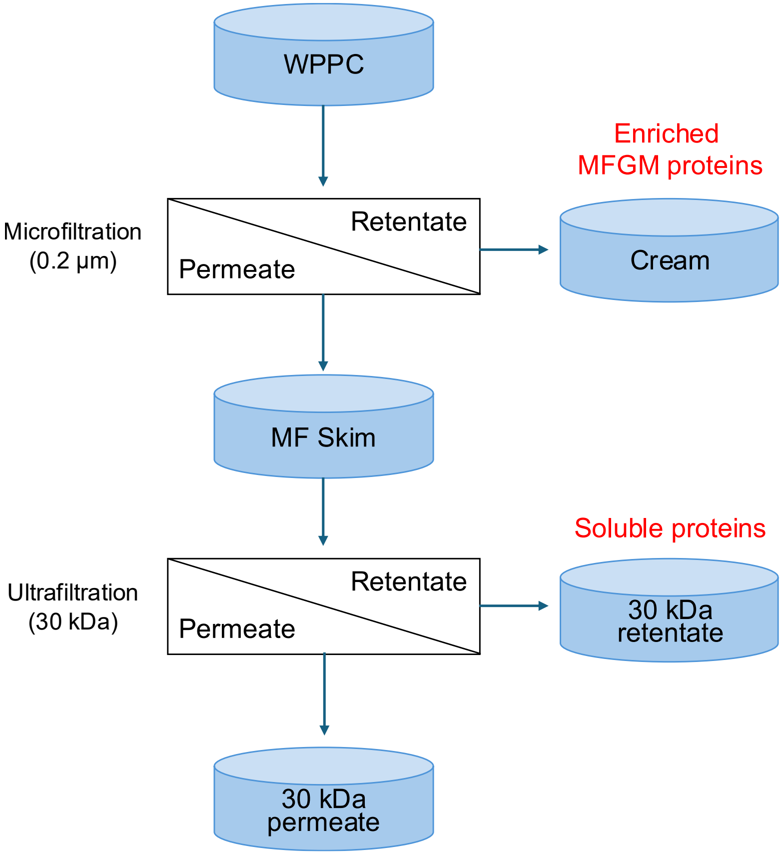
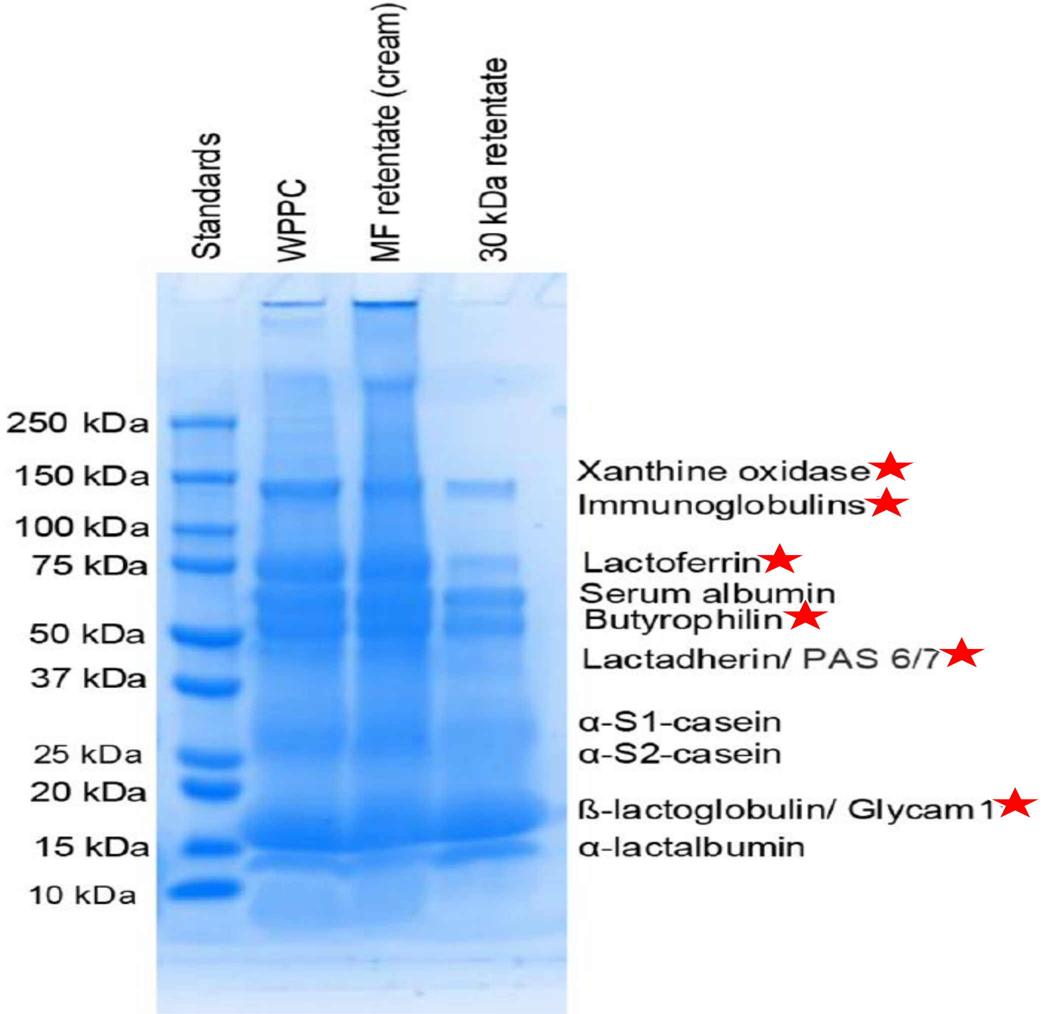
WPPC fractionation

Robert Mondavi Institute Milk Processing lab

Prof D. Barile





J. Dairy Sci. 108:3366-3381 (2025)

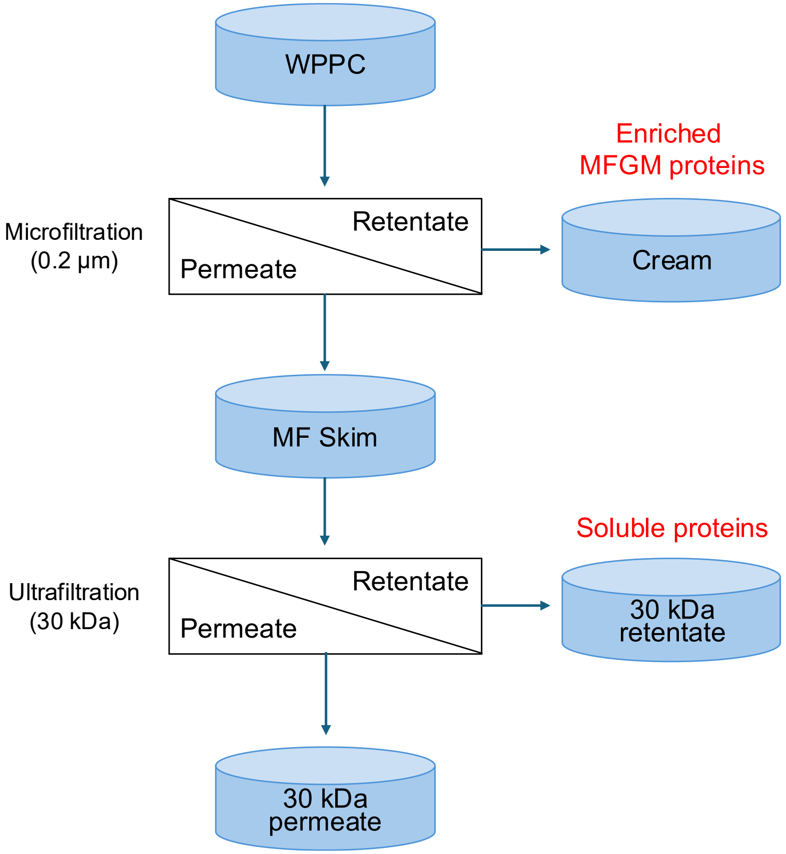
UCDAVIS

Growth of *Bifidobacterium* on WPPC fractions

RMI

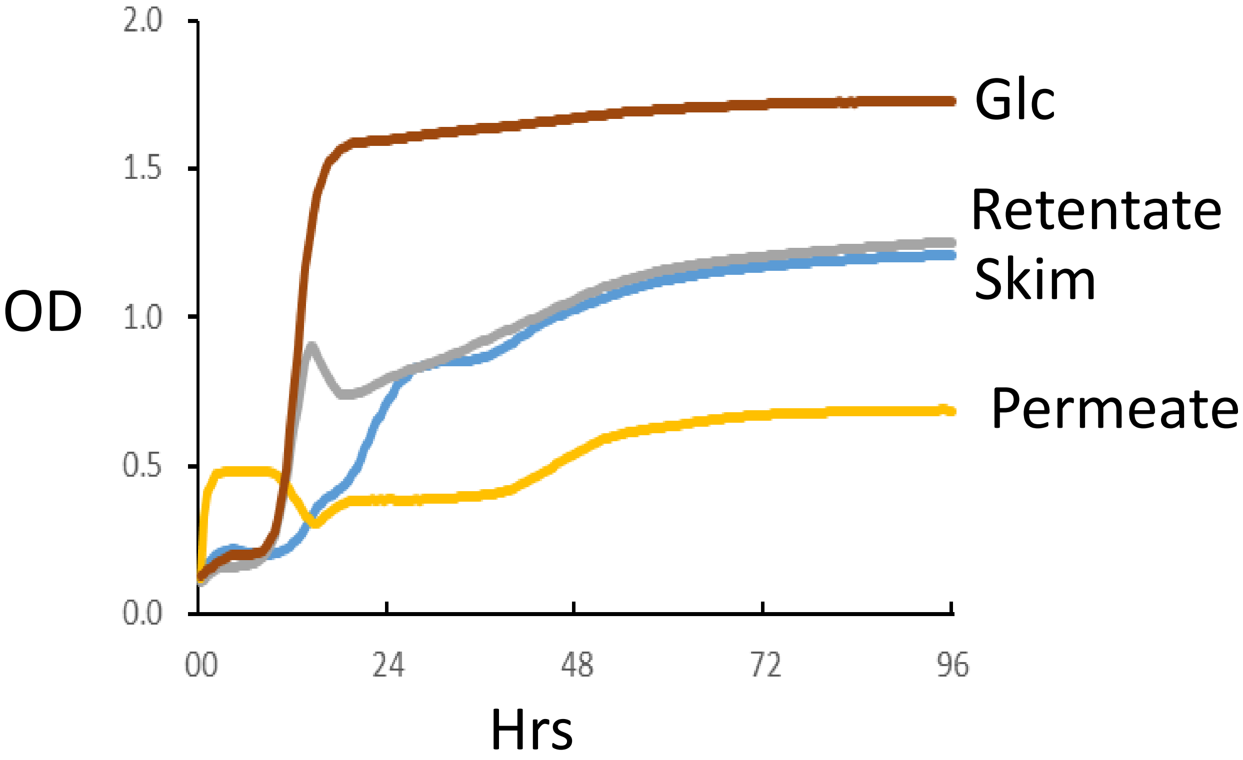
Dr. You-Tae Kim

Prof D. Barile

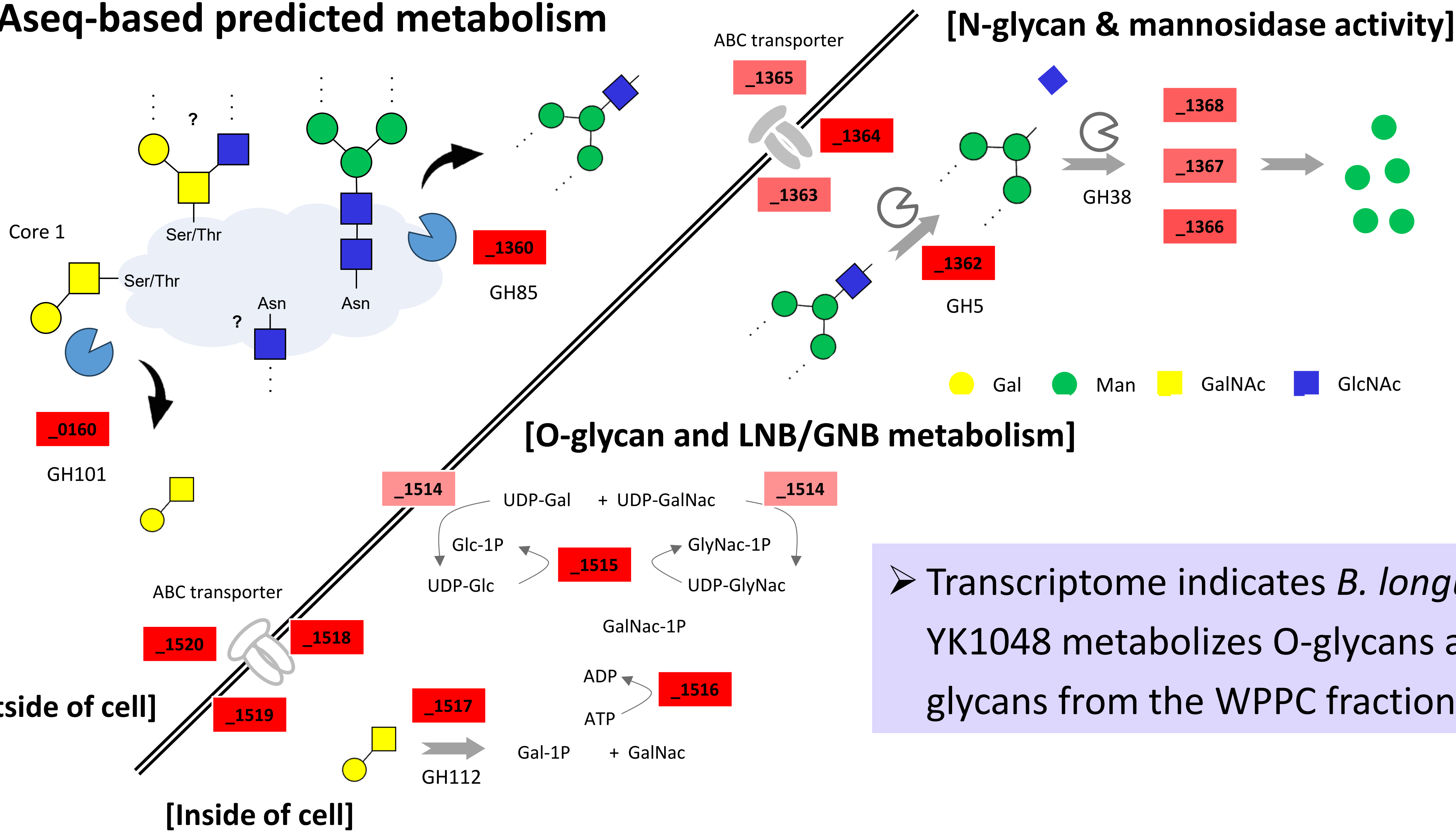


Bacterial growth

B. longum ssp. *longum* YK1048



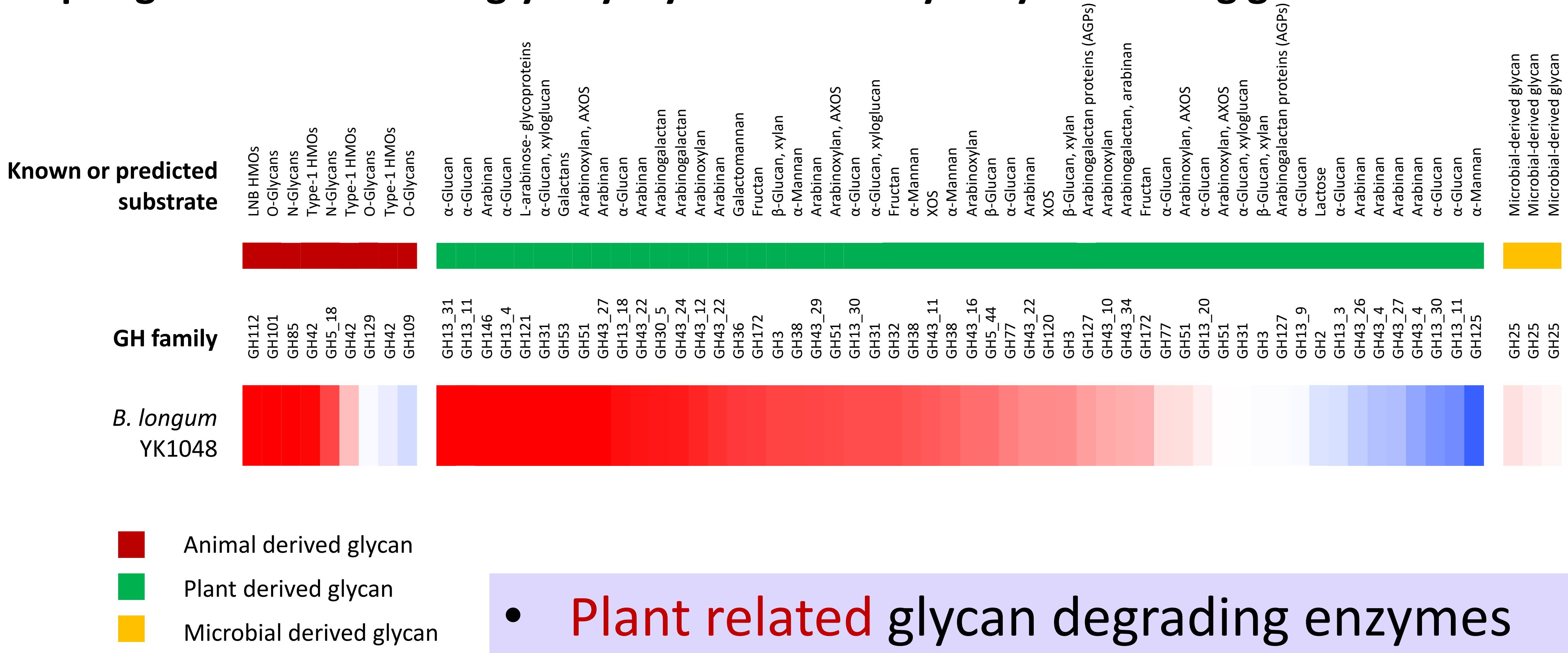
RNAseq-based predicted metabolism



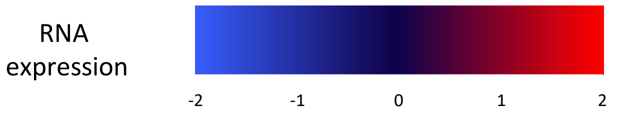
Dr. You-Tae Kim

- ➢ Transcriptome indicates *B. longum* YK1048 metabolizes O-glycans and N-glycans from the WPPC fraction

Up-regulation of various glycosyl hydrolase family enzymes during growth on WPPC

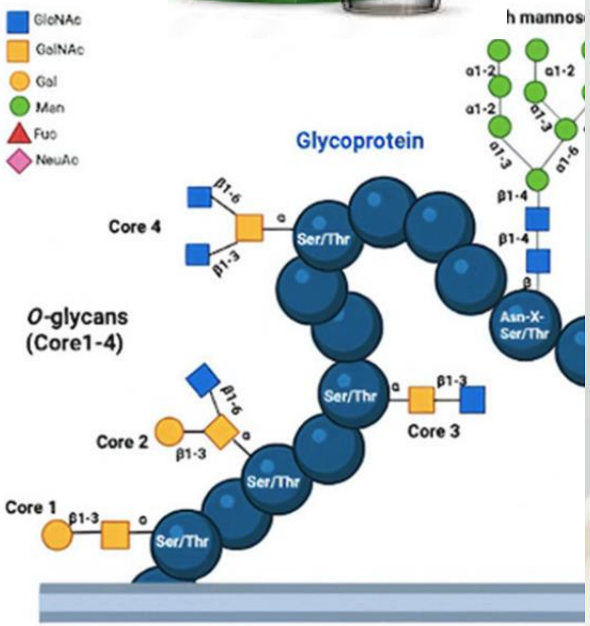


- Plant related glycan degrading enzymes were turned on by WPPC substrates!



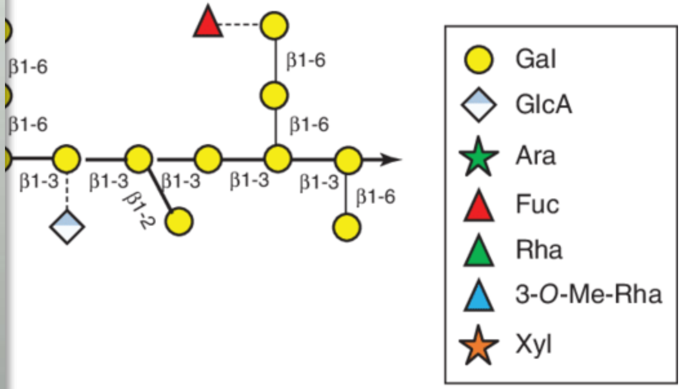
UCDAV

Milk



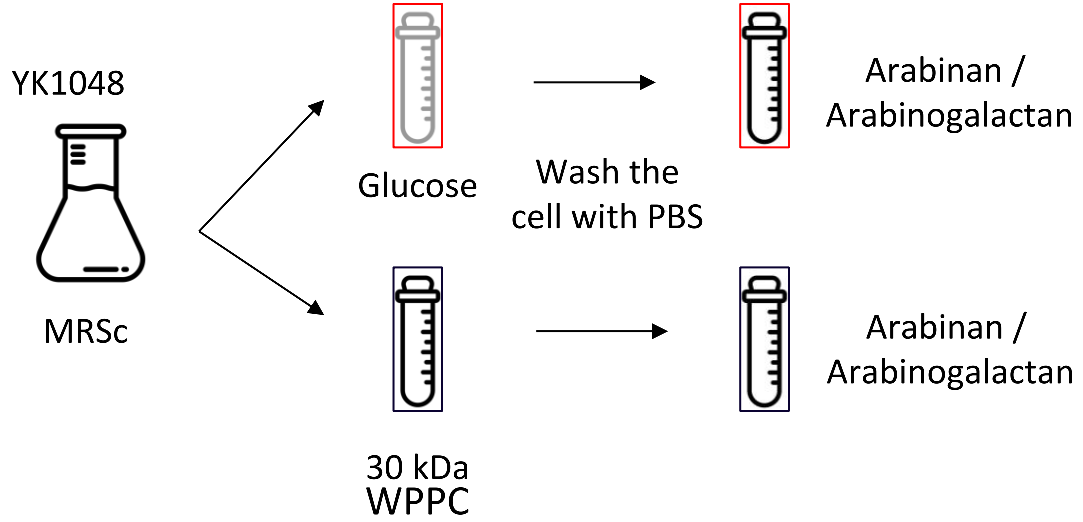
Conjugated G

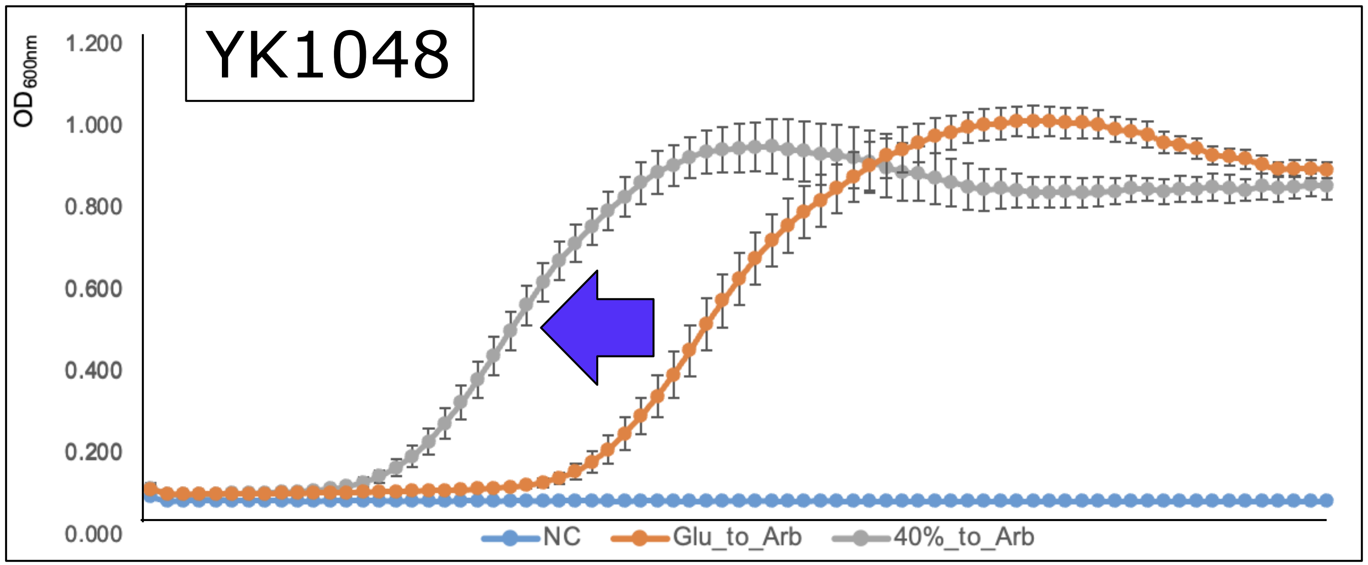
nt Glycans



UCDAVIS

Pre-activation with 30 kDa WPPC fraction



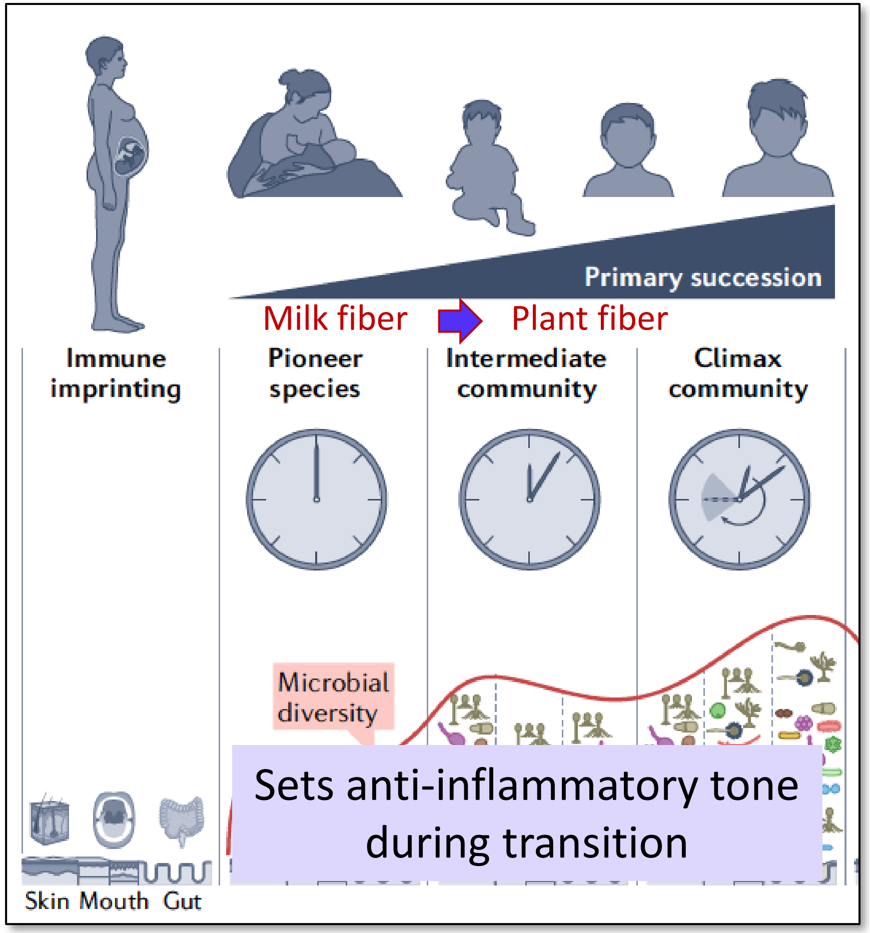


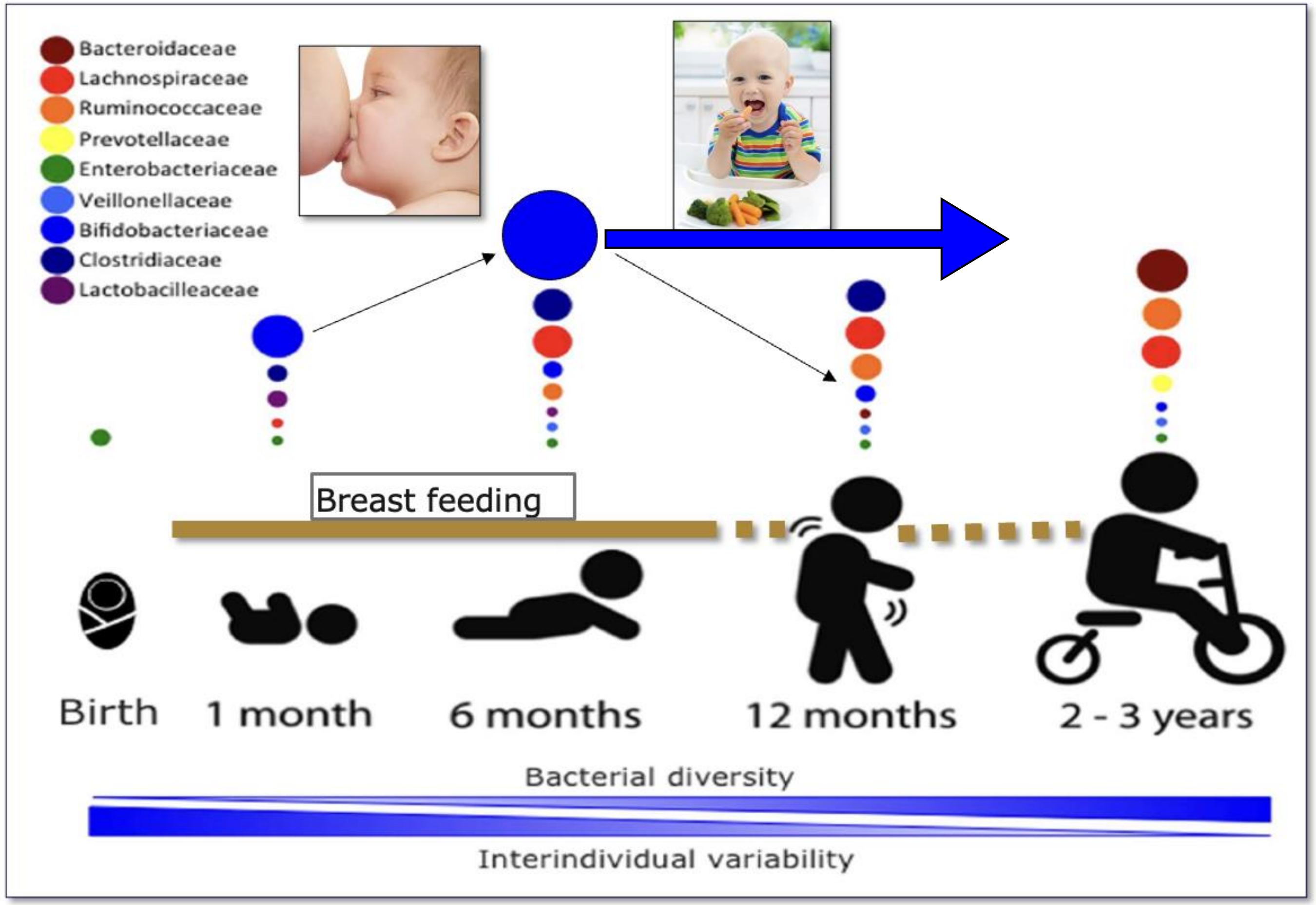
	Growth*		Pre-activation
	Arabinan	Arabino-galactan	
B. longum subsp. *infantis*			
B. infantis SC142	-	-	-
B. infantis ATCC 15697	-	-	-
B. infantis ATCC 25962	-	-	-
B. longum subsp. *longum*			
B. longum ATCC 15707	+++	++	✓
B. longum DJO10A	+	+	✓
B. longum SC536	+++	++	✓
B. longum SC596	+++	++	✓
B. longum SW1209	+++	++	✓
***B. longum* YK1048**	+++	++	✓
B. bifidum			
B. bifidum YK1043	-	-	-

*Optical density: +++, > 0.8; ++, > 0.6; +, > 0.2

In preparation

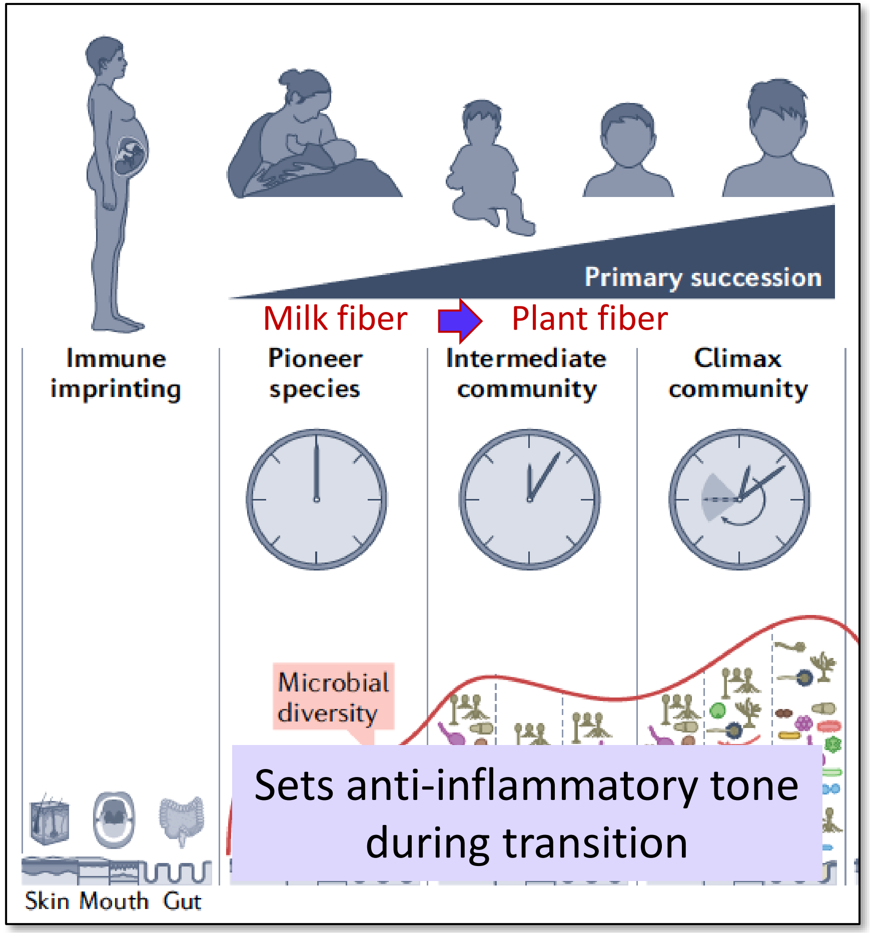
Gut microbiome "transitions" represent a common challenge in early life – how could we mitigate those risks?





Nature Rev Microbiology 2022

Gut microbiome "transitions" represent a common challenge in early life – how could we mitigate those risks?



Is weaning space an opportunity for Dairy to partner with Alternative Milks?

+

Do they have the right fiber?

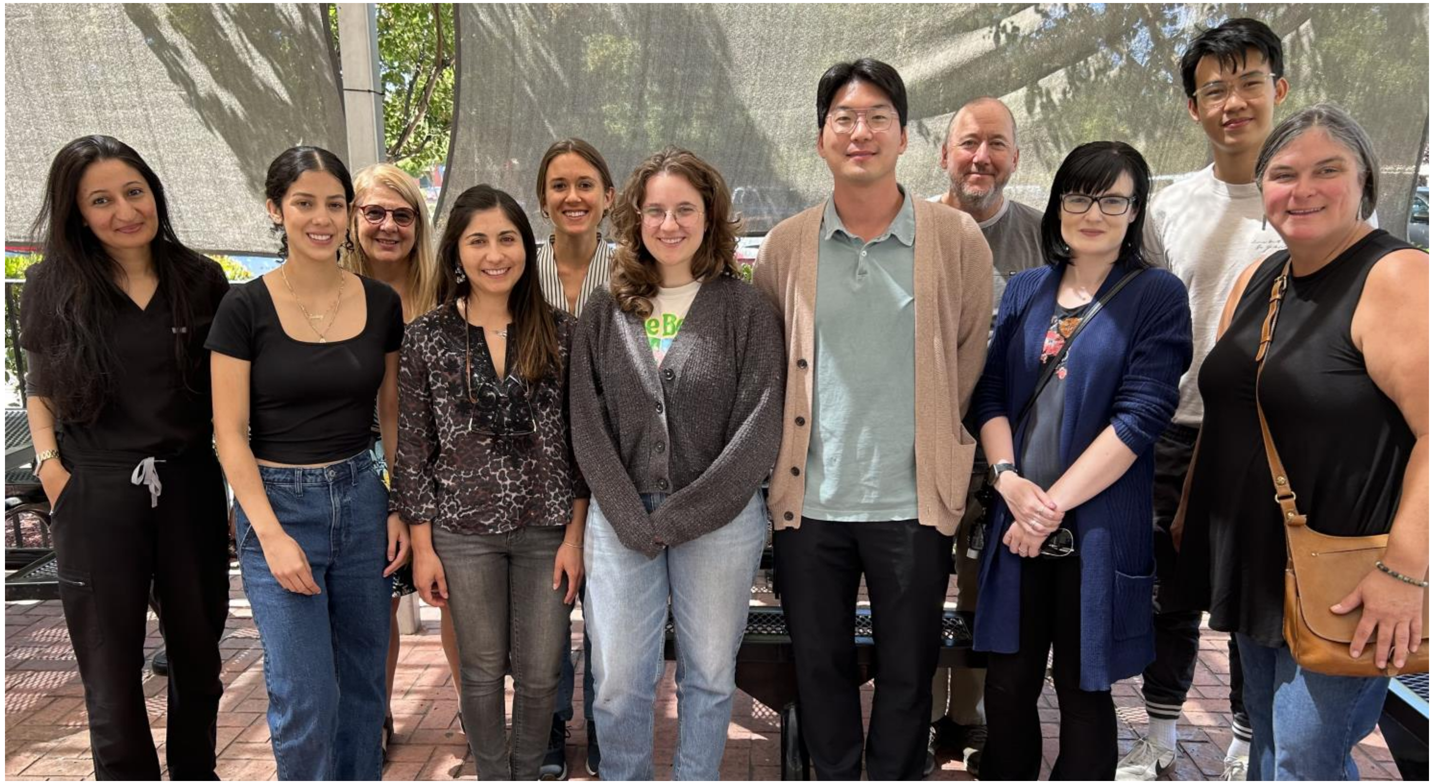
Nature Rev Microbiology 2022

UCDAVIS

Take home points….

- Milk "farms" that gut microbiota and provides a model of a food which expressly modulates the microbiota in a healthful way
- Specificity of that modulation is driven in part by glycan complexity and cognate bacterial catabolism
- *B. longum* subsp. *longum* strains are induced towards plant fiber consumption during growth on milk sugars
- Advances in food/fiber glycomics sets the stage for creation of novel weaning foods
- The collaborative, multi-discplinary environment at UC Davis drives both discovery, innovation *and translation!*

Acknowledgements



Mills Lab Collaborators

Carlito Lebrilla (UCD)
Bruce German (UCD)
Daniela Barile (UCD)
Ishita Shah (UCD)
Helen Raybould (UCD)
Carolyn Slupsky (UCD)
Ameer Taha (UCD)

Current & former students working on glycans:

Julia Finestone, **You-Tae Kim**, **Britta Heiss**, Maria Maldonado-Gomez, Vanessa Castagna, Jassim Al-Oboudi, Chad Masarweh, Nick Jensen, Jinxin Liu, Diana Taft, Zach Lewis, Guy Shani, Nina Kirmiz, **Santiago Ruiz-Moyeno, Saumya Wickramasinghe**

Funding Acknowledgements

USDA

NDC NATIONAL DAIRY COUNCIL™

BILL & MELINDA GATES foundation

cdfa

DMI DAIRY MANAGEMENT INC.™

NRF National Research Foundation of Korea

NIH NIDDK

CALIFORNIA DAIRY RESEARCH FOUNDATION
Science for a Sustainable Future

Arla Foods Ingredients
Discovering the wonders of whey
Arla

UC DAVIS

Proof Pudding (patent pending) was founded in 2025 by Dr. Kasey Schalich and Jade Schoenfeld. Proof was created to support brain health through nutrition. Proof is indulgent while still being low in sugar, high in protein and a good source of fiber.

UC DAVIS FOOD SCIENCE AND TECHNOLOGY

Understanding & Optimizing Fermented Foods for Improving Health

Maria Marco, Ph.D.
Professor & Chair of the Food Science Graduate Group
University of California at Davis

Understanding and optimizing fermented foods for health: role of gut health

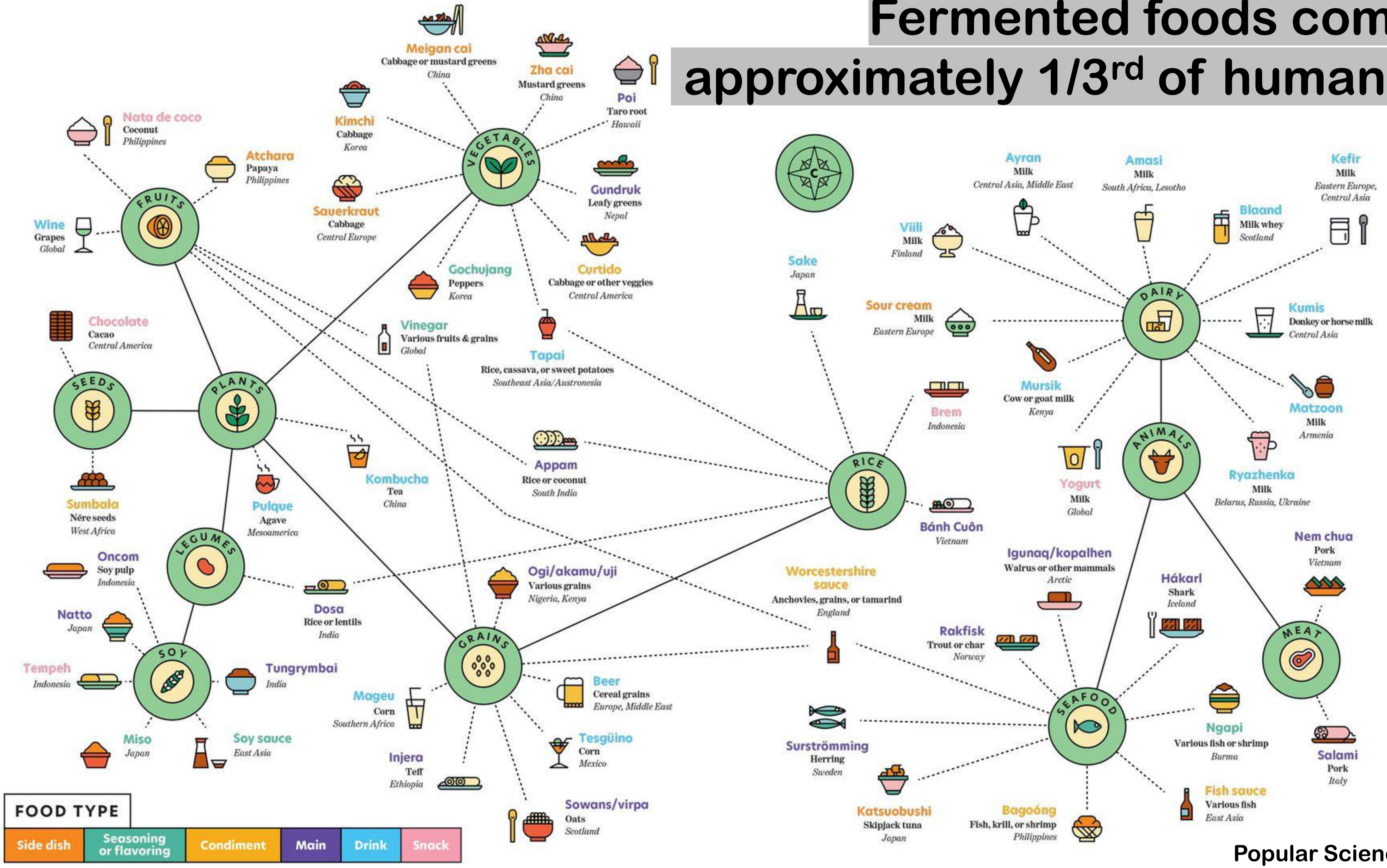
Maria Marco

Professor, UC Davis
President, ISAPP board of directors
mmarco@ucdavis.edu

UCDAVIS
FOOD SCIENCE AND TECHNOLOGY

Photo: Karen Wang-Diggs

Fermented foods comprise approximately 1/3rd of human diets



Popular Science Feb 2021

Fermented foods are microbial gardens

Fermented foods: Foods and beverages made through desired microbial growth and enzymatic conversions of food components.

Marco et al 2021 Nat Rev Gastroenterol Hepatol

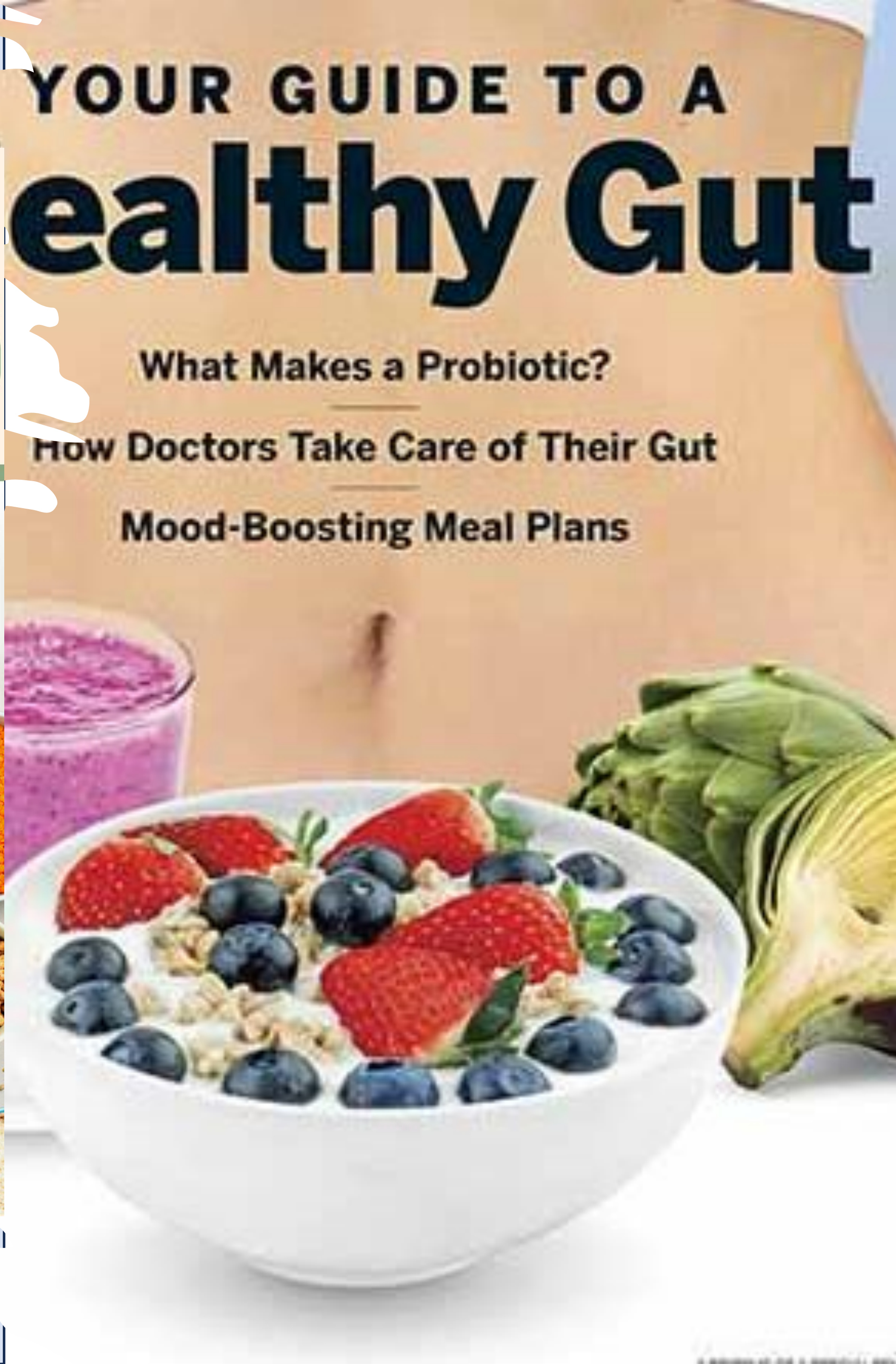
~ 50-80% microbial*

Fermented food microbes are responsible for

- ✓ Sensory attributes
- ✓ Shelf-life
- ✓ Safety
- ✓ Health promotion

* Based on average crop genome size and strain diversity predicted in fruit and vegetable fermentations

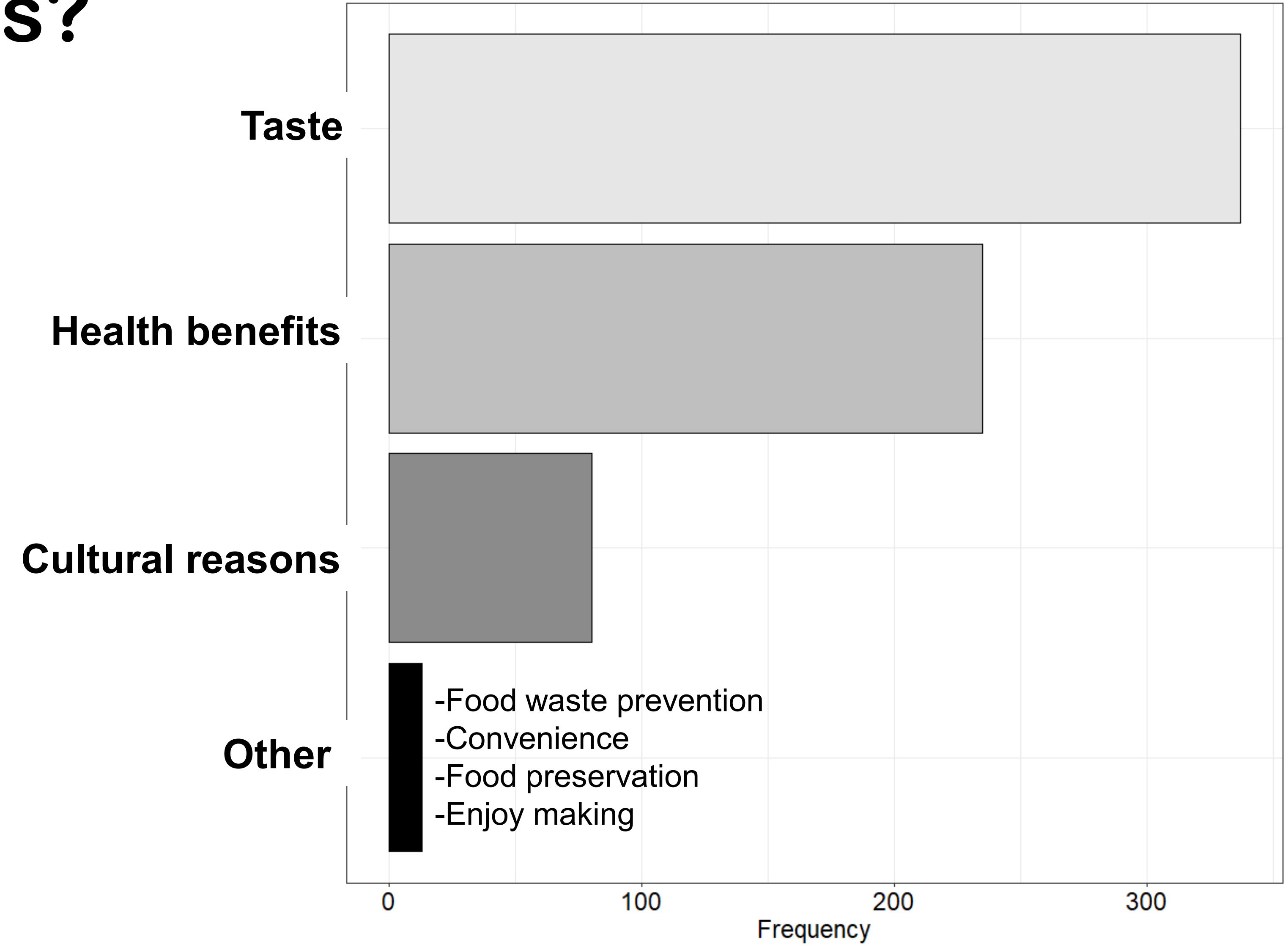
pollock communications
POWERING CHANGE
Food, Nutrition & Wellness Communications
Today's Dietitian
THE 13TH ANNUAL WHAT'S TRENDING IN NUTRITION SURVEY
THE TOP 10 SUPERFOODS 2025
Trends come and go, but these superfoods stay!
1 FERMENTED FOODS such as yogurt, pickles, kimchi, Kombucha Tea
NEW 2 BERRIES such as cranberries, blueberries, raspberries, etc.
NEW 3 BONE BROTH
4 SEEDS such as chia and hemp
5 AVOCADO
NEW 6 LEAFY GREENS such as kale and spinach
7 NUTS such as almonds and walnuts
8 ANCIENT GRAINS
874 Registered Dietition Nutritionists (RDNs) surveyed.



YOUR GUIDE TO A
ealthy Gut
What Makes a Probiotic?
How Doctors Take Care of Their Gut
Mood-Boosting Meal Plans

What is the main reason for consuming (non-alcoholic) fermented foods?

National fermented foods survey
751 respondents
(March-Sept 2022)



Hanlon, DiCaprio et al *manuscript under review*

Fermented foods & health benefits

Many fermented foods have only 1 or 2 human studies (RCT or observational)

Digestive heath
kefir, sourdough, yogurt

Inflammatory bowel syndrome
sauerkraut, sourdough
kimchi

Weight loss & obesity
yogurt, kimchi

Type 2 Diabetes
yogurt, cheese, kimchi,
sourdough, coffee, vinegar

Cancer
coffee, wine/beer

Mood & behavior
wine/beer, coffee

Immunity
kimchi, yogurt

Bone health
yogurt, kefir, natto

Cardiovascular disease
yogurt, cheese, coffee,
wine/beer, vinegar

Yogurt: inversely associated with inflammation, type 2 diabetes, and cardiometabolic disease risk

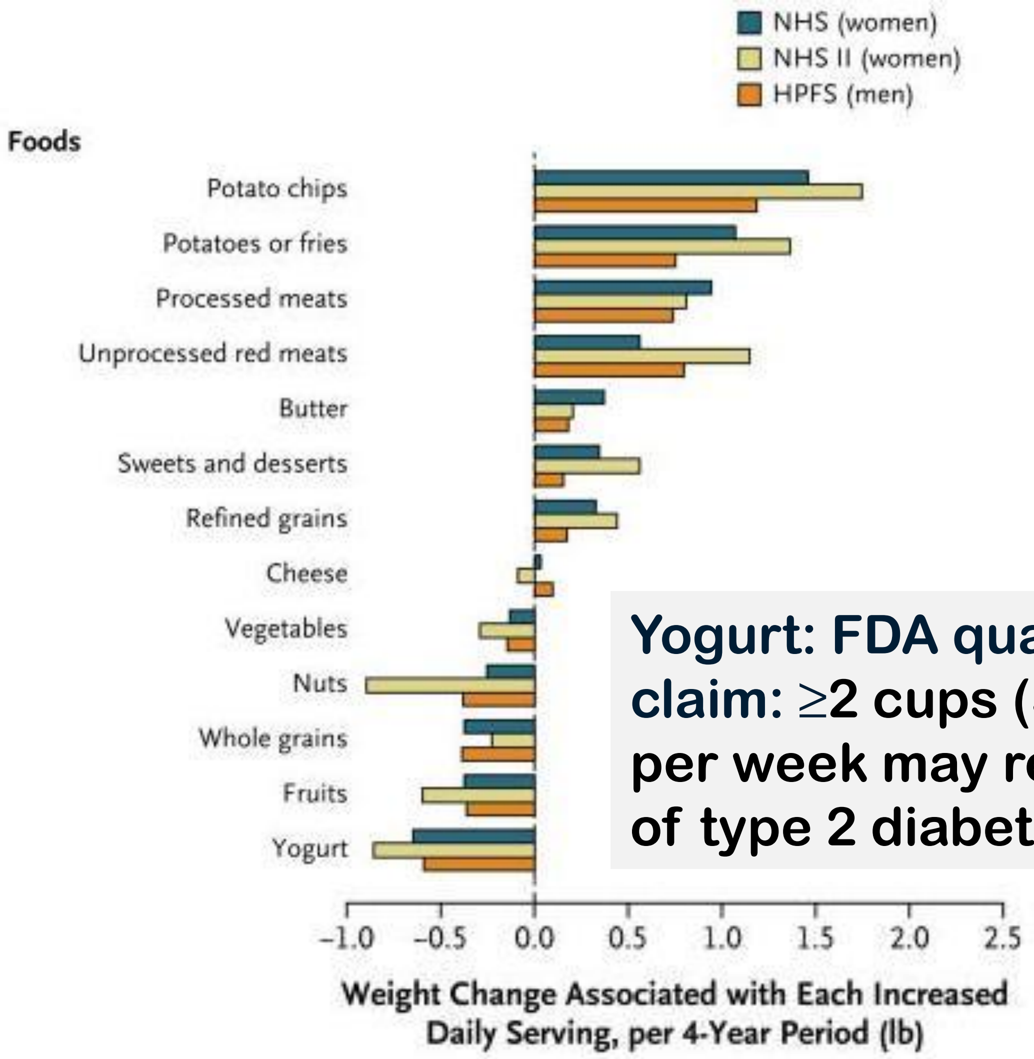
The NEW ENGLAND JOURNAL of MEDICINE

Changes in Diet and Lifestyle and Long-Term Weight Gain in Women and Men

Dariush Mozaffarian, M.D., Dr.P.H., Tao Hao, M.P.H., Eric B. Rimm, Sc.D., Walter C. Willett, M.D., Dr.P.H., and Frank B. Hu, M.D., Ph.D.

3 Cohort Studies (NHS I & II, HPFS)
~290,000 women and men

Yogurt consumption is associated with -0.82 lb change in weight over 4 years



Yogurt: FDA qualified health claim: ≥2 cups (3 servings) per week may reduce the risk of type 2 diabetes

Mozaffarian et al 2011 New Engl J Med

How to connect diet & health?... Gut Health

Brit J Nutr 2002

Communicating about gut health to the consumer: presenting the BENEO® Programme

P. A. A. Coussement*

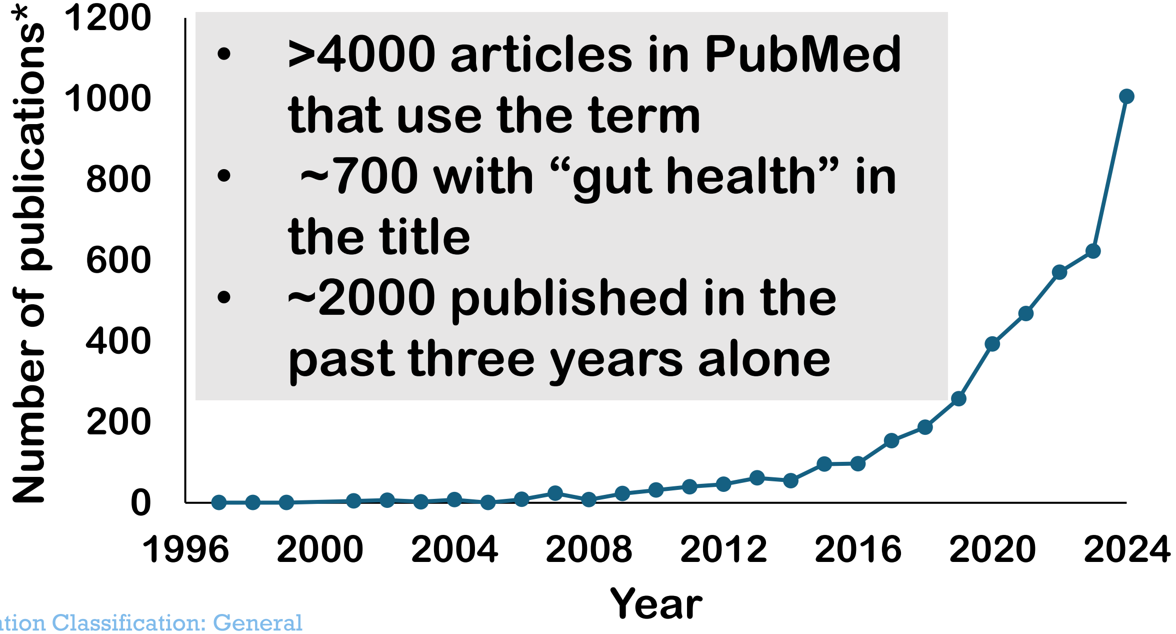
Sales & Marketing/Regulatory Affairs, ORAFTI Active Food Ingredients, Aandorenstraat 1, 3300 Tienen, Belgium

Consumer research: Concluded that ‘**gut health**’ and ‘**intestinal well-being**’ are meaningful for consumers.

How to connect diet & health?... Gut Health

2026

- >4000 articles in PubMed that use the term
- ~700 with “gut health” in the title
- ~2000 published in the past three years alone



* “gut health” in title and/or abstract

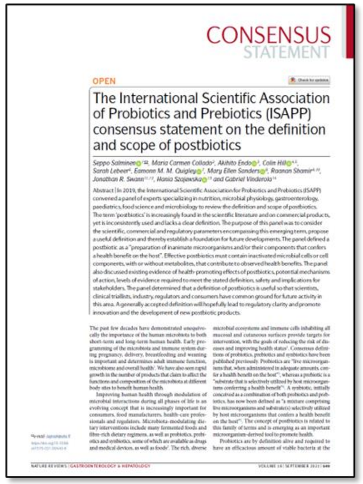
How to connect diet & health?... Gut Health

International Scientific Association for PROBIOTICS and PREBIOTICS

Non-profit scientific organization since 2002

Scientific leadership

Providing expert guidance and promoting rational, evidence-based approaches to biotic research and communication



Peer-reviewed publications and consensus guidance

Academic governance

Community building

Fostering a community of scientists and clinicians to build knowledge, connection and collaboration

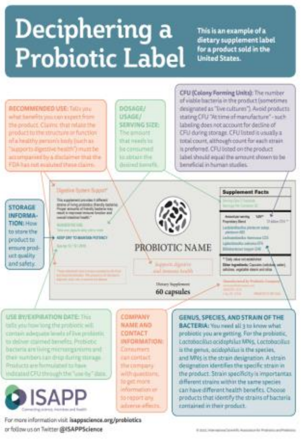
Scientific meetings

Expert panels and working groups

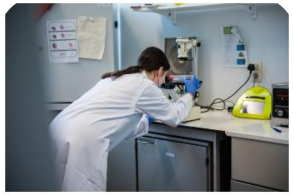
Early career development

Growing knowledge

Sharing evidence-based information with stakeholders and guiding appropriate implementation of biotic science



Educational resources



Microbiome endpoints in clinical trials for biotics – where do we stand and what have we learnt?

News and blog

Podcast

Gut health: what does it mean, can we measure it, and, if so, how?

ISAPP
International Scientific Association for PROBIOTICS and PREBIOTICS

London, UK. September 2024

Eamonn Quigley (co-chair): Gastroenterology
Maria L Marco (co-chair): Microbiology
Marla Cunningham: Biotics science

Stephan C. Bischoff: Gastroenterology
James D. Lewis: Gastroenterology
Daniel Merenstein: Family medicine
Hania Szajewska: Pediatrics
Heidi M. Staudacher: Nutrition and dietetics

Gerard Clarke: Gut-brain-microbiome axis
Nathalie Delzenne: Gut endocrine function
Marlies Meisel: Immunology
Paul W. O'Toole: Gut microbiology
Jerry M Wells: Intestinal cell biology

nature reviews gastroenterology & hepatology
https://doi.org/10.1038/s41575-026-01176-x

Consensus statement

Check for updates

The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of gut health

Maria L. Marco[1], Marla Cunningham[2], Stephan C. Bischoff[3], Gerard Clarke[4], Nathalie Delzenne[5], James D. Lewis[6], Marlies Meisel[7], Daniel Merenstein[8], Paul W. O'Toole[9], Heidi M. Staudacher[10], Hania Szajewska[11], Jerry M. Wells[12] & Eamonn M. M. Quigley[13]

ISAPP
International Scientific Association for PROBIOTICS and PREBIOTICS

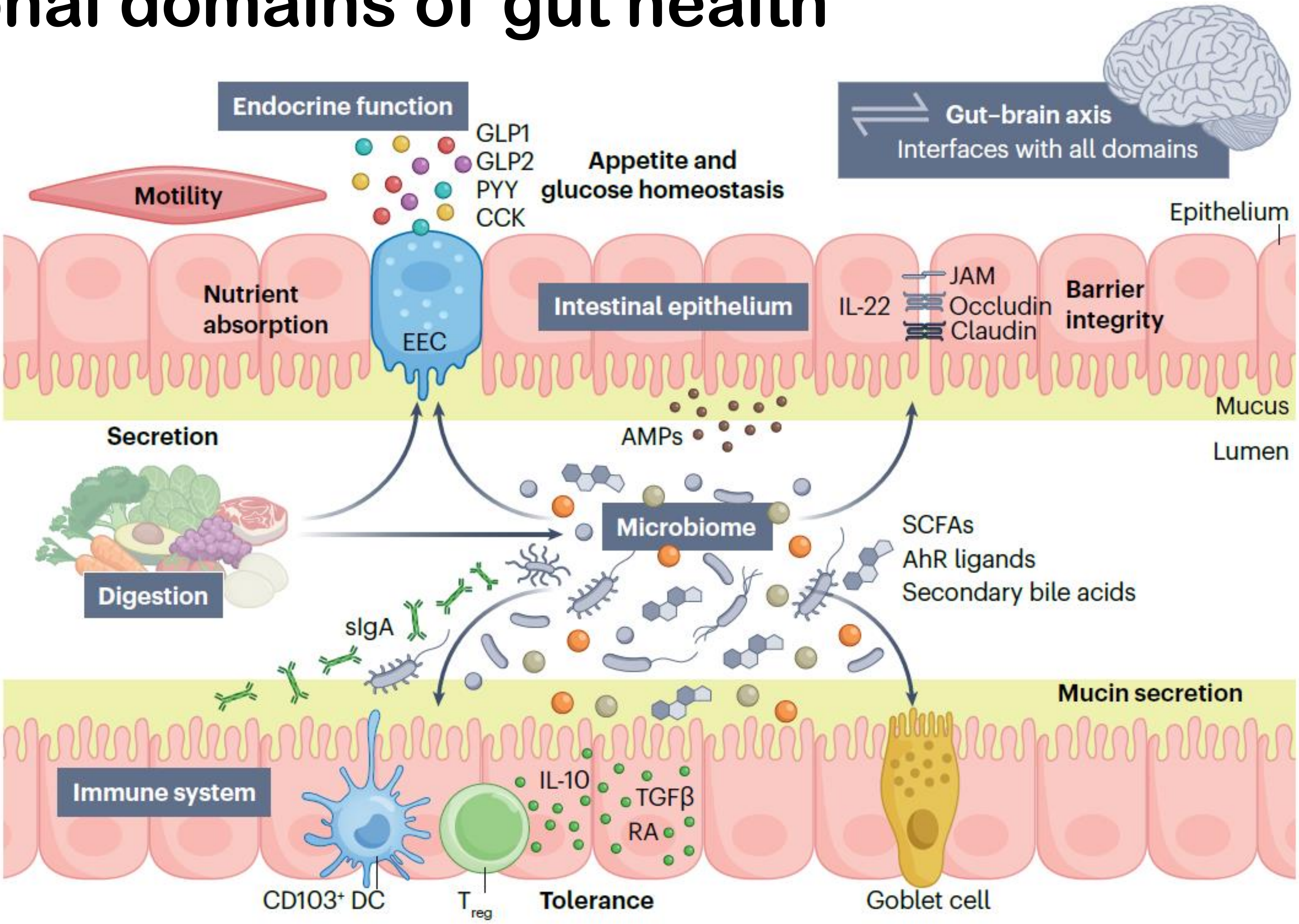
Non-profit scientific organization since 2002

a state of normal gastrointestinal function without active gastrointestinal disease and gut-related symptoms that affect quality of life

Published: 2/18/2026

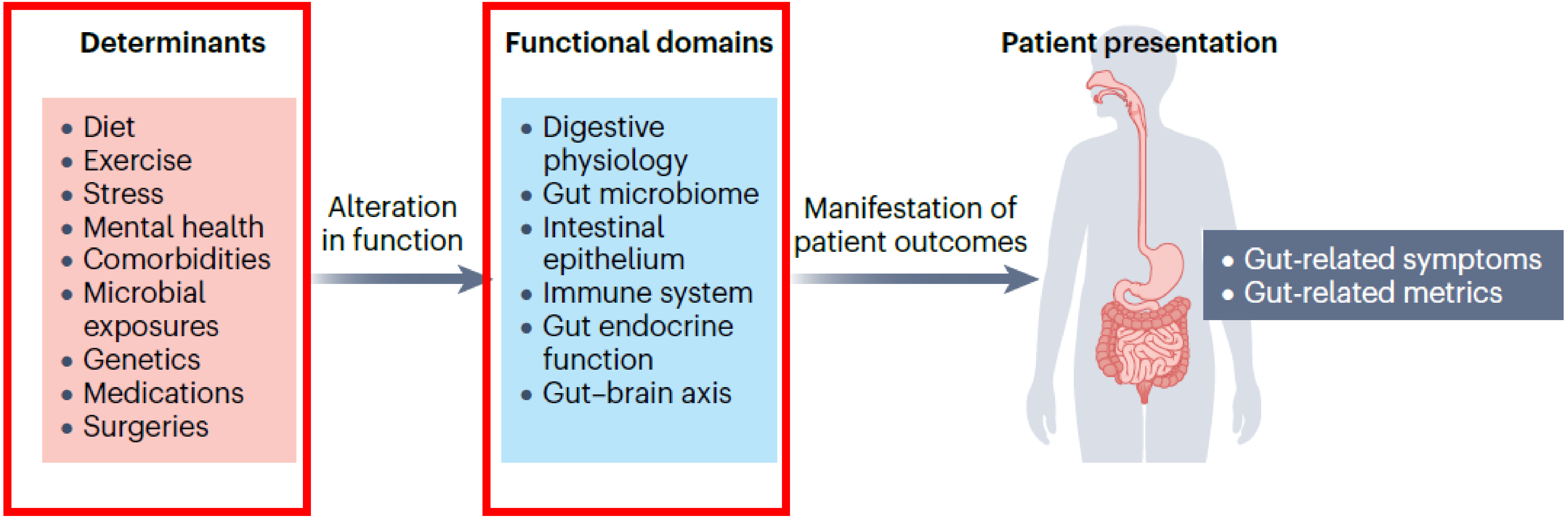
Marco *et al* 2026 Nat Rev Gastroenterol Hepatol

Functional domains of gut health



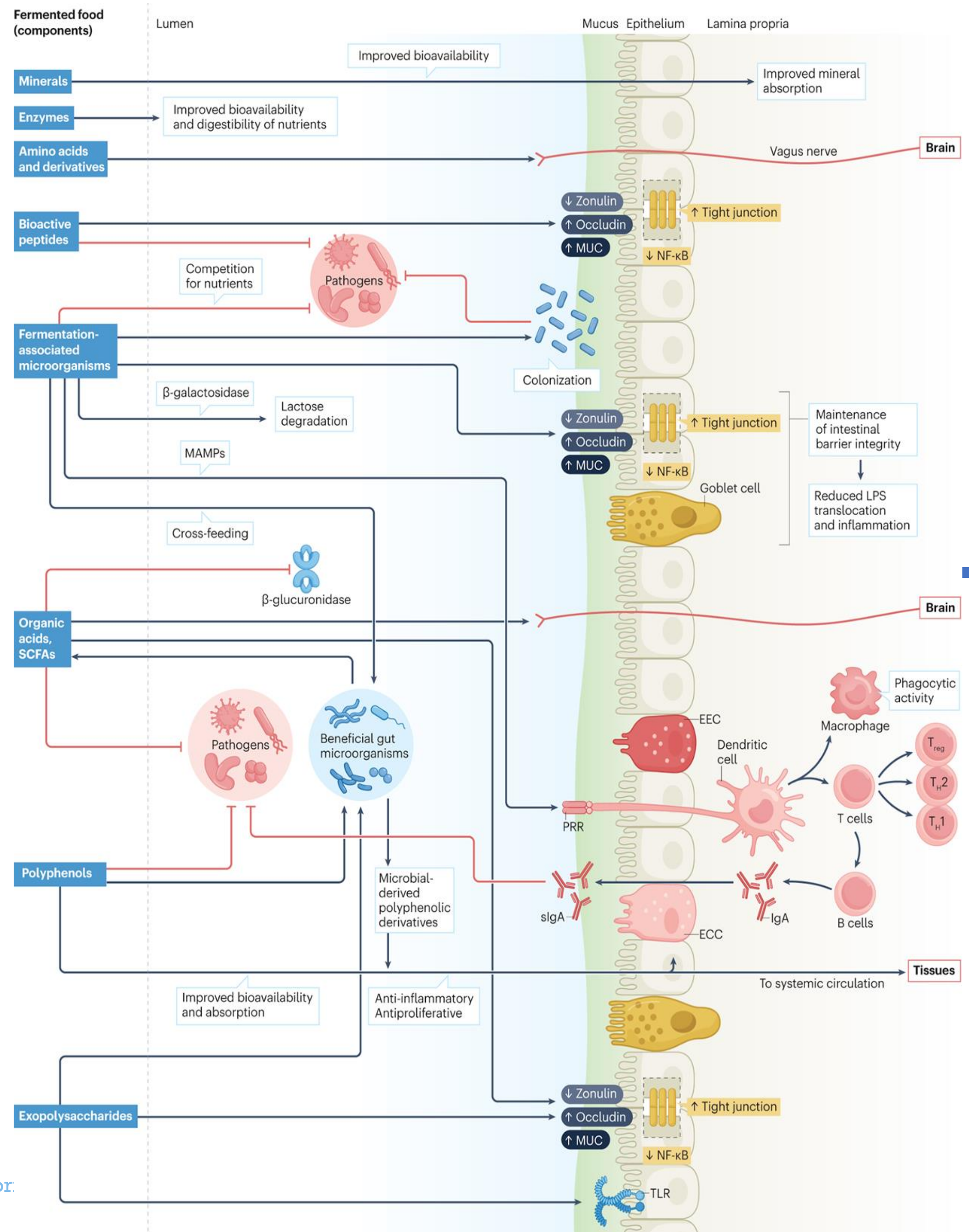
Marco *et al* 2026 Nat Rev Gastroenterol Hepatol

Holistic approach to gut health



- **Few validated metrics for assessing the functional domains.**
- **Risk factors for future gut health have yet to be determined.**

Marco *et al* 2026 Nat Rev Gastroenterol Hepatol



Review article

Fermented foods and gastrointestinal health: underlying mechanisms

Arghya Mukherjee[1,6], Samuel Breselge[1,2,6], Eirini Dimidi[3], Maria L. Marco[4] & Paul D. Cotter[1,2,5]

Nat Rev Gastroenterol Hepatol 2024

Examples of metabolites acting within and beyond the gut:

- **Organic acids**
- **Antimicrobial peptides**
- **Serotonin, melatonin, GABA**
- **Biogenic amines (histamine)**
- **Mycotoxins**
- **Cyanogenic glycosides (cassava)**

Infor

How can fermented foods support (gut) health?

Modifications to food ingredients

- ✓ Improve digestibility
- ✓ Remove toxic compounds

Delivery of new bioactive compounds

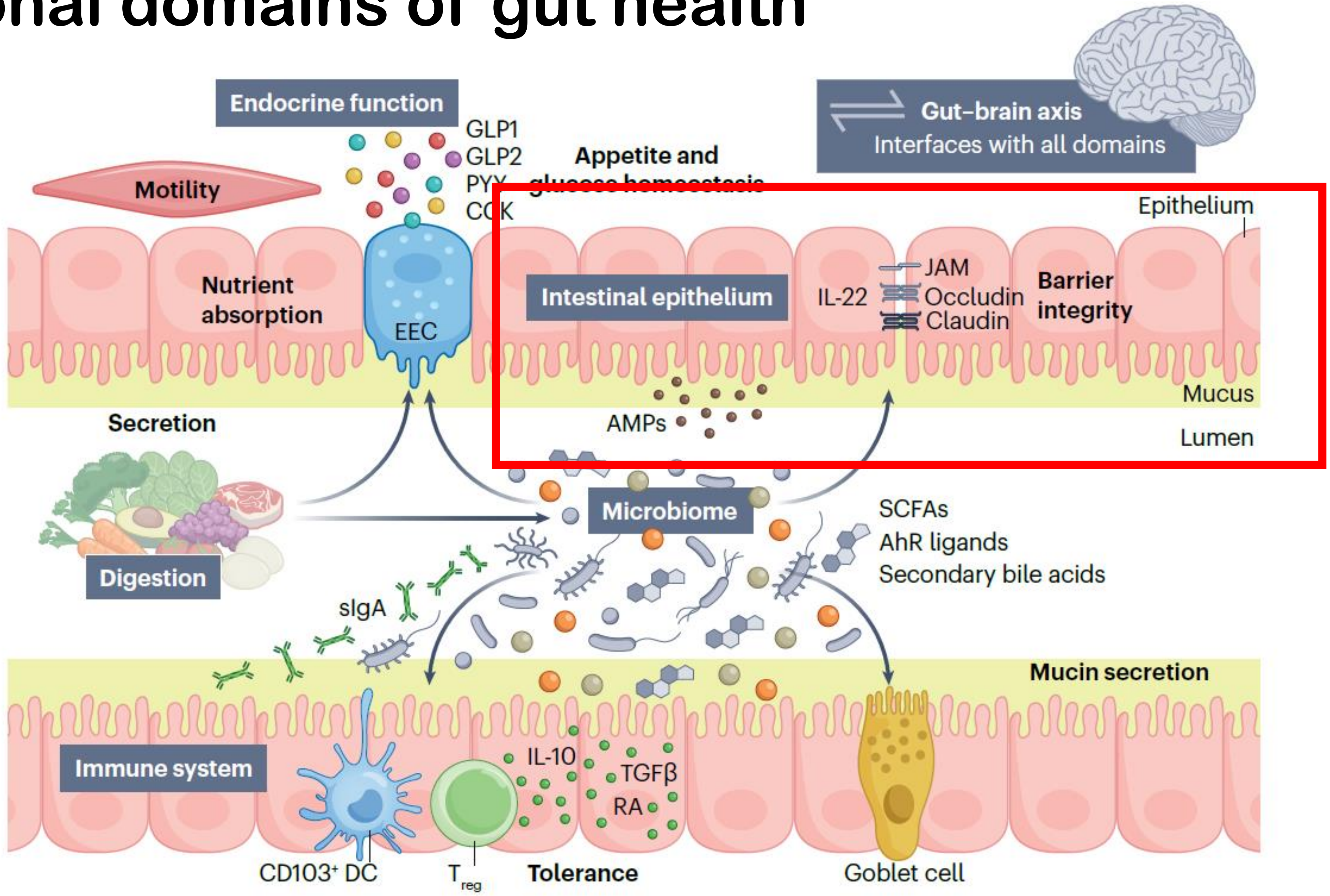
- ✓ Vitamins
- ✓ Bacteriocins
- ✓ Organic acids

Increased numbers of (living) microbes

- ✓ Increased live microbe intake
- ✓ Food microbes: ~3% of gut microbiome

Marco et al 2017 Curr Op Biotechnol; Marco et al 2021 Nat Rev Gastroenterol Hepatol

Functional domains of gut health



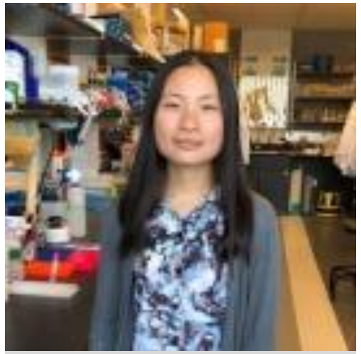
Information Classification:

Marco *et al* 2026 Nat Rev Gastroenterol Hepatol

Sauerkraut metabolites & intestinal barrier function

- Does (fermented) cabbage support intestinal barrier function?

- How consistent are the effects across ferments?
  - homemade vs commercial
  - fermentation time
  - with an added probiotic strain

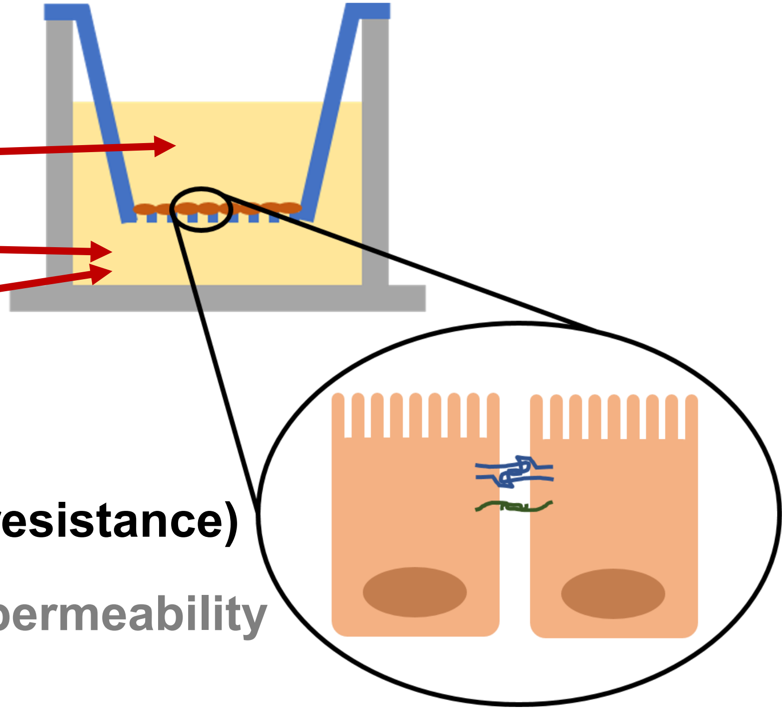


Lei Wei

Intestinal barrier model:

Intestinal epithelial Cells (IECs) form a barrier which regulates interactions between the luminal contents and the body, limiting permeability.

- Differentiated Caco-2
- 0 h: + (fermented) foods**
- 3 h: + IFNγ
- 24 h: + TNFα
- 48 h: Measure TER (Transepithelial electrical resistance)
- 60 h
- 72 h: FITC-Dextran paracellular permeability



Inflammatory cytokines (IFNγ and TFNα) increase barrier permeability.

** (Fermented) cabbage + brine homogenized, filtered (0.2 um), and adjusted to pH 7.4. 1:10 ratio in DMEM

Donato et al 2010 Microbiology

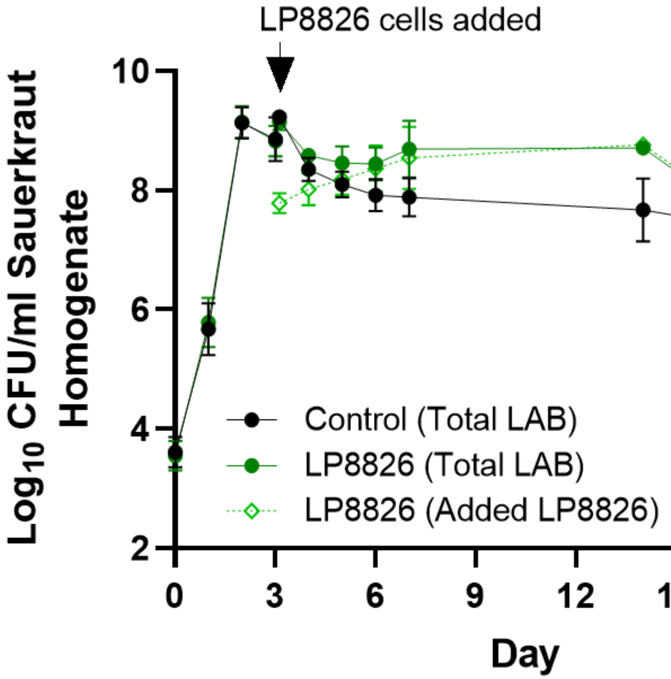
Laboratory and commercial cabbage ferments

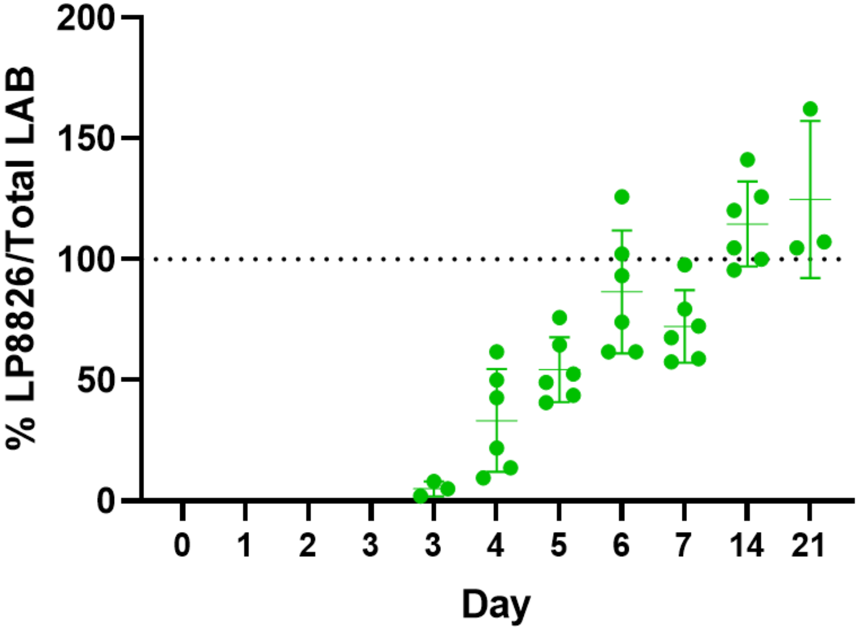
Cabbage + Brine (day 0)

Fermented cabbage day 7 (D7) & day 14 (D14)

...with *L. plantarum* NCIMB8826R day 7 (D7) & day 14 (D14)

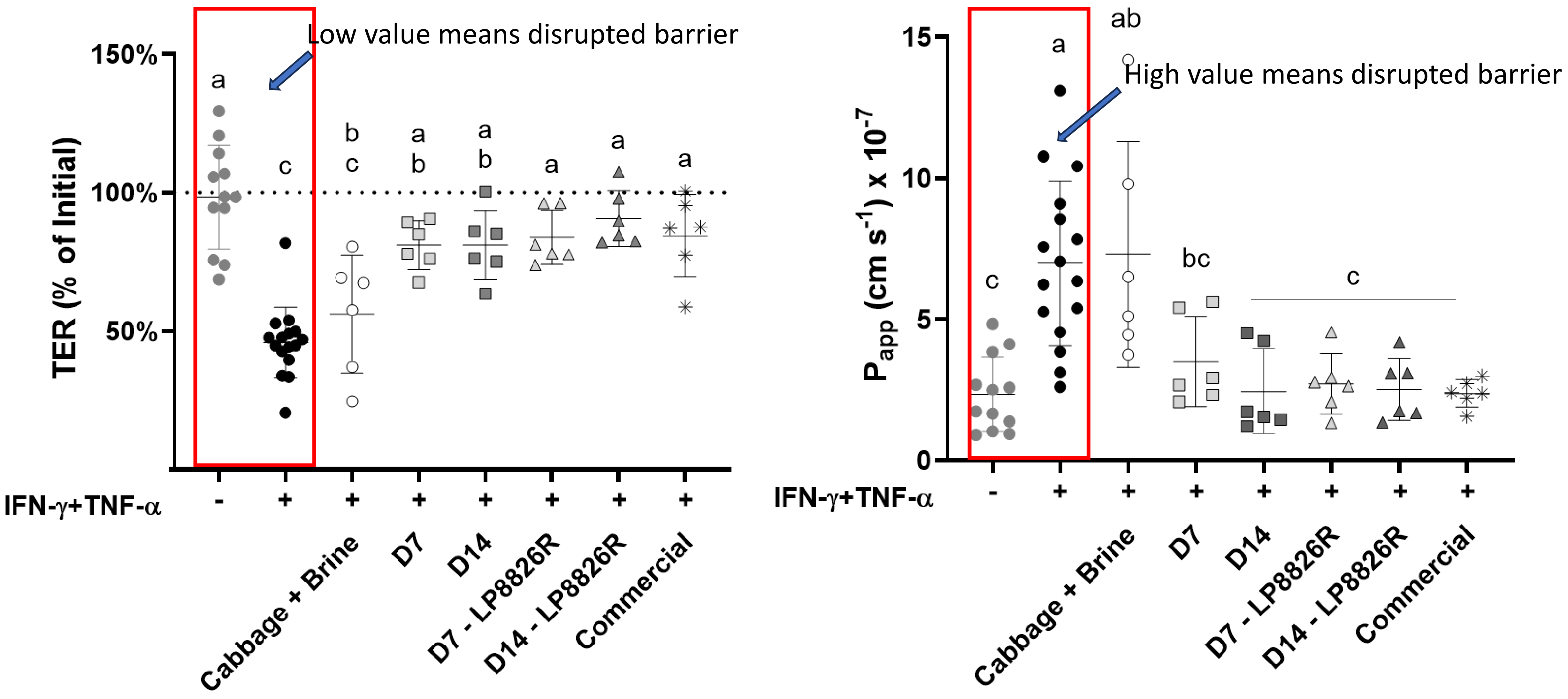
Store-bought (commercial)





Lei Wei et al 2025 Appl Environ Microbiol

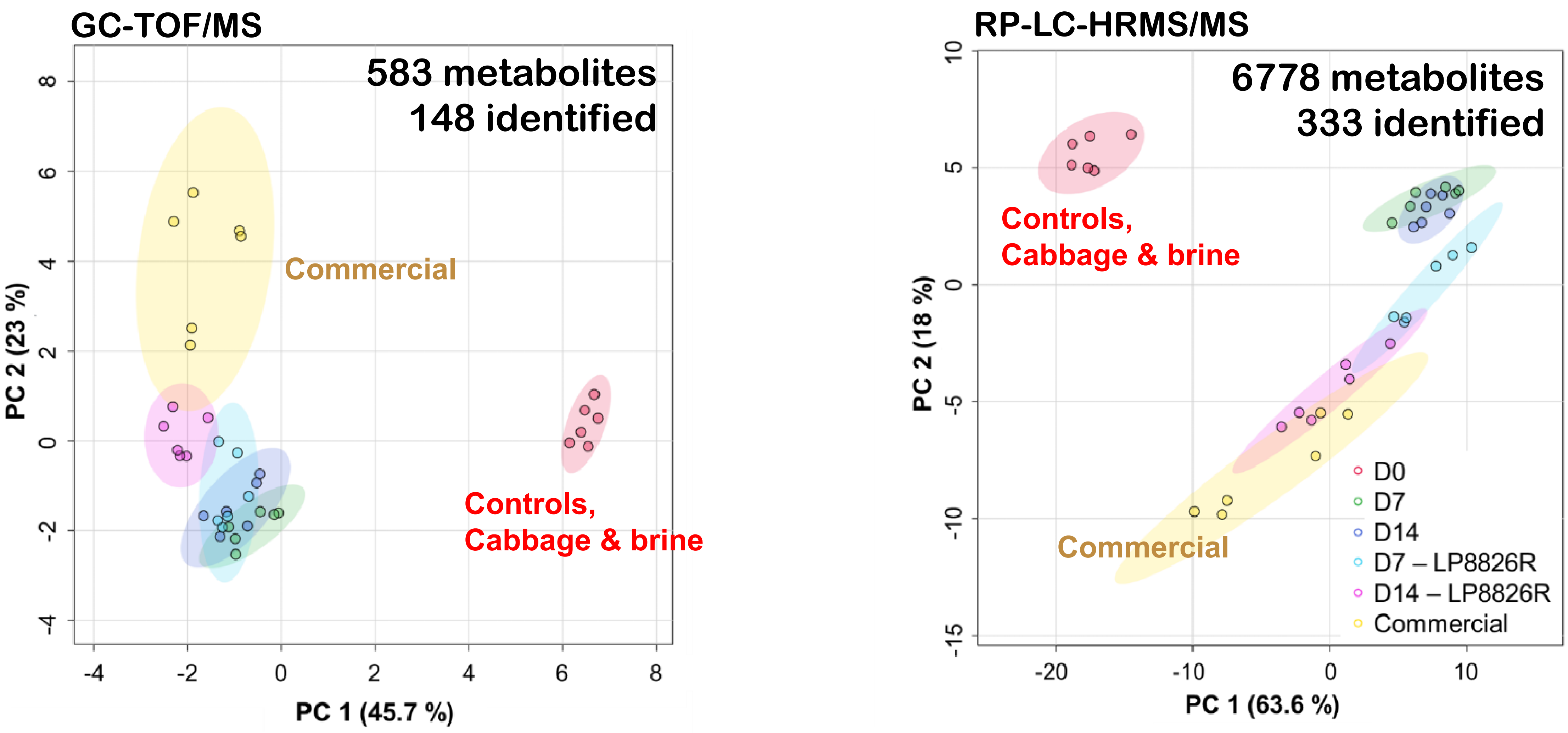
Fermented cabbage protects the intestinal barrier



TER normalized to time 0.
Data are from four independent experiments.
Mean ± SD. One-way ANOVA with Tukey's multiple comparison test; $p < 0.0001$.

Fermentation changes cabbage metabolomes

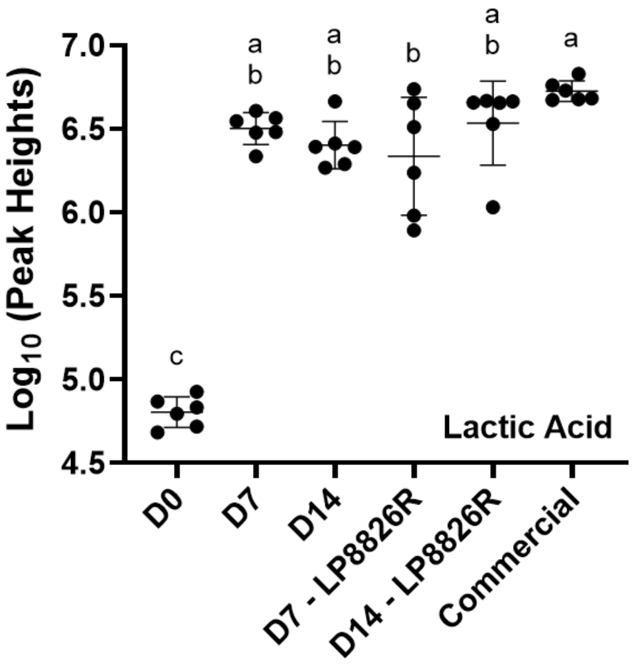
Soluble metabolites from filtered cabbage homogenates and brine



Significantly different, PERMANOVA P < 0.001

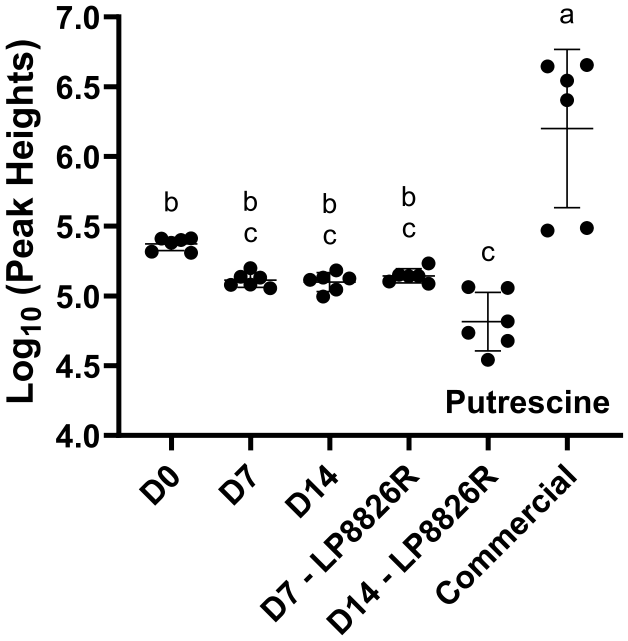
Lei Wei et al 2025 Appl Environ Microbiol

Core and ferment-specific metabolites

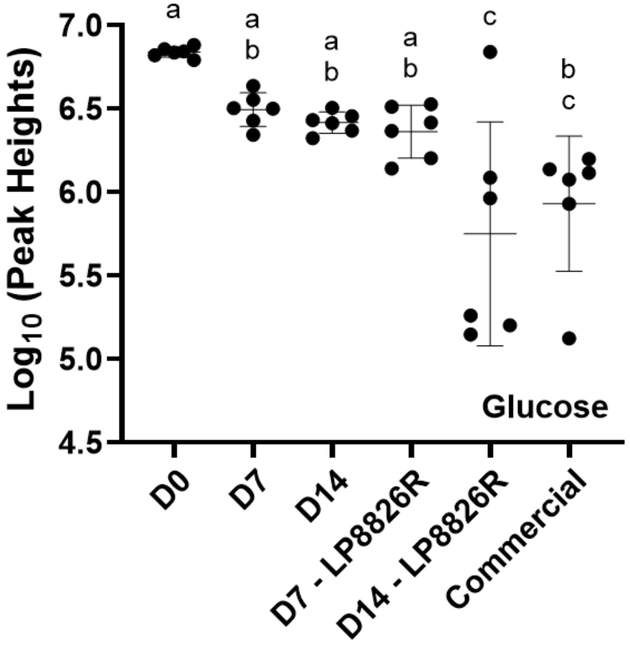


Core metabolites enriched (depleted) <u>across</u> ferments

Metabolites <u>specific</u> to commercial ferments

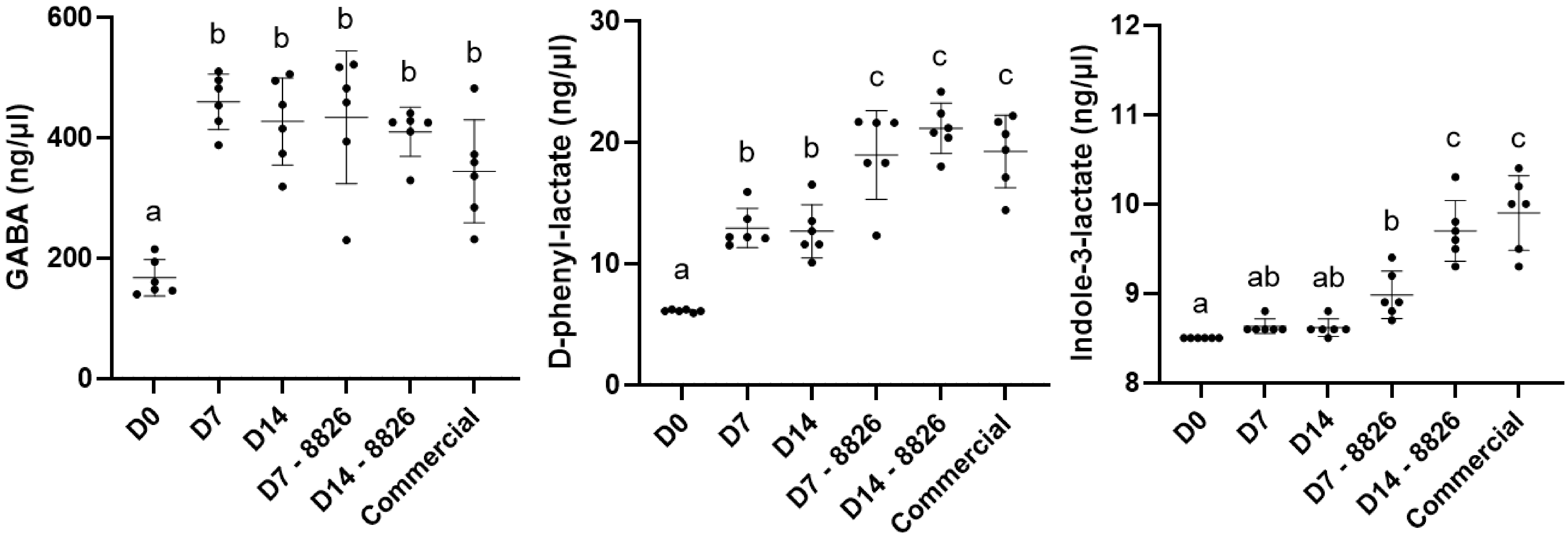


Metabolite changes <u>shared</u> between LP8826R and commercial ferments



Lei Wei et al 2025 Appl Environ Microbiol

Fermentation increases gut-microbe metabolites



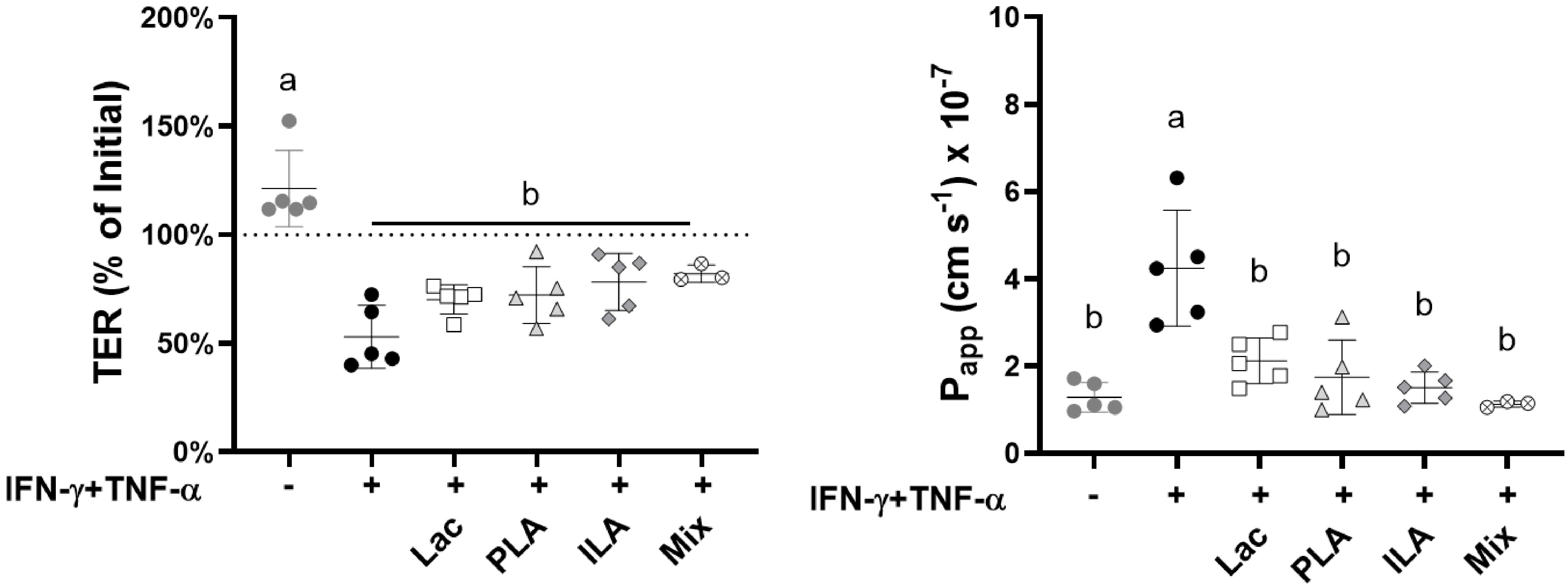
gamma-aminobutyric acid (GABA): a neurotransmitter

D-phenyl-lactate (PLA): immune and energy homeostasis

indole-3-lactic acid (ILA): anti-inflammatory, epithelial barrier

Targeted GC-TOF/MS. Mean ± SD. One-way ANOVA with Tukey's multiple comparisons test, $p < 0.05$; $n = 6$.

Individual metabolites provide incomplete protection against proinflammatory cytokines

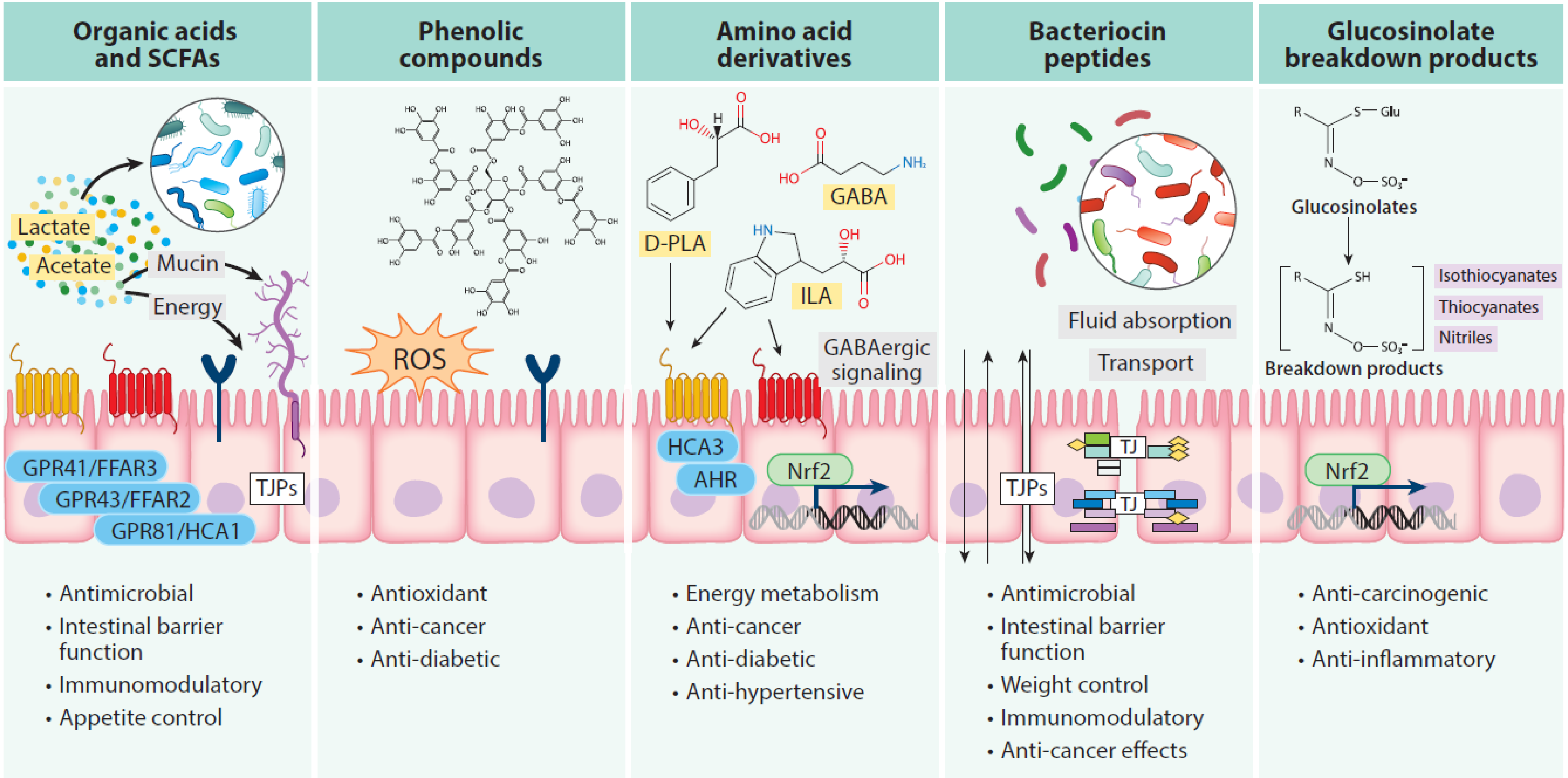


Lac: 50 mM lactate (n = 5); PLA: 60 μM D-phenyl-lactate (n = 5); ILA: 25 μM indole-3-lactate (n = 5); Mix: a mixture of the three metabolites (n = 3).

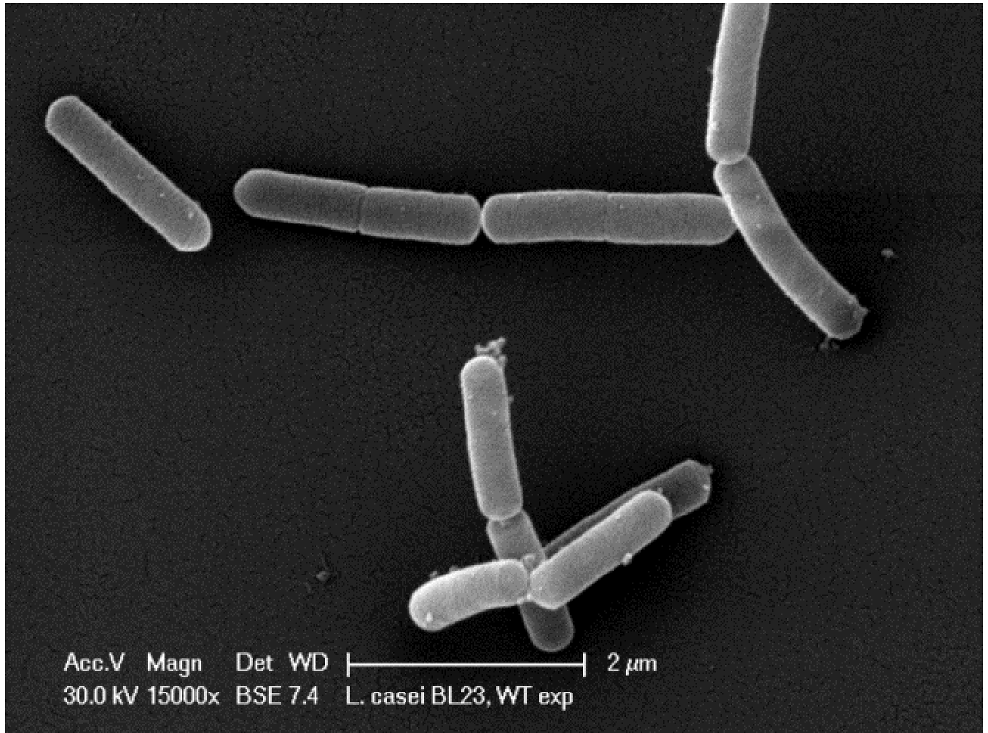
Mean ± SD. Mean values not sharing any letter are significantly different based on (TER) two-way or (FITC) one-way ANOVA with Tukey's multiple comparisons test.

Lei Wei et al 2025 Appl Environ Microbiol

Fermented fruits and vegetables



Lei Wei et al 2025 Ann Rev Food Sci Technol


Acc.V Magn Det WD 2 µm
30.0 kV 15000x BSE 7.4 L. casei BL23, WT exp

Fermented dairy and gut health

- RCT and observational studies on fermented dairy with comparisons to milk, non-dairy controls, or no dairy consumption.

- Probiotic-fermented or probiotic-containing fermented dairy studies were included if on fermented dairy, not the probiotic.

- 37 human studies (mainly RCTs), including adults and children, with and without underlying conditions. (21 included probiotic strains).

Bui and Marco 2025 Nutr Rev

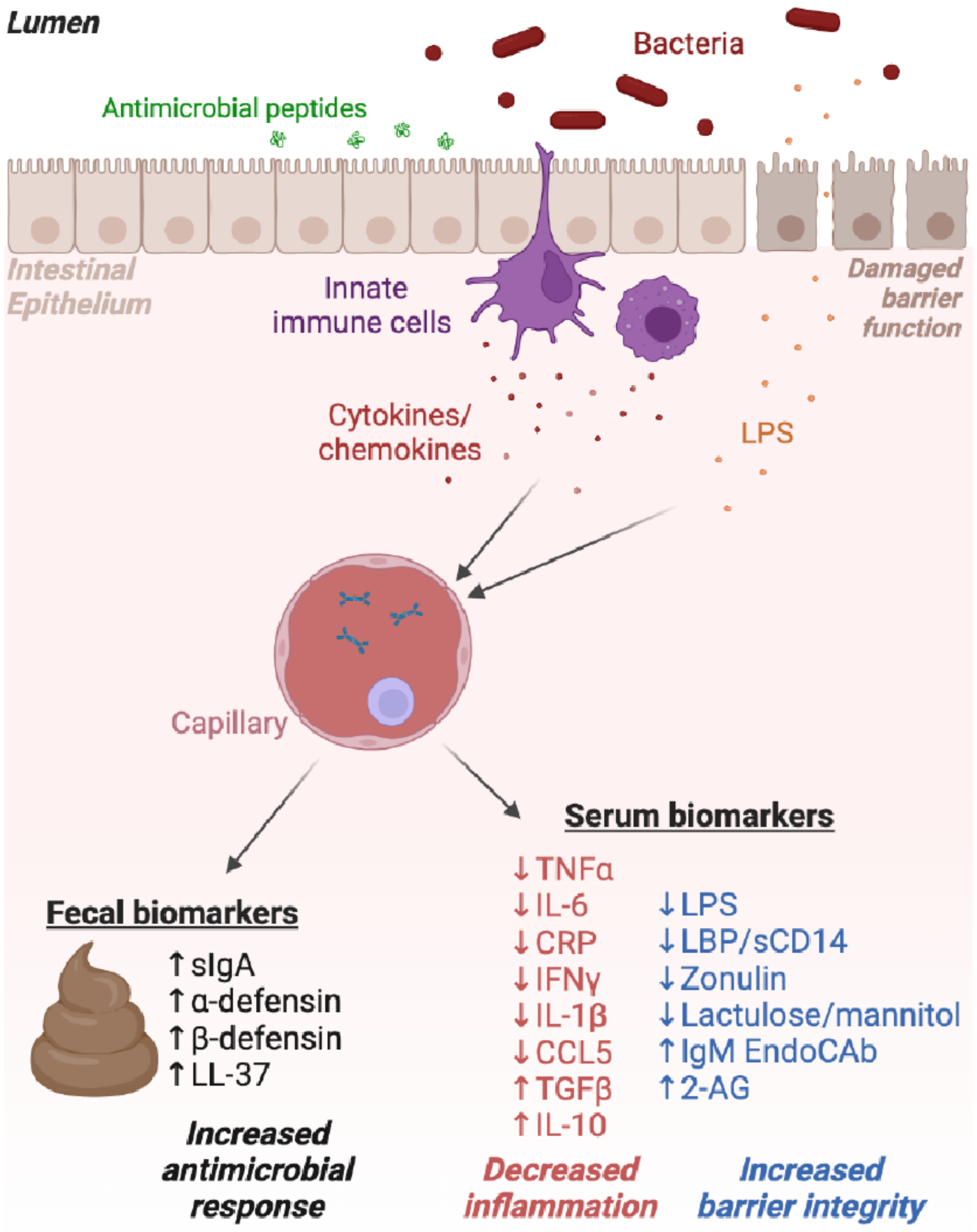
Fermented dairy and gut health

- No study reported a harmful effect
- 10 reported no benefit (symptom; immune)
- 27 with significant changes in one or more gut symptoms or gut health biomarkers
  (including 14 out of 20 studies measuring symptoms)

✓ Improved stool frequency and transit times

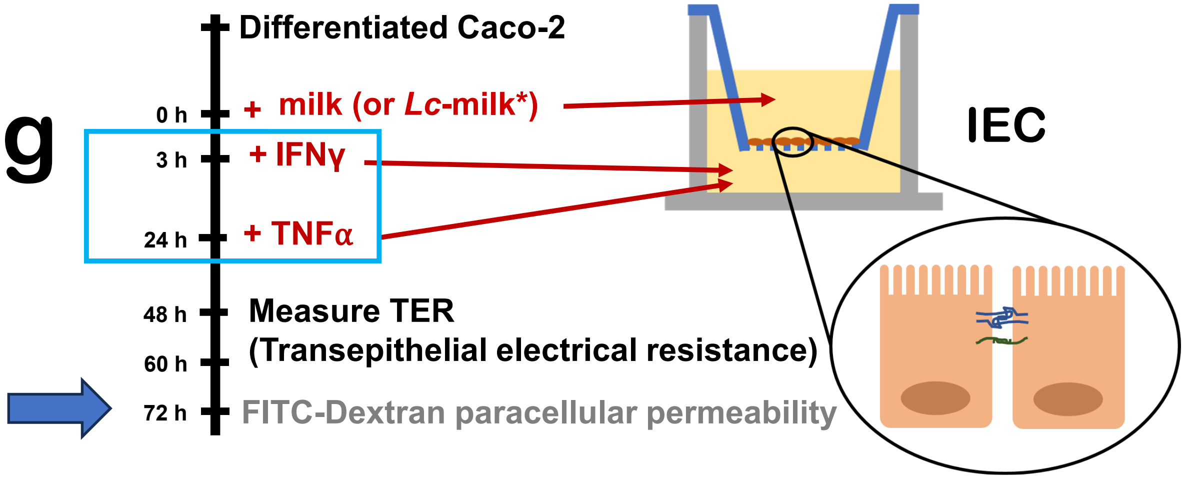
✓ Reduced abdominal and rectal symptoms

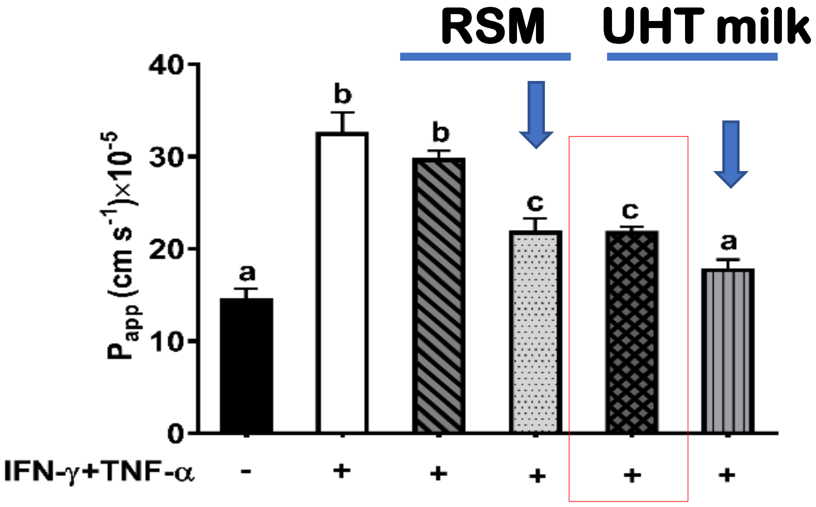
✓ Reductions in intestinal inflammation and serum TNFα levels (6 of 9 studies)



Bui and Marco 2025 Nutr Rev

L. paracasei fermented milk reduces IEC permeability during cytokine challenge





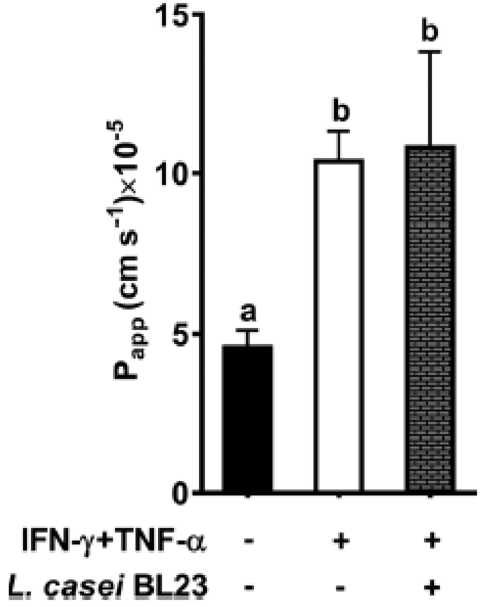
25% v/v Reconstituted skim milk (RSM)

25% v/v *L. paracasei* fermented RSM (FRSM)

25% v/v 2% Ultra-High Temperature (UHT) pasteurized milk

25% v/v *L. paracasei* fermented UHT milk (FUHT)

L. paracasei alone is ineffective



DMEM
(culture medium)

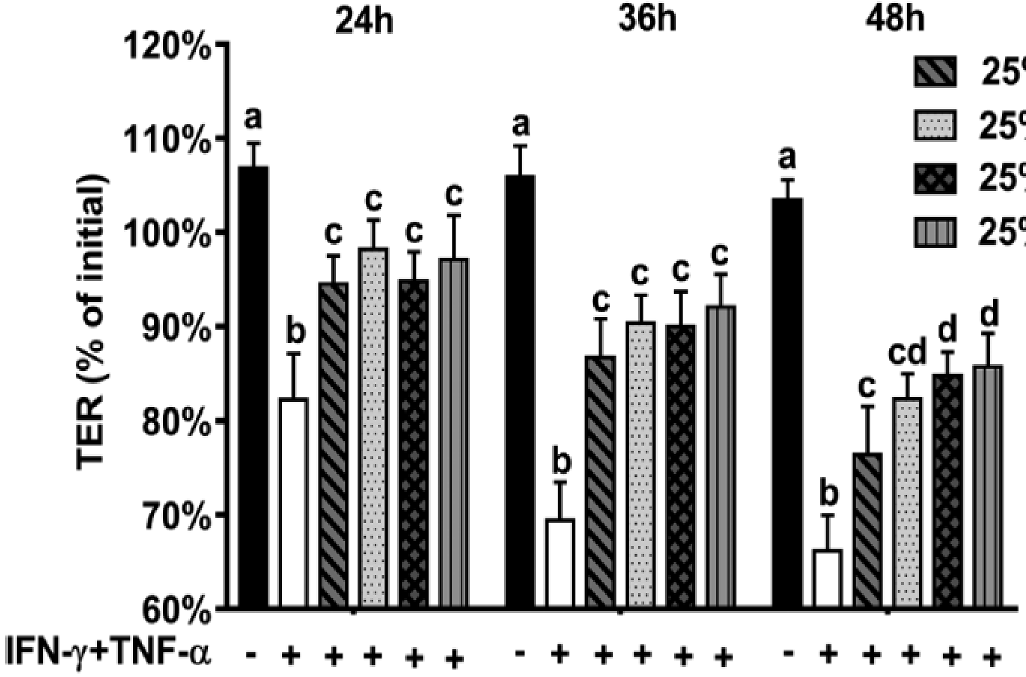
IEC: Intestinal epithelial cell

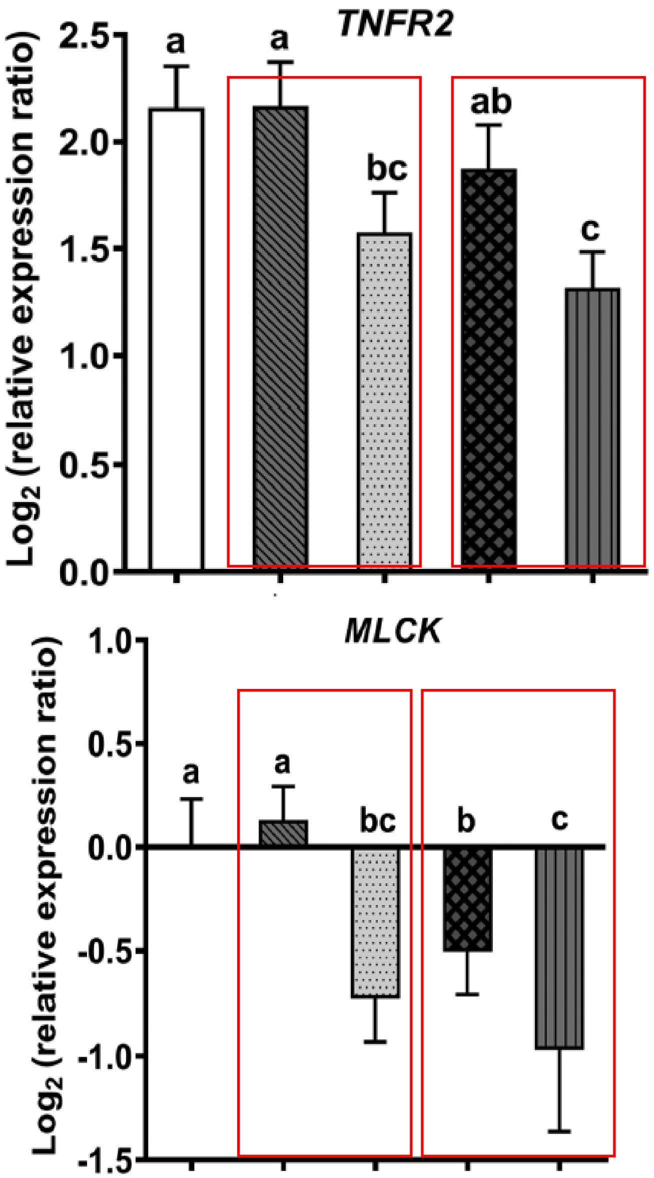
P_{app} : FITC-Dextran permeability

Cell-free filtrate of (fermented) milk was applied

Zhai *et al* 2019 J Ag Food Sci

L. paracasei fermented milk preserves IEC barriers





25% v/v Reconstituted skim milk (RSM)
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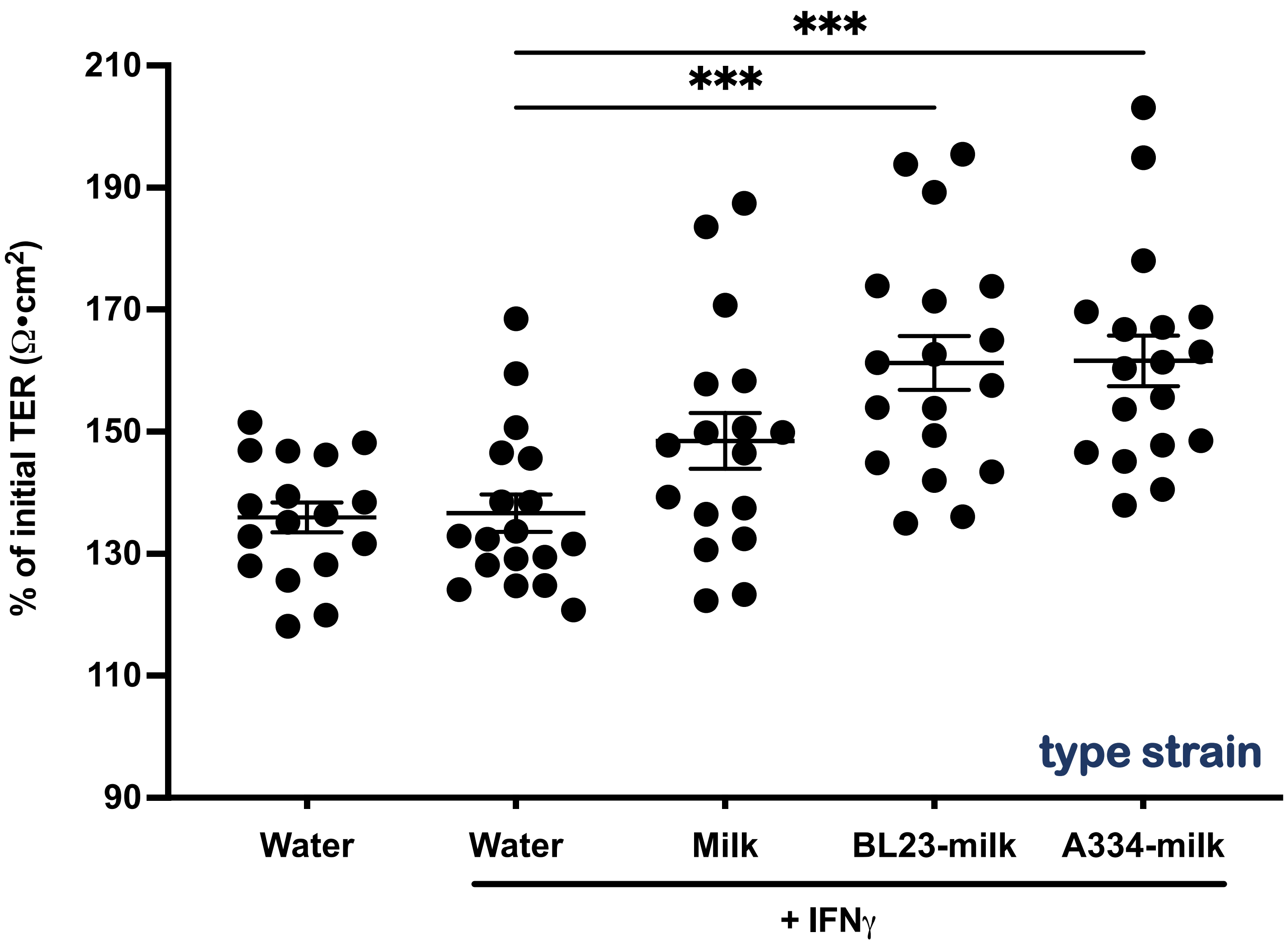
25% v/v 2% Ultra-High Temperature (UHT) pasteurized mil
25% v/v *L. paracasei* fermented UHT milk (FUHT)

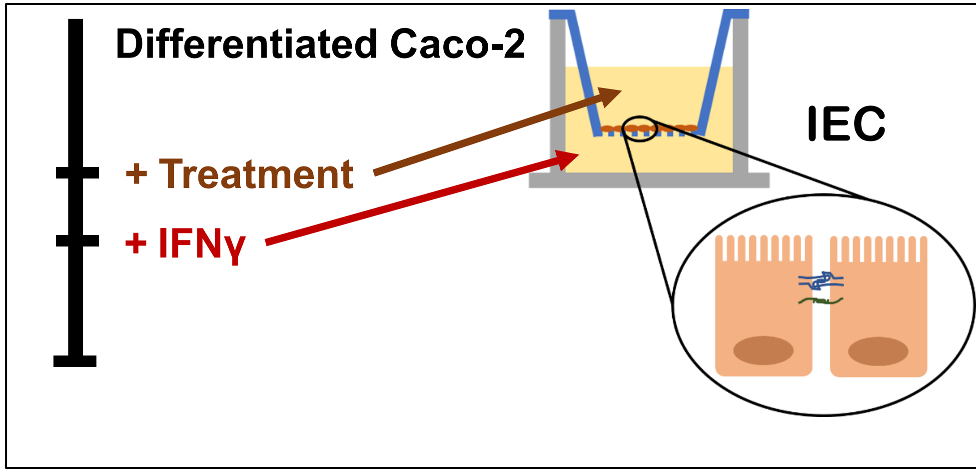
TNFR2 - TNF receptor

MLCK – myosin light-chain kinase

Zhai *et al* 2019 J Ag Food Sci

L. paracasei fermented milk - IFNγ interactions





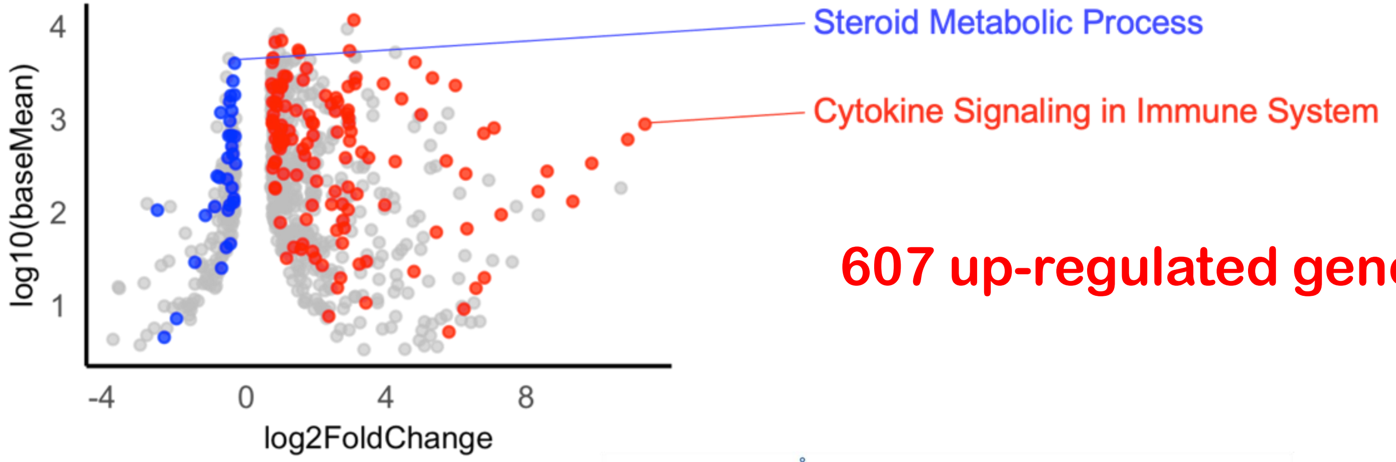
IFNγ (100 ng/ml)

***p < 0.0005 according to Kruskal Wallis and Dunn's multiple comparisons test

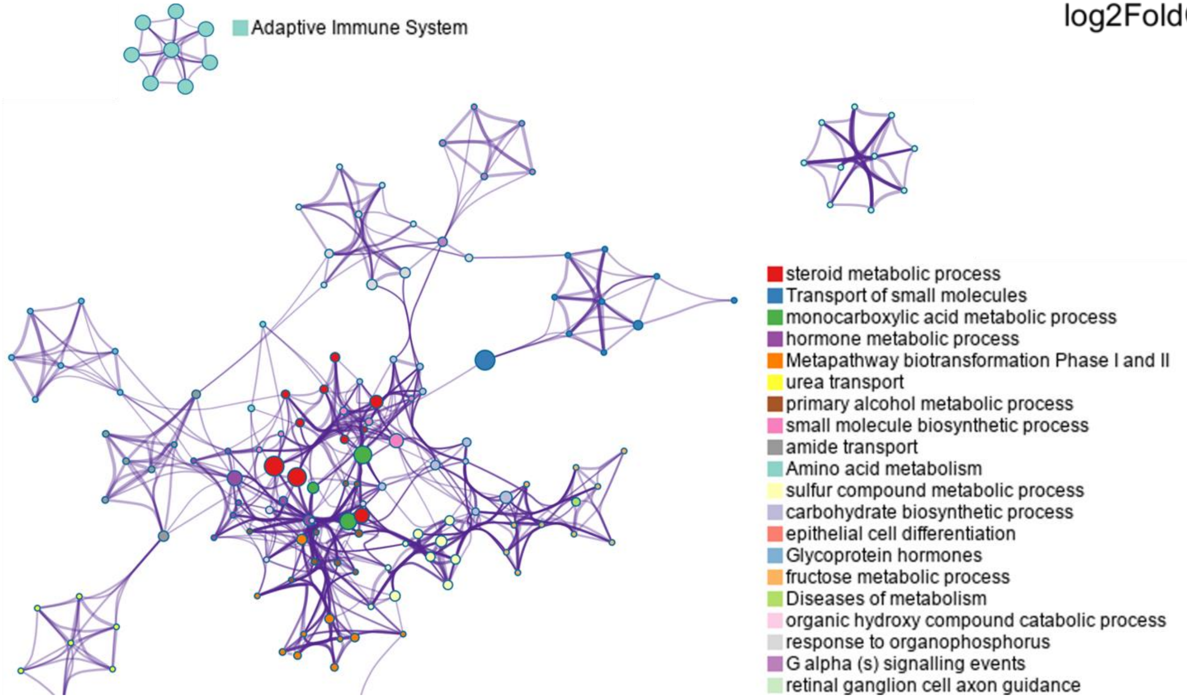
Bui *et al submitted*

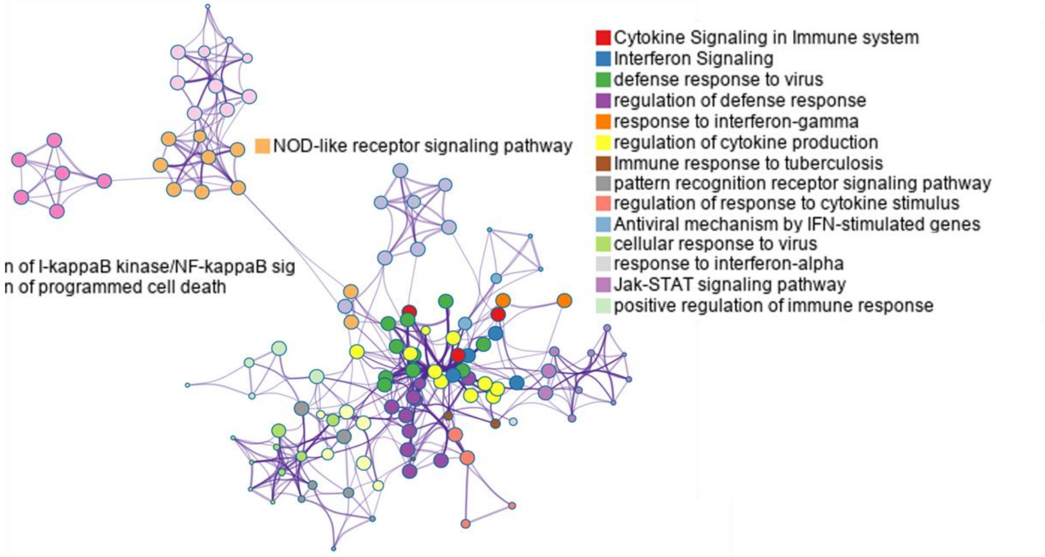
Intestinal cells respond to IFNγ

152 down-regulated genes



607 up-regulated genes

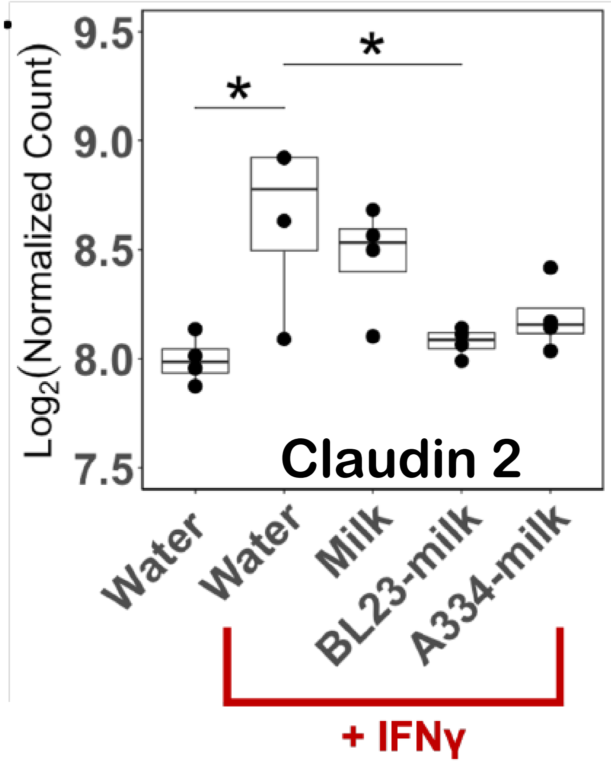




Network map of (Metascape). Node size reflects gene count, node color signifies cluster function, connecting lines indicate similar terms

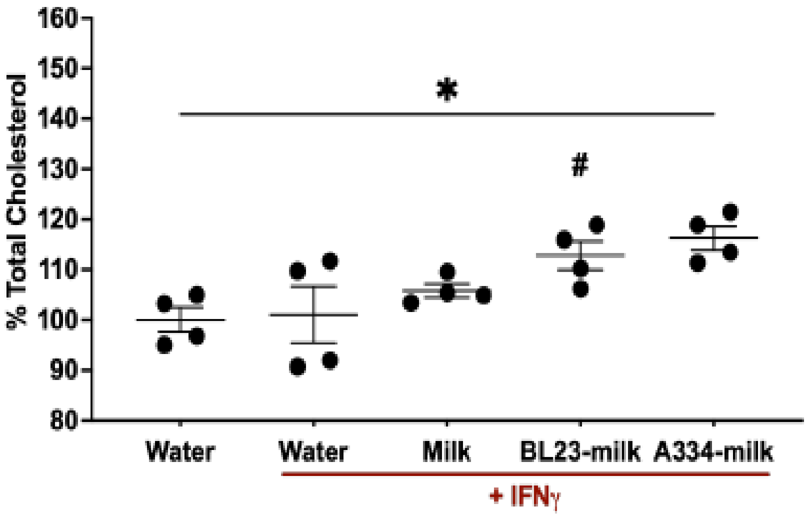
Bui *et al submitted*

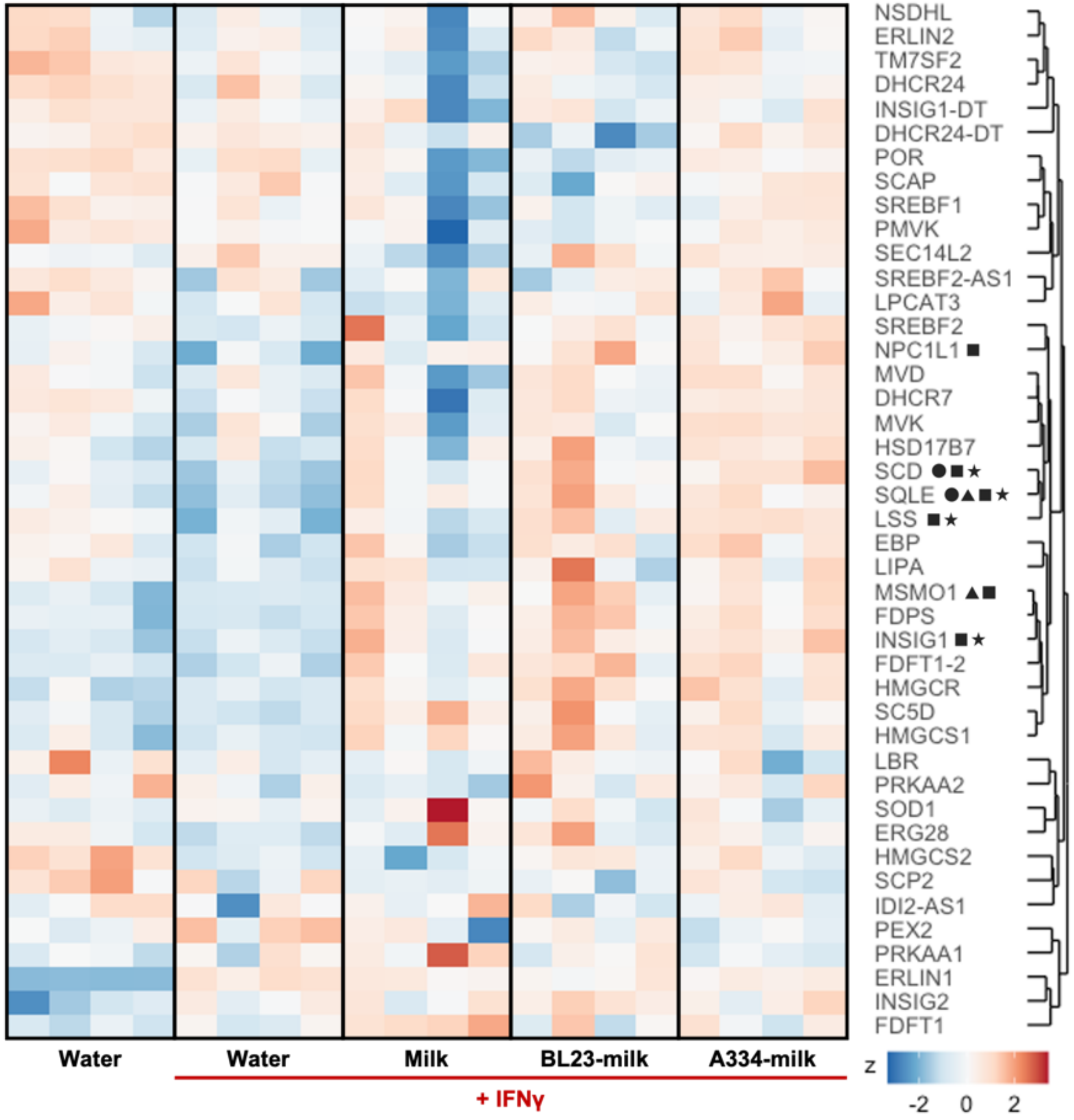
L. paracasei fermented milk prevents IFNγ changes to IEC



Sterol metabolism

normalized read counts across all genes associated with sterol biosynthesis

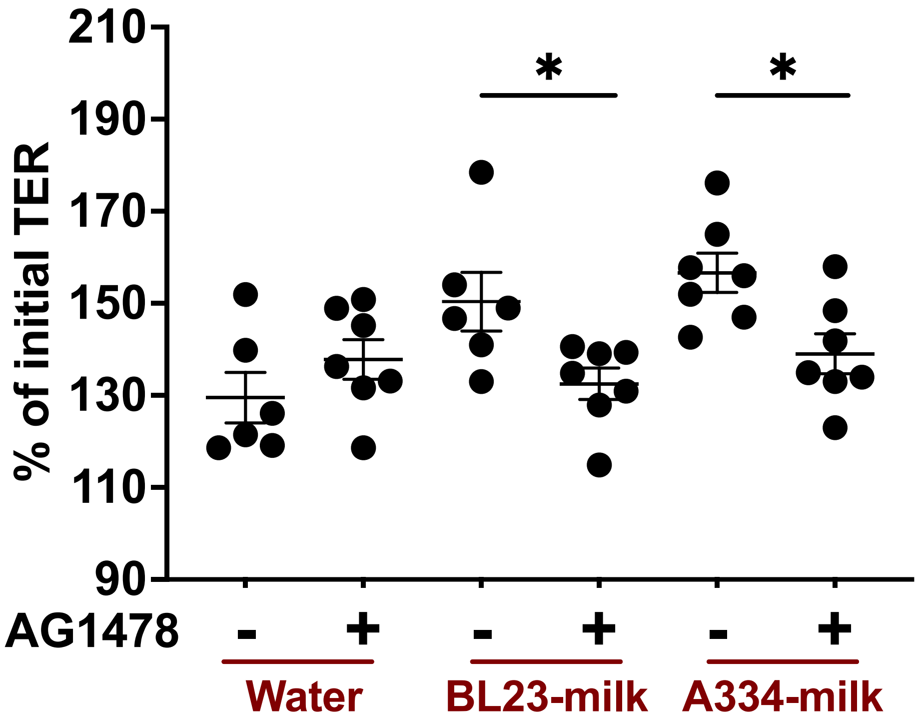




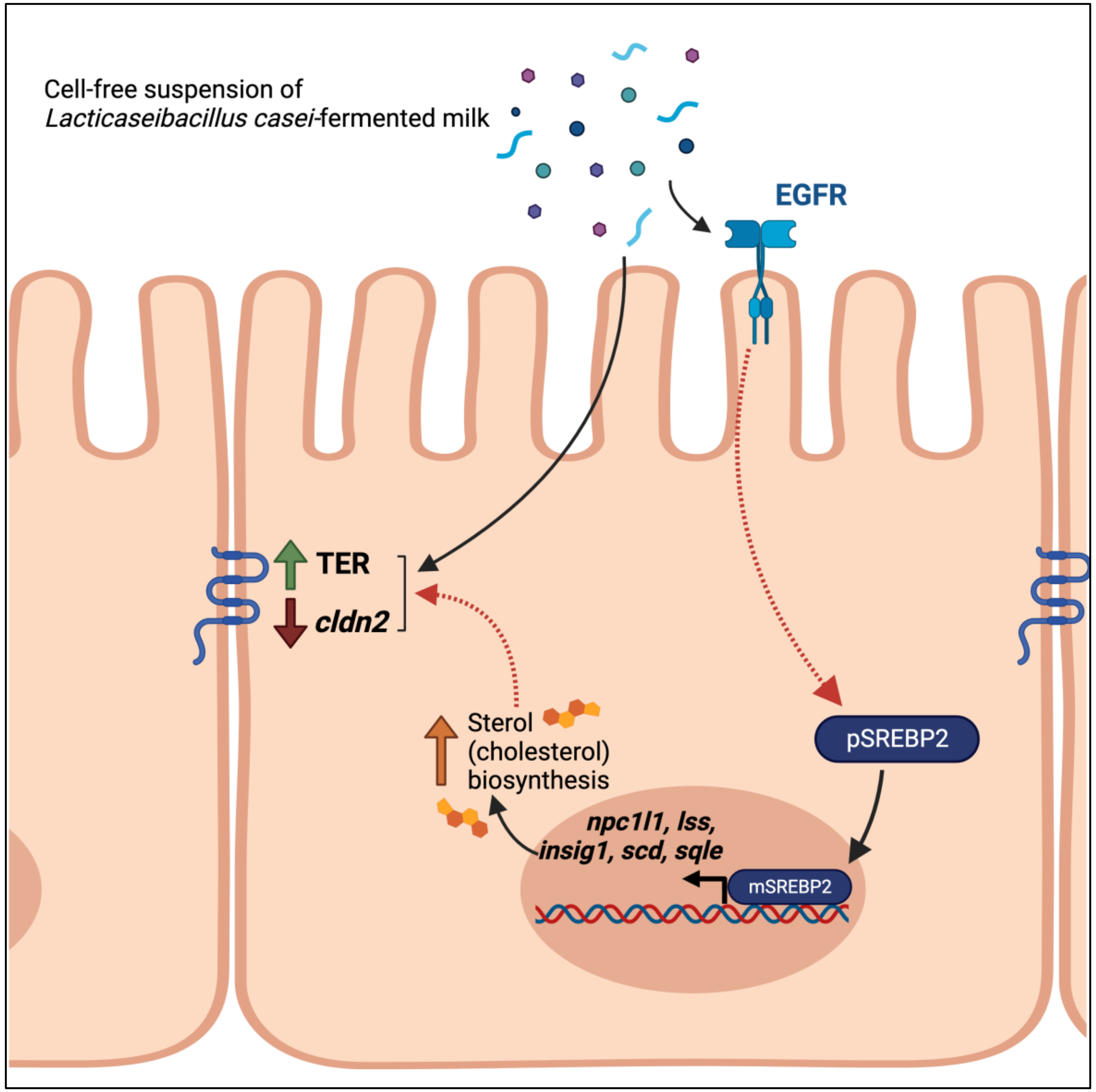
* P < 0.05 Kruskal Wallis

Bui *et al submitted*

Model for *L. paracasei* fermented milk – IEC interactions



AG1478: Antagonist of the Epidermal Growth Factor Receptor (EGFR)



Bui *et al submitted*

How can fermented foods support (gut) health?

Modifications to food ingredients

- ✓ Improve digestibility
- ✓ Remove toxic compounds

Delivery of new bioactive compounds

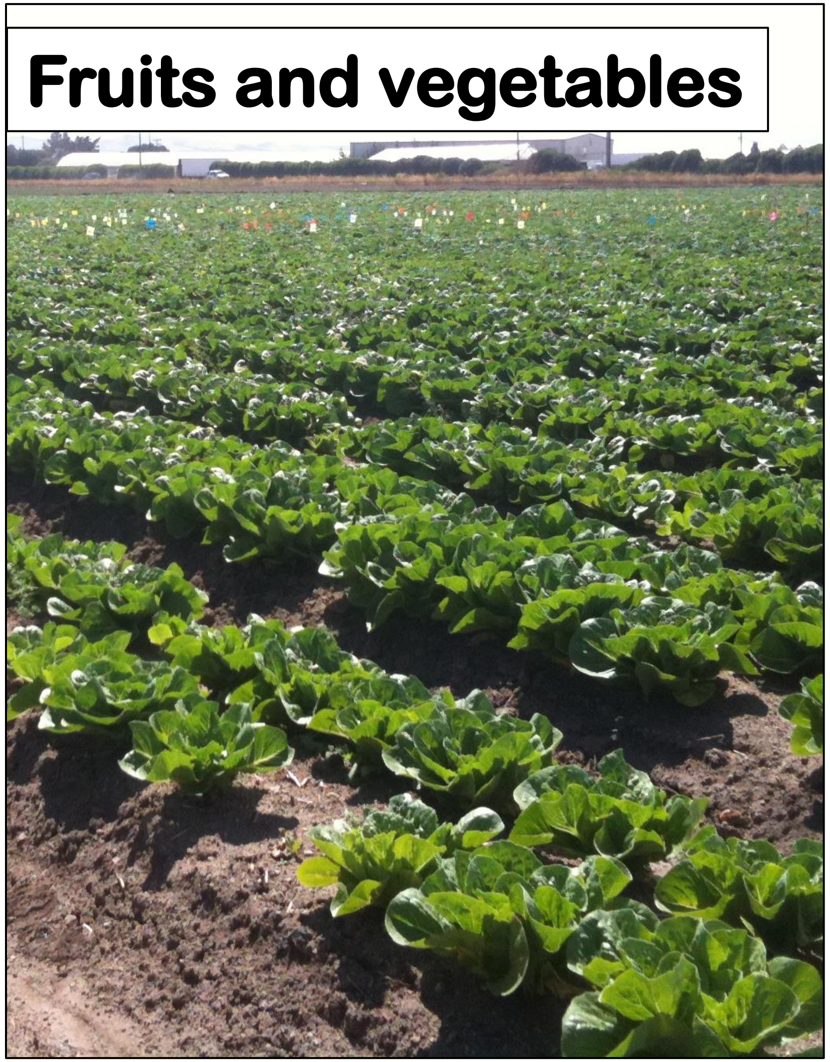
- ✓ Vitamins
- ✓ Bacteriocins
- ✓ Organic acids

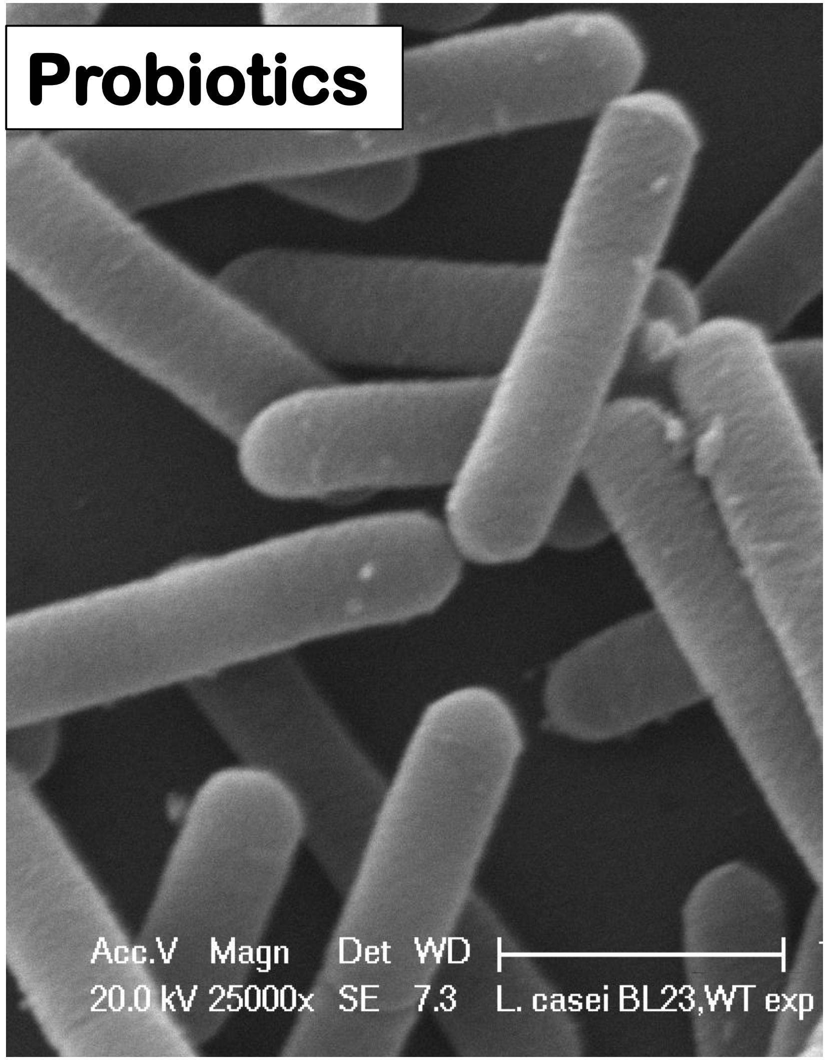
Increased numbers of (living) microbes

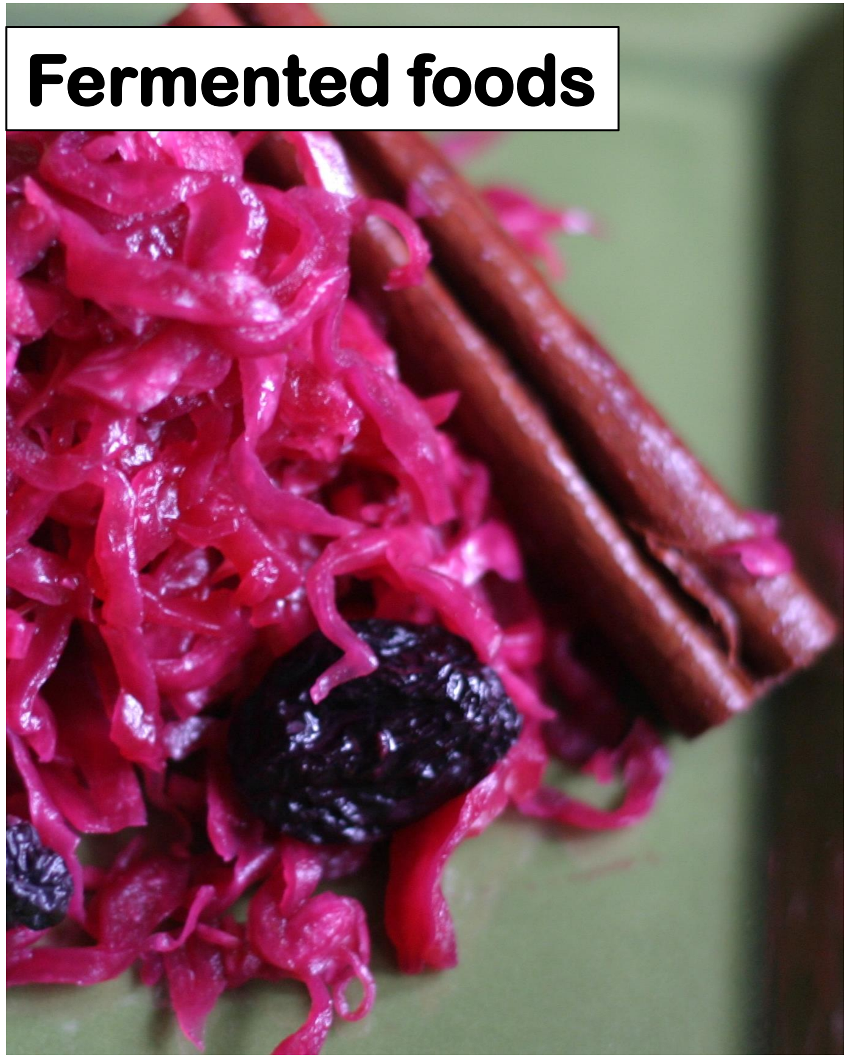
- ✓ Increased live microbe intake
- ✓ Food microbes: ~3% of gut microbiome

Marco et al 2017 Curr Op Biotechnol; Marco et al 2021 Nat Rev Gastroenterol Hepatol

Edible microbes







Benefits from commensal microbe exposures?

ISAPP
International Scientific Association for PROBIOTICS and PREBIOTICS

The NEW ENGLAND JOURNAL of MEDICINE

Eat Dirt — The Hygiene Hypothesis and Allergic Diseases

*Eating dirt or moving to a farm are at best **theoretical** rather than practical clinical recommendations for the prevention of asthma.*

Certain environmental factors are associated with a lower incidence of allergic disease in early life, such as oral supplementation with Lactobacillus, presence of a dog or other pet in the home, and attendance at day care…

- Scott T Weiss MD (2002)

The Journal of Nutrition
Nutritional Epidemiology
ASN
December 2020

Should There Be a Recommended Daily Intake of Microbes?

Maria Marco, Colin Hill, Robert Hutkins, Joanne Slavin, Daniel Tancredi, Daniel Merenstein, Mary E Sanders

Invite Some Germs to Dinner

Live Dietary Microbes Working Group

ISAPP
International Scientific Association for PROBIOTICS and PREBIOTICS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Chris Cifelli
National Dairy Council


Jaime Gahche
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Joanne Slavin
University of Minnesota


Dan Merenstein
Georgetown University


Dan Tancredi
University of California Davis


Mary Ellen Sanders
ISAPP


Bob Hutkins
University of Nebraska

Formulate hypotheses and how to test them

Estimate consumption of foods containing live microbes

Correlate consumption with disease risk

The National Health and Nutrition Examination Survey

Cross-sectional survey to assess the health and nutritional status of adults and children in the US

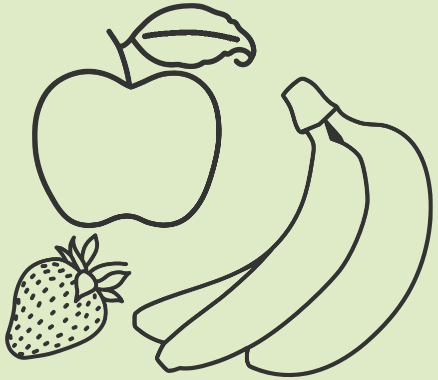
nhanes
The Nation's Mobile Health Survey

Estimating microbial numbers in foods

nhanes
The Nation's Mobile Health Survey

National Health and Nutrition Examination Survey

9,388 individual product food codes in NHANES

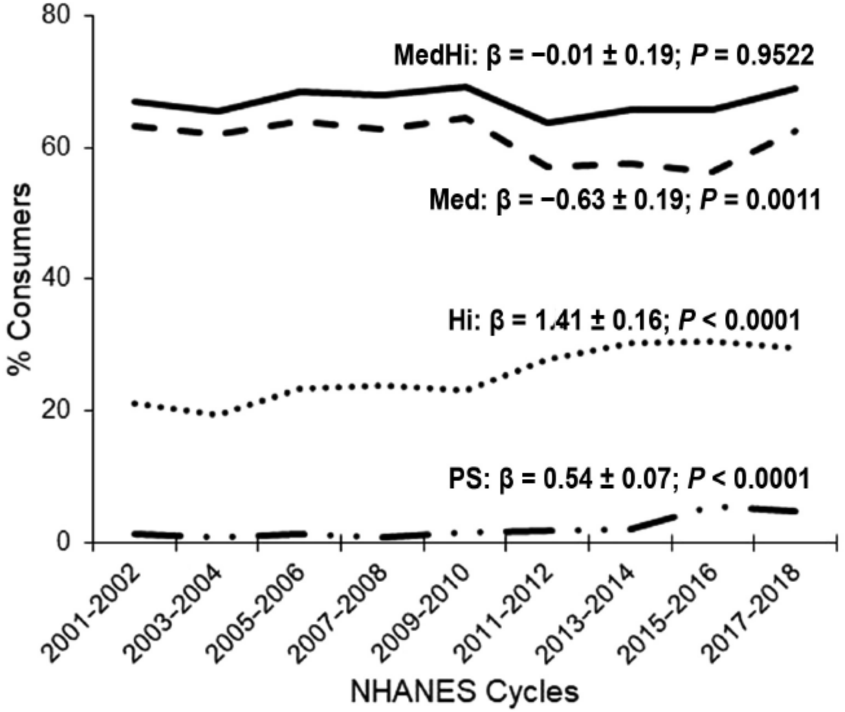
Low ($<10^4$ CFU/g)	Medium (10^4 to 10^7 CFU/g)	High $>10^7$ CFU/g
Pasteurized foods	Raw fruits & vegetables few fermented foods	Unpasteurized fermented foods and probiotic supplements
		
8,998 (96%)	**284 (3%)**	**106 (1%)**

ISAPP
International Scientific Association for PROBIOTICS and PREBIOTICS

Marco *et al* 2020 J Nutrition

Key Point 1. About 2/3 of those surveyed eat (any!) microbe-containing foods

~20% of consumers eat High microbe foods
~approximately 60% eat Medium or High microbe foods



Key Point 2. When included in the diet, 100 g/day of microbe-containing foods are consumed

~$10^{8\text{-}9}$ microbes/day*
***mostly from fermented foods**

Per capita consumption of live-microbe foods

Age, y	*n*	Percent consumers	Consumption (g/day)	Live microbes (CFU/day)
2 - 8	11,626	63	89	> 2.7×10^8
9 - 18	**16,749**	**56**	**83**	> 2.0×10^8
19 - 50	25,071	65	119	> 2.9×10^8
≥ 51	**21,020**	**70**	**139**	> 2.9×10^8

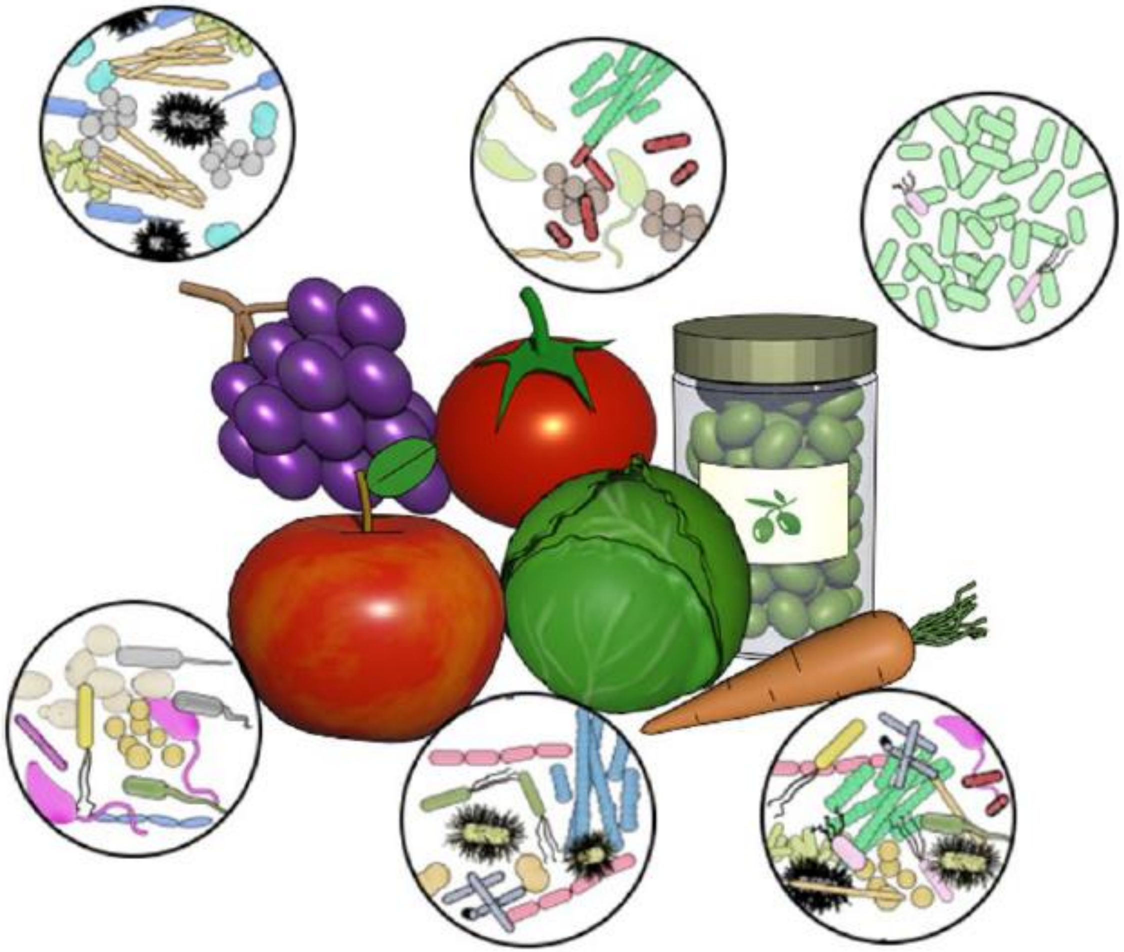
Adjusted associations of dietary intake (per 100 g) of fermented foods with physiological parameters in

Outcome	N	Regression Coefficient (95% CI)	p-value
BP systolic (mean rdg mm hg)	41,077	-0.768 (-1.136, -0.399)	**<0.001**
Body Mass Index (kg/m^2)	41,697	-0.309 (-0.465, -0.154)	**<0.001**
HDL-cholesterol (mg/dL)	40,313	0.696 (0.294, 1.098)	**<0.001**
Insulin (µU/mL)	18,163	-0.644 (-0.995, -0.292)	**<0.001**
Triglyceride (mg/dL)	18,327	-4.844 (-7.674, -2.014)	**<0.001**
Waist Circumference (cm)	40,804	-0.793 (-1.166, -0.421)	**<0.001**

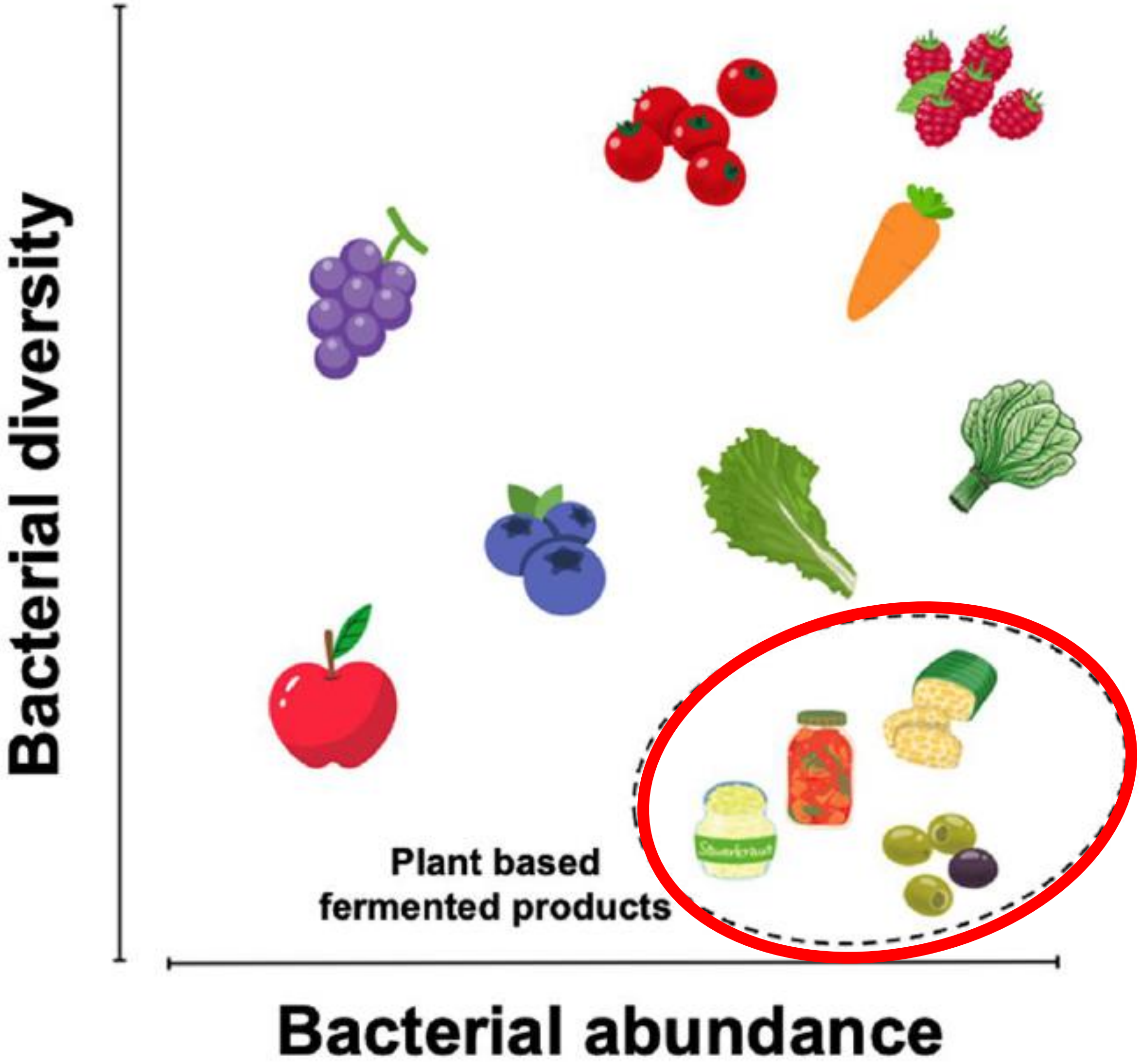
Not significant: Mean diastolic BP (mm Hg), C-reactive protein (mg/dL), Plasma glucose (mg/dL), LDL cholesterol (mg/dL), total cholesterol (mg/dL), weight (kg)

Hill, Tancredi, et al, 2023. Results adjusted for covariate set 1.

Which microbes?



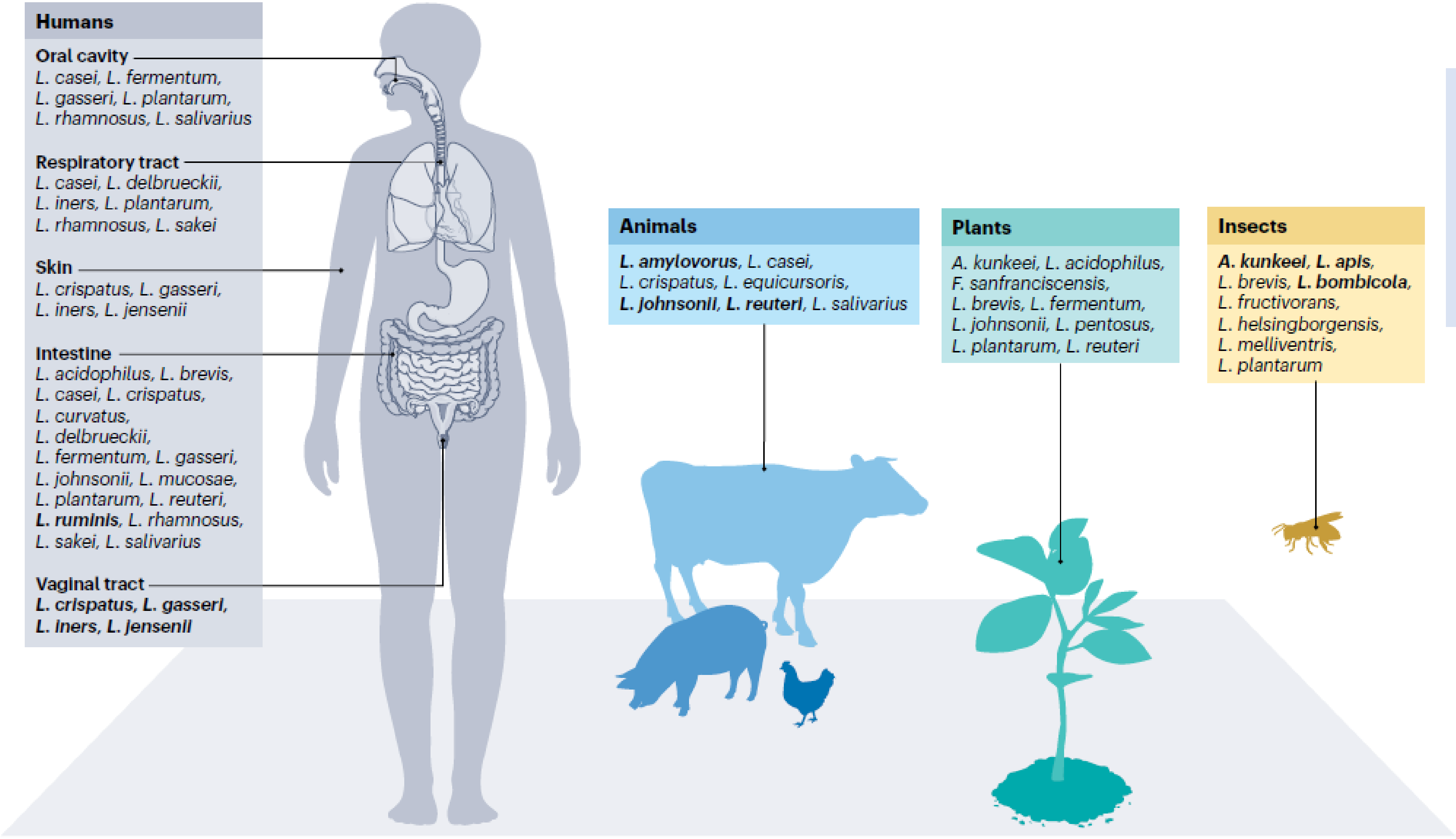
Proteobacteria, Bacteroidetes, Actinobacteria, Firmicutes



Berg et al 2025 Gut Microbes

Lactobacilli

Pervasive in plant, animal, and human microbiomes



Alejandra Mejia Caballero

Alejandra Mejia Caballero & Marco 2025 Nat Rev Microbiol

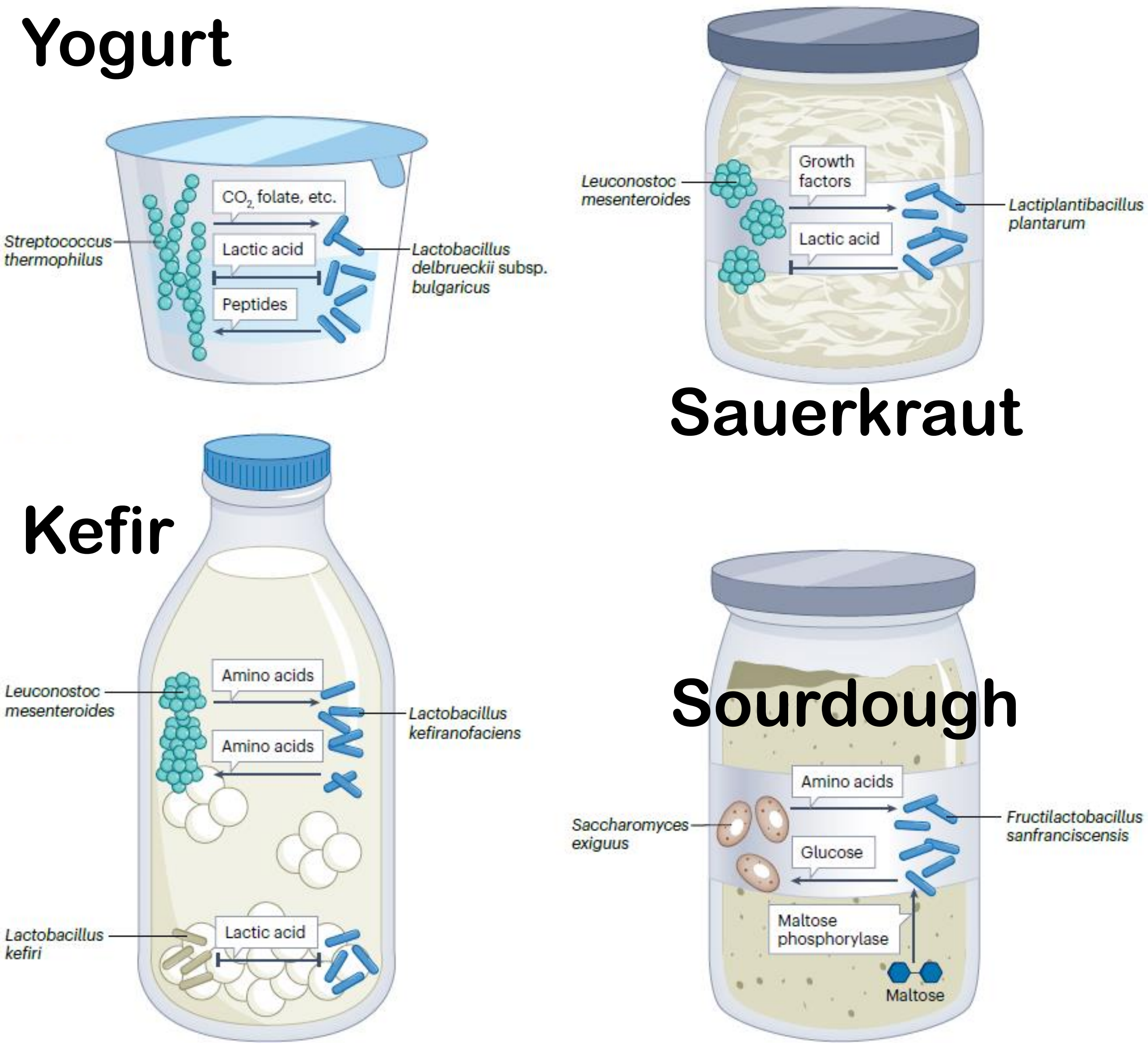
Lactobacilli in our diets

Yogurt

Sauerkraut

Kefir

Sourdough

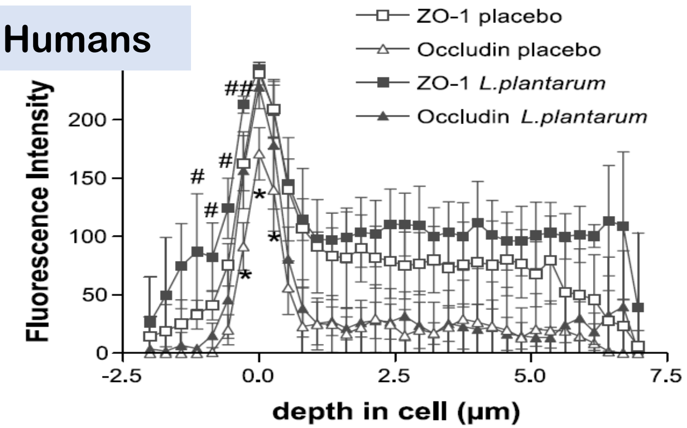


Wannes Van Beeck

Alejandra Mejia Caballero & Marco 2025 Nat Rev Microbiol

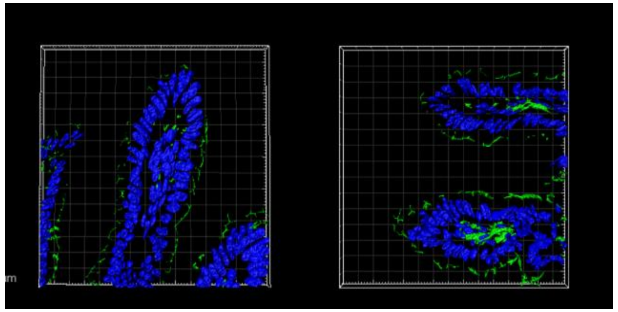
Lactiplantibacillus plantarum NCIMB8826R

Humans

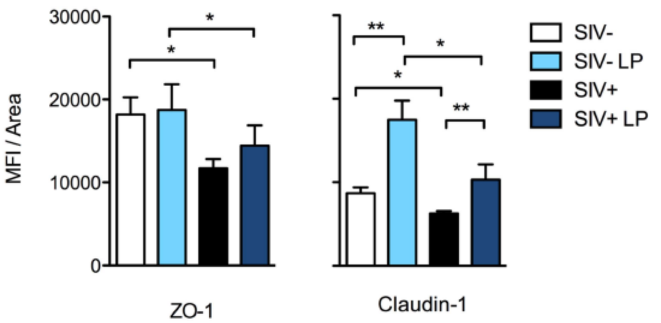


Mice

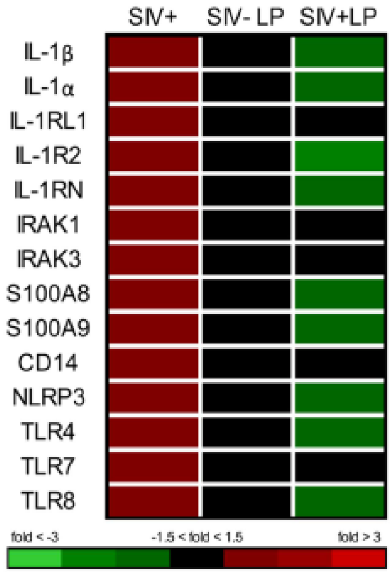
+LP (ZO-1)

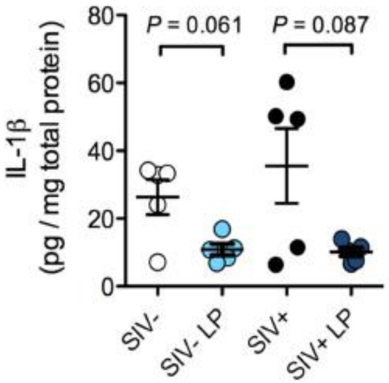


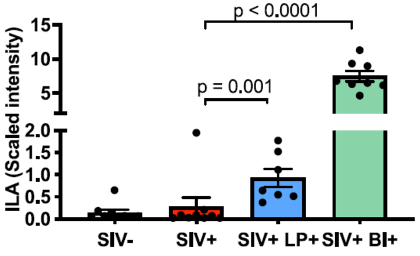
Rhesus macaques



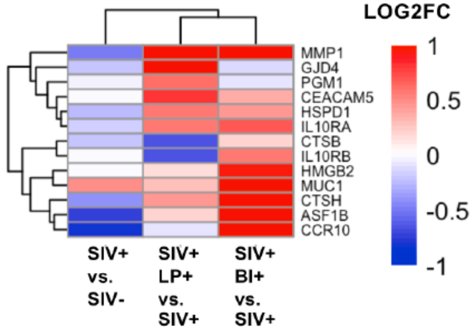
Improves intestinal barrier (ZO-1, Occludin, Claudin-1)





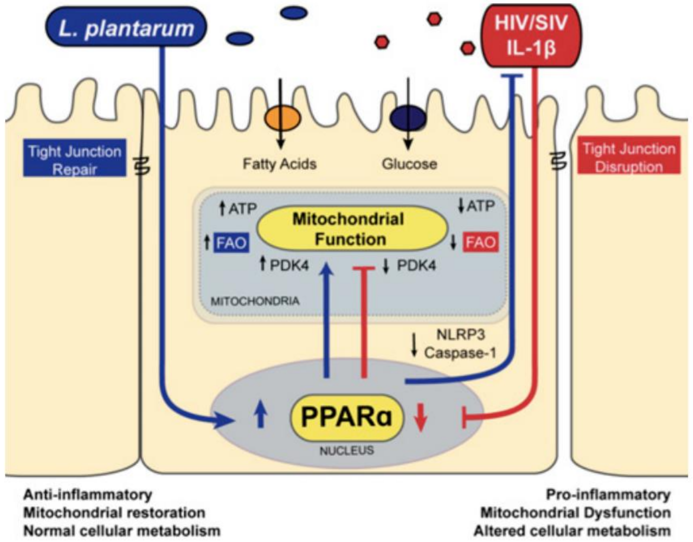


IL22/STAT3 signaling



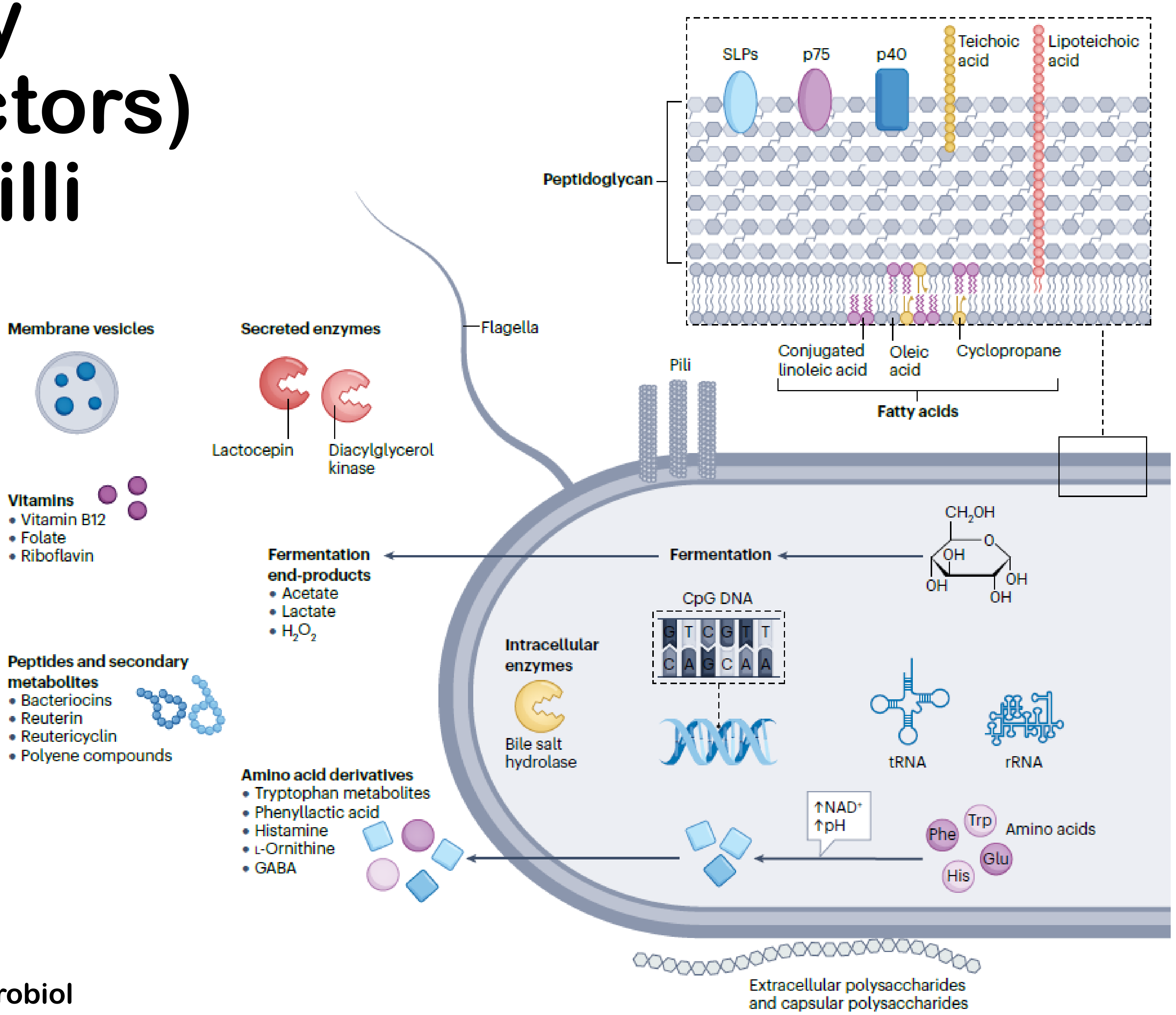
Simian Immunodeficiency Virus (SIV) infected rhesus macaques

Induces barrier restoration and protective, anti-inflammatory responses



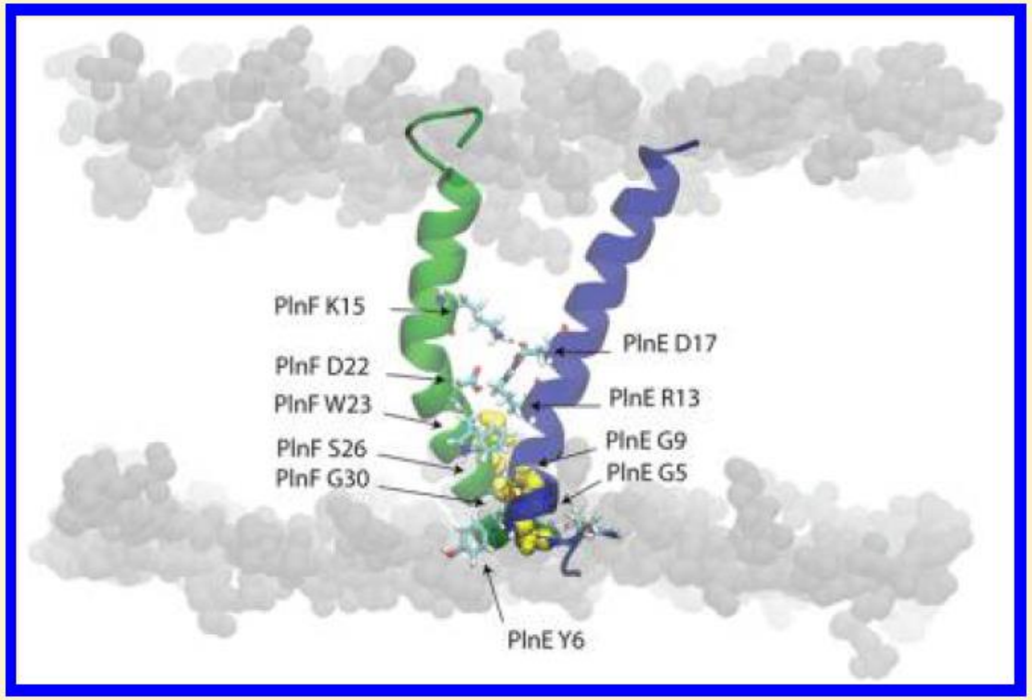
Karczewski et al 2010 AJPGLP
Heeney et al 2018 Gut MIcrobes
Hirao et al 2014 PLoS Path
Crakes et al 2019 PNAS

Health modulatory compounds (effectors) made by lactobacilli are known:



Alejandra Mejia Caballero & Marco 2025 Nat Rev Microbiol

Bacteriocins: Plantaricin EF (PlnEF)



Ekblad *et al* Biochemistry 2016

Bacteriocins are potent (nM range) antimicrobial peptides which typically kill related bacteria

Plantaricin EF (PlnEF) made exclusively by *L. plantarum*

Plantaricin genes are induced in the digestive tracts of mice & humans

Tachon et al 2010 EM
Marco et al, 2007 AEM
Marco et al, J 2010 ISME J

L. plantarum plantaricin: diet-induced obesity

C57Bl/6J
N = 10/group

High fat (HF) diet 42% energy from fat

+ *L. plantarum* NCIMB8826 (WT)

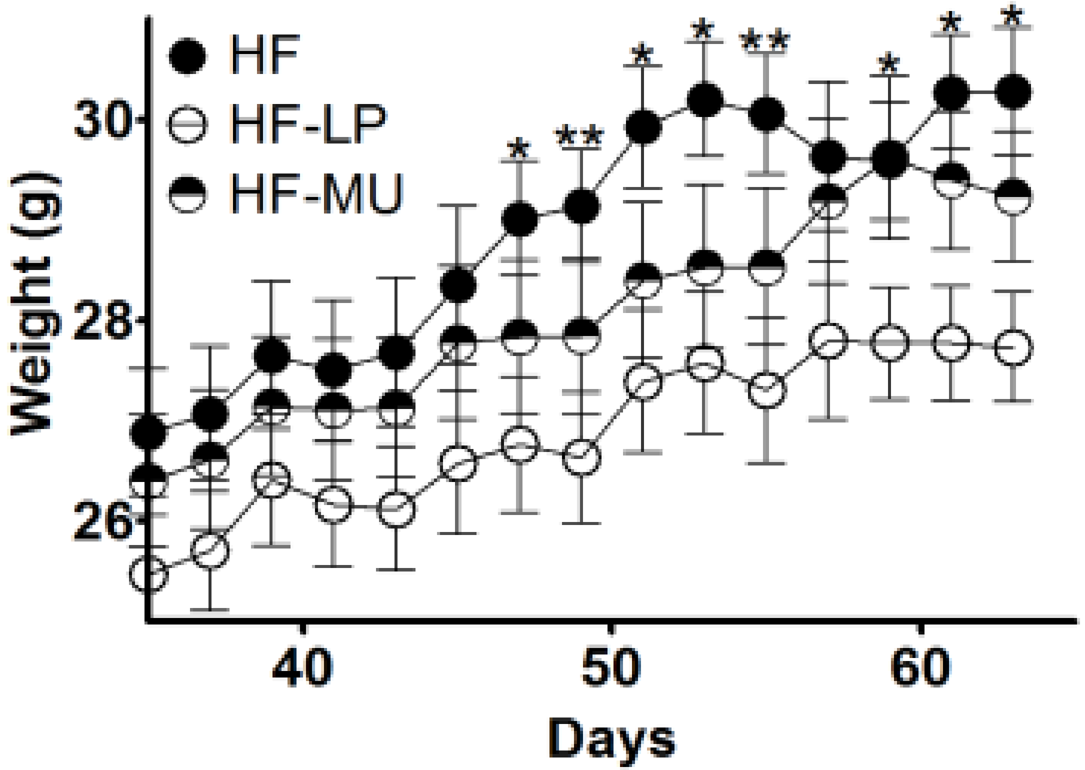
+ L. plantaricin
Plantaricin EFI deficient mutant (MU)

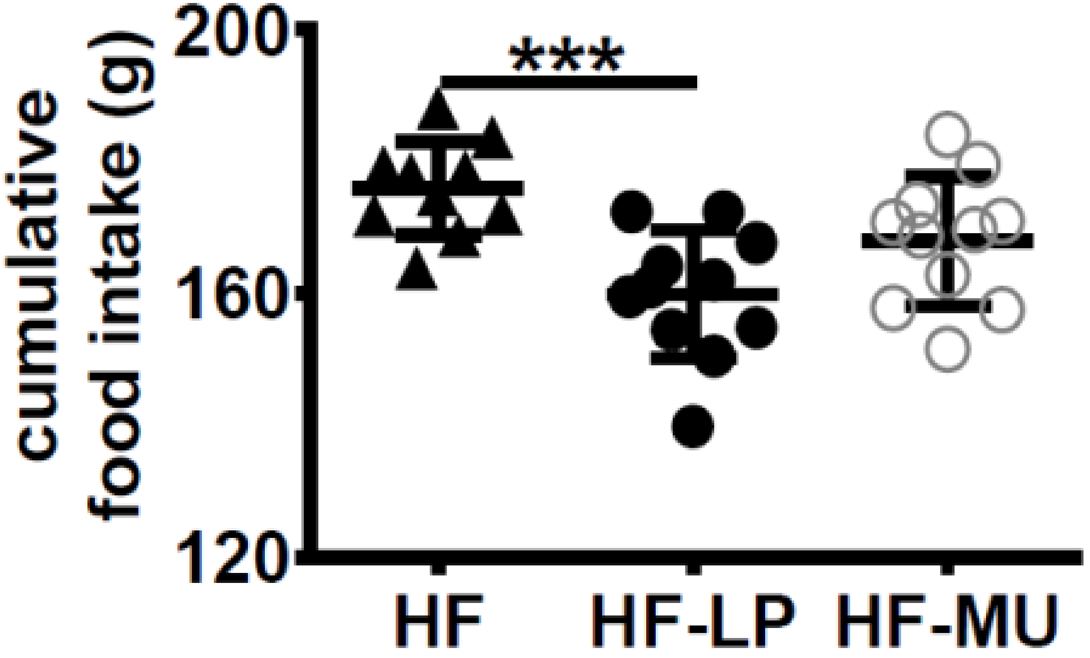
10^9 cells every 48 h

9 Weeks

Heeney *et al* 2018 Gut Microbes

L. plantarum requires PlnEF to prevent DIO





HF = high fat diet; LP = *L. plantarum;* MU = LP mutant. HF

* = p≤ 0.05, ** = p≤0.01; *** = p≤0.001

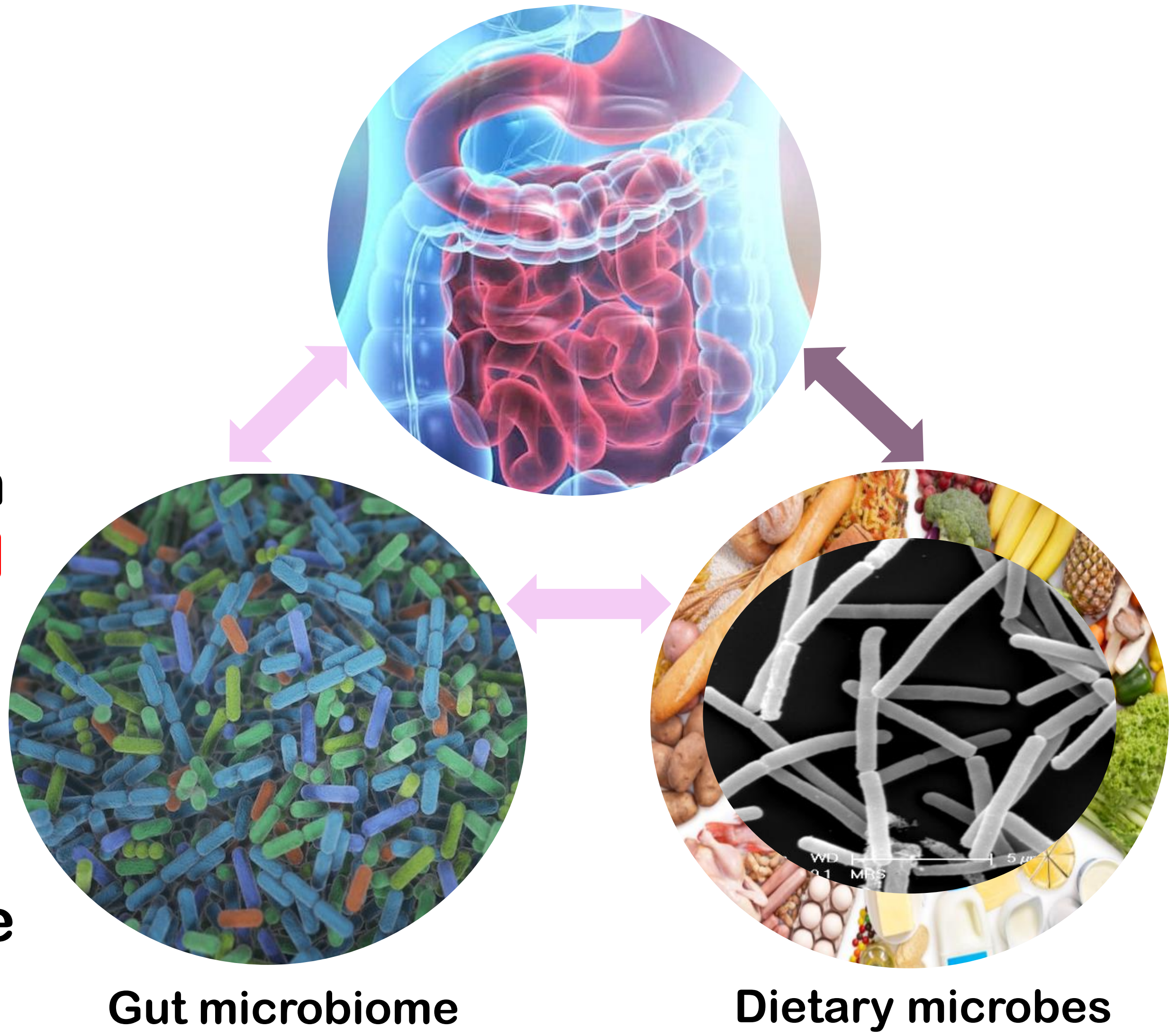
Heeney *et al* 2018 Gut Microbes

Summary

- Fermented dairy foods provide a "complete package" of beneficial microbial microbes and compounds.

- Fermented foods can support gut health by modulation of key domains: intestinal barrier function, immunity, & the gut microbiome.

- However, research is needed to identify suitable claims and improve and validate the quality and composition the final products.



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Collaborators (UC Davis)

Dr. Gail Bornhorst
Dr. Melanie Gareau

USDA United States Department of Agriculture National Institute of Food and Agriculture

NDC NATIONAL DAIRY COUNCIL™

novo nordisk fonden

NATIONAL INSTITUTES OF HEALTH

NSF

CALIFORNIA DAIRY RESEARCH FOUNDATION
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WiKim 세계김치연구소
World Institute of Kimchi

Eat.lac.project

Marcolab

Improving health with food and gut microbiome design

Gut feeding. Bratislav Milenkovic

Food as Medicine Across the Lifespan

Carolyn Slupsky, Ph.D.
Professor Food Science, Technology, & Nutrition |
Endowed Chair in Food, Nutrition, & Health
University of California at Davis

Food as Medicine Across the Lifespan

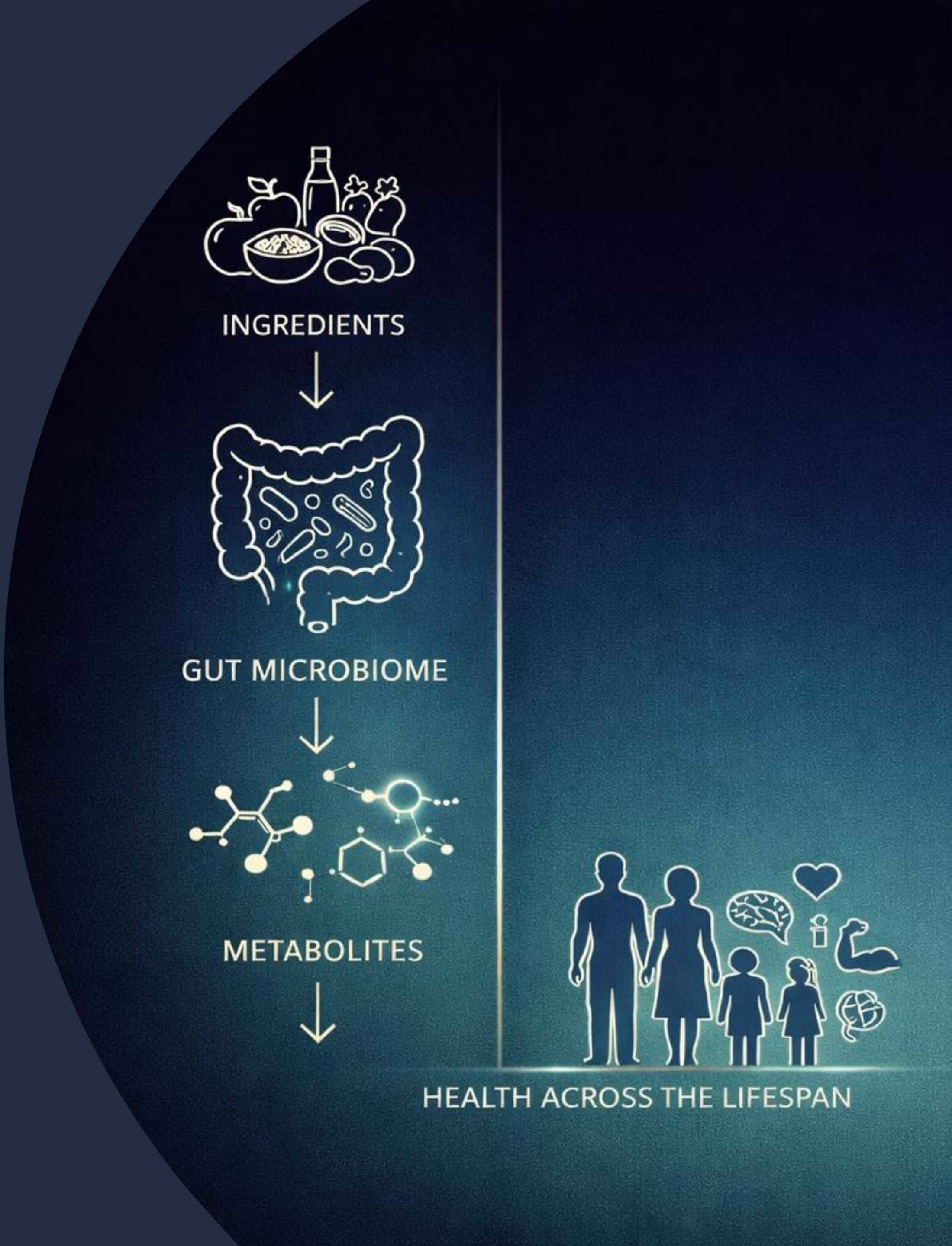
Carolyn M Slupsky, PhD

Department of Nutrition

Department of Food Science & Technology

University of California, Davis

Natural Products Expo West. March 4, 2026



Food → Microbiome → Metabolites → Host

- We don’t just digest food – we translate it
- Microbes convert dietary substances into bioactive metabolites
- Metabolites are measurable ‘functional outputs’ for product development

Making 'Food as Medicine' real: guardrails

- Mechanism-backed (microbial conversion → metabolite)
- Biomarker-verified (metabolomics as receipt)
- Clinically meaningful endpoints (or validated proxies)
- Transparency + reproducibility
- Equity / responder logic (who benefits and why)

The Roadmap

1. Define the target signal (metabolite / pathway / phenotype)
2. Choose the substrate + delivery matrix
3. Verify microbial conversion (microbiome function + metabolomics)
4. Confirm host engagement (biomarkers and outcomes)
5. Build responder logic (who benefits, and why)

Why lifespan matters

- Early life: highest biological plasticity (programming)
- Adulthood: metabolic resilience
- Old age: inflammation and cognition

A Hypothesis that Changed Infant Nutrition: The Early Protein Hypothesis

High protein intake with infant formula feeding

Results in

Higher levels of insulinogenic amino acids (leucine)

Stimulates

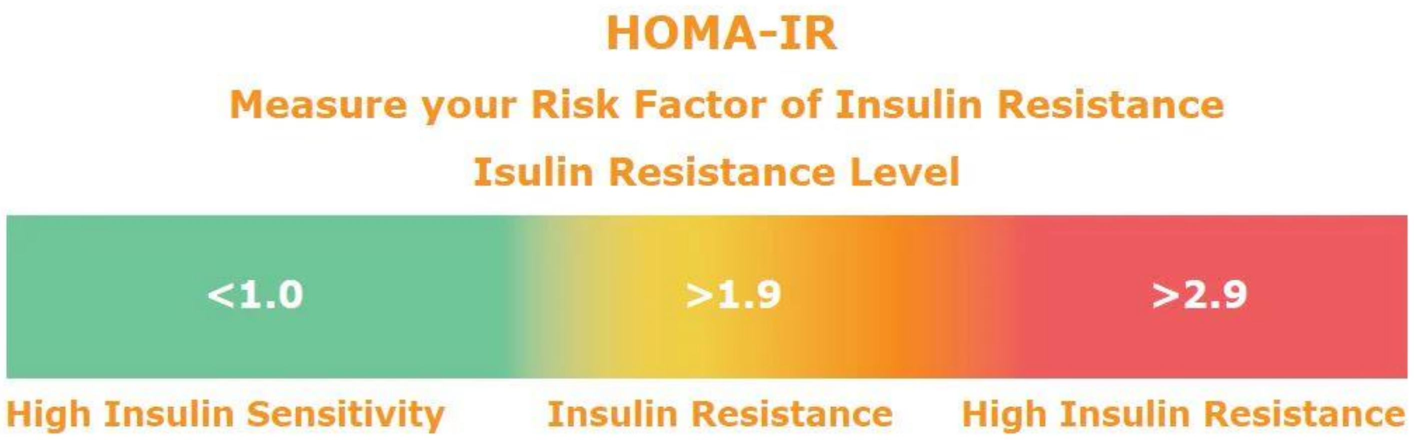
Insulin and mTORC1

Leads to

Increased weight gain and higher HOMA-IR

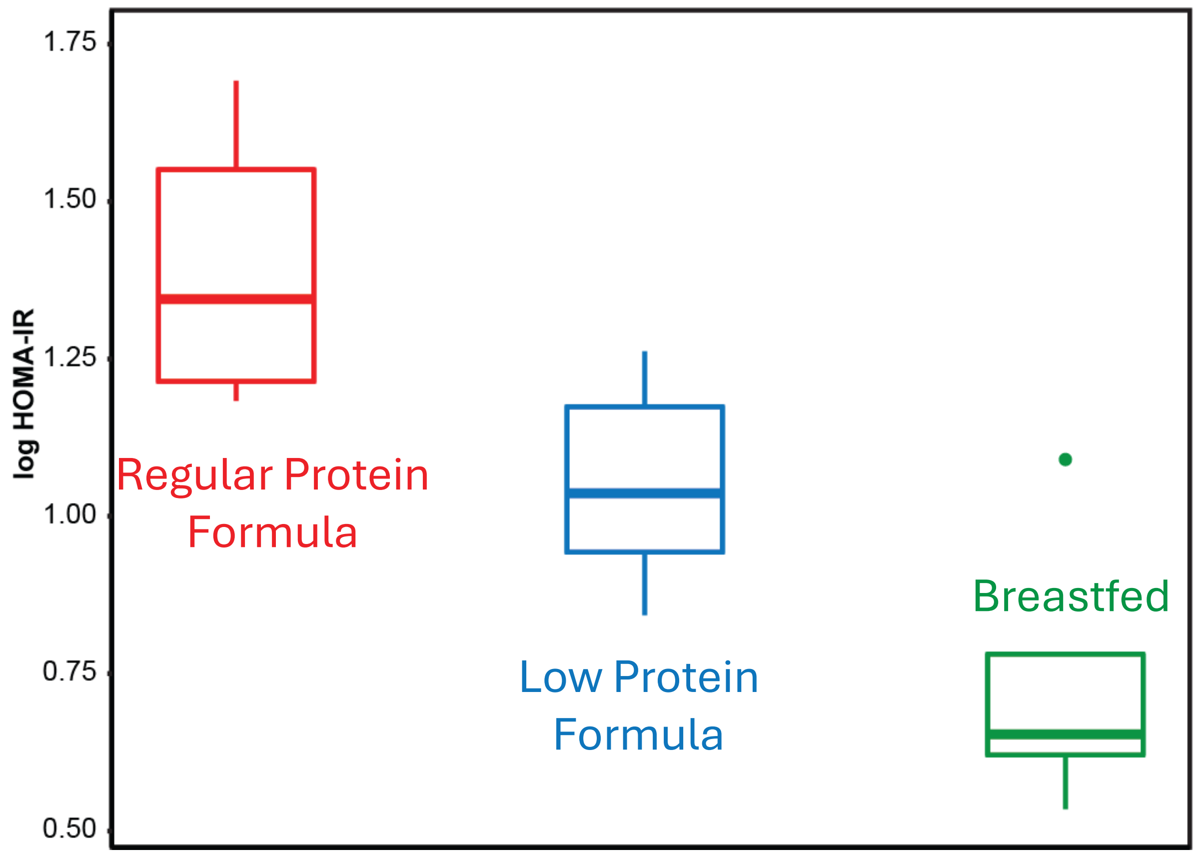
HOMA-IR
(Homeostatic Model Assessment of Insulin Resistance)

- Higher insulin and glucose indicates **insulin resistance**

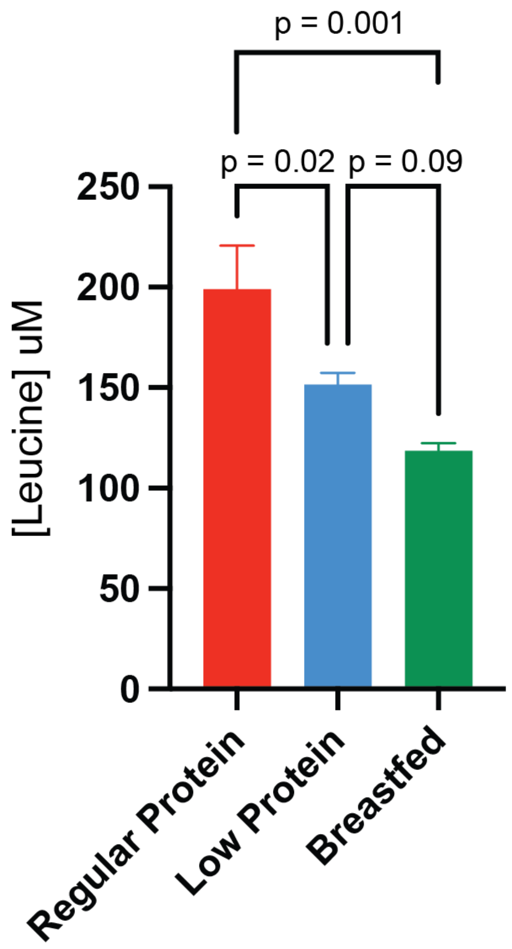


$$HOMA-IR = \frac{insulin\left(\frac{\mu U}{dL}\right) \times \; glucose\left(\frac{mmol}{L}\right)}{22.5}$$

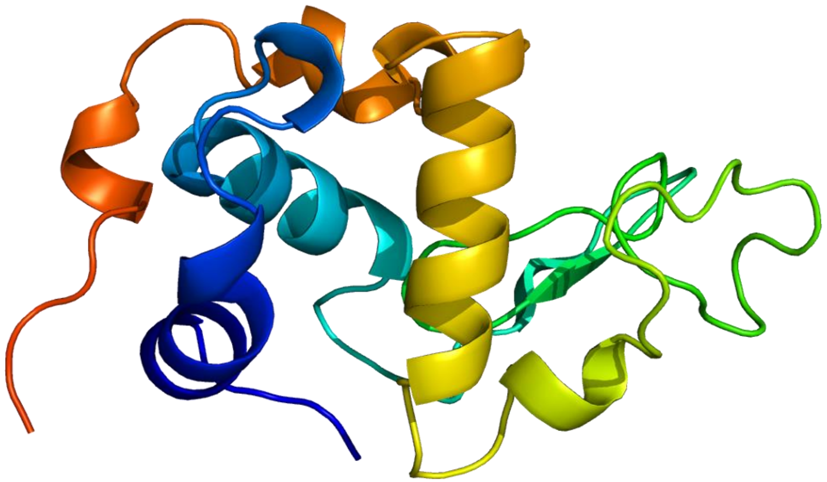
In infants, HOMA-IR is related to dietary protein level



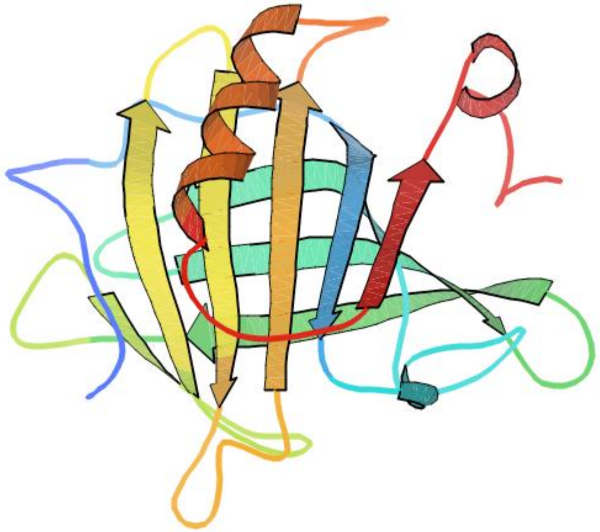
From: He et al. Front Pediatrics 7:563 (2020)



Protein quality is a signaling lever



α-lactalbumin
22% of total protein in human milk
3.5% of total protein in bovine milk
Contains 2x more Trp than β-lactoglobulin



β-lactoglobulin
0% of total protein in human milk
10% of total protein in bovine milk
Contains 1.5x more BCAA than α-lactalbumin

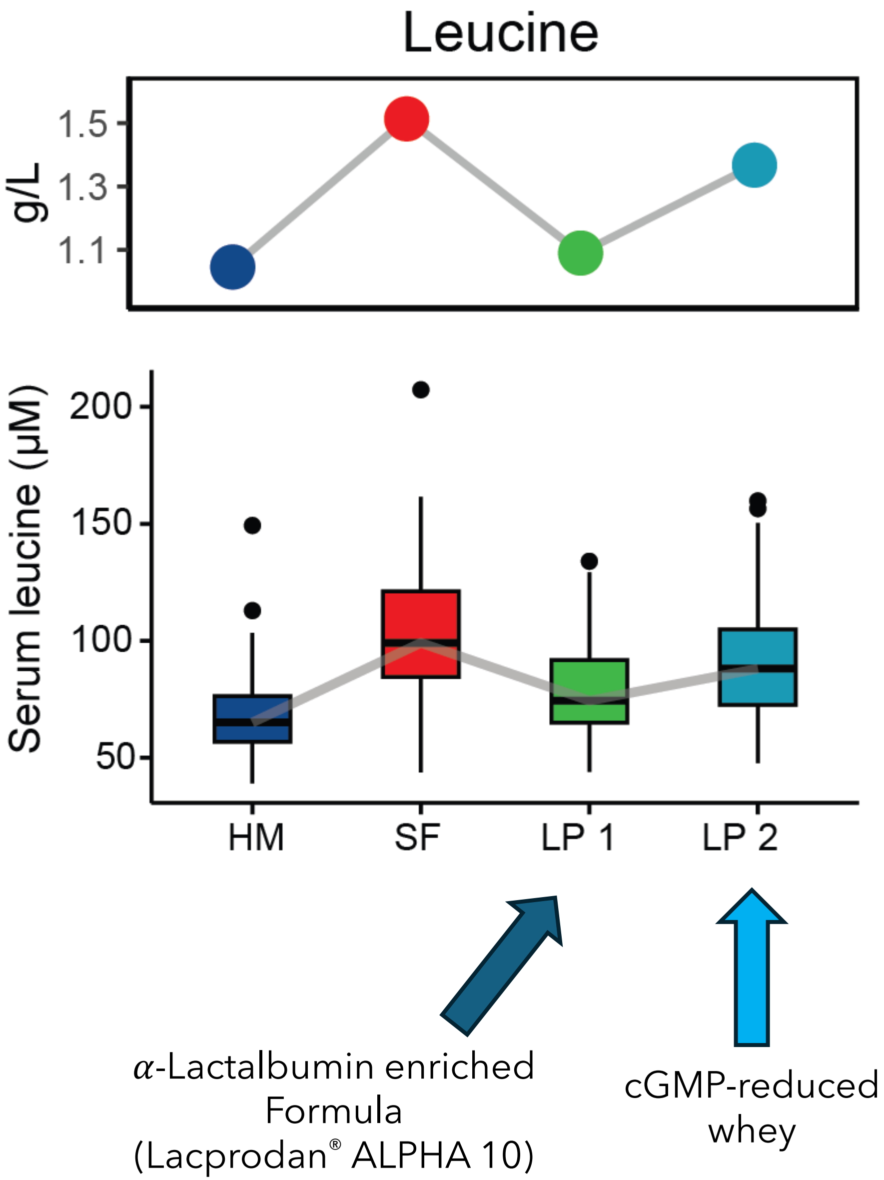
In Infant Formula
60:40 Whey:Casein

~10% of total protein

~30% of total protein

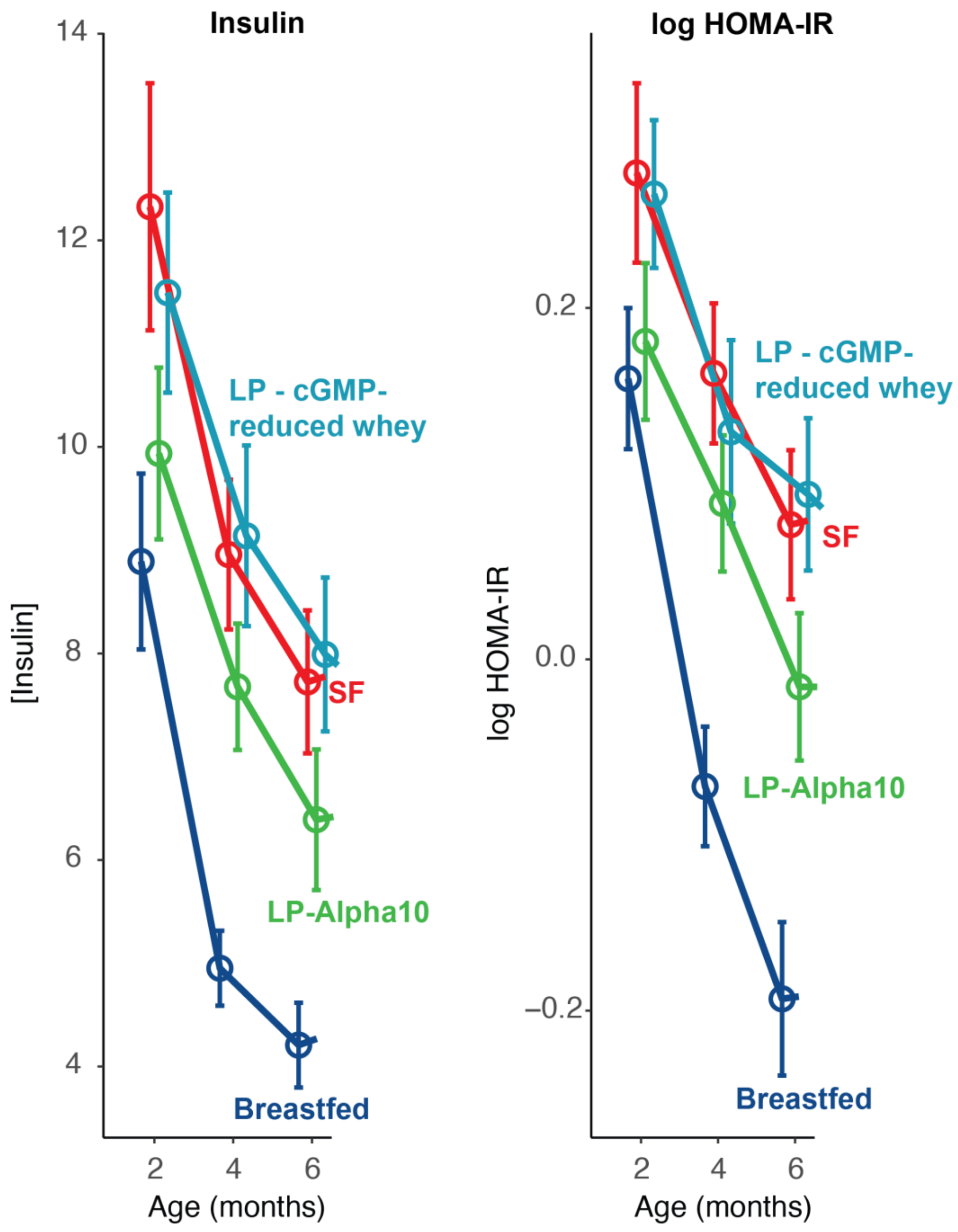
Formulation can tune insulinogenic amino acids

- Using α-lactalbumin in a formula allowed for reduced Leu compared to cGMP-reduced whey



From: He et al. Am J Clin Nutr 121(4):853-864 (2025)

Human Proof: Physiology moves with Formulation

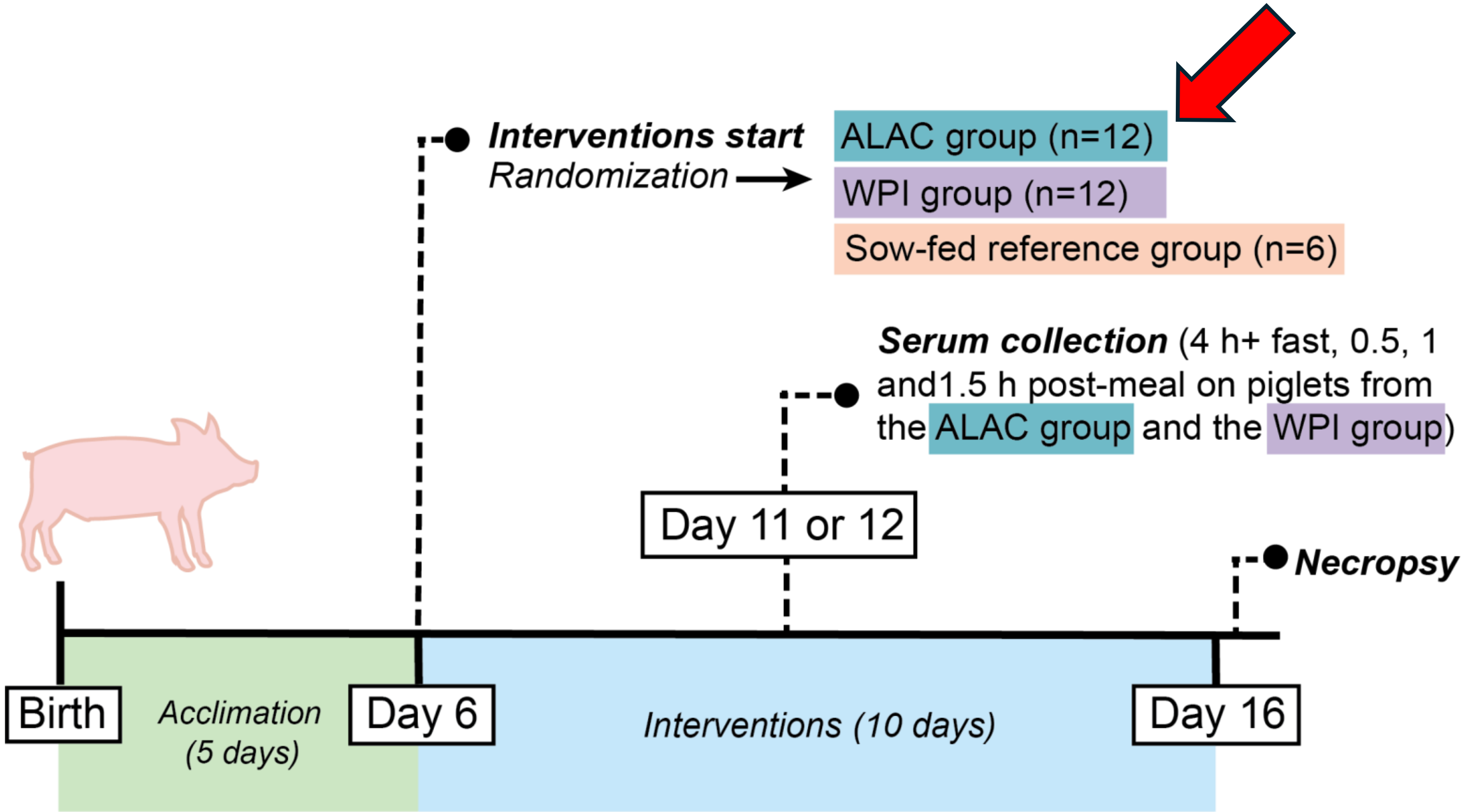


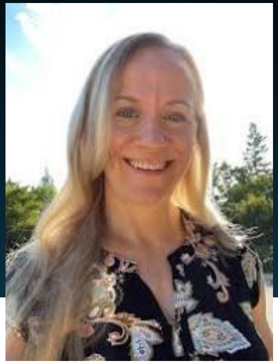
A translational model to see the whole system

- Similar anatomical features of the gastrointestinal tract
- Endocrine regulation of food intake is similar
- Overall brain anatomy and development is like humans
- Allows for mechanistic studies that could not be performed in humans

Study design…

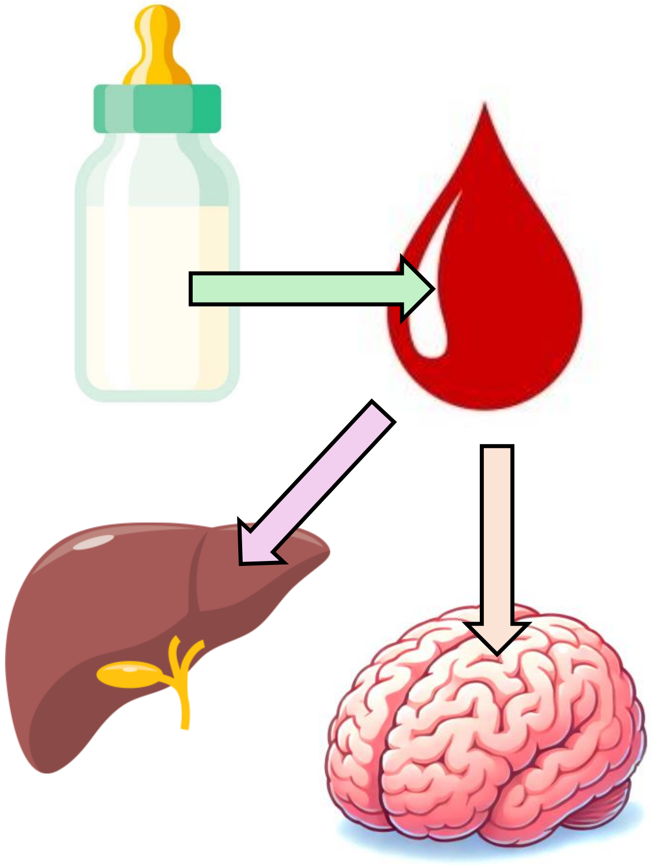
Lacprodan® ALPHA-50

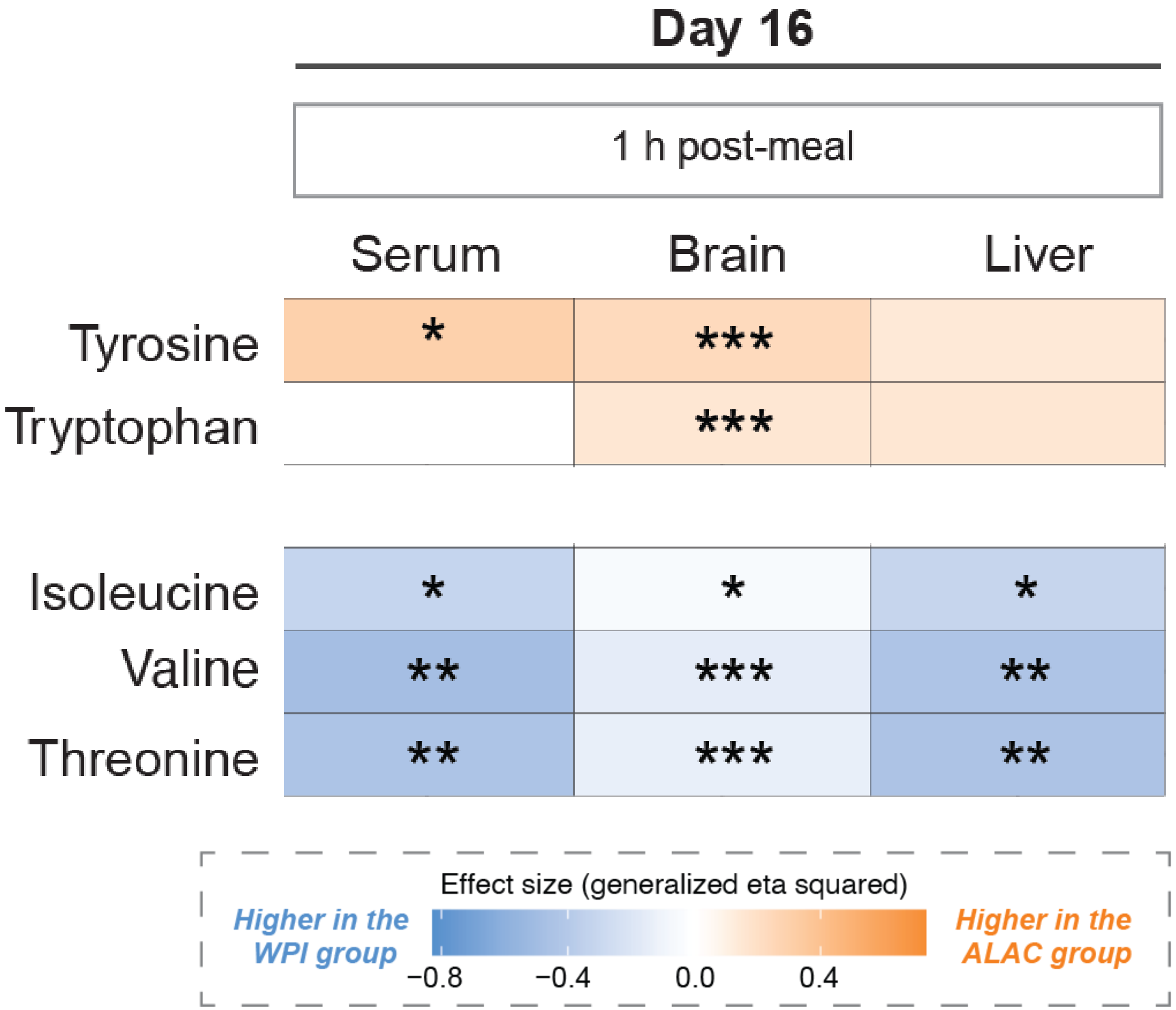




From: Shoff et al. npj Sci Food 9(1):120 (2025); He et al npj Sci Food 9(1):207 (2025)

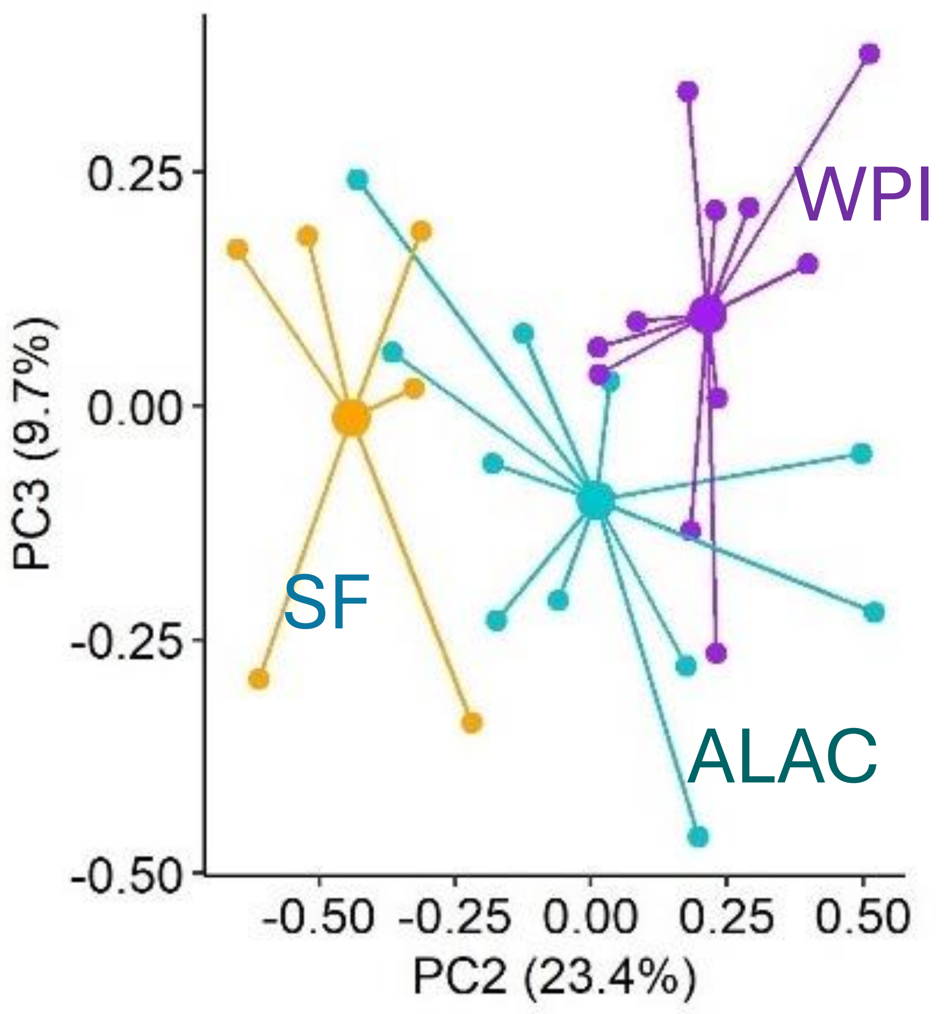
Correlation between diet, blood metabolites and tissue metabolites

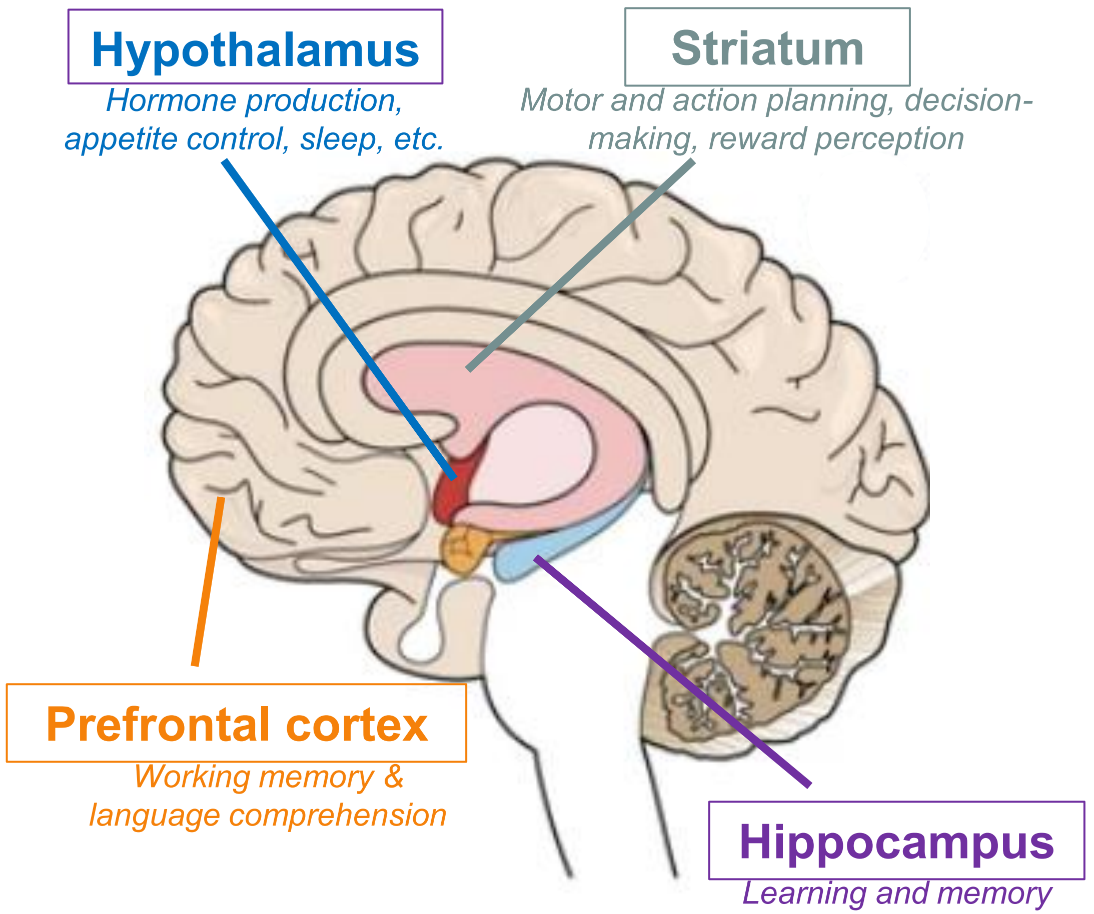




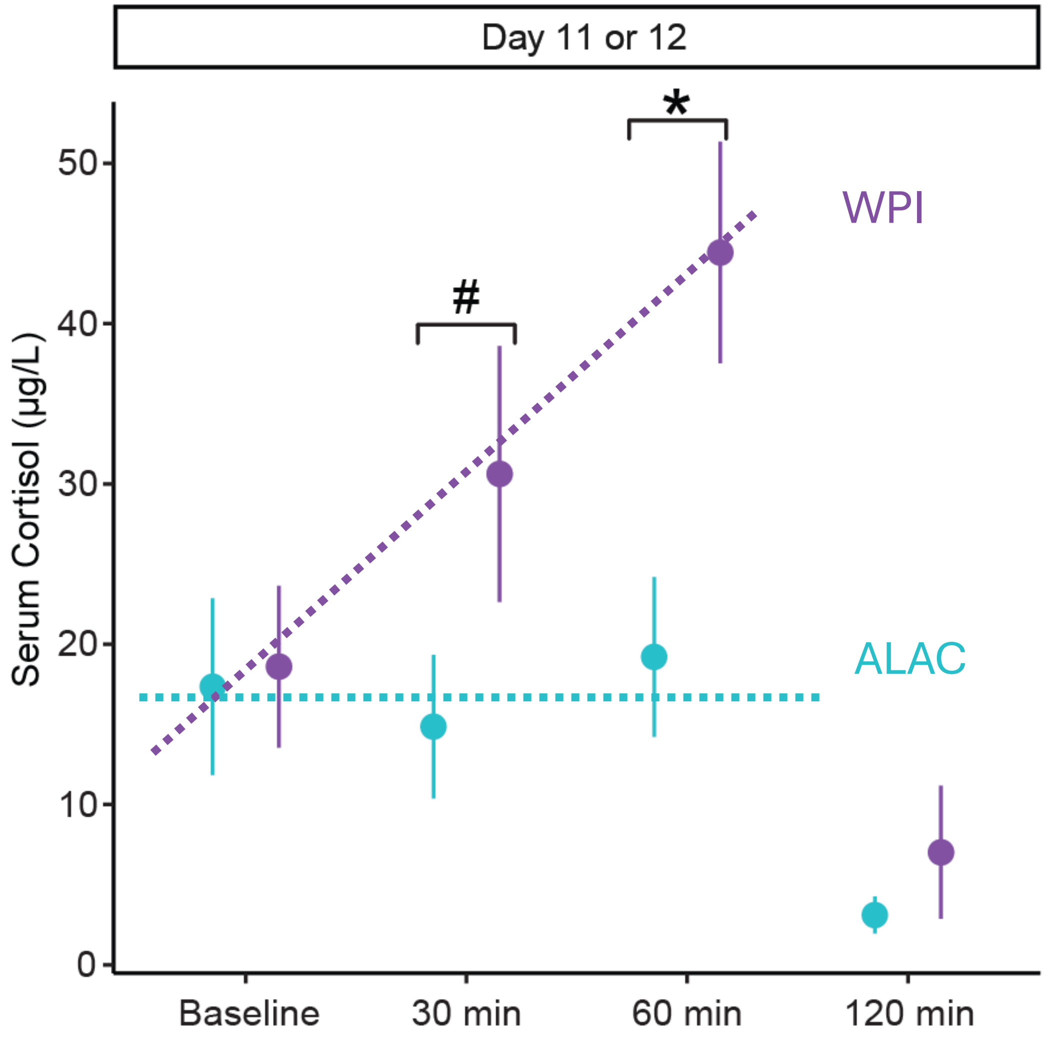
From: Shoff et al. npj Sci Food 9(1):120 (2025)

Diet can move the brain metabolome



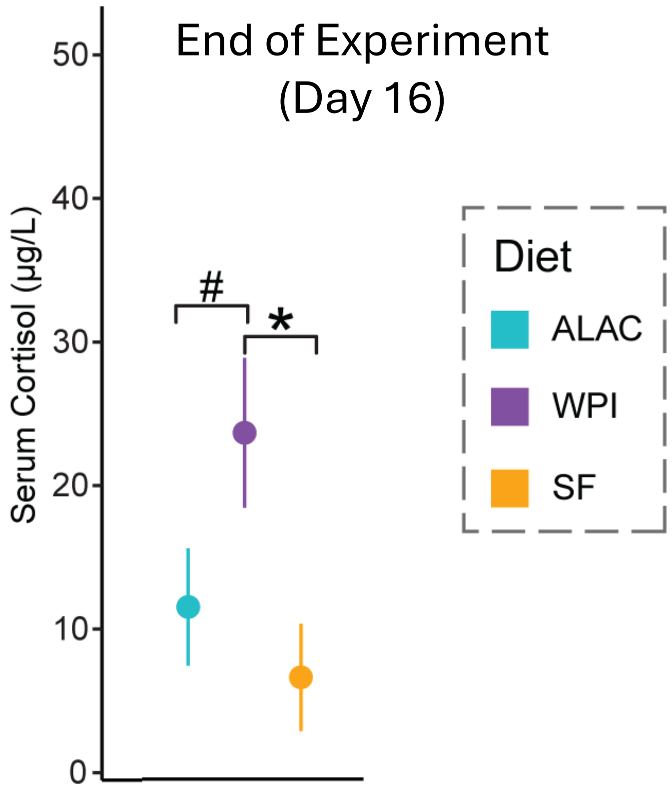


Stress resilience is a biochemical outcome

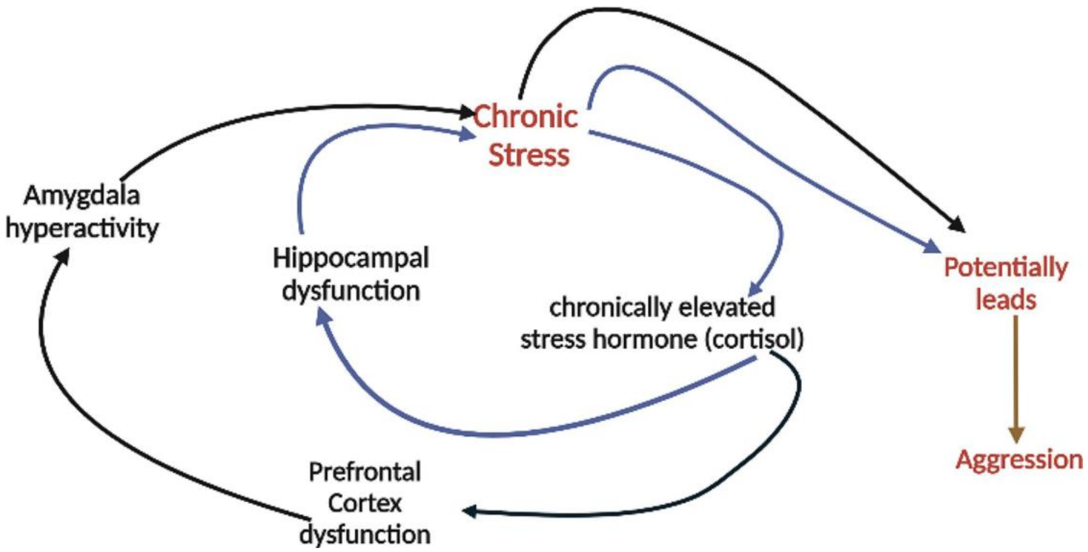


From: Shoff et al. npj Sci Food 9(1):120 (2025)

Chronic stress can affect cognition



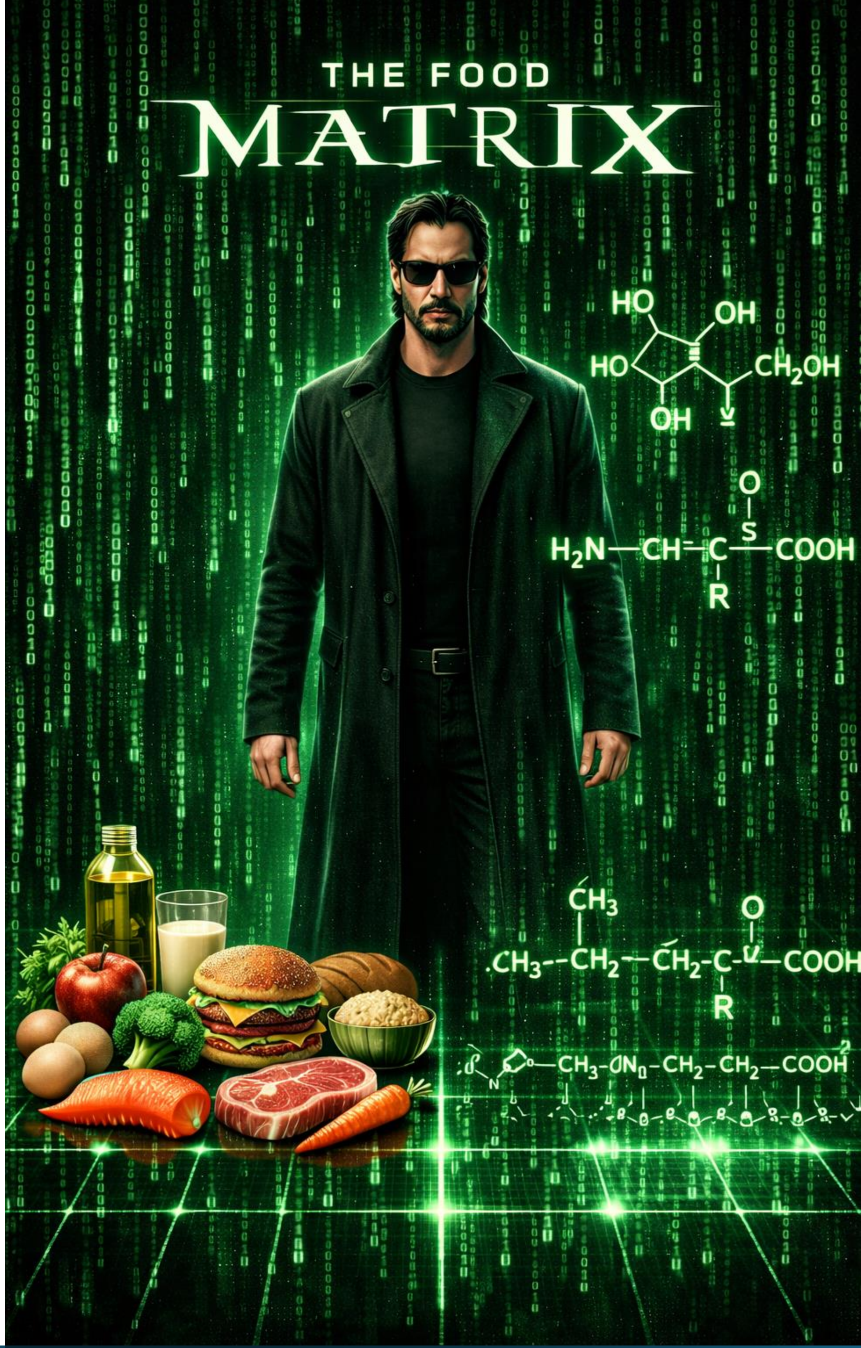
From: Shoff et al. npj Sci Food 9(1):120 (2025)



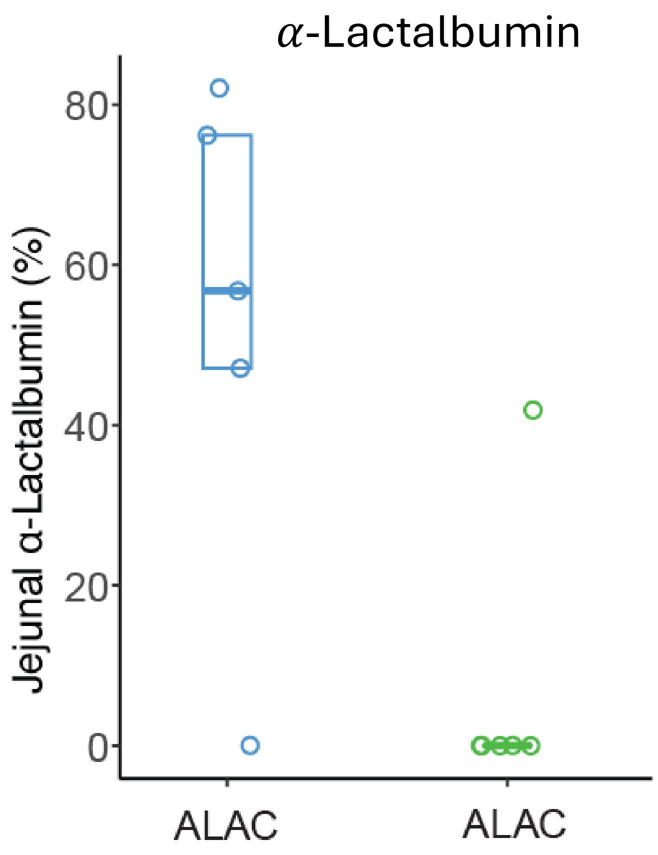
From: Mbiydzenyuy and Aulu Metab Brain Dis 39: 1613 (2024)

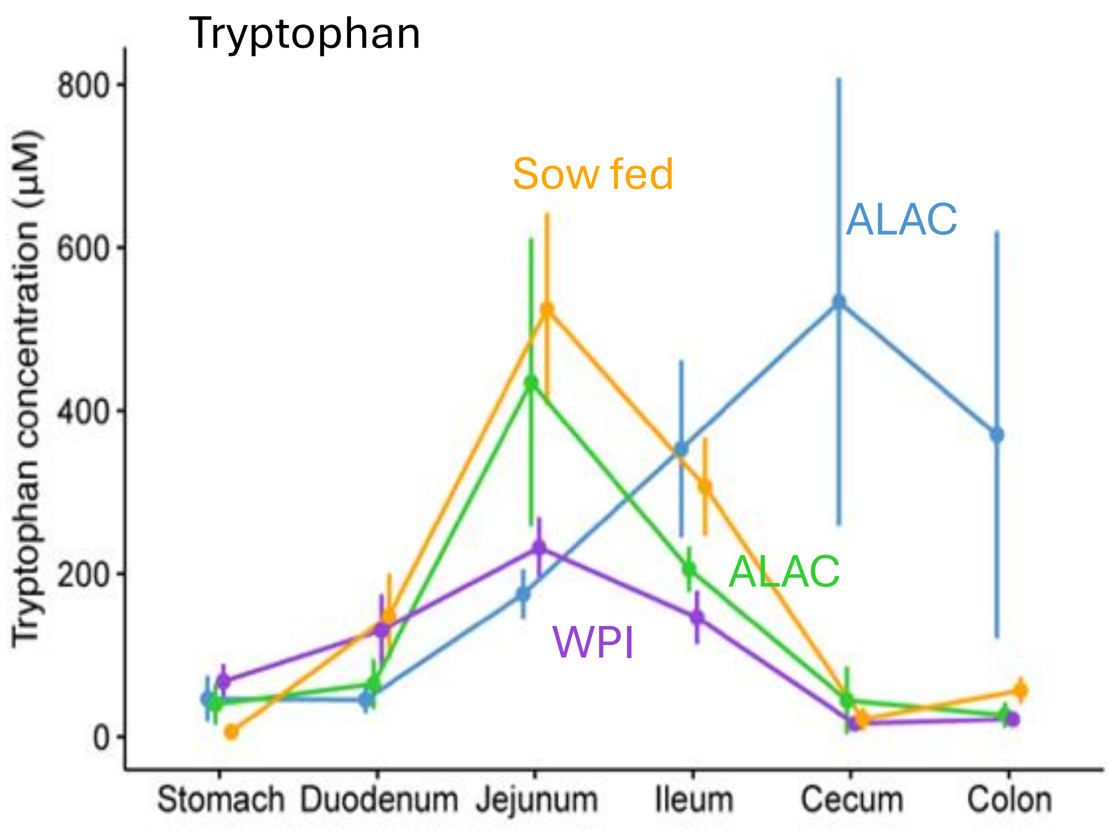
Delivery matters: matrix beats free nutrients

- Free tryptophan is rapidly absorbed in the small intestine
  - Most absorbed tryptophan is quickly shunted to the kynurenine pathway in the liver
- α-Lactalbumin needs to be digested
  - Resulting in a gradual and sustained tryptophan release



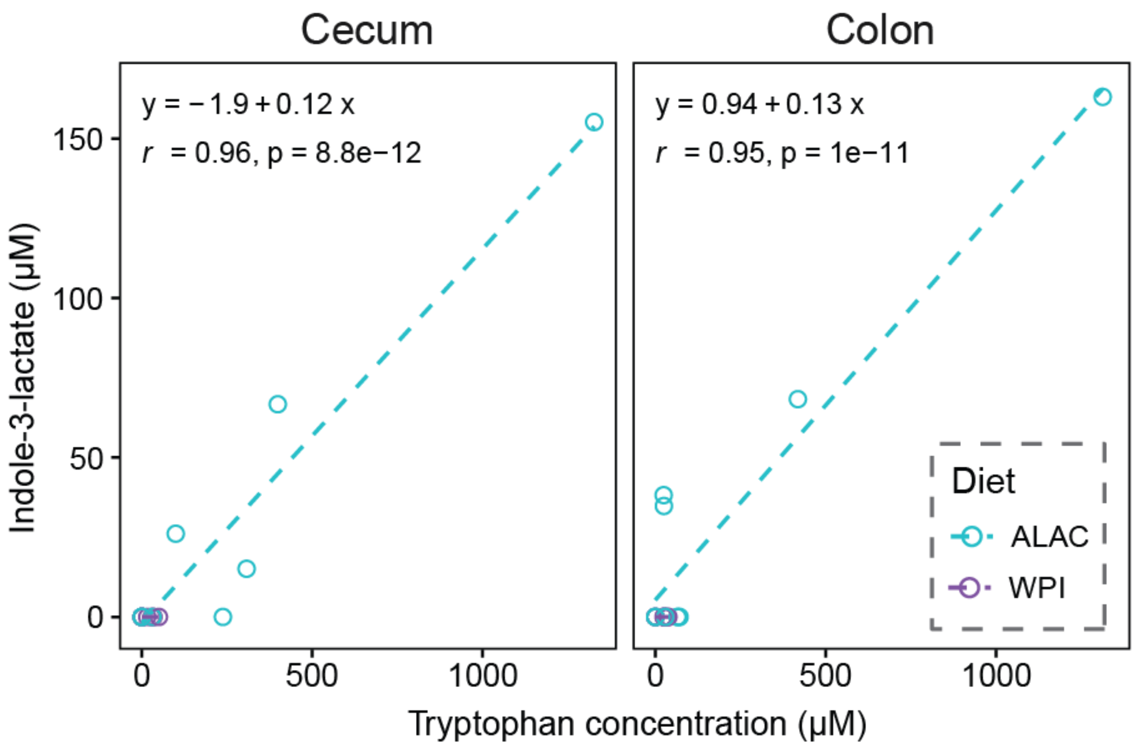
What reaches the colon becomes microbial substrate



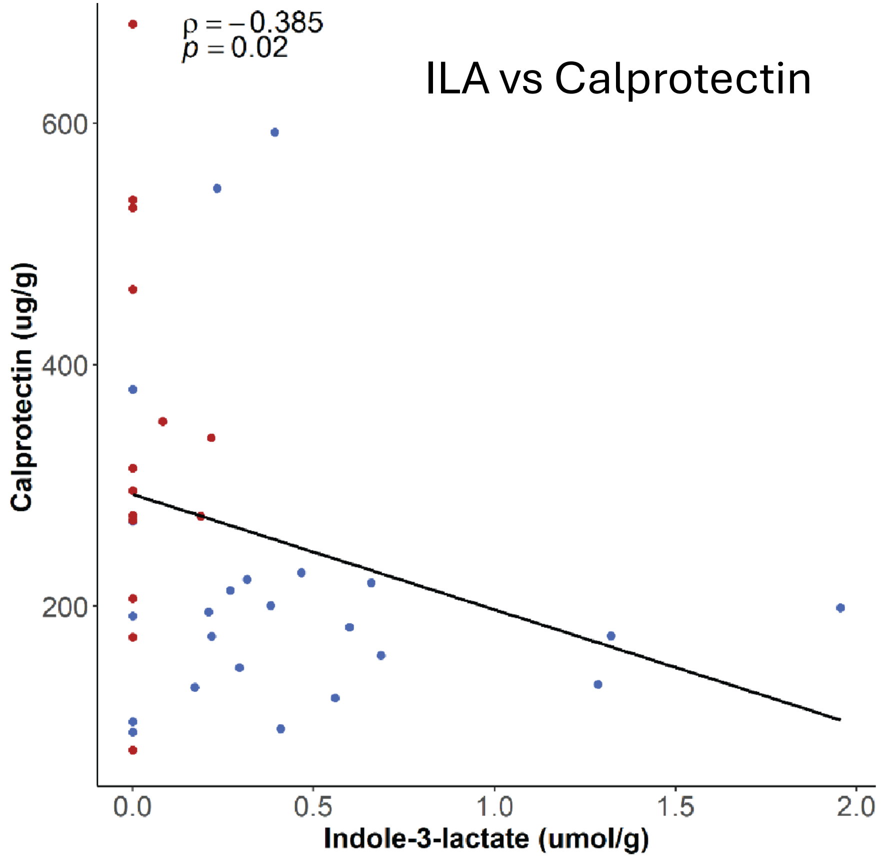


From: He et al. npj Sci Food 9(1):207 (2025)

Microbial metabolites can track inflammation



From: He et al. npj Sci Food 9(1):207 (2025)



From: Larke et al., J Pediatr Gastroenterol Nutr 75(4): 535-542 (2022)

Microbial signals reshape host biology systematically

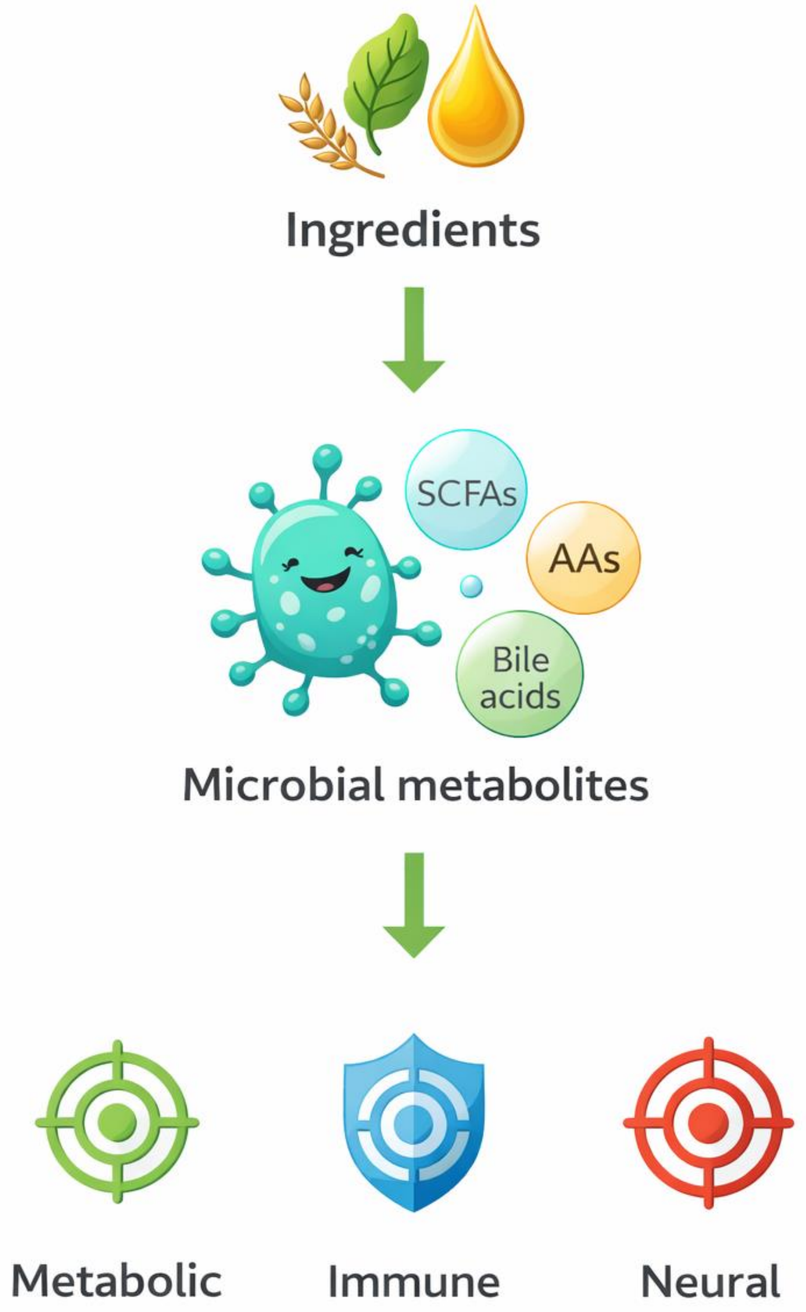
ALAC (ILA producer)
vs.
ALAC (ILA nonproducer)

	up	down
Small intestine	3	8
Colon	52	40
Liver	22	11
Brain	15	5

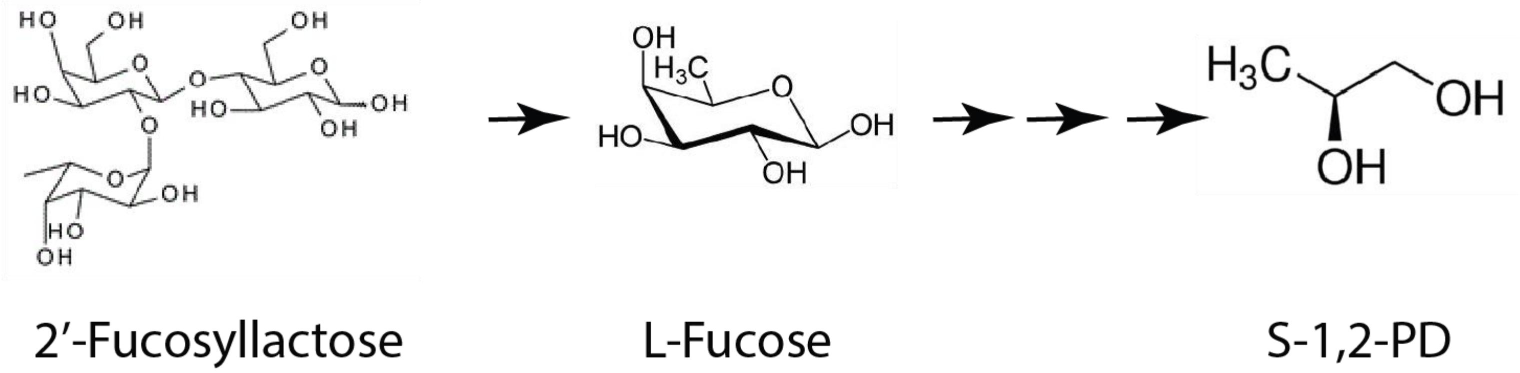
From: He et al. npj Sci Food 9(1):207 (2025)

Synthesis: from ingredients to signals

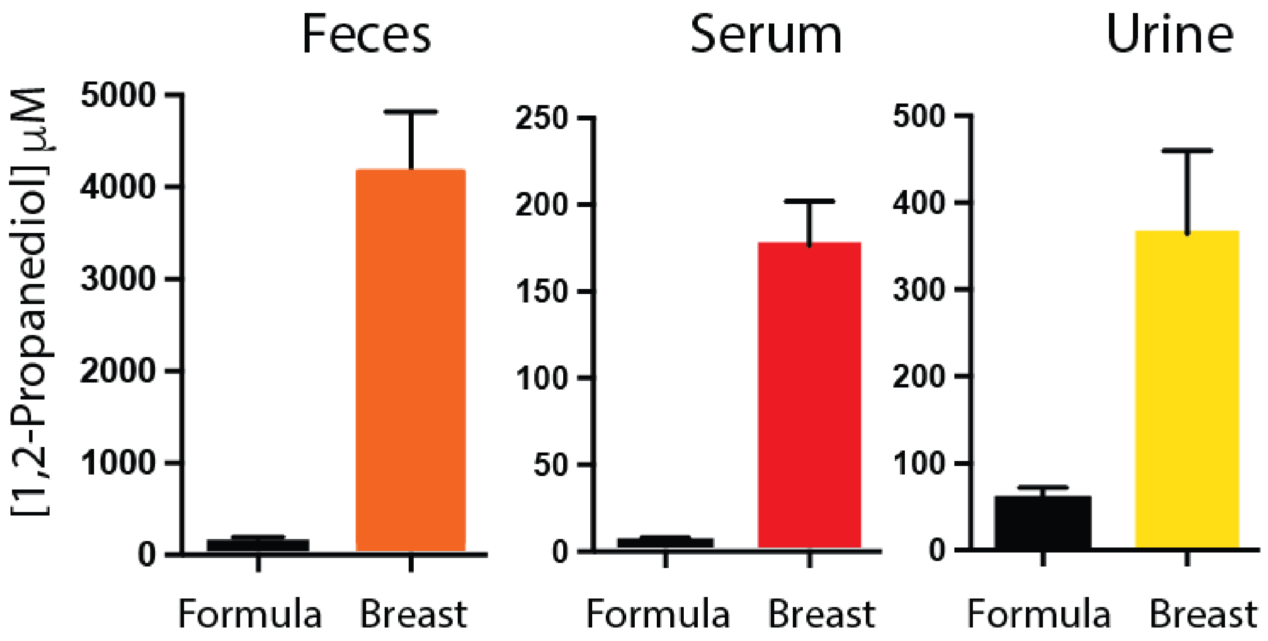
- Protein quantity and quality is important in the infant diet
  - α-Lactalbumin is rich in tryptophan and lower in BCAA than β-lactoglobulin, so it can provide essential tryptophan and decrease levels of BCAA in infant formula
  - Lower BCAA is related to lower insulin levels and HOMA-IR and may have long-term impacts on health
- α-Lactalbumin incorporation into infant formulas is beneficial
  - Can lower cortisol levels
  - Can provide tryptophan usable by colonic bacteria to produce ILA, a beneficial microbial metabolite

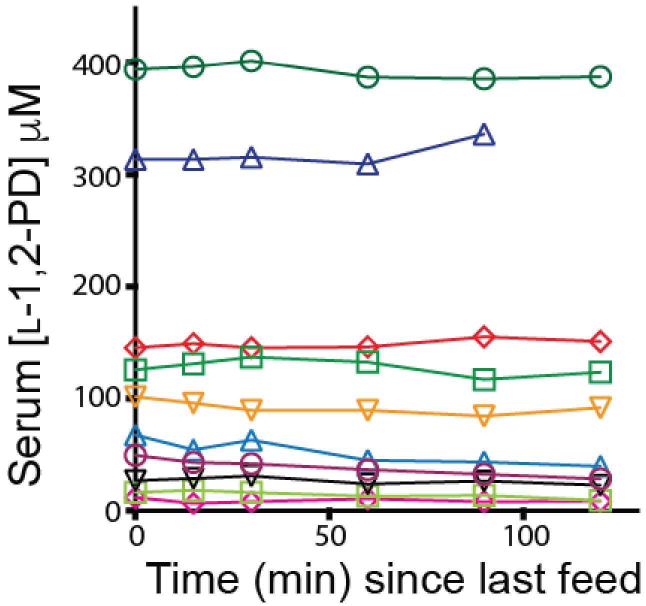


Other microbial metabolites can impact health systemically

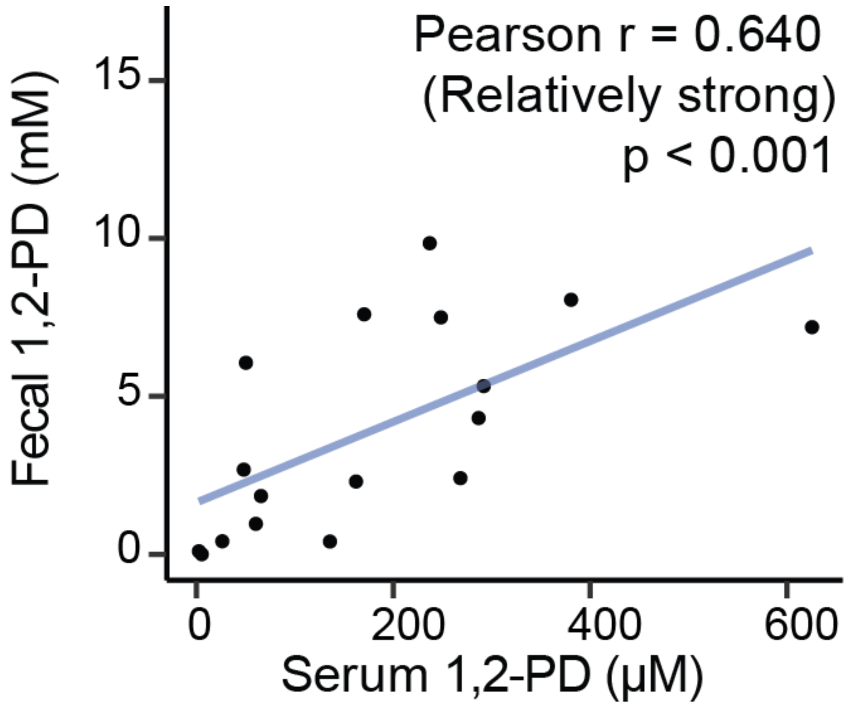


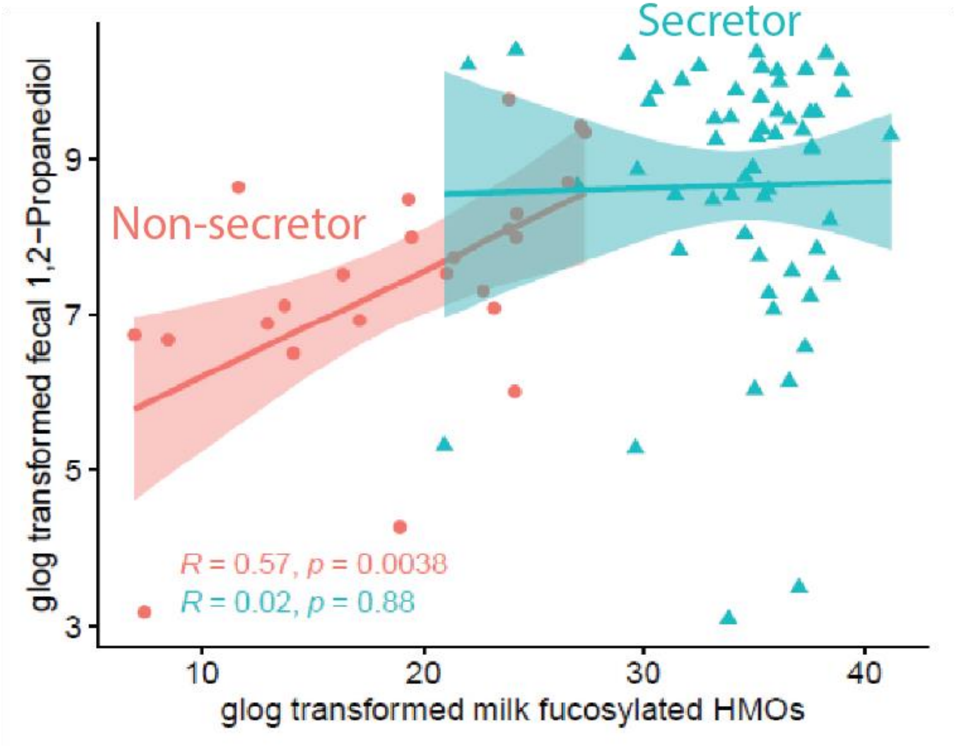
Breastfed infants have high levels of 1,2-PD





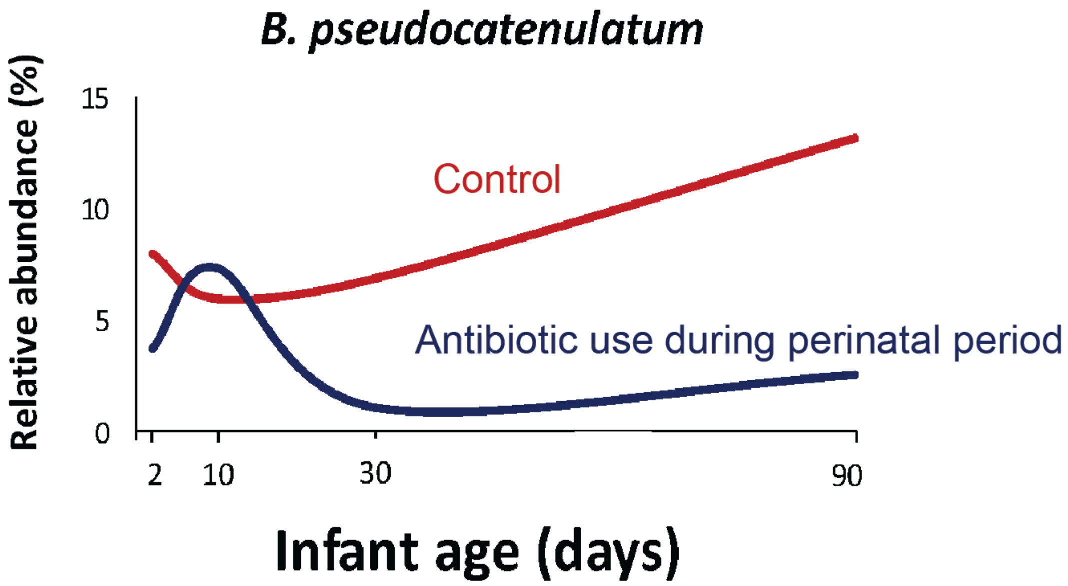
Fecal and serum SPD correlate, and SPD correlates with levels of milk HMOs





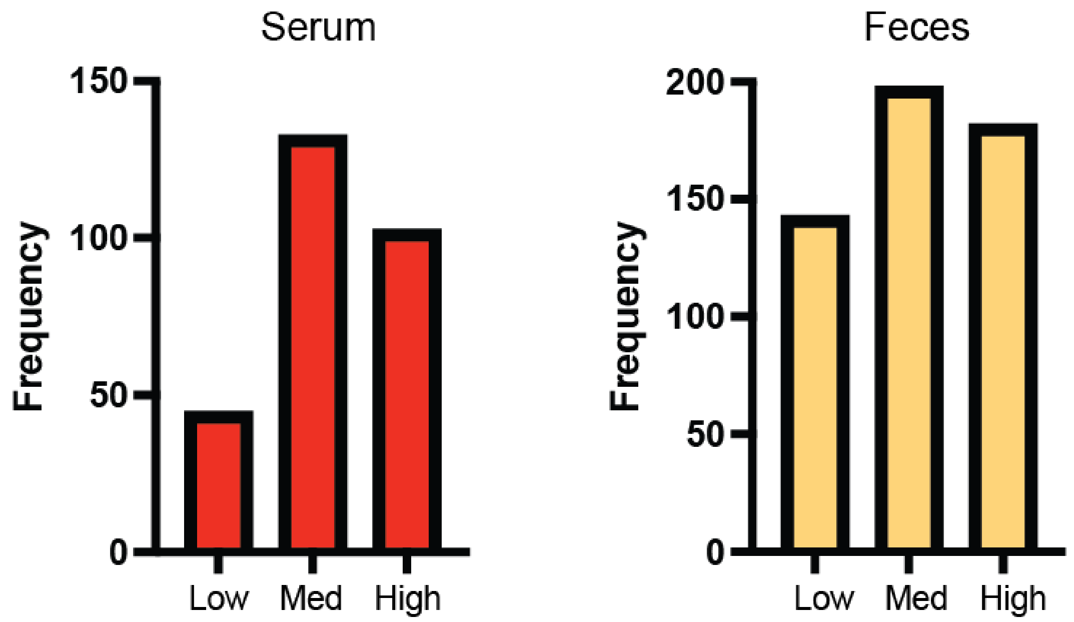
From: Wang et al., Gut Microbes 15(2):2257273 (2023)

Even in exclusively breastfed infants, levels of SPD vary

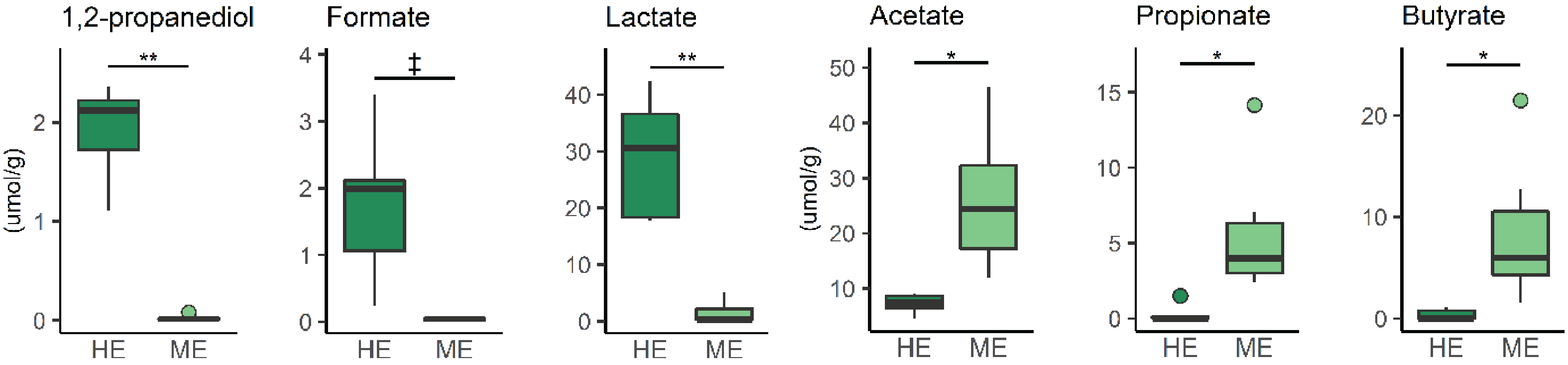


From: Saturio et al., Microorganisms: 9(9), 1867 (2021)

Distribution of SPD concentrations among breastfed infants 0-6 months

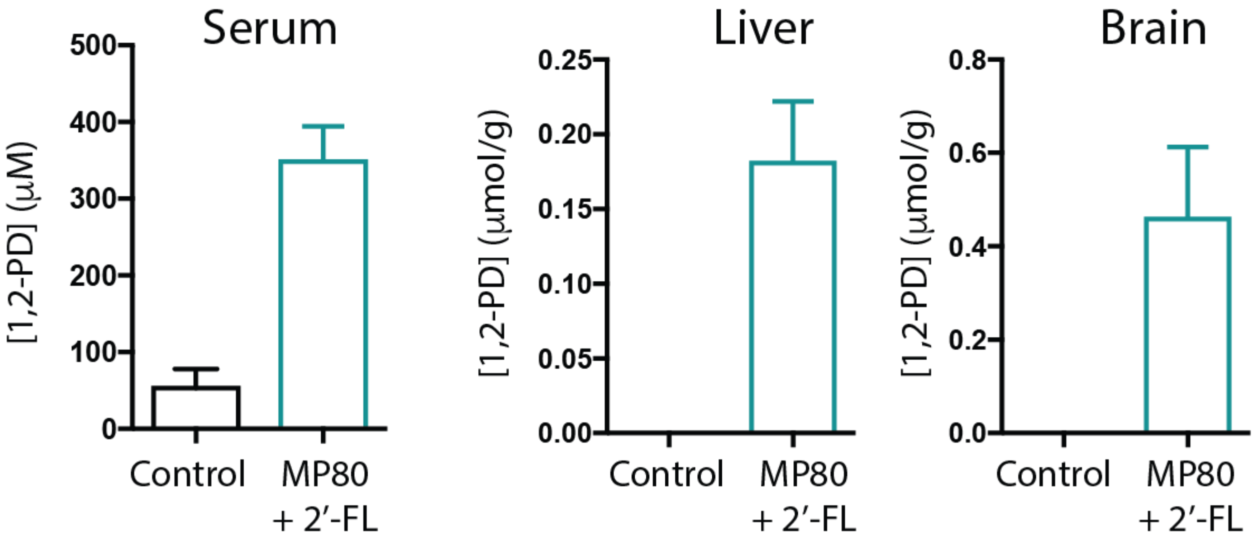


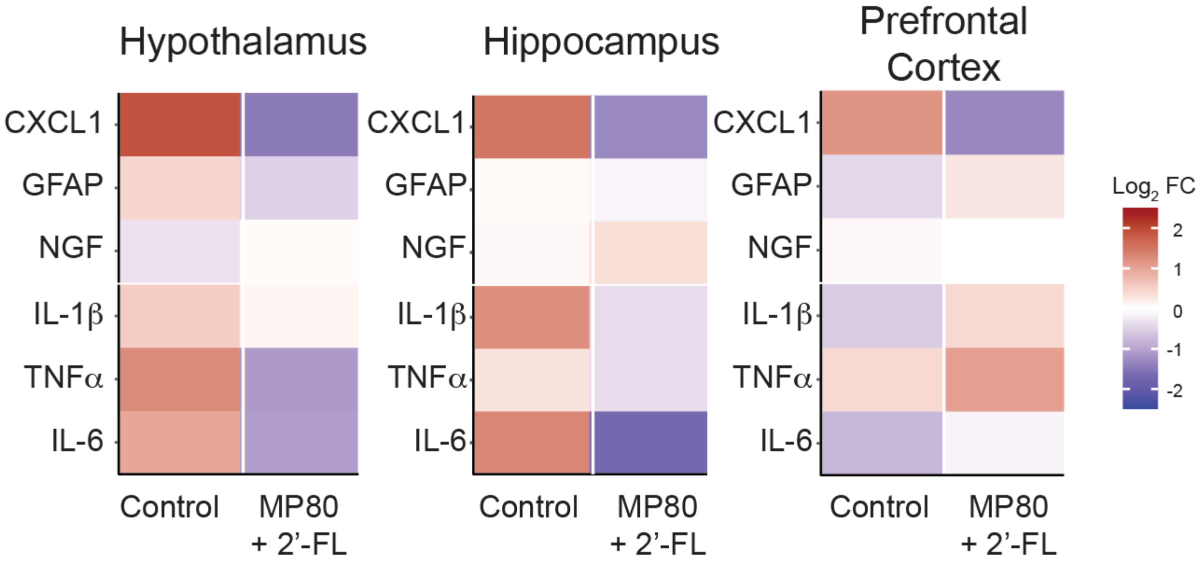
Colonization and bacterial levels matter



From: Larke et al. Microbiome 11:194 (2023)

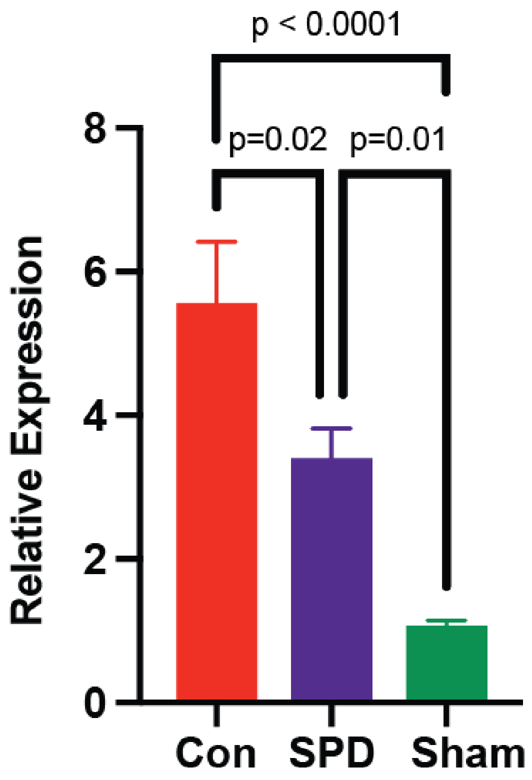
1,2-PD accumulates in the brain and attenuates inflammation

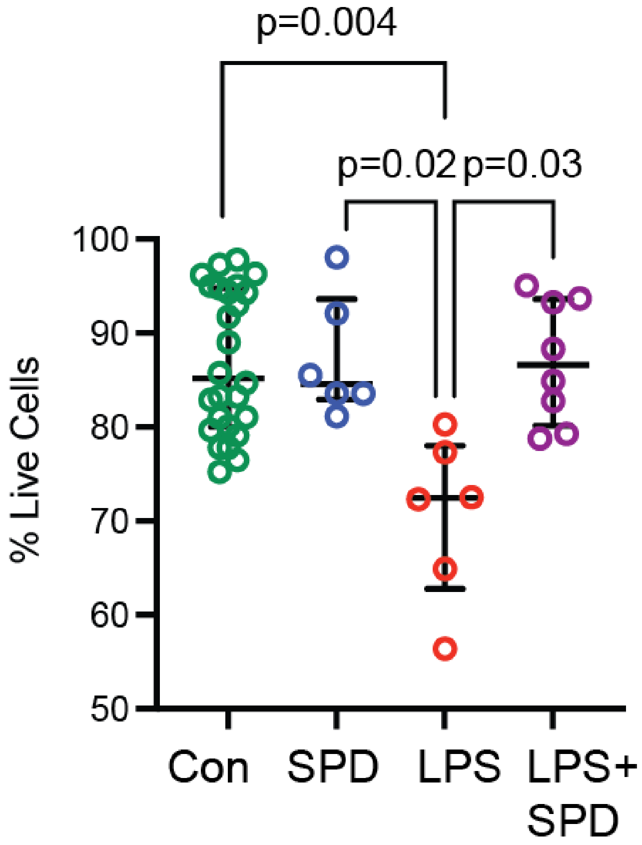


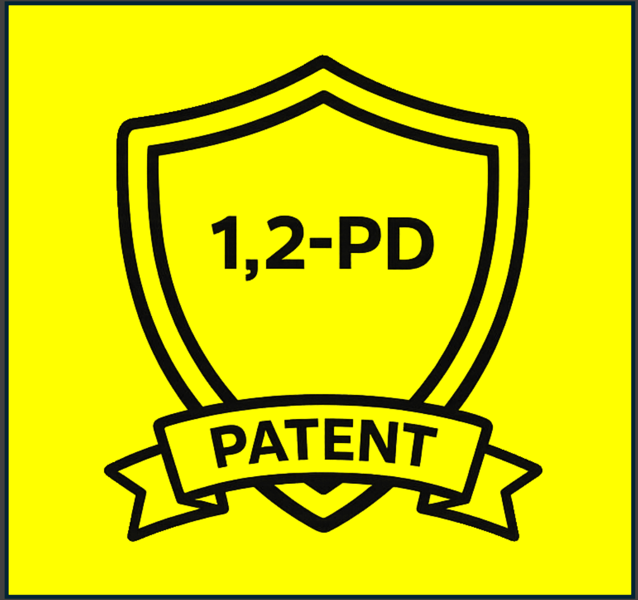


From: Heiss et al. Gut Microbes 13(1):1986666 (2021)

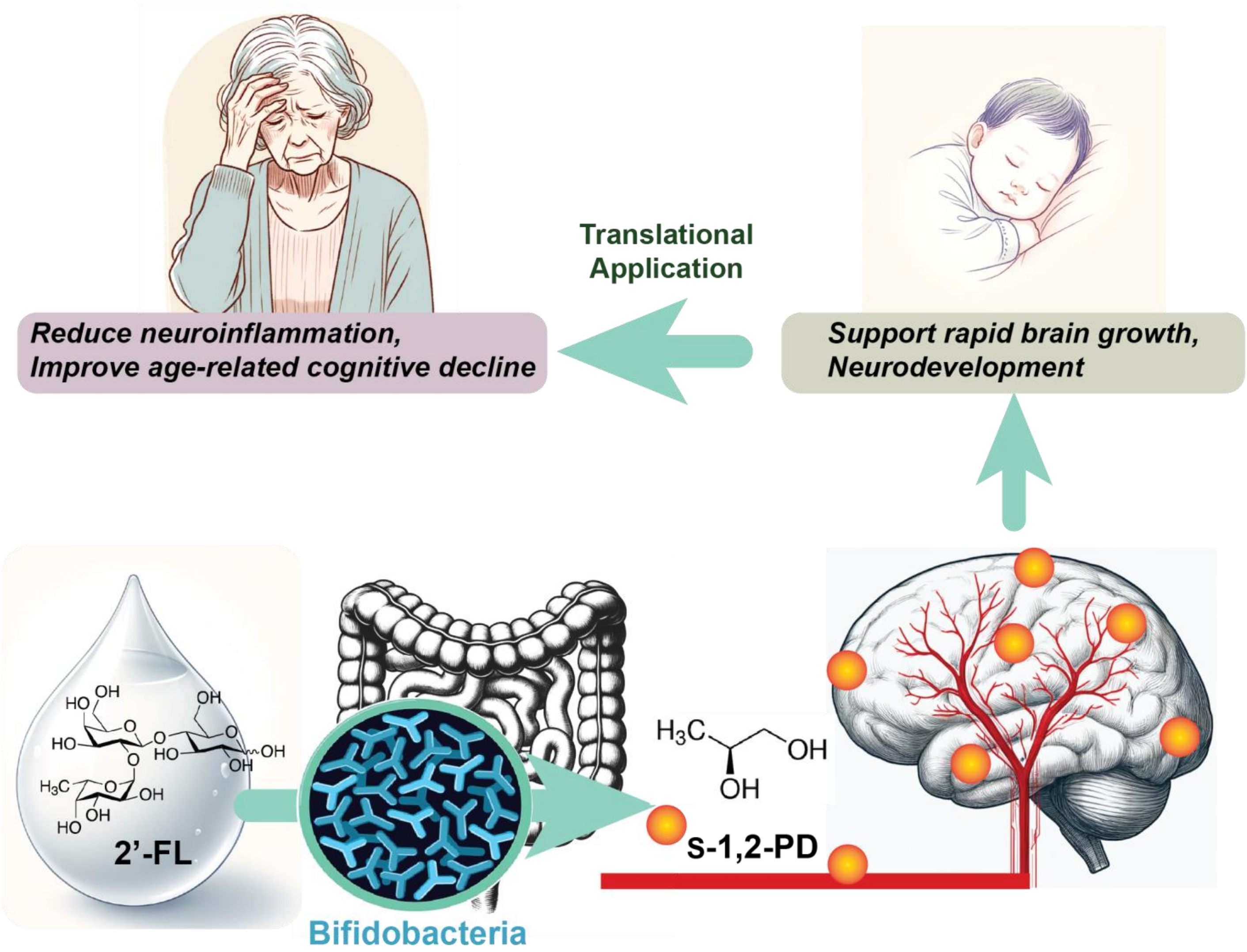
1,2-PD attenuates inflammation with an LPS challenge






1,2-PD
PATENT

Designing new products to impact health across the lifespan



Forward look: Designing foods for microbial transformation

- Design for what foods BECOME in the gut, not only what they CONTAIN.
- Pair substrate classes with microbial functions that manufacture beneficial metabolites.
- Use metabolomics as a development compass: reliability, dose-response, durability.
- Build products for life stage + responder profiles (microbiome function).

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- Olle Hernell

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