

POSTBIOTICS +
postbioticsplus.com

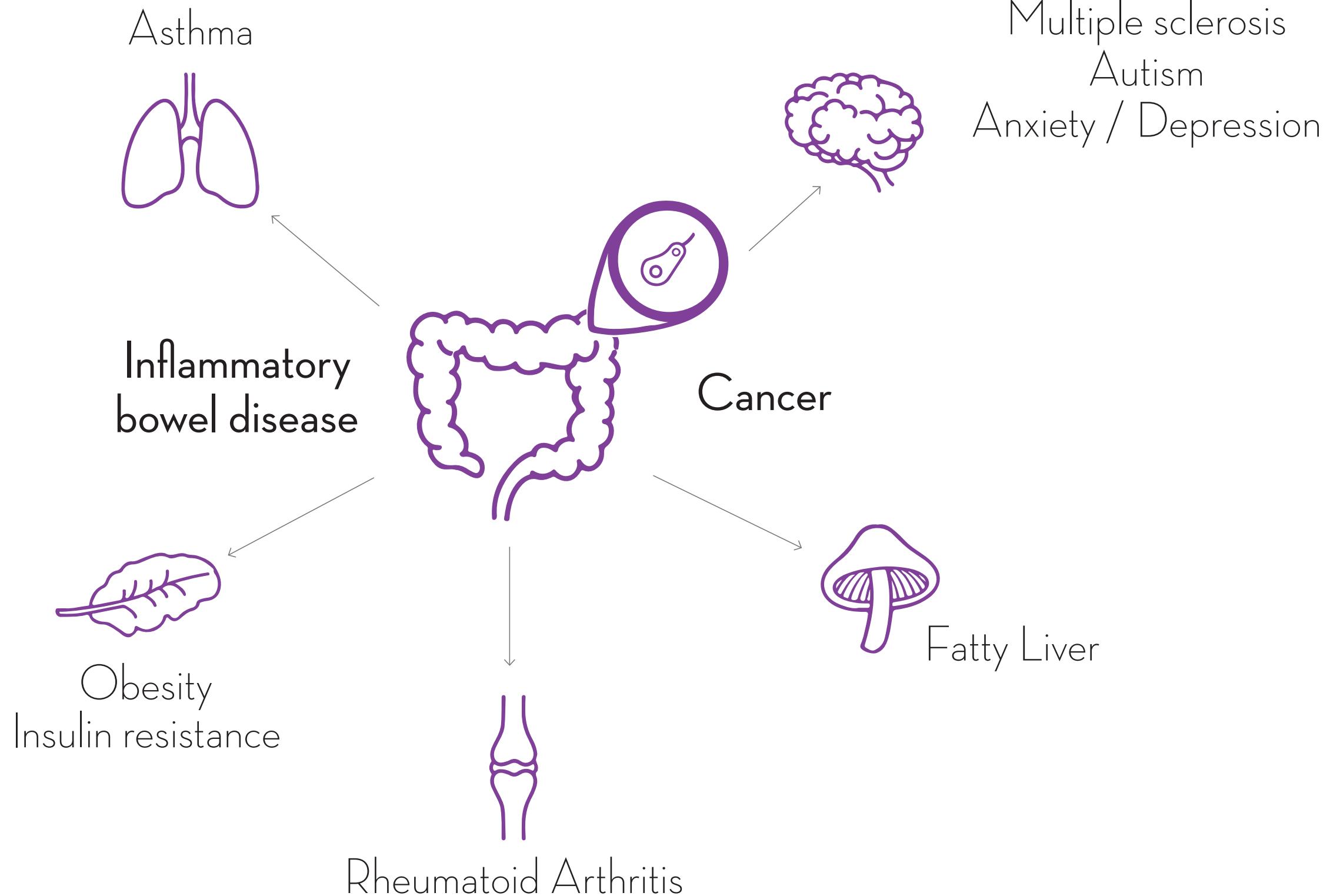
WHY POSTBIOTICS ARE
PROBIOTICS 2.0

Trends in probiotics

- Started out as digestive, but moving toward new claims and new categories
- Consumers have realized that gut health is related to women's health, mood, skin
- And that the microbiome can influence the immune system and inflammation
- Probiotics come in food and drinks that are convenient and taste good
- New strains and new ways to differentiate, like synbiotics

HIPPOCRATES

All disease begins in the gut



When probiotics
eat prebiotics (fiber),
they create the good stuff,
postbiotics.



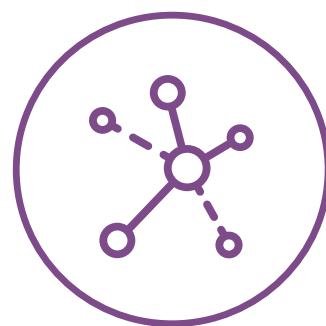
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PROBIOTICS

(microbes)

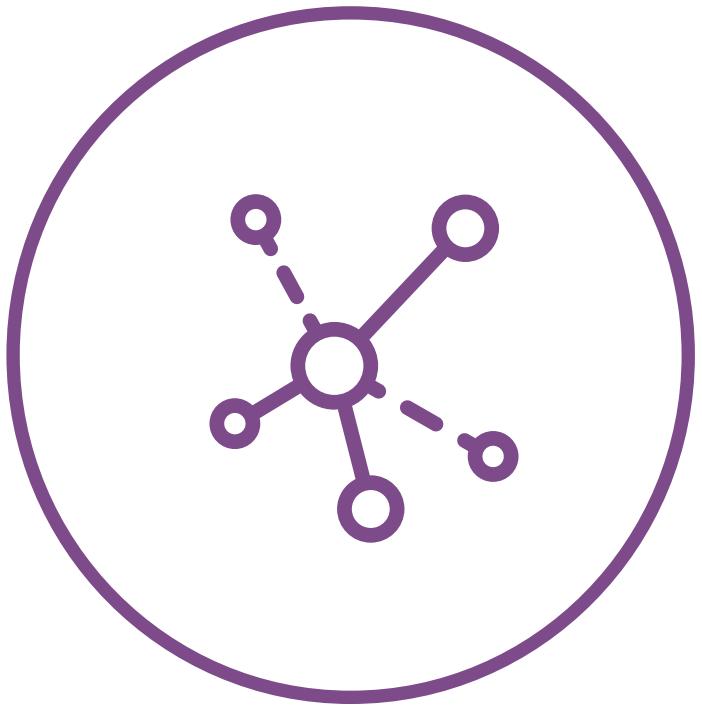
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POSTBIOTICS

(metabolites)

Calpis-
prehypertensive



Postbiotics are metabolic byproducts secreted by probiotics during fermentation, or released after cell lysis, that positively effect the host locally and systemically.

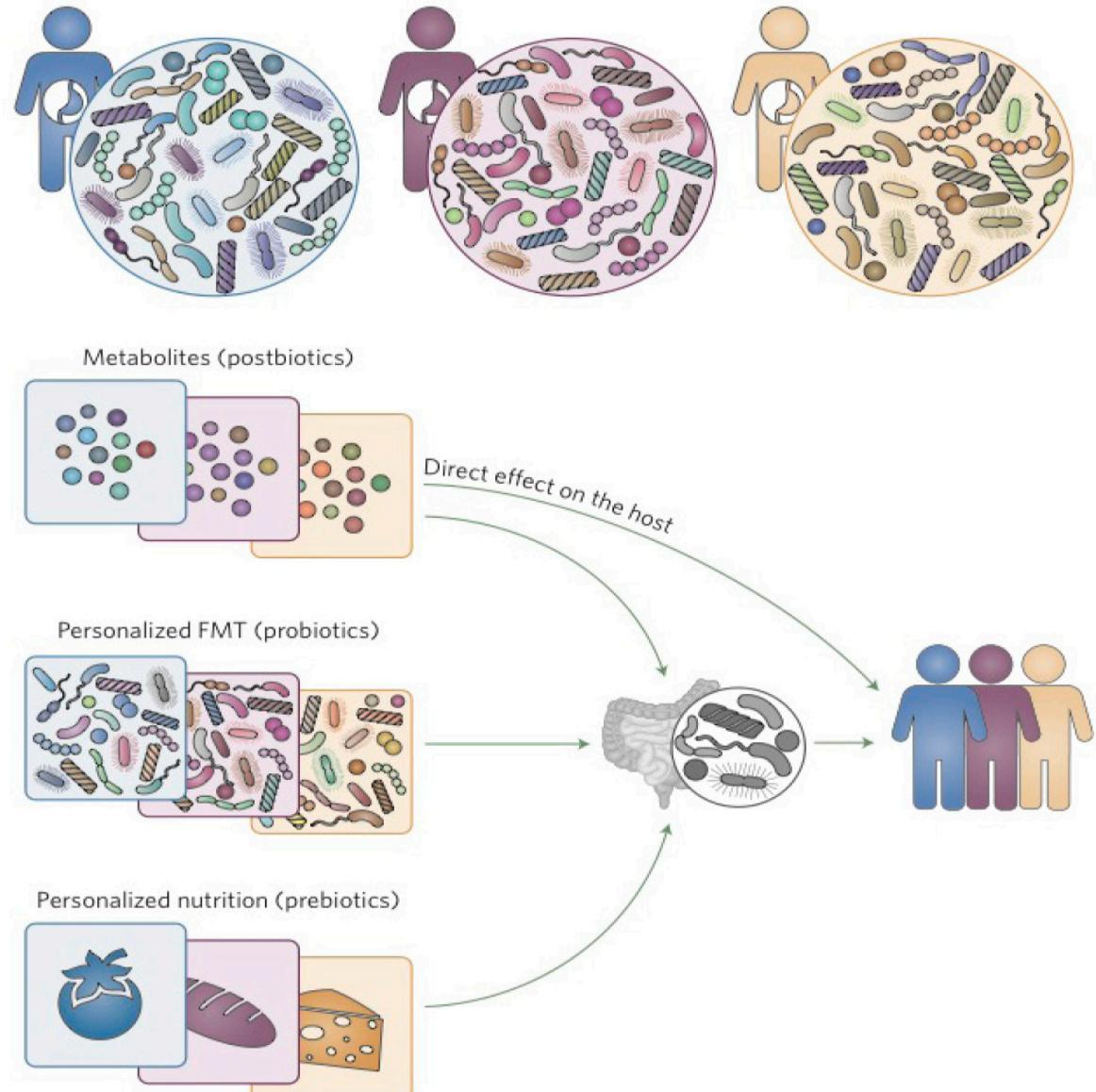
What is a postbiotic?

the good stuff bacteria create



- cell lysis
- inactivated probiotics
- probiotics cell wall
- metabolites
- quorum sensing molecules
- exopolysaccharide
- probiotic cell-free supernatants
- bacteriocins

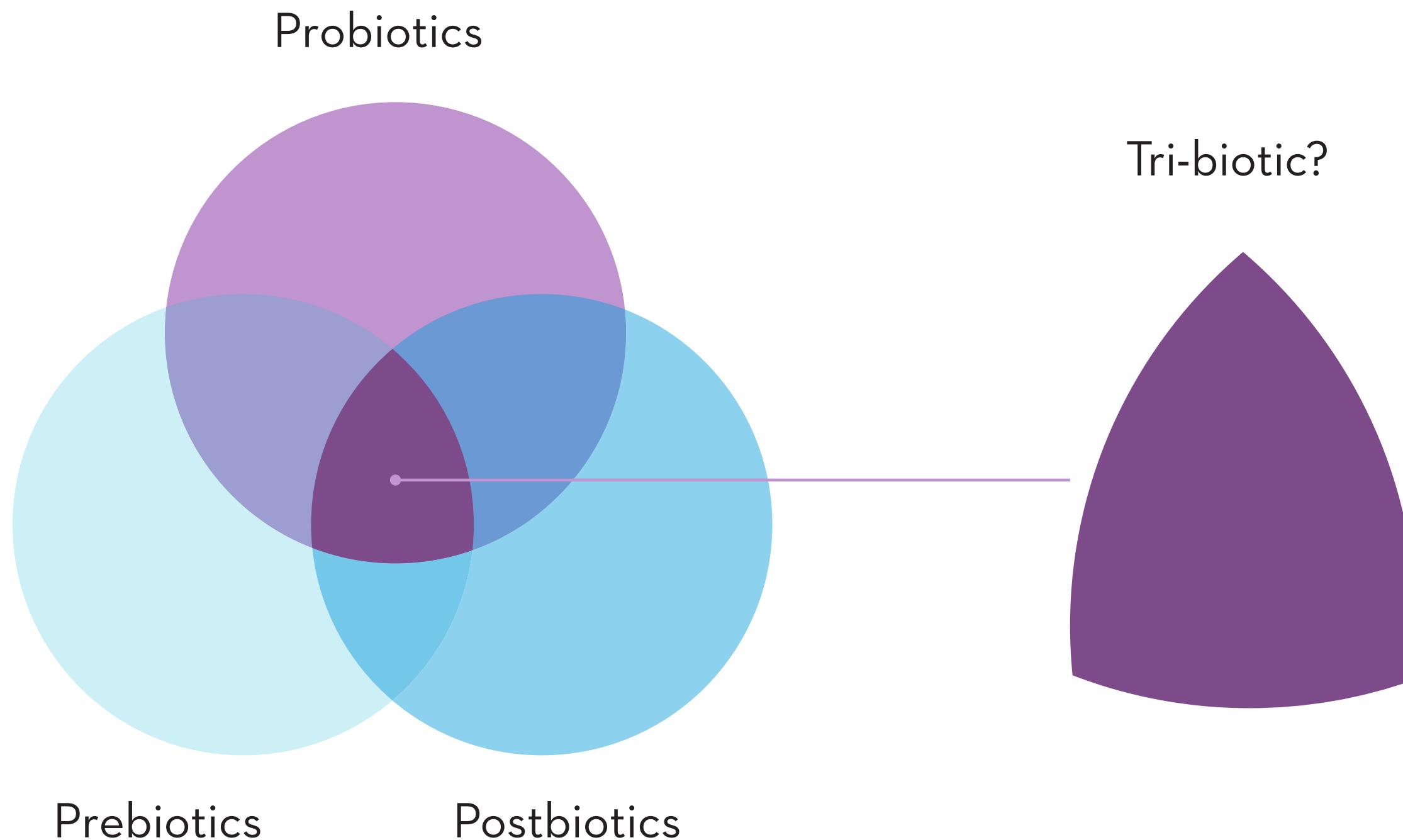
How do they work?



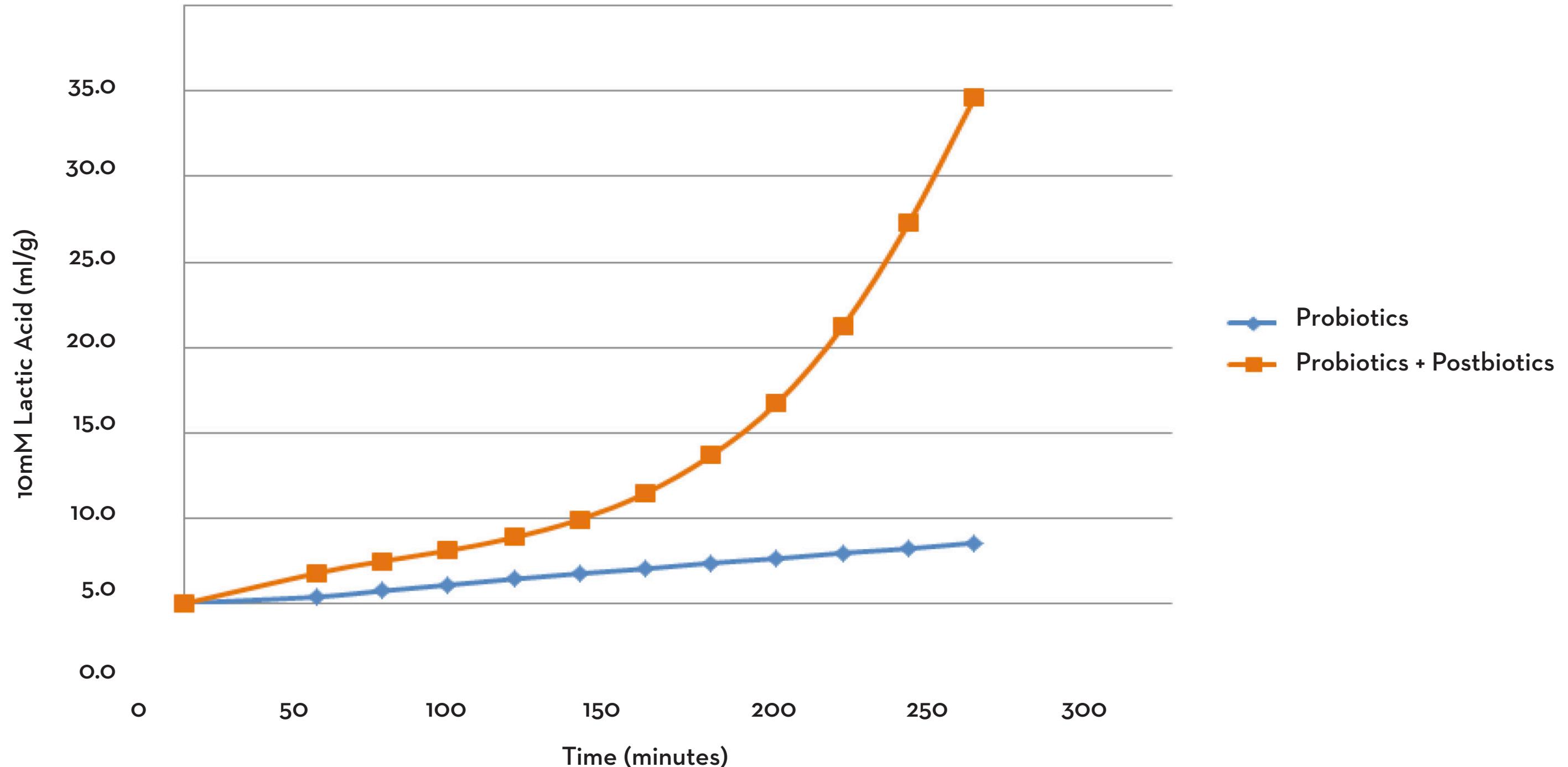
NATURE MICROBIOLOGY 2, 17075 (2017) |
DOI: 10.1038/nmicrobiol.2017.75 | www.nature.
com/naturemicrobiology

- reduce inflammation
- stimulate the immune system
- directly affect the body
- promote probiotic growth in the gut
- support a healthy gut lining
- provide bioavailable vitamins and nutrients
- support mood with GABA, dopamine, and other neurotransmitters
- support a healthy ecosystem

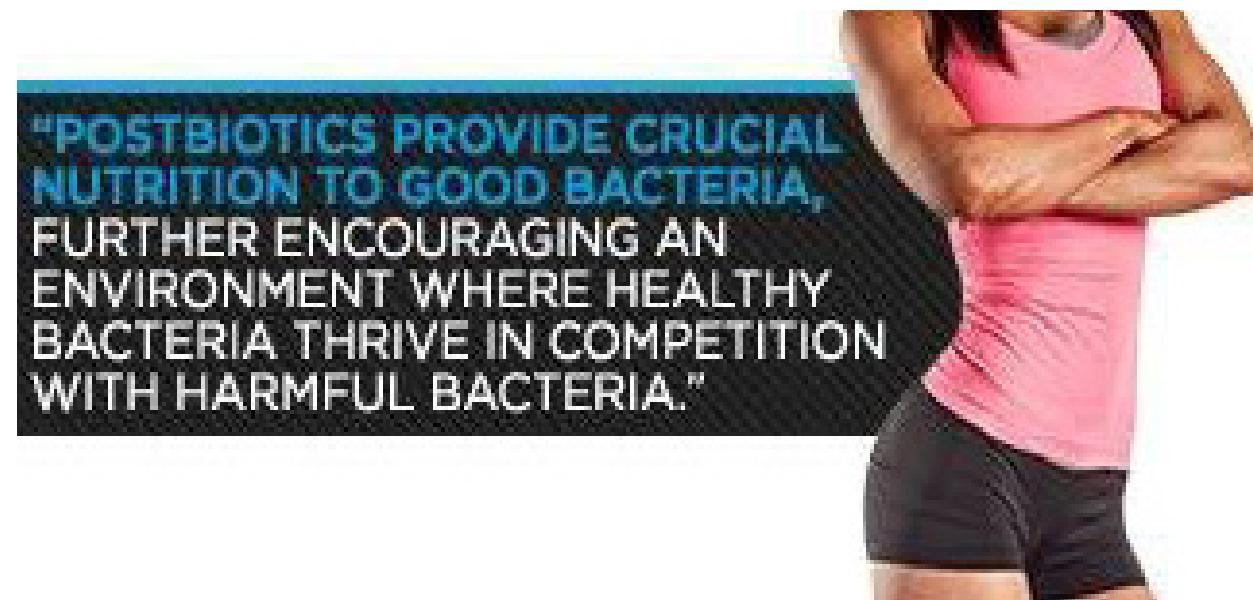
“metabolite treatment may enable an improved efficacy when coupled with other microbiome-based treatments, such as probiotics and nutritional interventions.”



POSTBIOTICS + Postbiotics boost probiotic activity



What people are saying...



SCIENCE

Contents ▾ News ▾ Careers ▾ Journals ▾

SHARE WEBINAR | TECHNOLOGY

The new era of postbiotics: Gut microbiome-derived lipid metabolites for health and wellness

This webinar is brought to you by the Science/AAAS Custom Publishing Office

Postbiotics Is the Latest Beauty "Buzzword" You Need to Know

by VICTORIA HALL | UPDATED 04/30/19 | PRODUCT DISCLOSURE 

Are Postbiotics the Long Sought-After Solution for a Leaky Gut?

Rachel Claire Anderson 

1st GENERATION

PREBIOTIC

Substance that induce the growth or activity of micro-organism

PROBIOTIC

Live organism that when administered confer a **general** health benefit to the host

2nd GENERATION

PROTEOBIOTIC

Natural molecules from probiotics that confer a **specific** health benefit

EXPLAINING POSTBIOTICS

FOOD for your beneficial bacteria

FERMENTATION by your beneficial bacteria

Production of beneficial POSTBIOTIC compounds

PREBIOTICS

To have a healthy microbiome you **MUST** feed your probiotic bacteria well! Probiotic bacteria thrive on non-digestible carbohydrates or non-digestible fiber.



PROBIOTICS

Live microorganisms that confer a health benefit on the host. Different bacteria produce different metabolites so diversity is very important!



POSTBIOTICS

Postbiotics are the key regulators of gastrointestinal health! Probiotic bacteria produce numerous classes of postbiotic compounds.



TYPES OF POSTBIOTICS



VARIOUS NUTRIENTS

B-vitamins, vitamin K and various amino acids

ANTIMICROBIAL PEPTIDES

Natural antibiotics that suppress the growth of bad bacteria.

SHORT CHAIN FATTY ACIDS

Optimize acid/base balance in GI tract, promote growth of good bacteria, and suppress pathogens!

CARBOHYDRATE-ACTIVE ENZYMES

Helps probiotics digest fibers to produce postbiotics

HYDROGEN PEROXIDE

Suppresses the growth of Candida and other yeasts

TOP SOURCES OF POSTBIOTICS



Dr. Axe
FOOD IS MEDICINE

- ▶ Spirulina and chlorella
- ▶ Mycelium, which produces mushrooms
- ▶ Grape pomace
- ▶ Fermented aloe
- ▶ Shilajit
- ▶ Apple cider vinegar and coconut vinegar
- ▶ Humic and fulvic acid
- ▶ Bacterial protease
- ▶ Saccharomyces enzymes
- ▶ Grow BioGurt Nutrients

“During fermentation, these bacteria synthesize vitamins and minerals, produce biologically active peptides with enzymes such as proteinase and peptidase, and remove some non-nutrients.”

Sources of Postbiotics

Because postbiotics are a byproduct of probiotic fermentation, the direct source of postbiotics are probiotics. Foods that can help increase the concentration of postbiotics in the gut are (9):

- Yogurt
- Sauerkraut
- Miso soup
- Soft Cheeses
- Kefir
- Sourdough bread
- Buttermilk
- Pickles
- Tempeh

Additionally, postbiotics can be produced and extracted in laboratories to be used for therapeutic purposes, and delivered through pills and direct application (10).

The advantages of a postbiotic

- Shelf Stable
- Safer for compromised populations
- Added benefits with probiotics
- Easier to manufacture, package, store, and define

Could be the answer to worries about excessive immune stimulation, systemic infections, and horizontal gene transfer.

Interest in Postbiotics is Growing, March 27, 2019

“

For about 75% of the studies that included a comparison to a live microbe, no difference in efficacy between the live and killed microbe was observed.

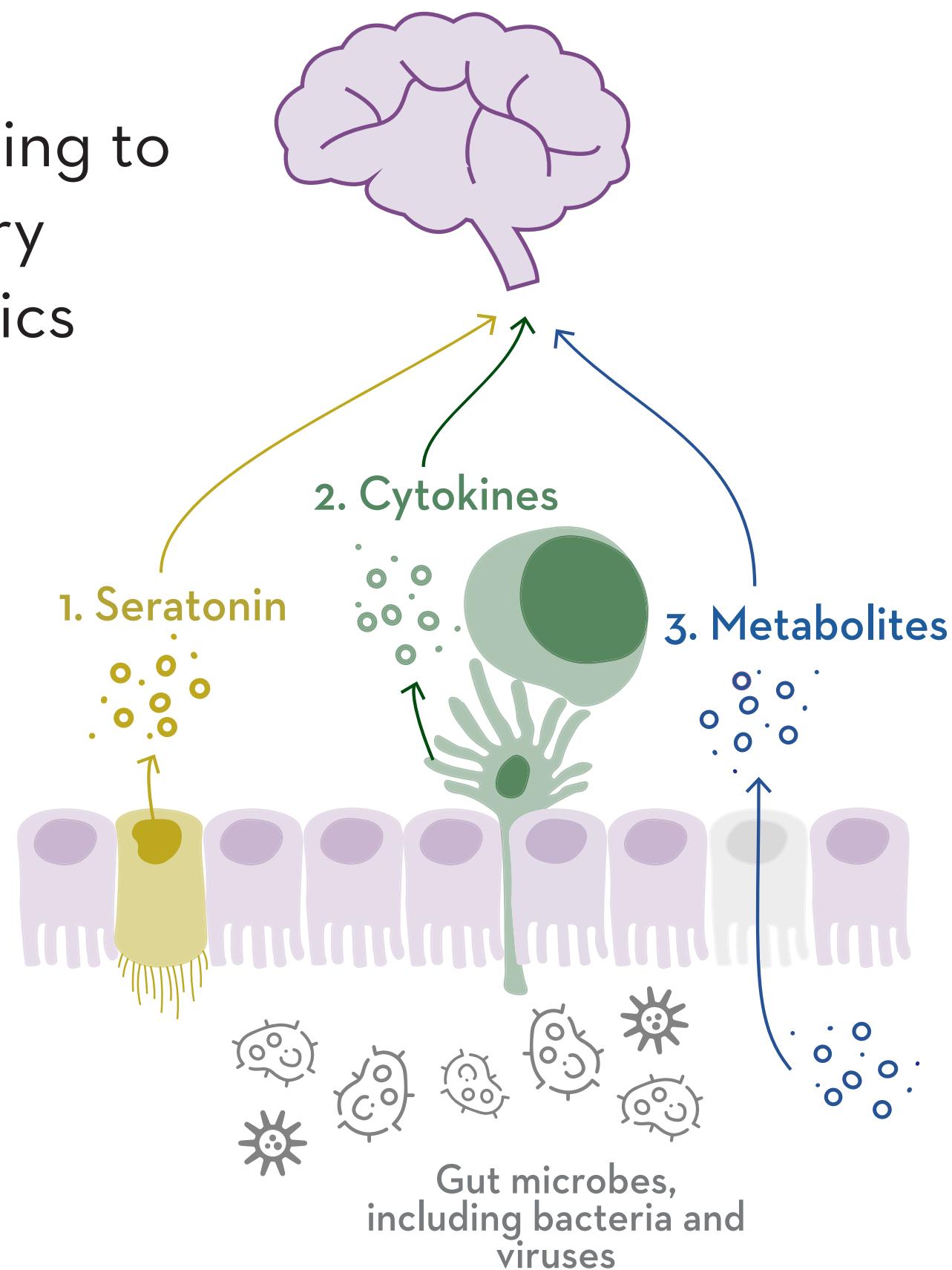
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About 40% of comparisons favored the postbiotic over the placebo or live microbe, supporting the idea that postbiotics may be a legitimate functional ingredient.

- Mary Ellen Sanders, PhD , Dairy & Food Culture Technologies

“Postbiotics have the same mechanism of action and capacity as probiotics owing to the presence of secondary metabolites from probiotics but without a living cell.”

Animals 2019, 9, 644



1. Peripheral Serotonin

Cells in the gut produce large quantities of the neurotransmitter serotonin, which may have an effect on signaling in the brain.

2. Immune System

The intestinal microbiome can prompt cells to produce cytokines that can influence neurophysiology.

3. Bacterial Molecules

Microbes produce metabolites, such as butyrate, which can alter the activity of cells in the blood-brain barrier.

Where they are being used currently

- Food and Beverage
- Baby formula
- Animal feed
- Cosmetics/Skin Care
- Dietary Supplements

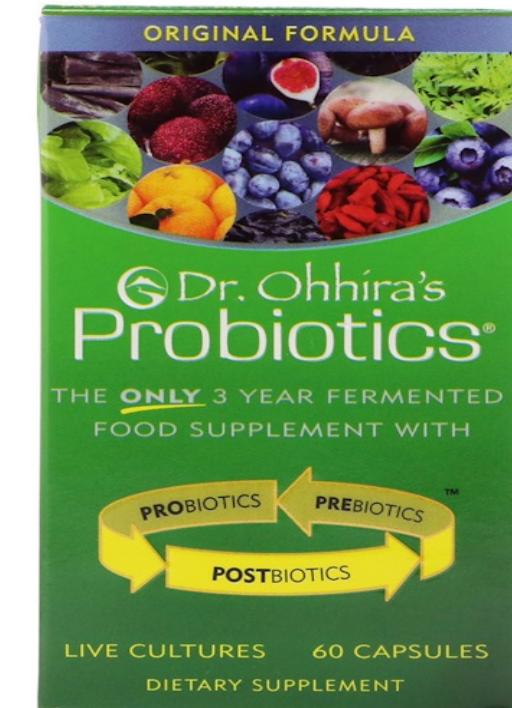
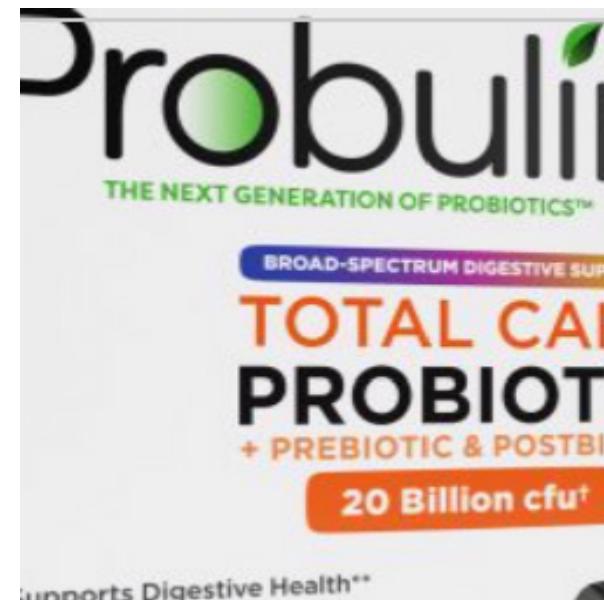
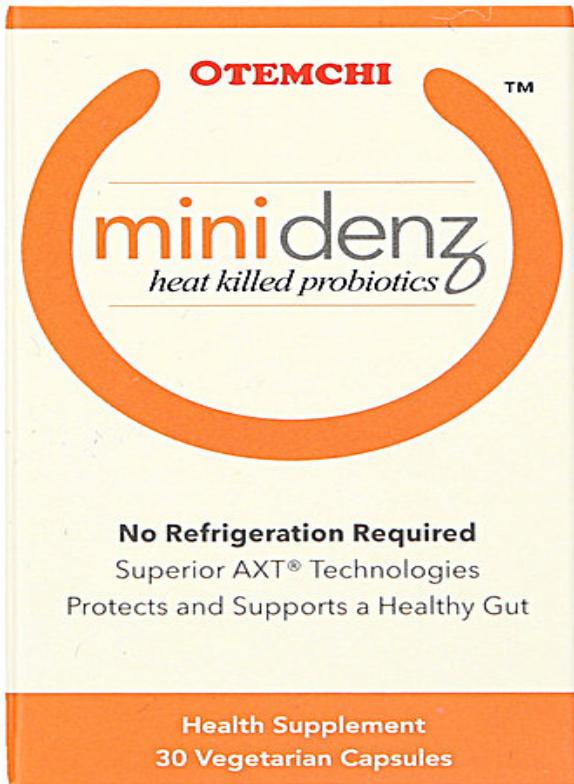
Next generation of infant formula - prebiotics, postbiotics and HMOs to support the immune system through the gut

Prof. Hania Szajewska (Chair)

The Medical University of Warsaw, Department of Paediatrics, Poland

“Thus, opportunities for further improvement of infant formulas exist. Despite the challenges, research on further improving infant formulas continues. Among others, efforts focus on metabolic programming and the potential impact on infant gut microbiota of adding probiotics, prebiotics, including human milk oligosaccharides, or postbiotics.”





PREMIER
RESEARCH LABS

Premier Fermented Greens Capsules

Fermented Multi-Greens With Probiotics, Prebiotics & Postbiotics

**DIETARY SUPPLEMENT
150 PLANT-SOURCE CAPSULES**

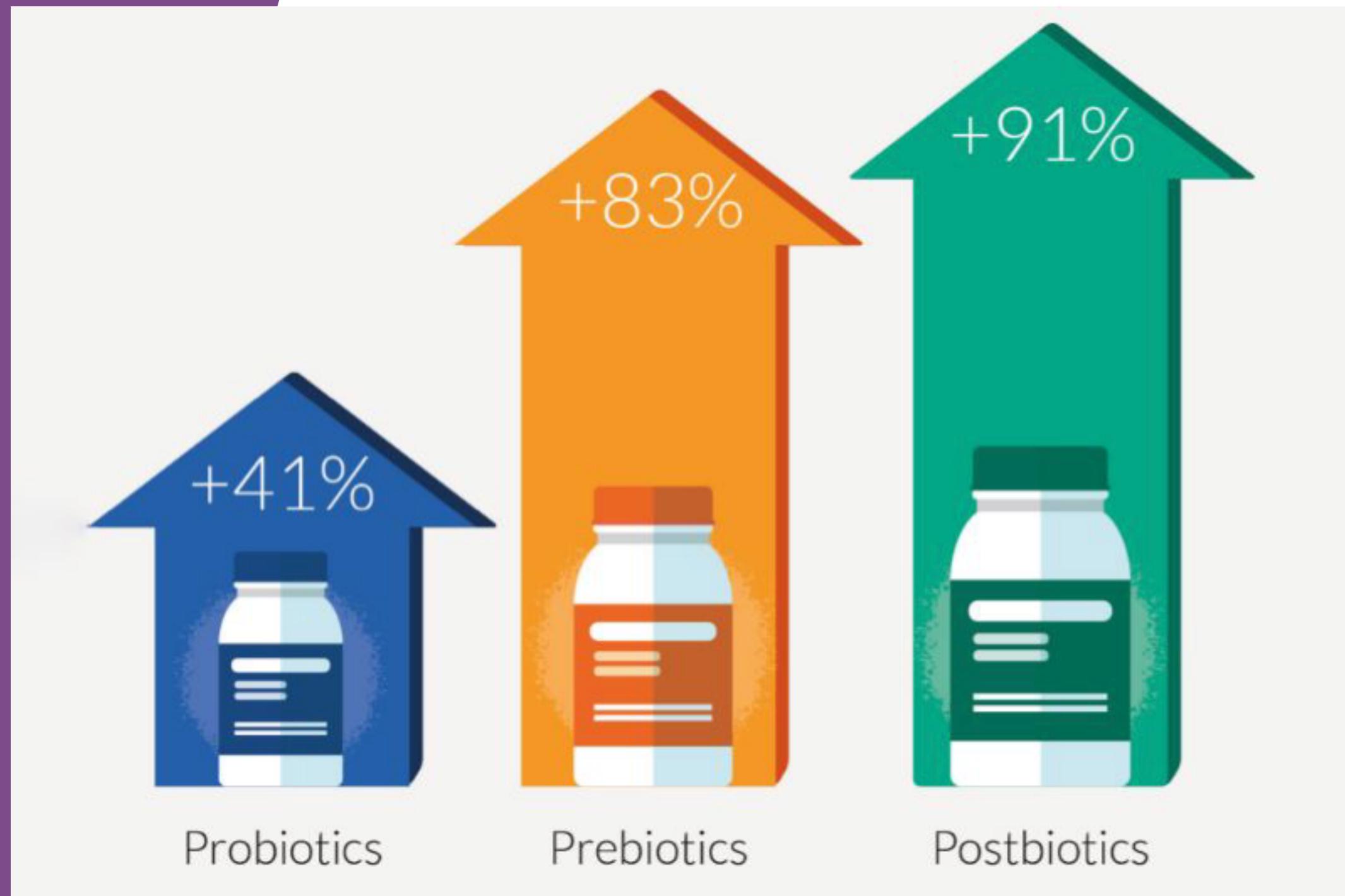
- PIL's Quality Guarantee**
 - Pure Vegan**
 - NON-GMO**
 - Gluten Free**
 - Soy Free**
 - Purity Verified**
 - No Chemical or Radiation Sterilization**
 - Pathogen Microbiology Performed**
 - Heavy Metal Tested**
 - FDA-Monitored cGMP Facility**



How postbiotics are labeled?

- Heat killed probiotics
- Sterilized probiotics
- Heat treated probiotics
- Inactivated probiotics
- Metabolites by name
- Fermented ingredients

What people are saying?



Source: MINTEL, Aug 2019 Report

Base: mentions of probiotics, prebiotic and postbiotics on Instagram, Pinterest and Twitter, July 2018-19

Original Source: Wageningen Academic; Science Direct; Infegy/Mintel (Digestive Health, Social media, US, August 2019)

Studies on postbiotics

Animal Feed:

Subsequently, postbiotics, which are metabolites of probiotics, have been used as feed additives in livestock as a potential replacement for antibiotics and probiotics.

The presence of antimicrobial metabolites, such as organic acids and bacteriocins, in postbiotics can reduce the gut pH and inhibit the proliferation of opportunistic pathogens in the feed and gut of animals.

Lactobacillus rhamnosus GG with a beneficial effect on intestinal barrier function:

Recently, increasing evidence supports the notion that certain probiotic-derived components, such as bacteriocins, lipoteichoic acids, surface layerprotein and secreted protein, have a similar protective role on intestinal barrier probiotics. These bioactive components have been named ‘postbiotics’ in the most recent publications.

<https://www.frontiersin.org/articles/10.3389/fmicb.2019.00477/full>

Heat-killed Lactococcus lactis strain helps athletes:

The severity of symptoms was tracked based on subjective questionnaires. In short, the heat-killed L. lactis group showed lower fatigue and symptom scores for sneeze/running nose, and the placebo group had a higher number of cumulative days with any upper respiratory tract symptom. Modest, but positive, results.

By Mary Ellen Sanders, PhD , Dairy & Food Culture Technologies, December 3, 2018

Infant Formula:

This pool of oligosaccharides in our new nutritional concept will further mimic the quantity, complexity and functionality of the total pool of HMOS. 2'-FL is known to inhibit pathogen binding and new data has shown that 2'-FL is more efficient in presence of scGOS/IcFOS (9:1). 3'-GL is reported to protect the gut barrier and is produced during Nutricia's unique, patented Lactofidus™ fermentation process, also introducing specific postbiotics in its formulations.

Dr. Bernd Stahl, R&I director Human milk Research at Danone Nutricia Research, the Netherlands

Lactobacillus casei CRL 431 and Bacillus coagulans GBI-30 strains

The metabolite profile revealed a variety of compounds (fatty acids, amino acids, coenzyme, protein, amino sugars), with significant probable activities ($P_a > 0.7$) as immune-stimulant, anti-inflammatory, neuroprotective, antiproliferative, immunomodulator, and antineoplastic

Postbiotics and Metabolism

Moreover, the products of microbiota metabolism, so-called postbiotics, are involved in the mechanisms that connect prebiotics and microbiota modulation with thermogenesis and protection against obesity and its associated metabolic disorders. Interestingly, the direct use of postbiotics, through dietary supplementation, can also be considered as an interesting strategy

<https://www.frontiersin.org/articles/10.3389/fphys.2018.01908/full>

Postbiotic metabolites produced by *Lactobacillus plantarum* strains exert selective cytotoxicity effects on cancer cells

In conclusion, PM produced by the six strains of *L. plantarum* exhibited selective cytotoxic via antiproliferative effect and induction of apoptosis against malignant cancer cells in a strain-specific and cancer cell type-specific manner whilst sparing the normal cells. This reveals the vast potentials of PM from *L. plantarum* as functional supplement and as an adjunctive treatment for cancer.

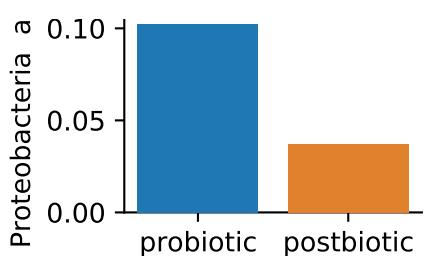
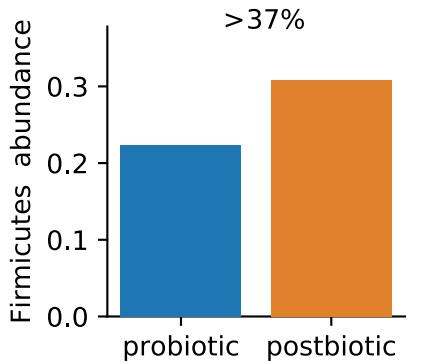
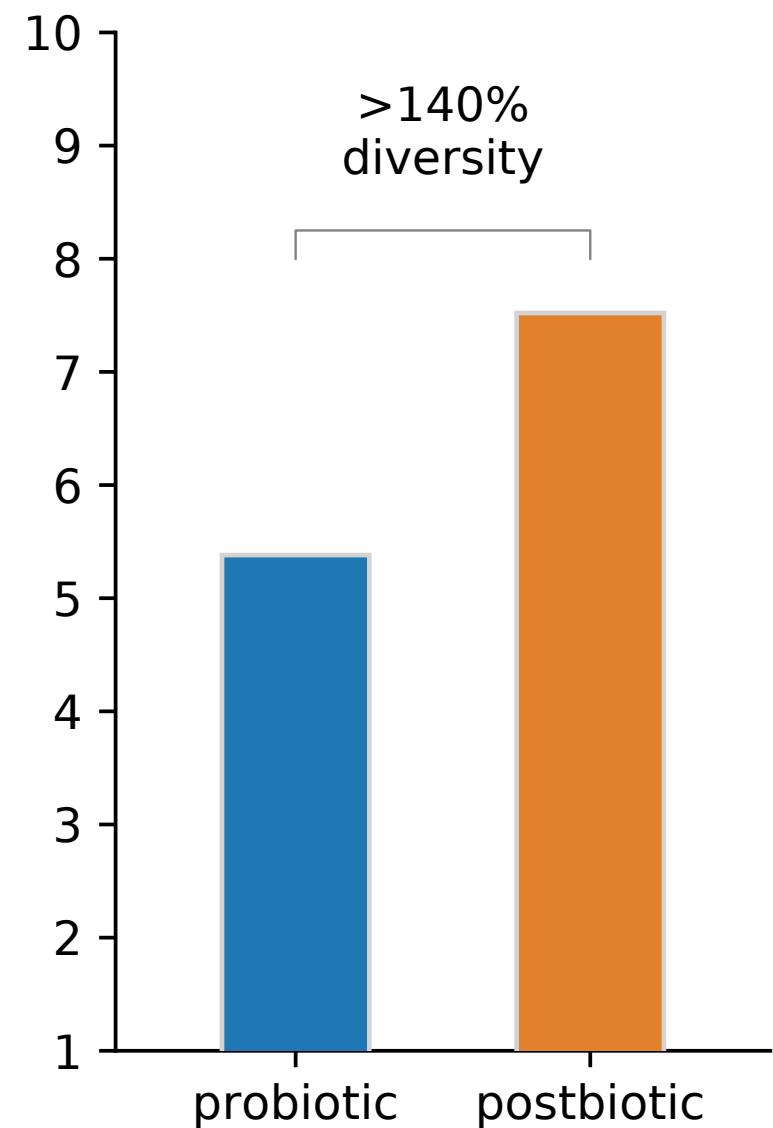
Li-Oon Chuah¹, Hooi Ling Foo^{1,2*}, Teck Chwen Loh^{3,4}, Noorjahan Banu Mohammed Alitheen^{2,5}, Swee Keong Yeap⁶, Nur Elina Abdul Mutalib¹, Raha Abdul Rahim^{2,5} and Khatijah Yusoff^{2,7}

May Help Lower Blood Sugar and Prevent Diabetes

We found that bacterial cell wall-derived muramyl dipeptide (MDP) is an insulin-sensitizing postbiotic that requires NOD2. Injecting MDP lowered adipose inflammation and reduced glucose intolerance in obese mice without causing weight loss or altering the composition of the microbiome.

[https://www.cell.com/cell-metabolism/fulltext/S1550-4131\(17\)30175-4](https://www.cell.com/cell-metabolism/fulltext/S1550-4131(17)30175-4)

40% improved gut
microbiome diversity
relative to top medical
grade probiotics.



Companies patenting postbiotics: Sacco, ADM, Chr. Hansen, Abbot Labs, Hills pet nutrition, Sofar

Danone recently launched Aptamil Follow On Milk with Pronutra-ADVANCE, which contains a patented formulation combining prebiotics and postbiotics, which Danone claims is immune and gut development, clinically proven to support immune and gut development.

MJN U.S. Holdings LLC, a subsidiary of **Mead Johnson Nutrition**, has a Patent Cooperation Treaty publication (WO2017078907A1), which describes the method of producing Lactobacillus rhamnosus GG (LGG) soluble mediators, and its use in pediatric nutritional composition. The soluble mediator is used instead of probiotics, to improve impaired gut barrier function and to reduce visceral pain in a pediatric subject.

DuPont Nutrition Biosciences filed a PCT (WO2018050623A1) claiming L. crispatus LMG18199 or its metabolite, to be used as an active ingredient in food products. These metabolites are resistant to acid and bile fluid and helps in preventing and/or treating gastrointestinal disorders.

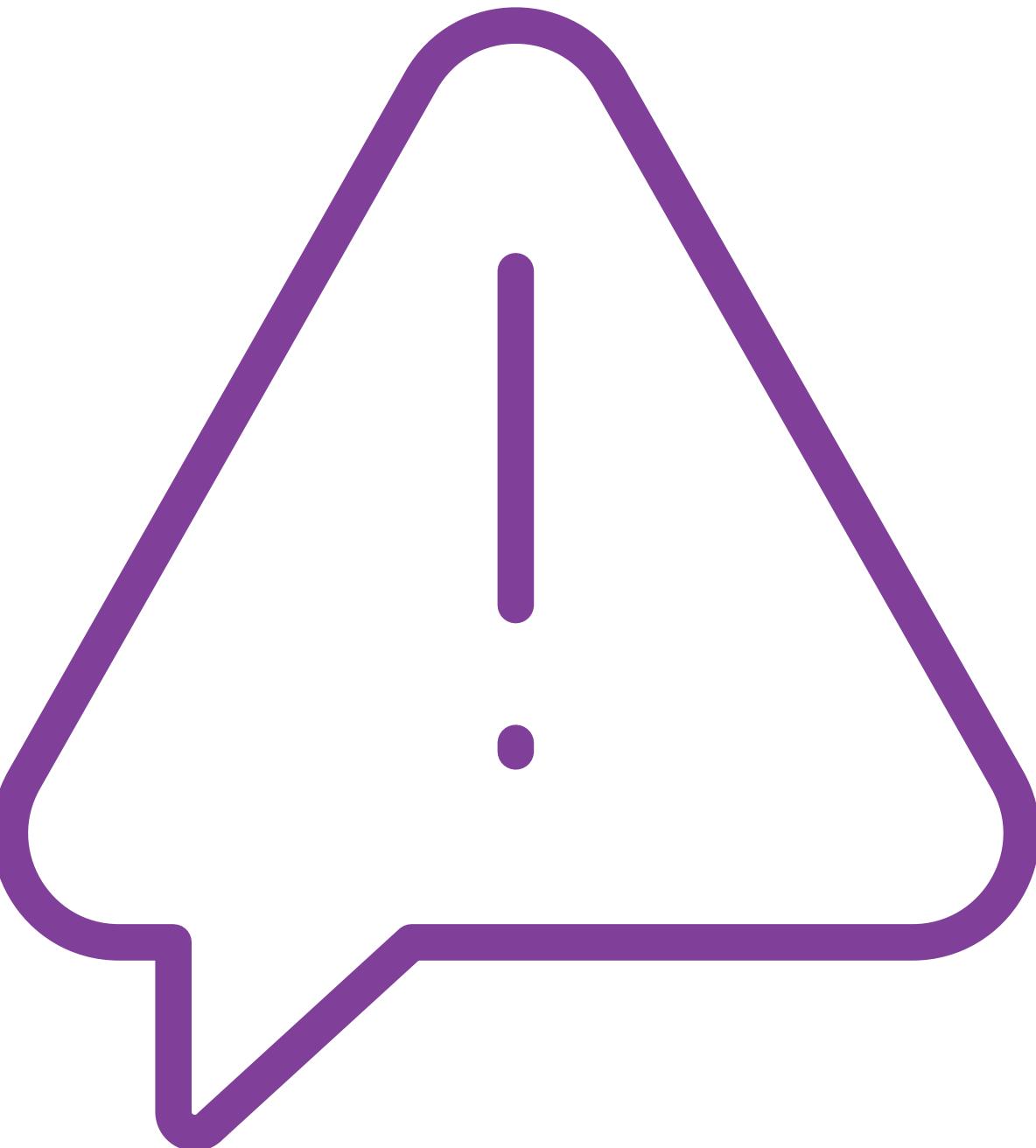
A pending Indian patent publication (IN201838007857A) filed by **Amano Enzyme Group**, discloses a novel -galactosidase derived from Bacillus circulans to produce low lactose milk, which can be used as food additive in infant formula, for lactose intolerant infants.

TCI Co filed a US patent application (US20180264054A1), which claims Lactobacillus plantarum TCI378. The pending application further discloses the use of either the bacteria or its metabolite as an active ingredient in food, pharmaceuticals or animal feed, to improve gastrointestinal functions and to reduce weight by enhancing fat metabolism.

A US pending publication (US20190099438A1), filed by **Nitto Pharmaceutical Industries**, discloses exopolysaccharide produced by Leuconostoc mesenteroides to treat metabolic disorders, like obesity, diabetes, etc. These metabolites helps in decreasing a ratio of bacteria belonging to the Firmicutes to bacteria belonging to the Bacteroidetes in the intestine and increasing the amount of short-chain fatty acid in the intestine

Challenges

- Standardizing
- Defining
- Re-educating market



BENEFITS

“metabolites has the potential to counteract and correct the negative effects of dysbiosis”

Metabolite-based interventions are therapeutically attractive for several reasons. These small molecules are physiologically abundant at high concentrations, and thus the potential for toxicity is low. In contrast to the administration of live organisms, their dosage and routes of administration follow the principles of pharmacokinetics. Moreover, metabolites are present at most body sites and thus suitable for different routes of administration. Additionally, metabolites are generally stable in the systemic circulation and thus amenable for scalable modulation of their concentration.

DOWNSIDE

Among the downsides of metabolite-based therapeutics are the shorter half-lives than administration of live bacteria; hence, repeated dosing may be required for the treatment of dysbiosis-associated conditions. In addition, the effects of some microbiome-associated metabolites are pleiotropic and highly cell type specific. As such, further characterization of the full effects of different metabolites is necessary in order to understand potential side effects of postbiotics.

“

As the full importance of the gut microbiome is uncovered, and we learn more about the active metabolites generated by the microbiome, the role of these postbiotic metabolites is attracting greater attention.

”

sciemag.org

It is up to us to push
postbiotics forward...

- Define postbiotics
- Standardize postbiotics
- Clinically study postbiotics
- Educate the market