Hana KOUTNIKOVA ROUSSELIN
Danone

Yogurt consumption and metabolic diseases

AXE INTESTIN-MICROBIOTE-CERVEAU

DANS LES MALADIES MÉTABOLIQUES :

PRÉVENTION ET TRAITEMENT

September 30th 2021

DANONE
ONE PLANET. ONE HEALTH

ADEBIOTECH
THINK TANK ONE HEALTH

DISCLOSURE

- Employee of Danone Nutricia Research, Paris region
- One of the main R&I center serving Danone's divisions worldwide and particularly focusing on the Essential Dairy, Plant-Based and Waters divisions

DANONE
ONE PLANET. ONE HEALTH

- INTRODUCTION
- EVIDENCE
- MODE OF ACTION
- FUTURE
- CONCLUSION

Our mission

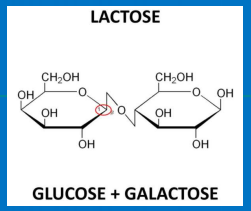
Bringing health through food
to as many people as possible

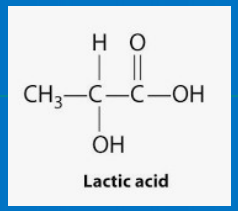
YOGURT IS PART OF DIETARY GUIDELINES

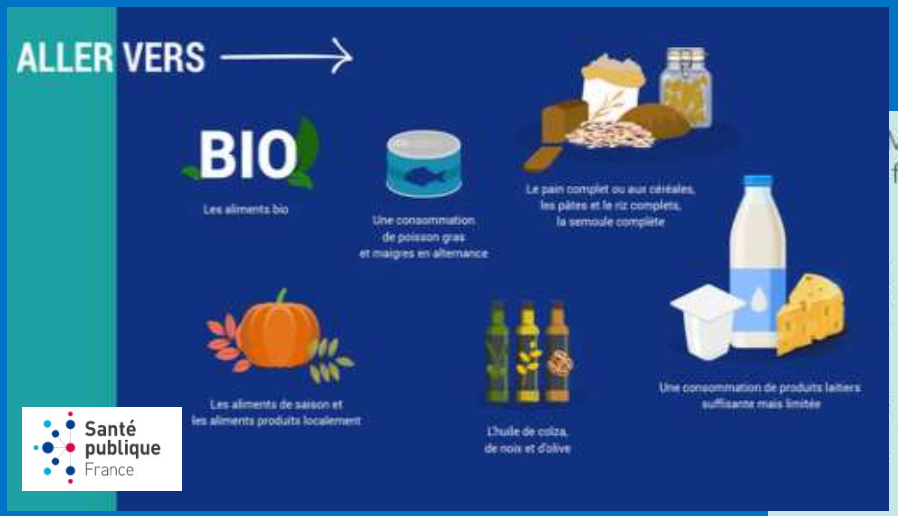
> 10^6 cfu/g

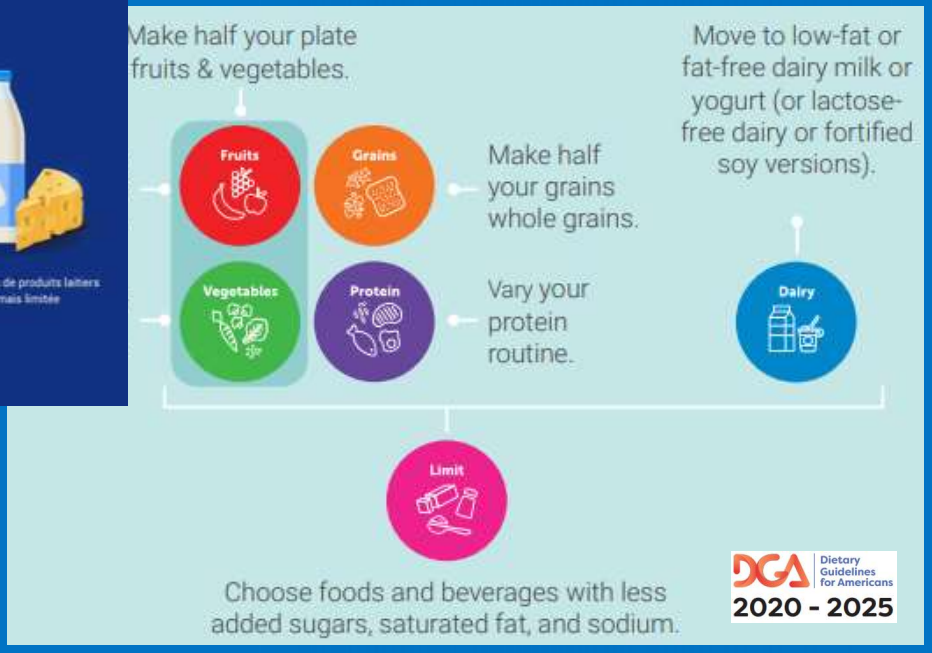
L. delbrueckii subsp. bulgaricus

Streptococcus salivarius subsp. thermophilus







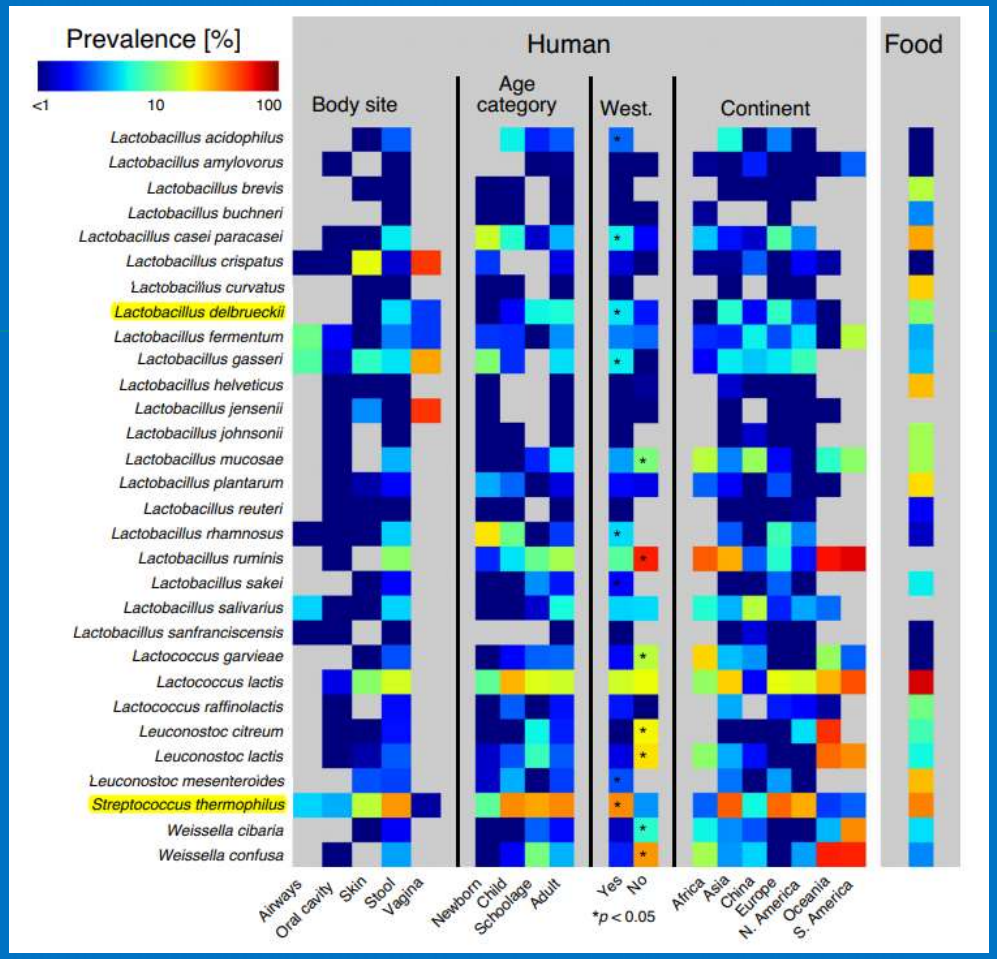


https://www.dietaryguidelines.gov/
https://www.santepubliquefrance.fr/

LIVE LACTIC ACID BACTERIA ARE CONSUMED WITHIN FERMENTED FOODS

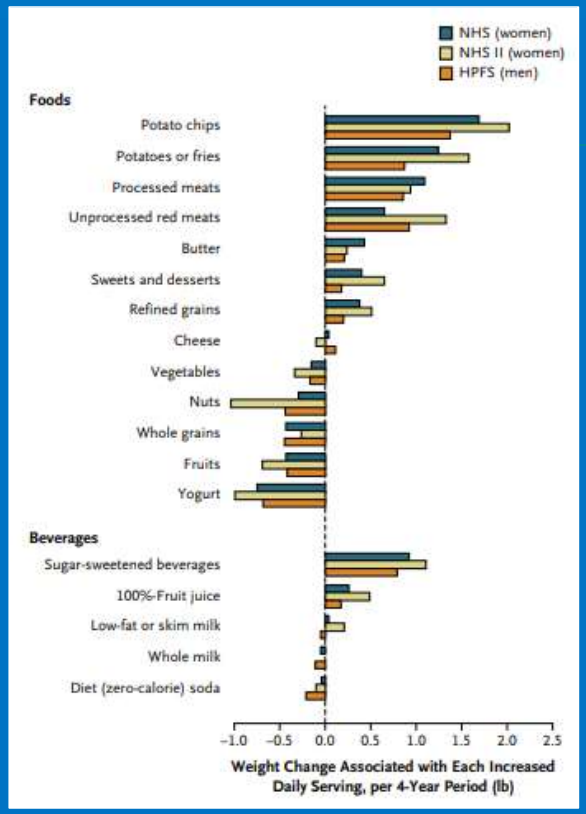
POSSIBLE SOURCE FOR THE GUT MICROBIOME

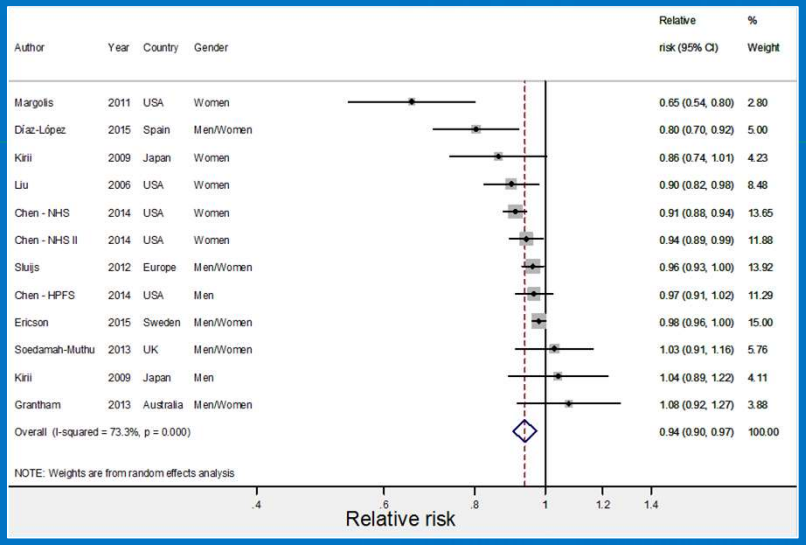
https://www.yogurtinnutrition.com/

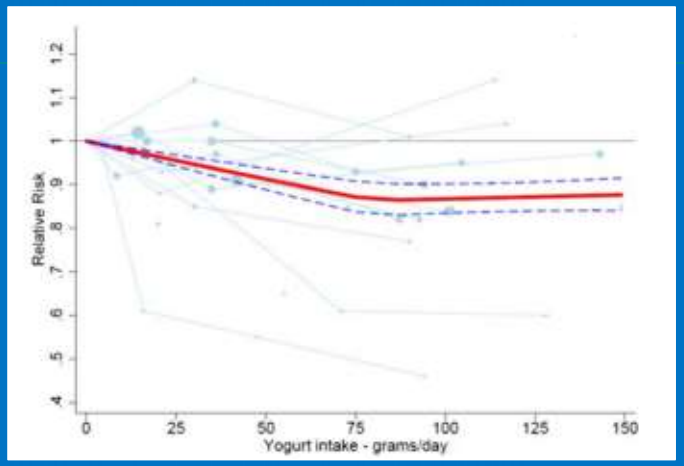


Pasolli et al., Nat Commun. 2020 May 25;11(1):26102020

YOGURT ASSOCIATES INVERSELY WITH METABOLIC DISEASES







Inversely associated with weight change	−0.82 lb, 95% CI −0.99 to −0.67
Inversely associated with diabetes	RR = 0.86, 95% CI: 0.83–0.90 at 80 g/d
Inversely associated with NAFLD	OR = 0.86, 95% CI: 0.76- 0.98 at ≥ 4 times/week

Mozaffarian et al., 2011; Gijsbers et al., 2016, Soedamah-Muthu et al., 2018, Zhang et al., 2019

YOGURT IMPROVES INSULIN RESISTANCE

220 g/day
24 weeks

Yogurt improves insulin resistance and liver fat in obese women with nonalcoholic fatty liver disease and metabolic syndrome: a randomized controlled trial

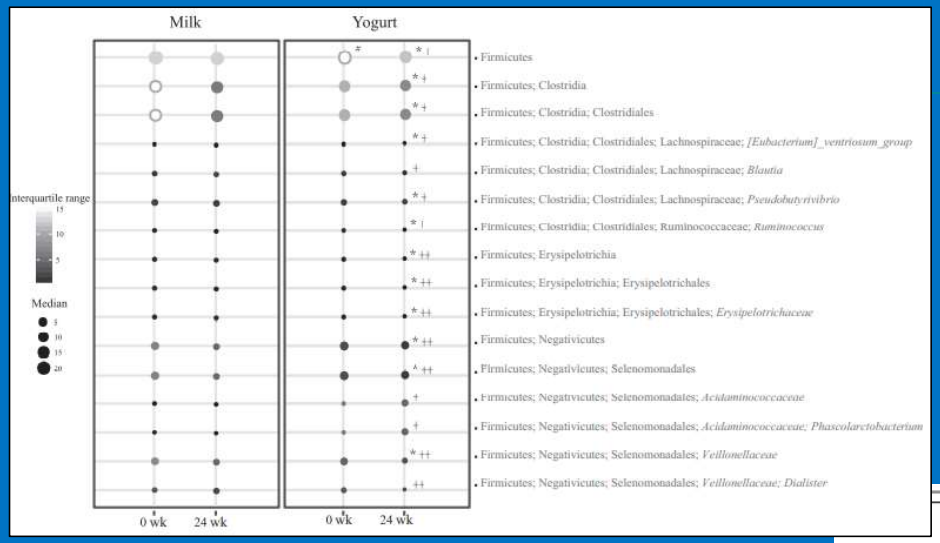
Yang Chen,[1] Rennan Feng,[1,4] Xue Yang,[1] Jiaxing Dai,[5] Min Huang,[1] Xiaoning Ji,[1] Yong Li,[4] Akinkunmi Paul Okekunle,[1] Guanghui Gao,[6] Justina Ucheojor Onwuka,[2] Xiuyu Pang,[1] Cheng Wang,[3] Chunlong Li,[7] Ying Li,[1] and Changhao Sun[1]

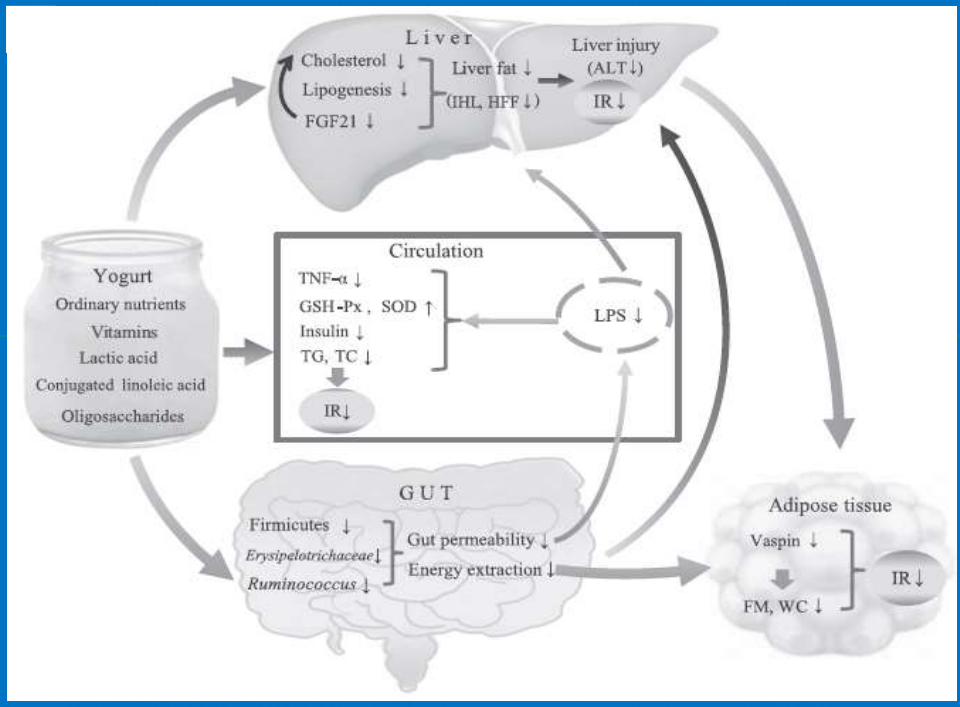
	Milk ($n = 44$)		Yogurt ($n = 48$)		
Variables	Baseline	24 wk	Baseline	24 wk	Adjusted differences of yogurt vs milk at 24 wk
BMI, kg/m^2	31.81 ± 2.76	31.97 ± 2.82	32.18 ± 3.18	32.02 ± 3.35	−0.28 (−0.33, 0.88)
FM, kg	31.04 ± 4.13	30.83 ± 3.31	32.88 ± 6.65	31.60 ± 6.54**	−2.26 (−3.51, −1.00)†
WC, cm	99.66 ± 7.39	100.89 ± 5.87*	100.68 ± 6.66	98.84 ± 7.64**	−1.85 (−3.00, −0.69)†
FBG, mmol/L	5.38 ± 0.53	4.85 ± 0.46**	5.40 ± 1.15	4.92 ± 0.64**	−0.08 (−0.19, 0.03)
Fasting insulin, mU/L	16.61 ± 8.43	14.34 ± 6.84*	15.33 ± 7.25	12.55 ± 6.53**	−2.77 (−4.91, −0.63)††
HOMA-IR	4.11 ± 2.48	3.10 ± 1.61**	3.78 ± 2.12	2.80 ± 1.68**	−0.53 (−1.03, −0.02)†
ALT, U/L	27.30 ± 13.56	25.32 ± 15.69	24.83 ± 13.07	19.44 ± 10.46**	−4.65 (−8.67, −0.64)†
AST, U/L	22.05 ± 6.19	21.48 ± 8.05	24.08 ± 13.20	20.19 ± 5.08	−2.56 (−5.22, 0.09)
IHL, %, $n = 20$	27.34 ± 7.87	27.84 ± 8.15	30.10 ± 5.22	25.13 ± 6.01**	−3.44 (−6.19, −0.68)†

Adapted from Chen et al., Am J Clin Nutr 2019;109:1611–1619.

*Continuous data are presented as mean ± SD or mean (95% CI). *P < 0.05 or **P < 0.01 compared with baseline in each group; †P < 0.05 or ††P < 0.01 when comparing the 2 groups at 24 wk with the use of ANCOVA adjusted for baseline values, age, BMI, dairy intake, physical activity levels, menopausal status and energy intake change over 24-wk period. The IHL was measured in the 20 participants randomly selected from each group. ALT, alanine aminotransferase; AST, aspartate aminotransferase; FBG, fasting blood glucose; FM, fat mass; IHL, intrahepatic lipid;WC, waist circumference.*

YOGURT REDUCES ENERGY, LIPIDS, INFLAMMATION AFFECTS GUT MICROBIOTA





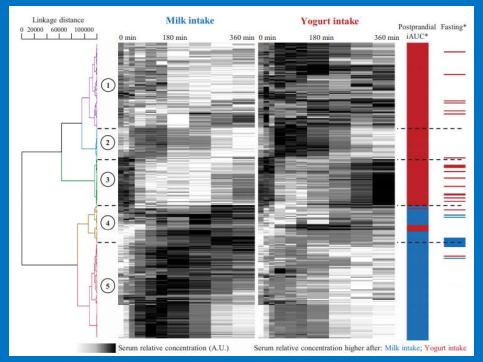
Variables	Milk ($n = 44$)		Yogurt ($n = 48$)	
	Baseline	24 wk	Baseline	24 wk
Dietary intakes				
Energy, kcal/d	2697.5 ± 609.2	2668.0 ± 883.3	2679.8 ± 766.7	2474.9 ± 925.5†
Protein, g/d	88.8 ± 23.2	88.2 ± 30.8	89.7 ± 26.8	87.0 ± 36.8
Fat, g/d	74.0 ± 20.2	80.9 ± 39.3	72.5 ± 32.9	69.3 ± 22.3
Carbohydrate, g/d	409.5 ± 109.8	383.4 ± 130.8	396.5 ± 77.4	386.0 ± 149.9

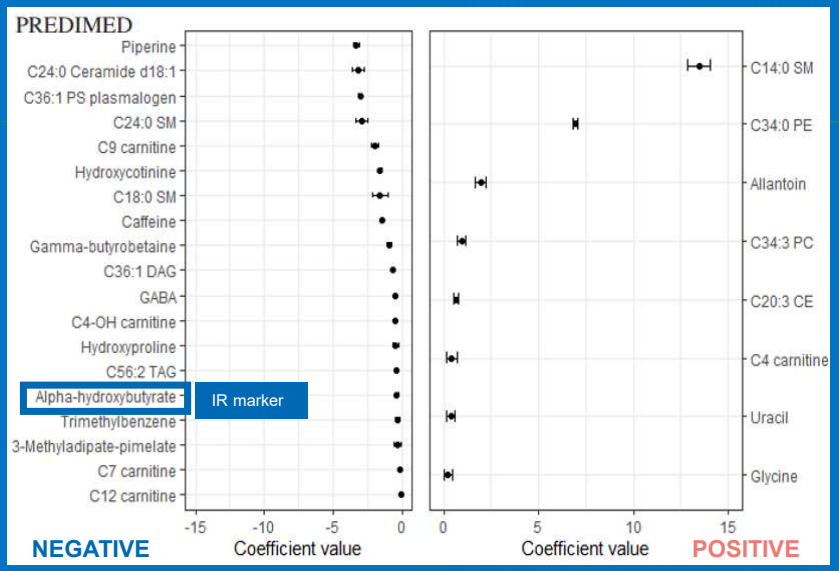
Adapted from Chen et al., Am J Clin Nutr 2019;109:1611–1619.

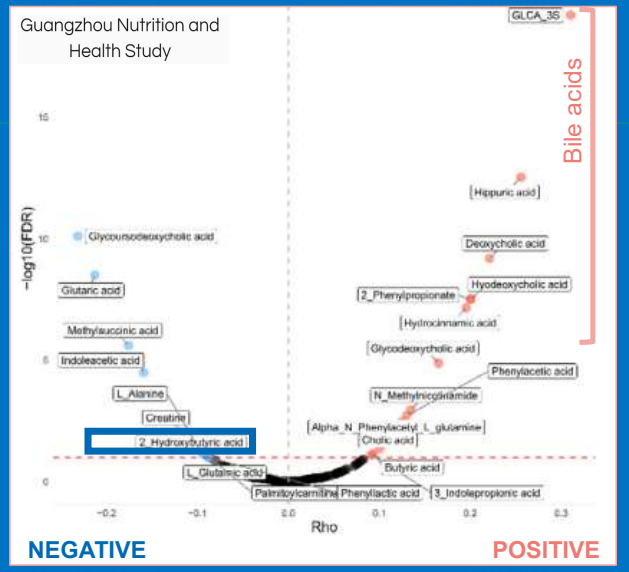
YOGURT ASSOCIATES WITH METABOLITES ACROSS COHORTS YET REPRODUCIBILITY IS CHALLENGE

NQplus

NS Proline
NS Lysine
NS Threonine
NS Phenylalanine
Asparagine
NS Tyrosine
NS Tryptophan
Citrulline
NS Indole-3-lactic acid
NS Indole-3-acetaldehyde







Framingham Heart Study Offspring

Metabolite		Quartile category of dairy intake Q1	Q2	Q3	Q4	*P*-trend	Third Generation (Gen3) Sig.[2]	In Gen3[3]
Yogurt (quartile median, servings/wk)		0.0	0.0	0.5	3.0			
C20:5 CE	1818	−0.420 ± 0.043	−0.376 ± 0.039	−0.354 ± 0.040	−0.263 ± 0.040	0.001	Y	n/a
C20:5 LPC	1818	−0.099 ± 0.036	−0.099 ± 0.033	−0.050 ± 0.034	−0.017 ± 0.034	0.03	N	n/a
C58:11 TAG	1818	0.324 ± 0.036	0.315 ± 0.033	0.345 ± 0.034	0.392 ± 0.034	0.03	N	n/a
Pyridoxate	1814	0.022 ± 0.049	0.062 ± 0.045	0.111 ± 0.047	0.168 ± 0.046	0.01	N	n/a
Salicylurate	1814	0.804 ± 0.116	0.673 ± 0.106	0.735 ± 0.109	0.859 ± 0.109	0.17	N	n/a

Pimentel, et al., 2018, Li et al., 2020; Drouin-Chartier et al., 2021; Shuai et al., 2021, Adapted from Hruby et al., 2020

YOGURT ASSOCIATES WITH CHANGES IN GUT MICROBIOME
INCREASE OF YOGHURT SPECIES

Lactobacillus delbrueckii ↑ *Zhernakova et al., 2016*
Bolte et al., 2020

Streptococcus thermophilus ↑ *Zhernakova et al., 2016*
Bolte et al., 2020
Asnicar et al., 2021
Le Roy et al. unpublished,
Jie et al., preprint

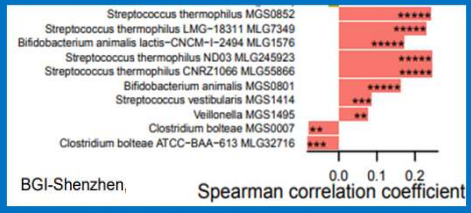
Bifidobacterium animalis ↑ *Asnicar et al.,2021*
Le Roy et al. unpublished
Jie et al., preprint

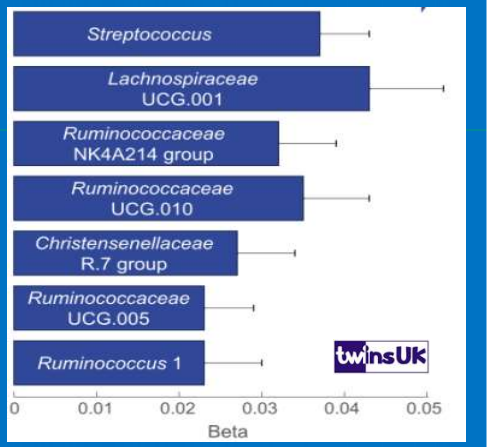
Clostridium bolteae ↑↓ *Bolte et al., 2020*
Jie et al., preprint

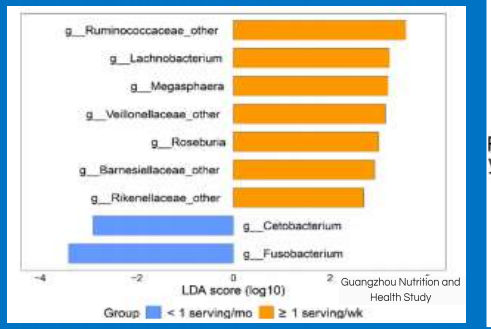
Lachnospiraceae ↑↓ *Asnicar et al., 2021*
Le Roy et al. unpublished

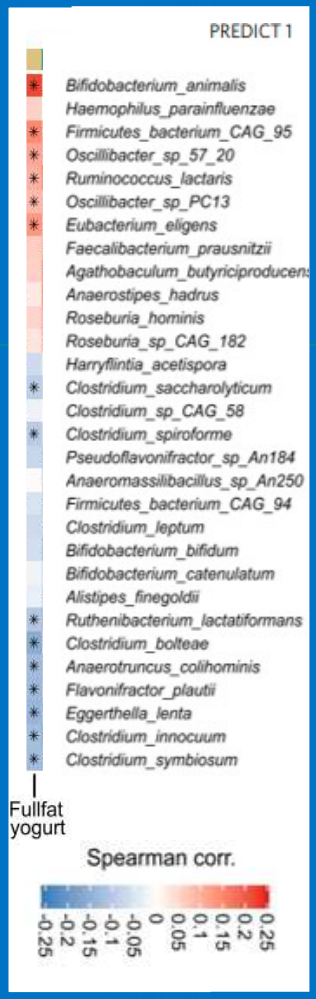
Ruminococcaceae ↑↓ *Shuai et al., 2021*
Le Roy et al. unpublished

Veillonellaceae ↑ *Shuai et al., 2021*
Jie et al., preprint



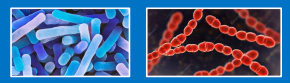




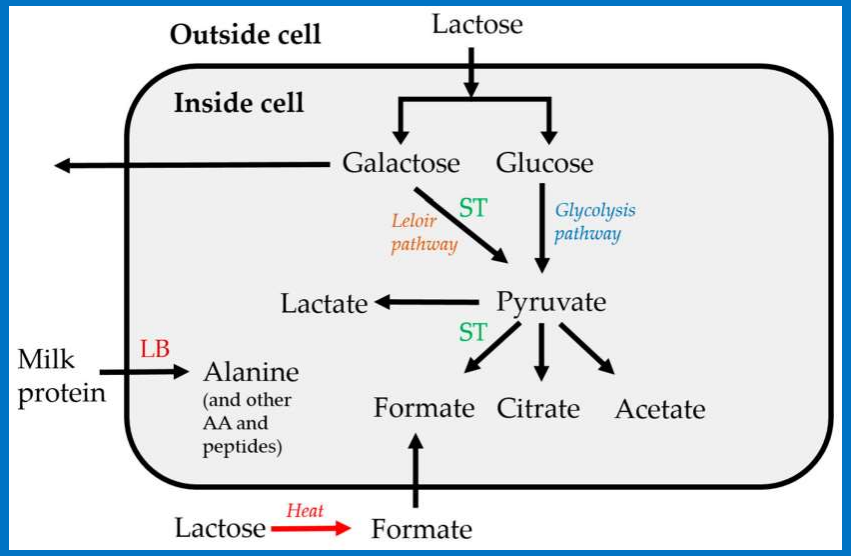


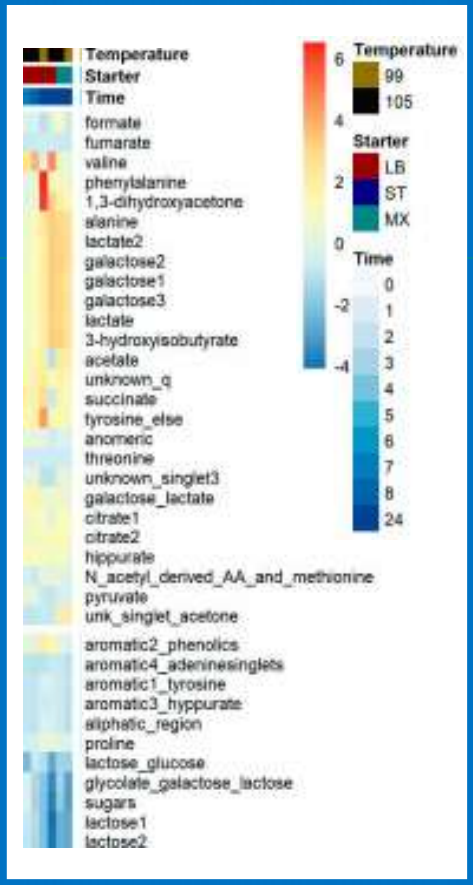
Zhernakova et al., 2016, Bolte et al., 2020, Adapted from Asnicar et al., 2021, Shuai et al., 2021, Le Roy et al. unpublished, Jie et al., preprint

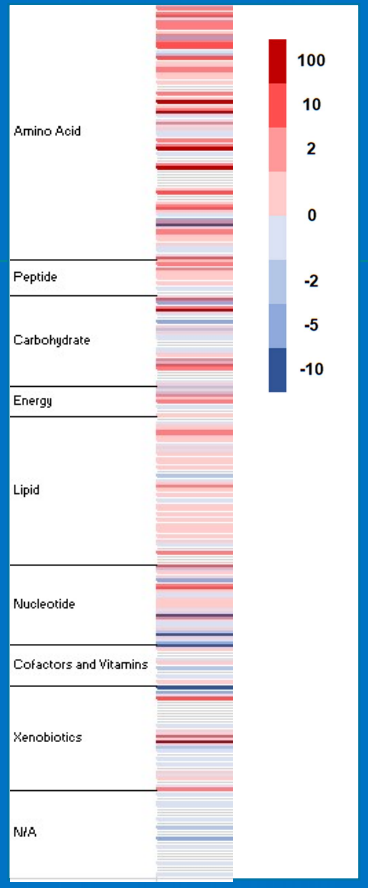
UNDERSTANDING ROLE OF YOGURT METABOLOME



L. delbrueckii subsp. Bulgaricus + Streptococcus thermophilus





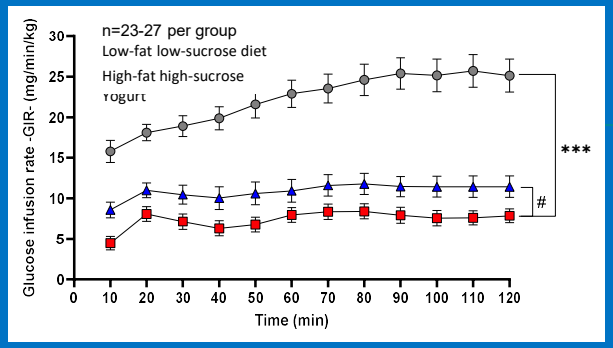


Adapted from Trimigno, et al., 2020

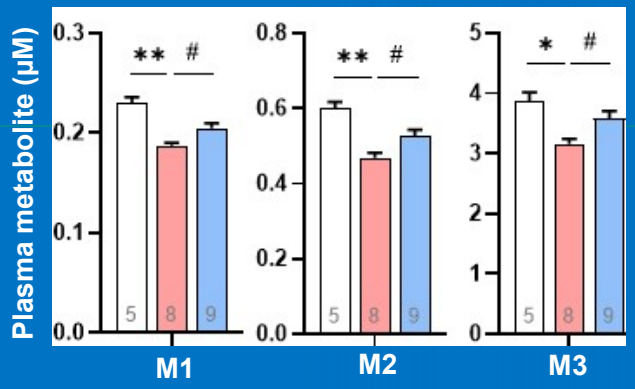
Daniel et al., unpublished

ROLE OF YOGURT DERIVED AMINO ACID METABOLITES IN YOGURT INCREASED INSULIN SENSITIVITY

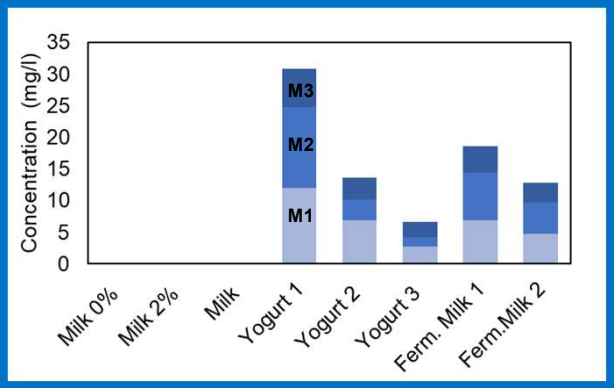
Hyperinsulinemic-euglycemic clamp in mice



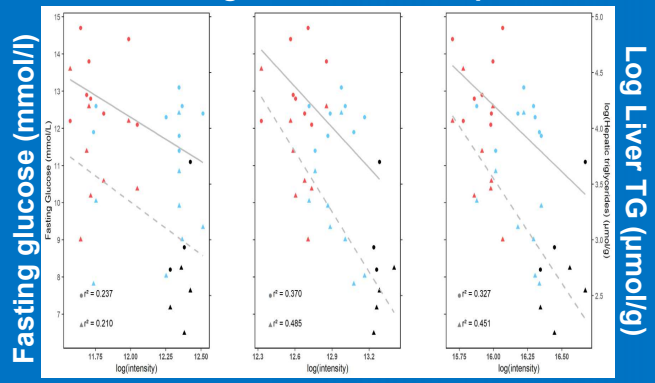
AA metabolites are increased upon yogurt intake

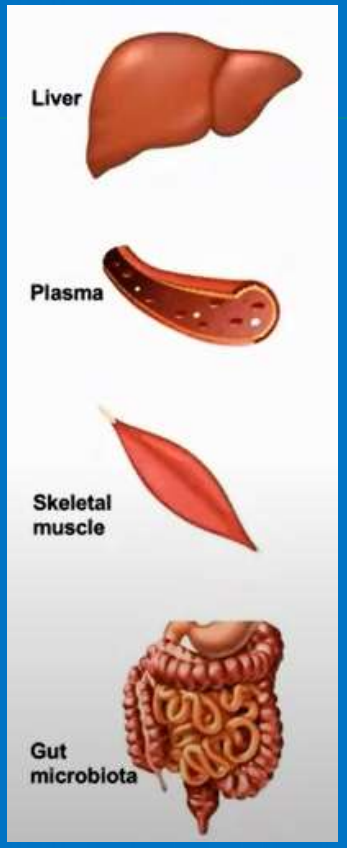


AA metabolites are undetected in milk



Hepatic AA metabolites inversely correlate with glucose and liver lipids





Reduced insulin resistance & steatosis

Improved glucose homeostasis

Reduced insulin resistance

Modified composition and function

Daniel et al., unpublished

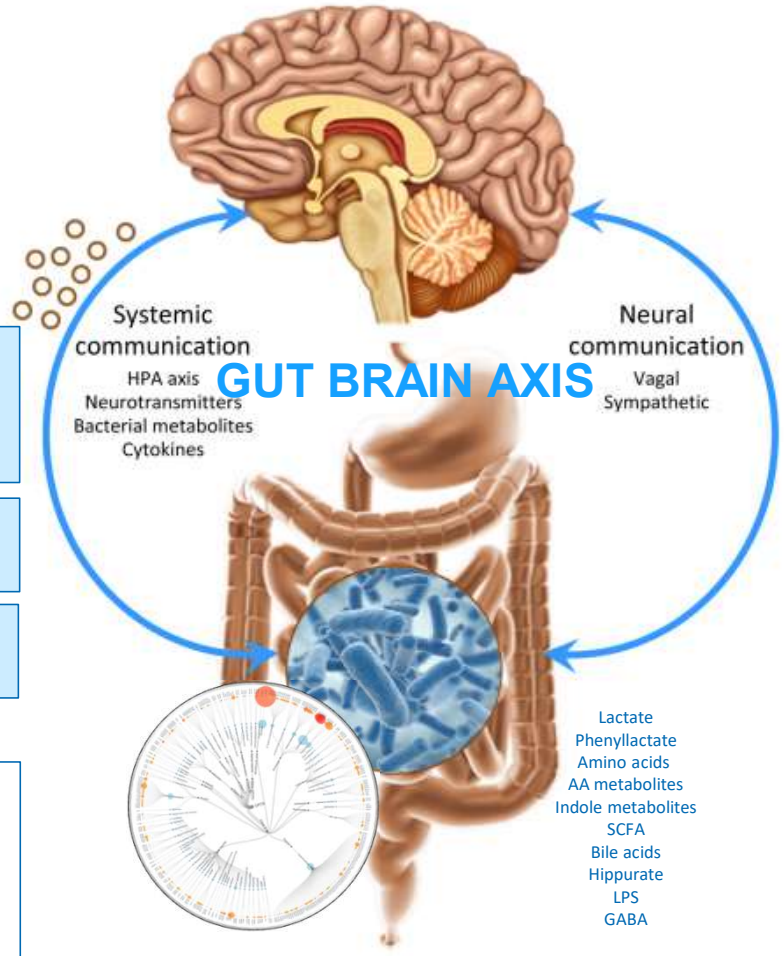
Brain
Food intake
Satiety
Neurotransmitters
Mood

Liver
Glucose production
Insulin sensitivity
Fat content

Pancreas
Insulin secretion

Muscle
Glucose uptake

Intestines
Microbiota composition
Metabolites
Gut endocrine factors
Nutrients
Cell component

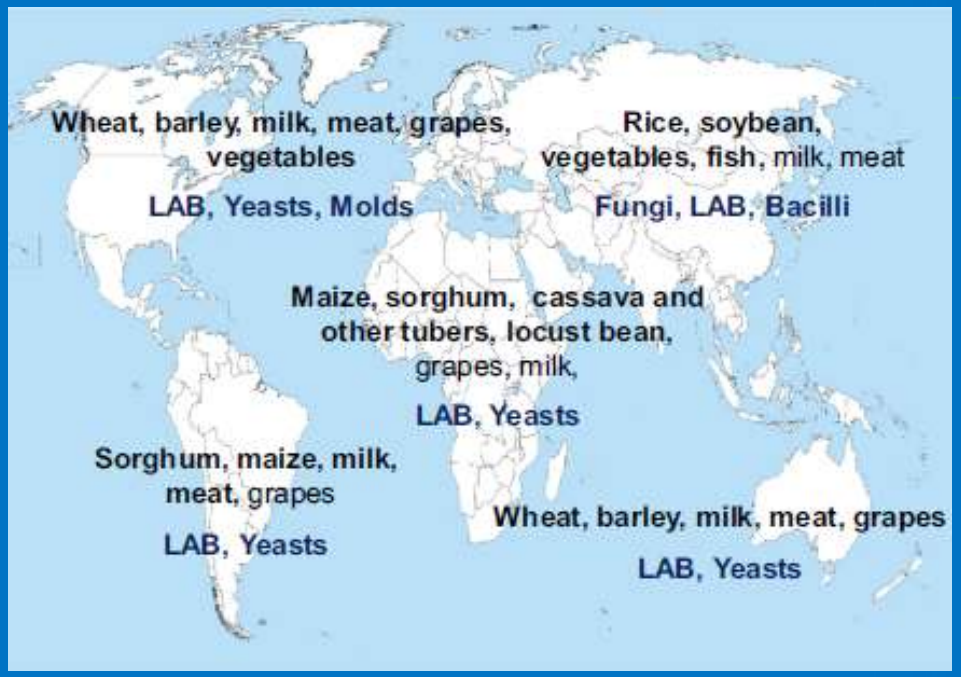


FUTURE

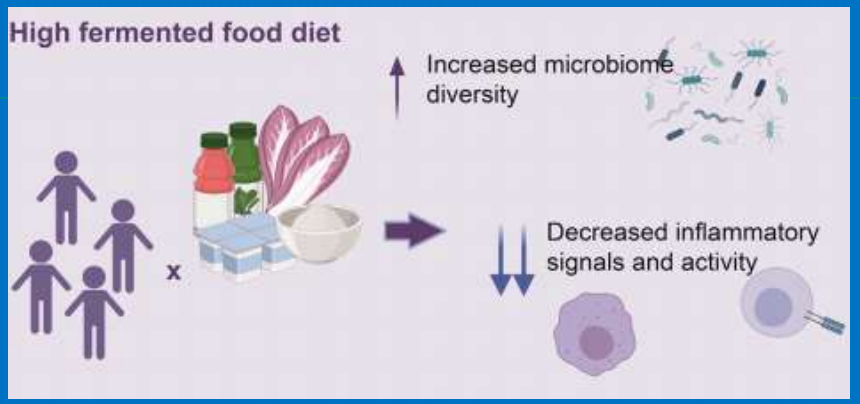
ABSORPTION
EXPOSURE
KINETICS
METABOLISM
SPECIFICITY
SELECTIVITY
HUMAN TARGET
BACTERIAL TARGET
REDUNDANCY

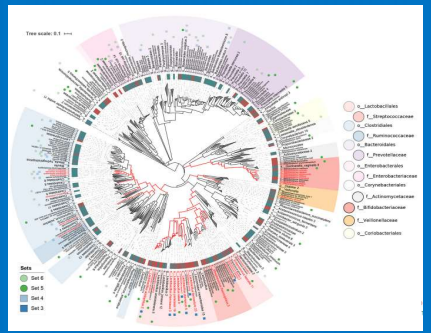
Adapted from Mayer et al., J. Neurosci., November 12, 2014 • 34(46):15490 –15496, Chen et al., 2019; Castellanos-Jankiewicz et al., 2021

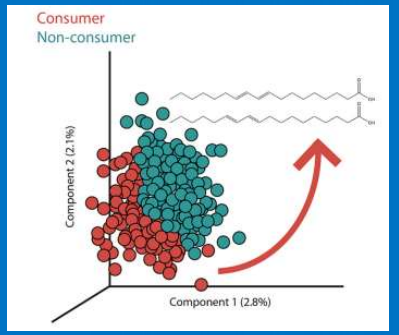
YOGURT IS POPULAR FERMENTED FOOD



Tamang et al., Compr Rev Food Sci Food Saf. 2020;19:184–217.







Wastyk et al., 2021, Cell 184, 1–17,
Taylor et al., 2021 mSystems . 2020 Mar 17;5(2):e00901-19

- Yogurt is associated with less body weight gain & lower incidence of diabetes and fatty liver disease
- Yogurt Improves insulin resistance in obese subjects with NAFLD
- Metabolite profiles of yogurt intake and yogurt itself are complex
- Lactic acid bacteria contribute to gut microbiome

RESEARCH ON YOGURT SPECIFIC EFFECTS RESPONSIBLE FOR METABOLIC HEALTH IS AREA OF ACTIVE GUT – MICROBIOME - LIVER / BRAIN RESEARCH

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CENTER FOR microbiome INNOVATION

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BIOASTER

METABOLON