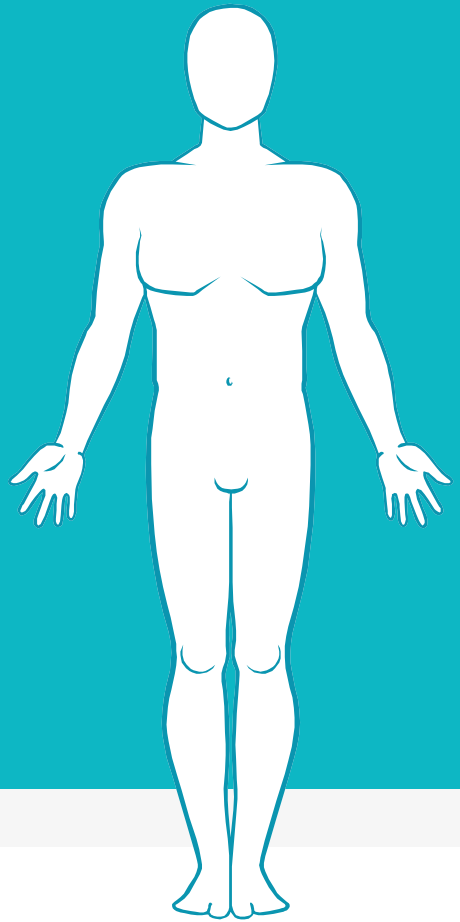
香港中文大學
The Chinese University of Hong Kong

Impact of Dietary Sugars & Sweeteners on GM and human health



5th year Phd student: PAN Mingfang; Supervisor: Prof. Margaret Ip

Department of Microbiology, CUHK, 14-Dec-2021

Sugar & artifical sweetener?

Sugars

Carbohydrates – they break down into energy in the body..

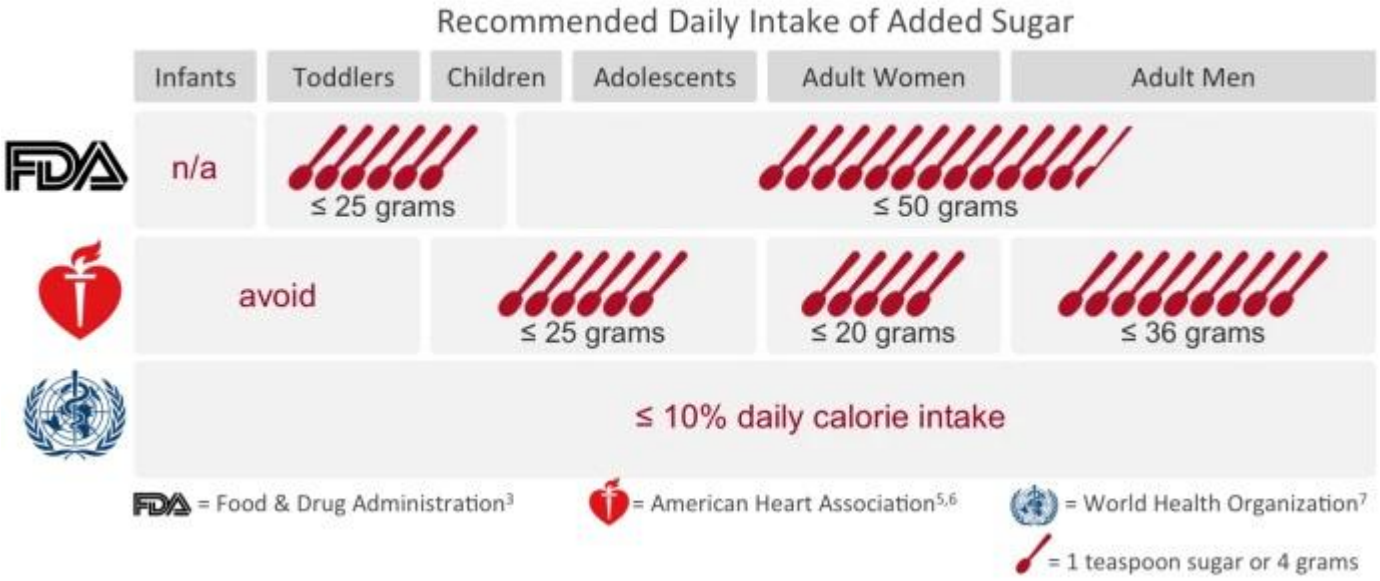
e.g., monosaccharide, glucose and fructose…Disaccharide, sucrose…

Artificial sweeteners

Or sugar substitutes, are chemicals added to some foods and beverages to make them taste sweet..

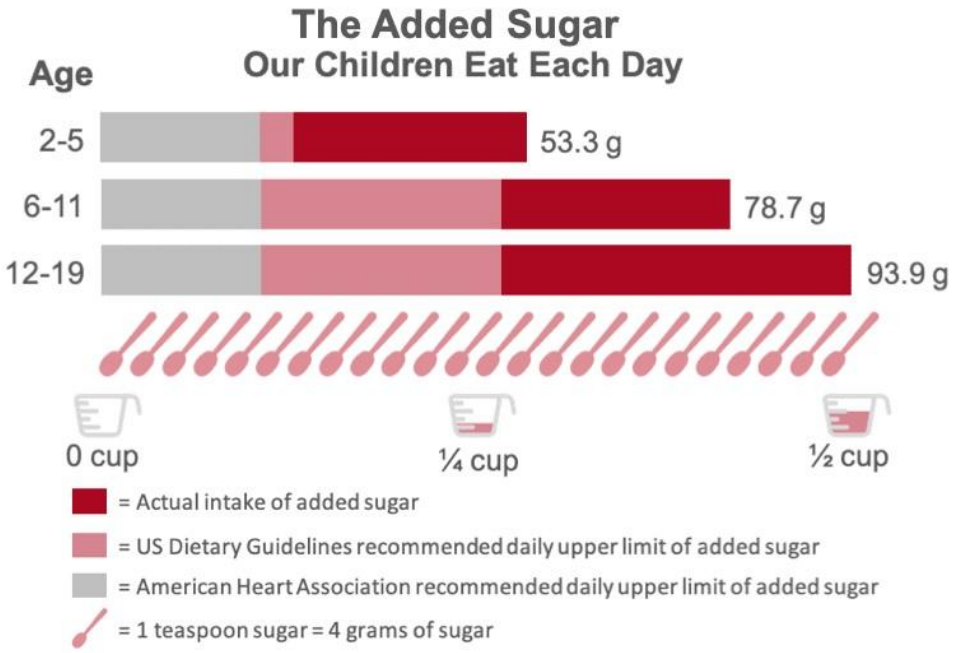
e.g., Equal (aspartame), Sweet'N Low (saccharin), and Splenda (sucralose)

Recommended sugar consumption



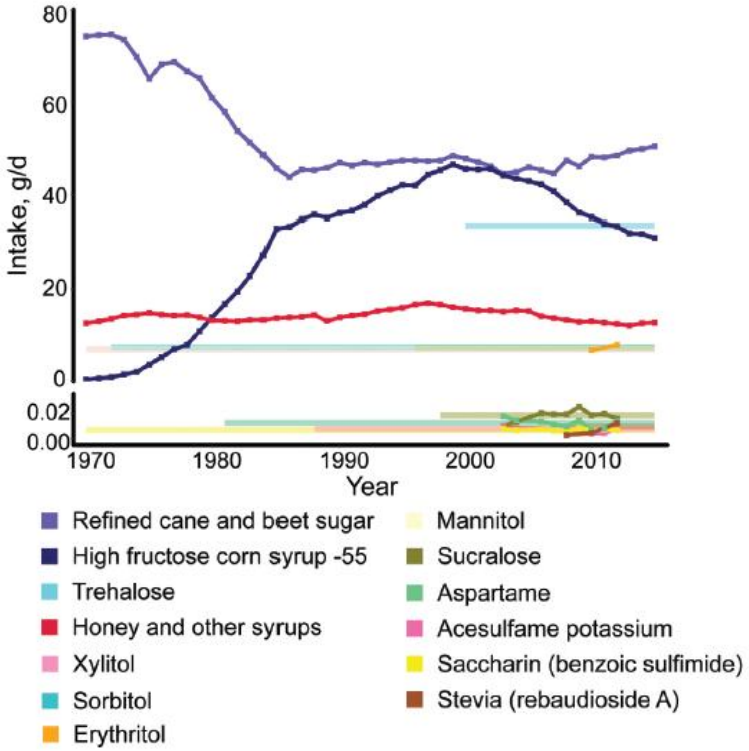
~50 grams

Consumption trends for common dietary sugars and sweeteners



- Excess sugar consumption is common, especially in western diet.
- Exceed more than one-fold of the recommendation.

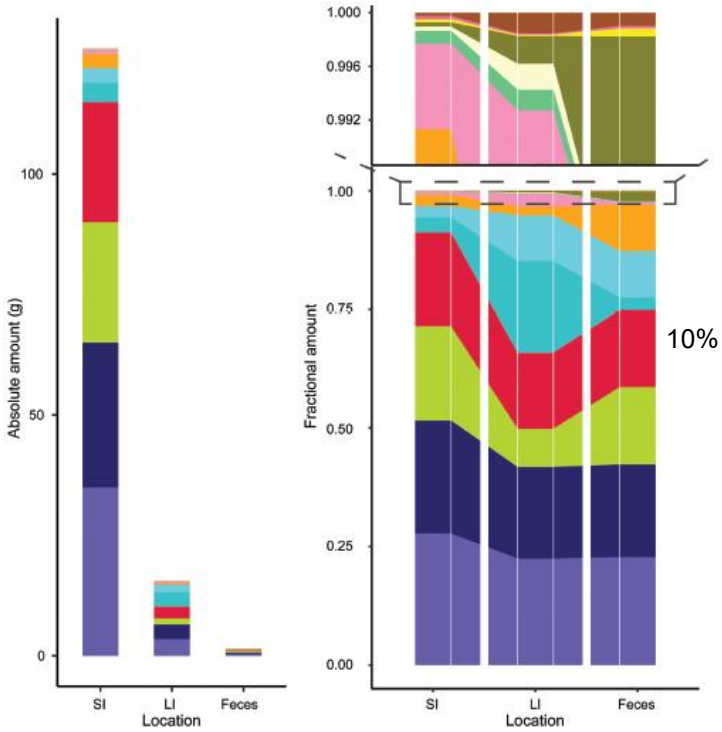
Consumption trends for common dietary sugars and sweeteners



- Consumption of fructose has increased 100-fold over the last century.
- Several novel sweeteners have been created and other natural sugars have been supplemented into foods.

Di Rienzi, et al. "Adaptation of the gut microbiota to modern dietary sugars and sweeteners." *Advances in Nutrition* (2020)

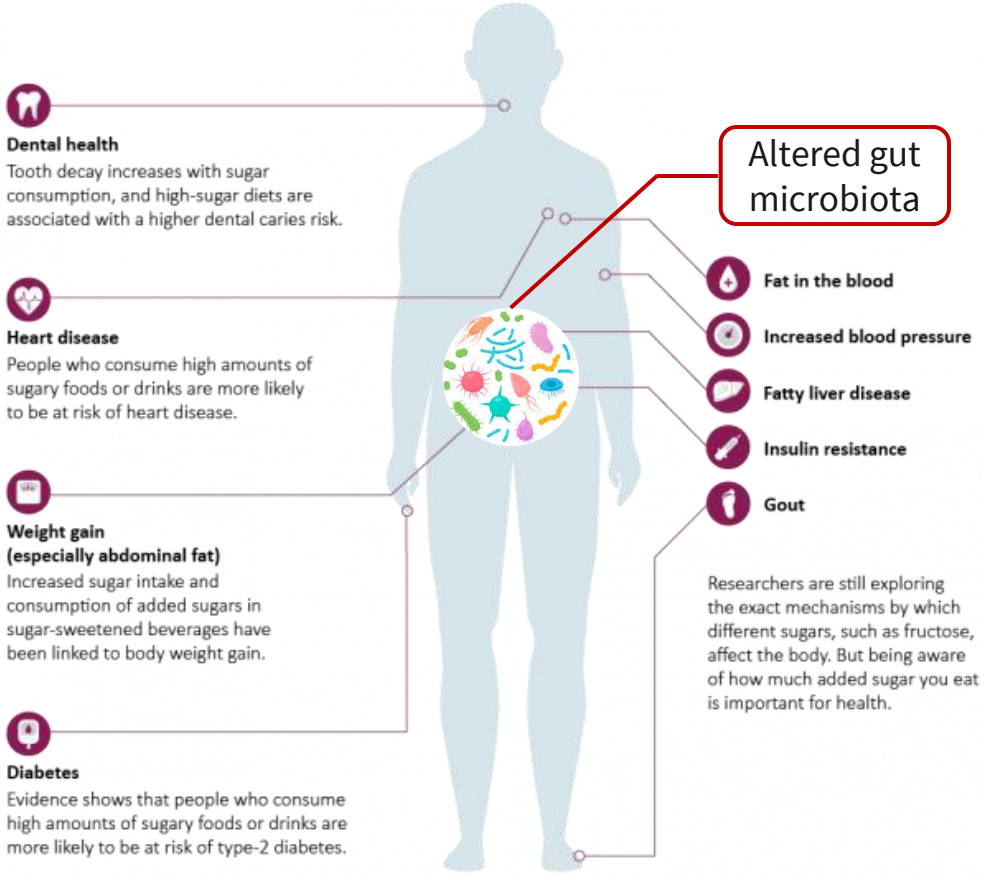
Absolute and fractional amounts of common dietary sugars and sweeteners in the SI and LI and in feces



- Small intestine : Most sugars and sweeteners
- Large intestine: 5–30%

Di Rienzi, et al. "Adaptation of the gut microbiota to modern dietary sugars and sweeteners." *Advances in Nutrition* (2020)

Health Concerns:
Weight Gain, Obesity, Diabetes, and Liver disease?



Hypothesis

Changes in sugar and sweetener consumption lead to transcriptional, compositional, and/or function in gut microbes, which lead to weight gain, obesity, diabetes, liver disease.

How dietary sugar & sweeteners affect the gut microbiota?

Gut colonization, bacterial virulence, composition and function…

1. Dietary sugar affects the gut commensals colonization?

Let’s start…

Dietary sugar and gut colonization

Dietary sugar silences a colonization factor in a mammalian gut symbiont

Guy E. Townsend II, Weiwei Han, Nathan D. Schwalm III, Varsha Raghavan, Natasha A. Barry, Andrew L. Goodman, and Eduardo A. Groisman

[a]*Department of Microbial Pathogenesis, Yale School of Medicine, New Haven, CT 06536;*

[b]*Yale Microbial Sciences Institute, West Haven, CT 06516*

– Hide authors and affiliations

PNAS January 2, 2019 116 (1) 233-238; first published December 17, 2018; https://doi.org/10.1073/pnas.1813780115

Dietary sugars

⊥

Colonization Factor: ROC

⊥

Gut commensal colonization

Bacteroides thetaiotaomicron

Dietary sugar and gut colonization

Dietary sugar silences a colonization factor in a mammalian gut symbiont

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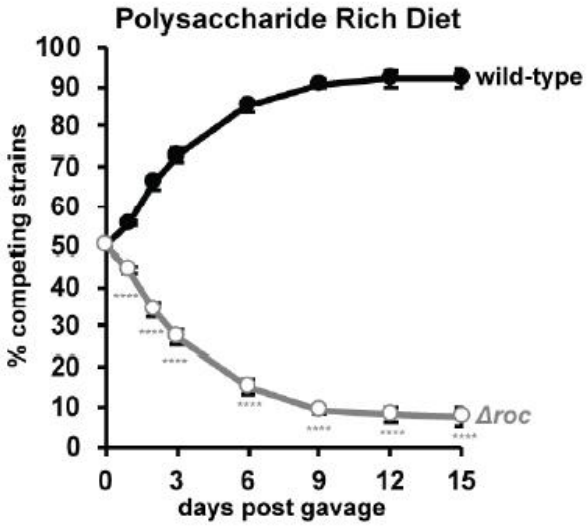
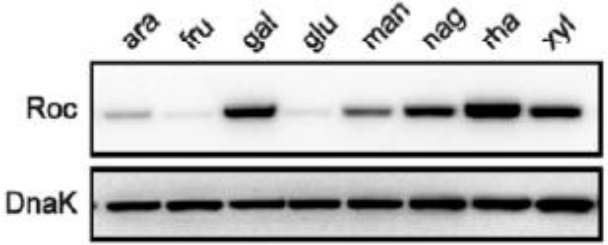
PNAS January 2, 2019 116 (1) 233-238; first published December 17, 2018; https://doi.org/10.1073/pnas.1813780115

Colonization factor, BT3172 gene, herein named **ROC** for "regulator of colonization," is required for ***B. thetaiotaomicron*** colonization of germ-free mice fed a polysaccharide-rich diet.

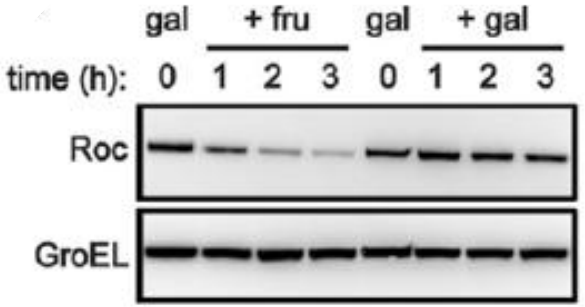


Sonnenburg ED, et al. A hybrid two-component system protein of a prominent human gut symbiont couples glycan sensing in vivo to carbohydrate metabolism. PNAS, (2006) .

Glucose and fructose suppress the ROC



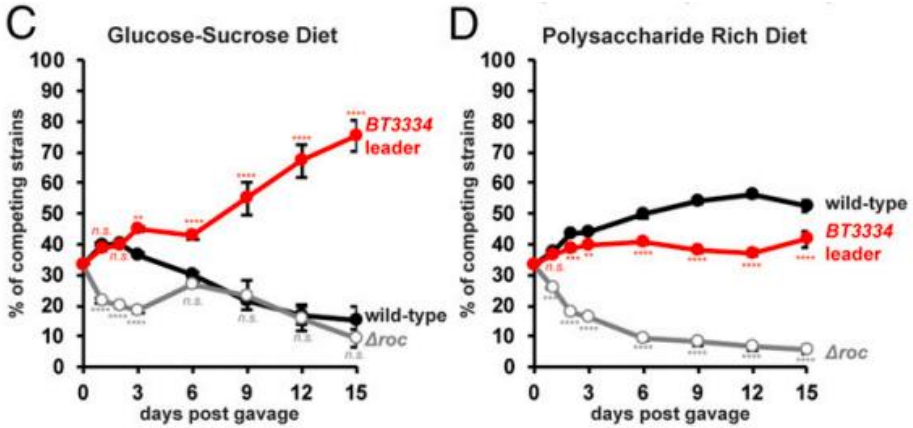
WB analysis of crude extracts from *B. thetaiotaomicron* grown to midexponential phase in minimal media monosaccharides



WB analysis of crude extracts from *B. thetaiotaomicron* grown in 0.25% galactose (0 h) and following addition of either 0.25% fructose or 0.25% galactose (1–3 h).

Townsend, Guy E., et al. "Dietary sugar silences a colonization factor in a mammalian gut symbiont." *PNAS*(2019).

Glucose and fructose suppress the ROC, affect gut colonization



Relative abundance of wild-type *B. thetaiotaomicron*, a strain deleted in the roc gene (Δroc;), and an engineered strain with the **roc leader replaced by the BT3334 leade**r determined by qPCR from genomic DNA prepared from fecal samples.

Dietary sugars
Glucose and fructose

⇩

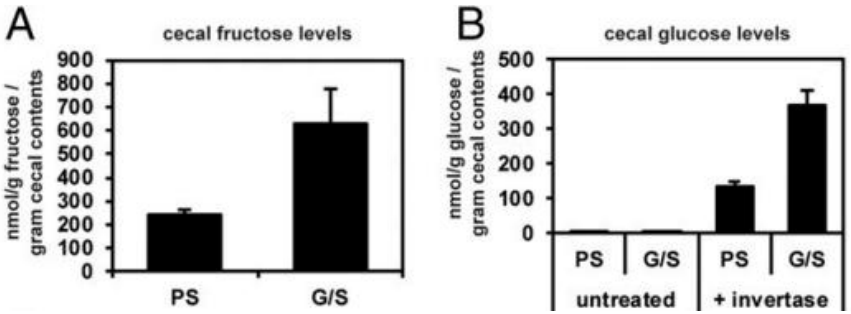
Colonization Factor
ROC

⇩

Gut commensal fitness

Townsend, Guy E., et al. "Dietary sugar silences a colonization factor in a mammalian gut symbiont." *PNAS*(2019).

Fructose is more risky



(A) The amounts of fructose per gram of cecal material from mice fed either a polysaccharide-rich or glucose–sucrose diet. (B) The amounts of glucose per gram of cecal material from mice fed either a polysaccharide-rich or glucose–sucrose diet before or after the addition of invertase

- Consumption of too much fructose can develop nonalcoholic fatty liver disease.

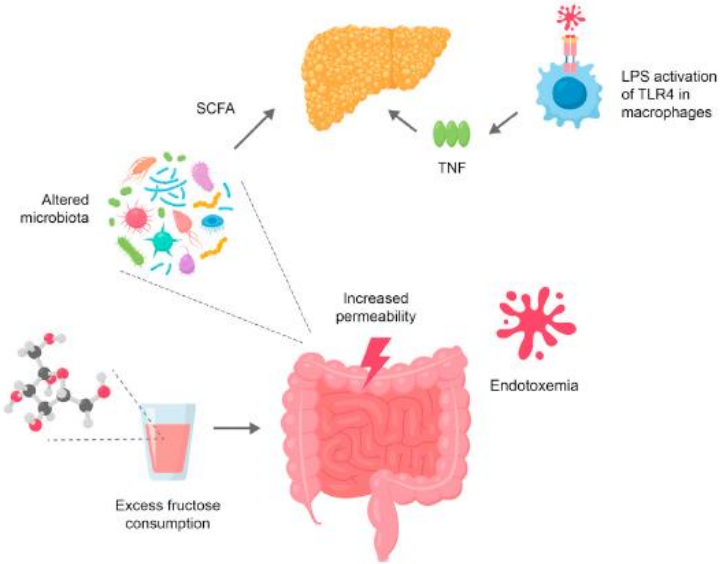
Townsend, Guy E., et al. "Dietary sugar silences a colonization factor in a mammalian gut symbiont." *PNAS*(2019).

Cell Metabolism

Perspective

"Sweet death": Fructose as a metabolic toxin that targets the gut-liver axis

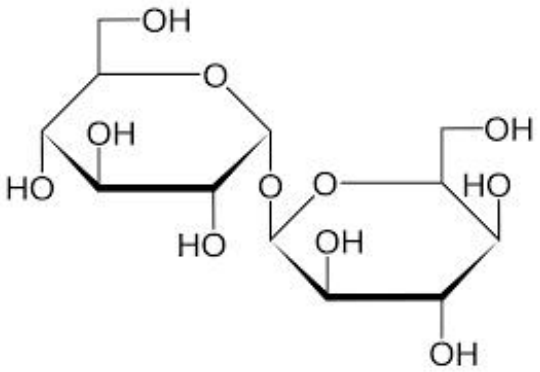
Mark A. Febbraio[1,*] and Michael Karin[2,*]
[1]Monash Institute of Pharmaceutical Sciences, Monash University, Parkville, VIC, Australia
[2]Department of Pharmacology, School of Medicine, University of California, San Diego, San Diego, CA, USA
*Correspondence: mark.febbraio@monash.edu (M.A.F.), mkarin@health.ucsd.edu (M.K.)
https://doi.org/10.1016/j.cmet.2021.09.004



2. Dietary trehalose affect the bacterial virulence?

Let’s start…

Dietary sugar: trehalose



- **Trehalose** is a sugar consisting of two molecules of glucose.
- In 2000, US FDA approved trehalose as a food additive and considered to be safe to human.

Published: 03 January 2018

Dietary trehalose enhances virulence of epidemic *Clostridium difficile*

J. Collins, C. Robinson, H. Danhof, C. W. Knetsch, H. C. van Leeuwen, T. D. Lawley, J. M. Auchtung & R. A. Britton

Nature **553**, 291–294 (2018) | Cite this article

25k Accesses | **177** Citations | **1178** Altmetric | Metrics

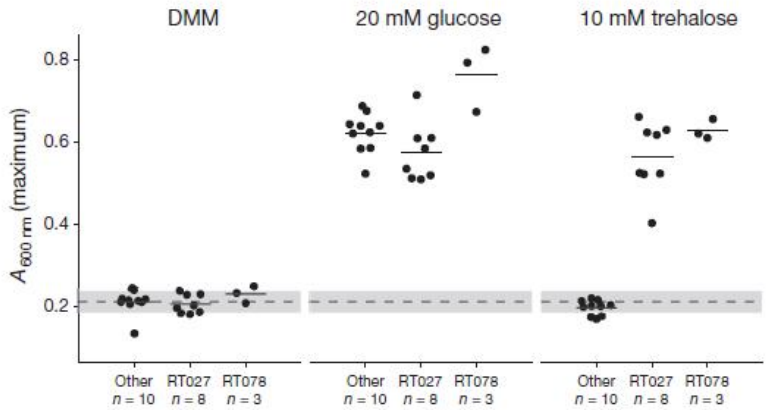
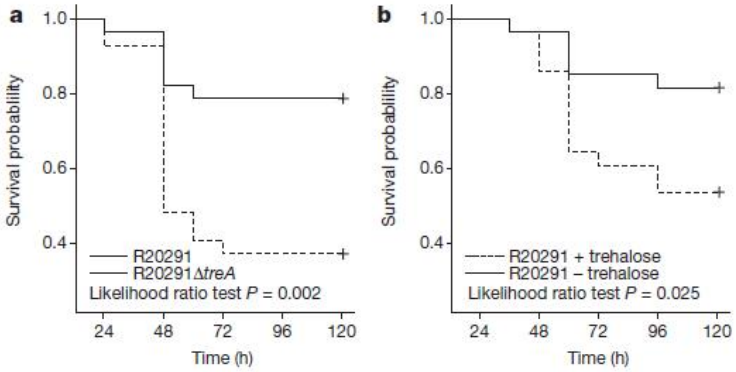


Figure 1 | Only RT027 and RT078 strains show enhanced growth on 10 mM trehalose. Dashed grey line and band indicate mean growth and s.d. in DMM without a carbon source for all samples ($n = 21$). Solid lines are mean growth yield (absorbance at 600 nm, $A_{600\ nm}$) for groups: non-RT027/078 ($n = 10$), RT027 ($n = 8$), and RT078 ($n = 3$). All points represent biologically independent samples.

- 21 *C. difficile* strains encompassing 9 ribotypes were grown on a defined minimal medium (DMM) supplemented with glucose or trehalose as the sole carbon source.
- Two epidemic stains RT027 and RT078 can use trace amount of trehalose.

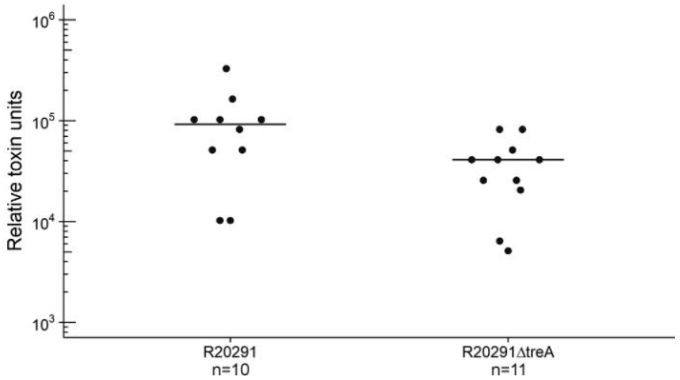
Trehalose metabolism increases virulence

Higher mortality



- Mice infected with R20291 (RT027) have a significantly higher risk of mortality when trehalose is supplemented in the diet.

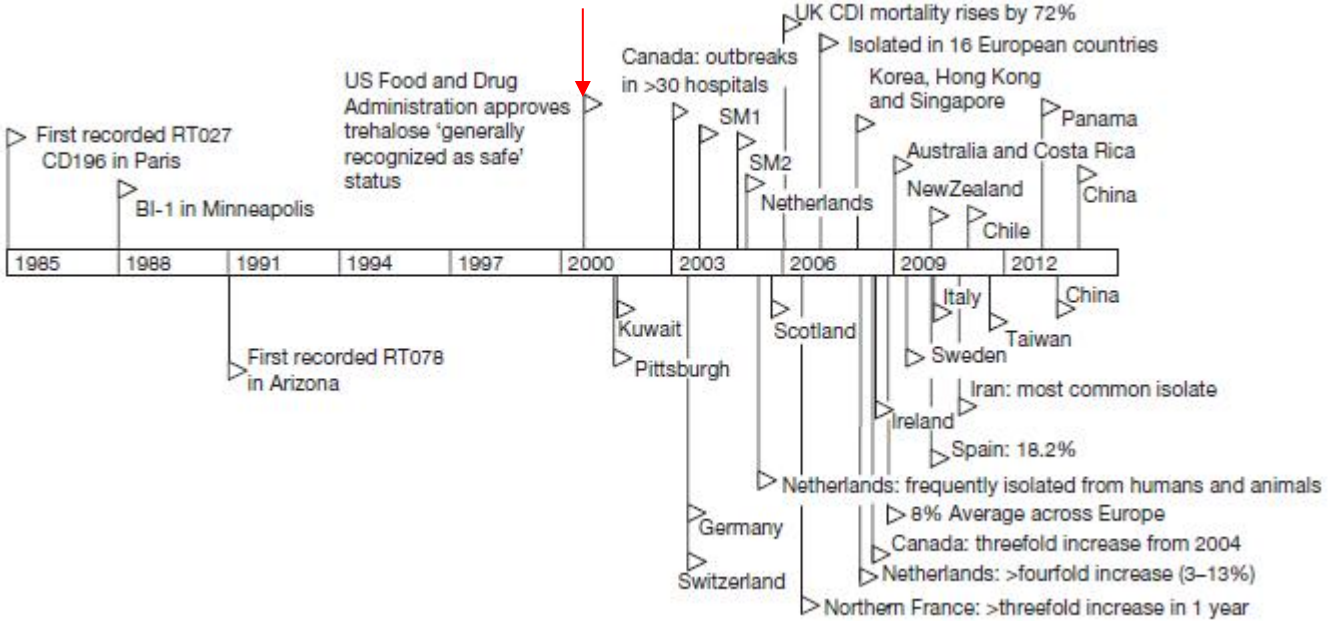
Higher Toxin



- Mice were gavaged with 10^4 spores of either R20291 or R20291ΔtreA and provided with 5 mM trehalose in drinking water.

Collins, J., et al. "Dietary trehalose enhances virulence of epidemic Clostridium difficile." *Nature* (2018).

Timeline of trehalose adoption and spread of RT027 and RT078 lineages



- *The widespread adoption and use of trehalose in the diet coincides with the emergence of both RT027 and RT078 outbreaks*

Collins, J., et al. "Dietary trehalose enhances virulence of epidemic Clostridium difficile." *Nature* (2018).

3. Artificial Sweeteners affect gut microbiota composition and function

Saccharin…

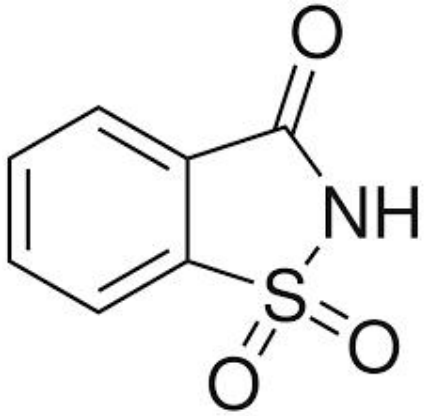
Published: 17 September 2014

Artificial sweeteners induce glucose intolerance by altering the gut microbiota

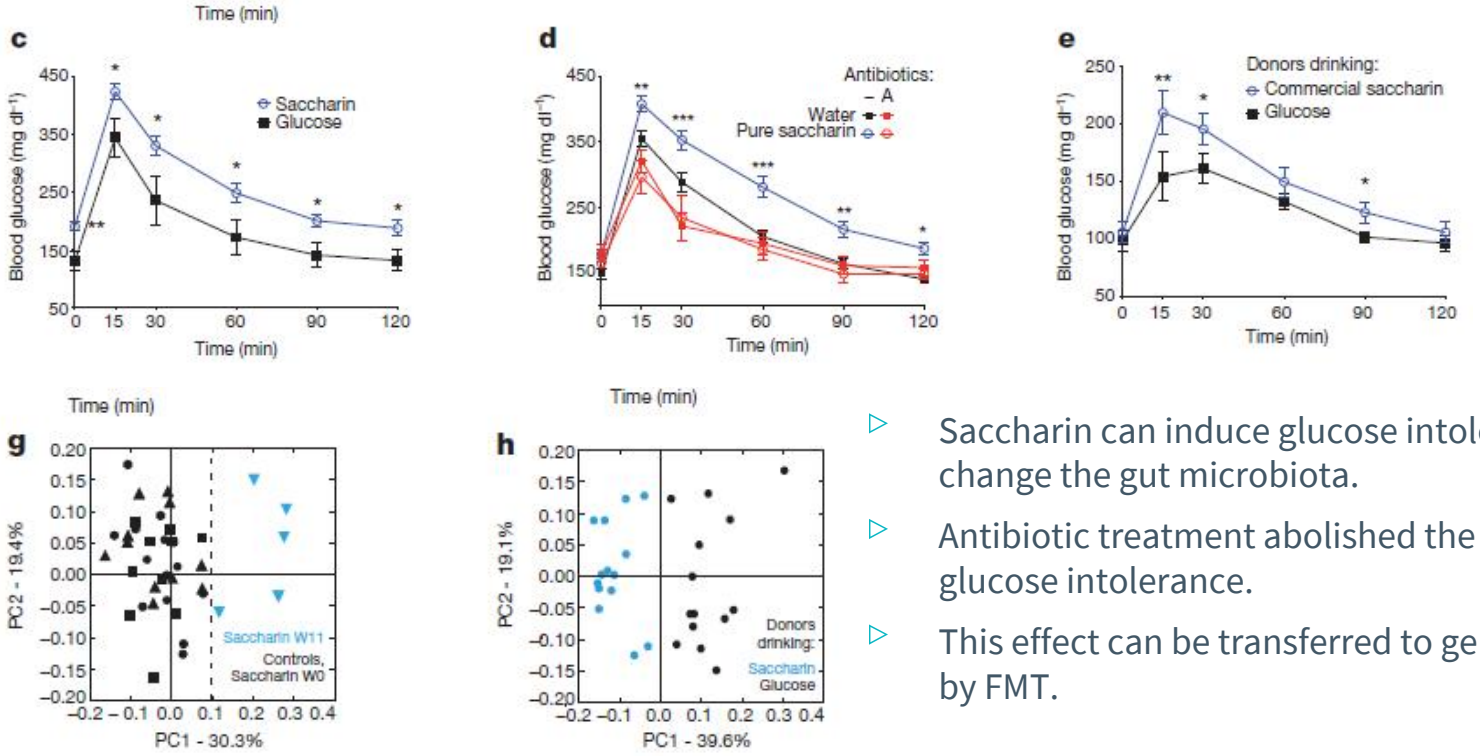
Jotham Suez, Tal Korem, David Zeevi, Gili Zilberman-Schapira, Christoph A. Thaiss, Ori Maza, David Israeli, Niv Zmora, Shlomit Gilad, Adina Weinberger, Yael Kuperman, Alon Harmelin, Ilana Kolodkin-Gal, Hagit Shapiro, Zamir Halpern, Eran Segal ✉ & Eran Elinav ✉

Nature **514**, 181–186 (2014) | Cite this article

Saccharin is an artificial sweetener with effectively no food energy. It is about 300–400 times as sweet as sucrose.



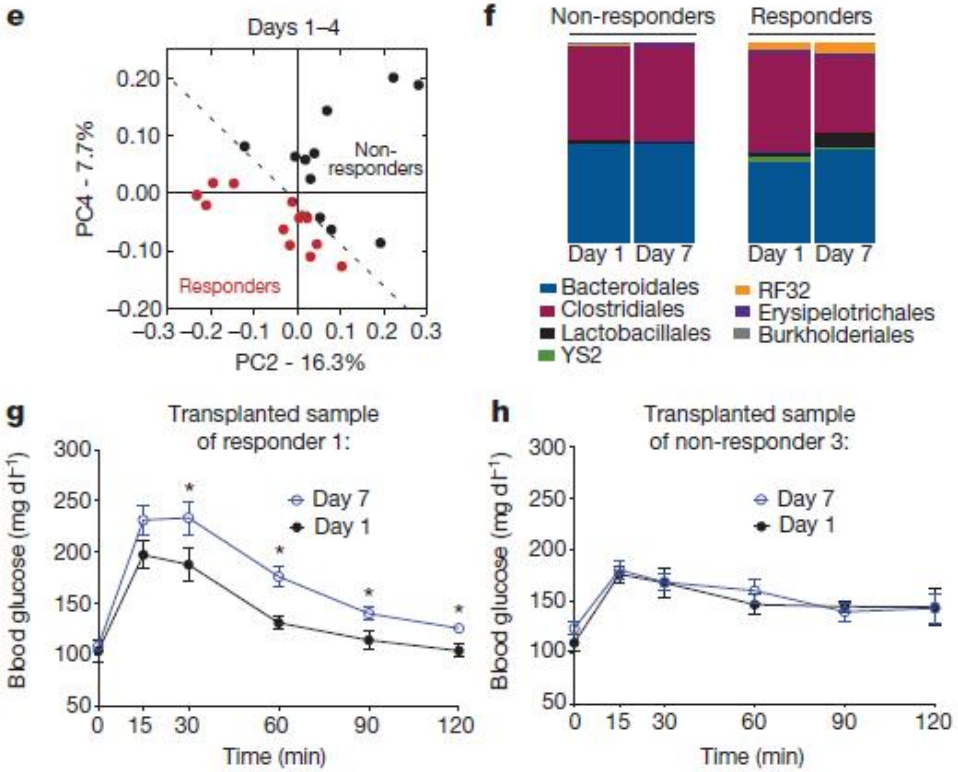
Saccharin induce glucose intolerance transferable to germ-free mice



- Saccharin can induce glucose intolerance and change the gut microbiota.
- Antibiotic treatment abolished the difference in glucose intolerance.
- This effect can be transferred to germ-free mice by FMT.

Suez, Jotham, et al. "Artificial sweeteners induce glucose intolerance by altering the gut microbiota." *Nature* 514.7521 (2014)

Saccharin in humans associate with impaired glucose tolerance

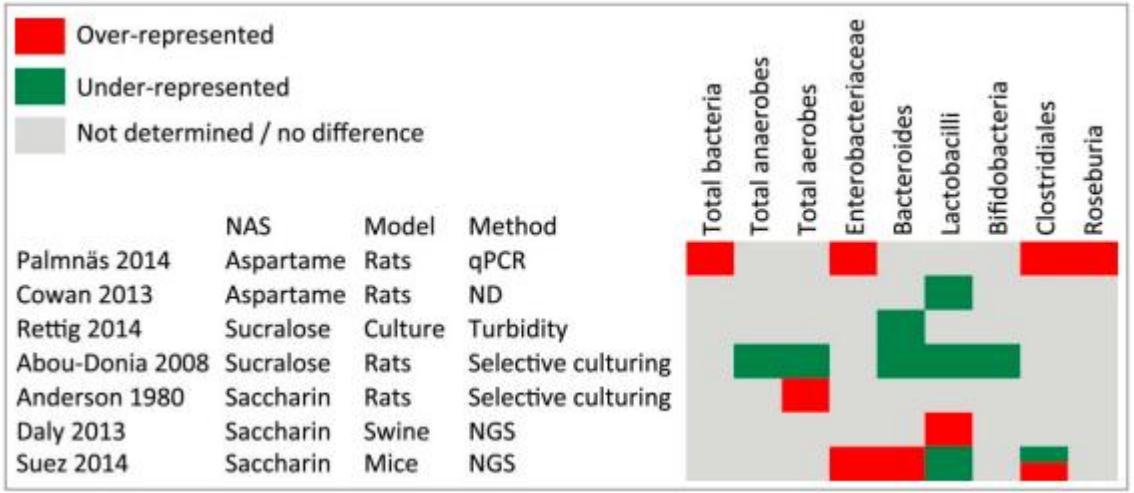


- Four out of seven healthy participants showed disrupted gut bacteria balance and poorer blood sugar control.
- When gut bacteria from these people were transferred into mice, the animals also developed poor blood sugar.

Suez, Jotham, et al. "Artificial sweeteners induce glucose intolerance by altering the gut microbiota." *Nature* 514.7521 (2014)

Artificial Sweeteners-Microbes interaction

Summary of studies describing effects of AS on members of the microbiome or bacteria in culture.



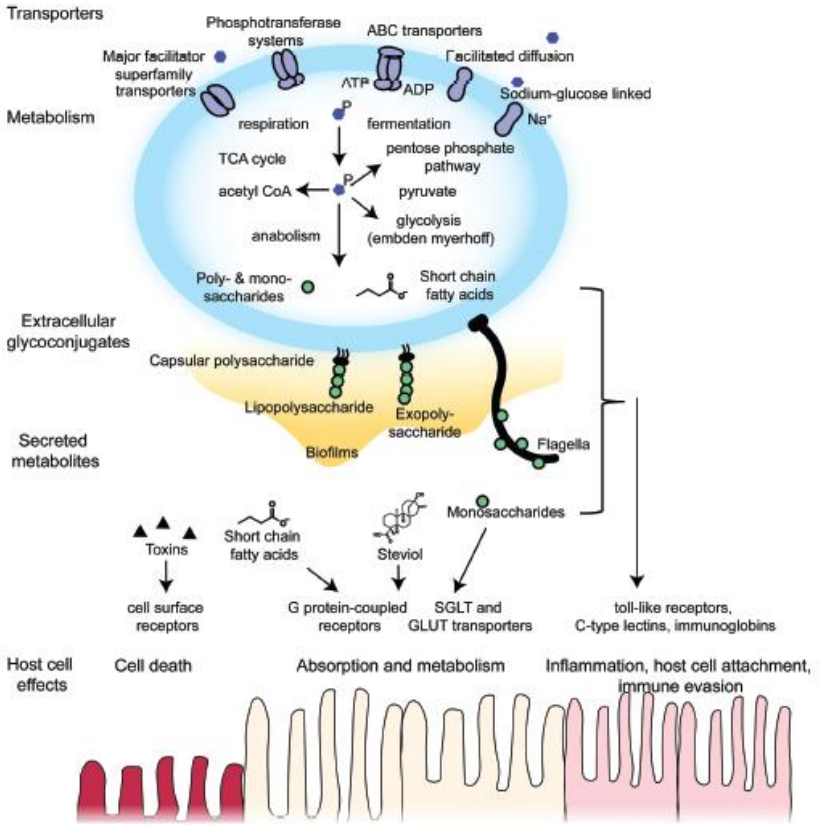
	NAS	Model	Method
Palmnäs 2014	Aspartame	Rats	qPCR
Cowan 2013	Aspartame	Rats	ND
Rettig 2014	Sucralose	Culture	Turbidity
Abou-Donia 2008	Sucralose	Rats	Selective culturing
Anderson 1980	Saccharin	Rats	Selective culturing
Daly 2013	Saccharin	Swine	NGS
Suez 2014	Saccharin	Mice	NGS

ND, no data; NGS, Next generation sequencing.

A **controversial** issue

Suez, Jotham, et al. "Non-caloric artificial sweeteners and the microbiome: findings and challenges." *Gut microbes* 6.2 (2015

Summary



Take-home message:

- Sugar consumption one day: < 50 g, 12 teaspoons;
- Fructose is bad than glucose;
- Avoid trehalose, especially during *C. diff* infection;
- Avoid artificial sweeteners e.g., saccharin.

Di Rienzi, et al. "Adaptation of the gut microbiota to modern dietary sugars and sweeteners." *Advances in Nutrition* (2020)

THANKS!

Any questions?