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RESEARCH

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ESSENTIAL DAIRY  
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## From Probiotics to Precision Probiotics

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# Probiotic research: any doubts?



SCIENTIFIC AMERICAN. English Cart

SCIENCES MIND HEALTH TECH SUSTAINABILITY EDUCATION VIDEO PODCASTS BLOGS STO

THE BODY

## Do Probiotics Really Work?

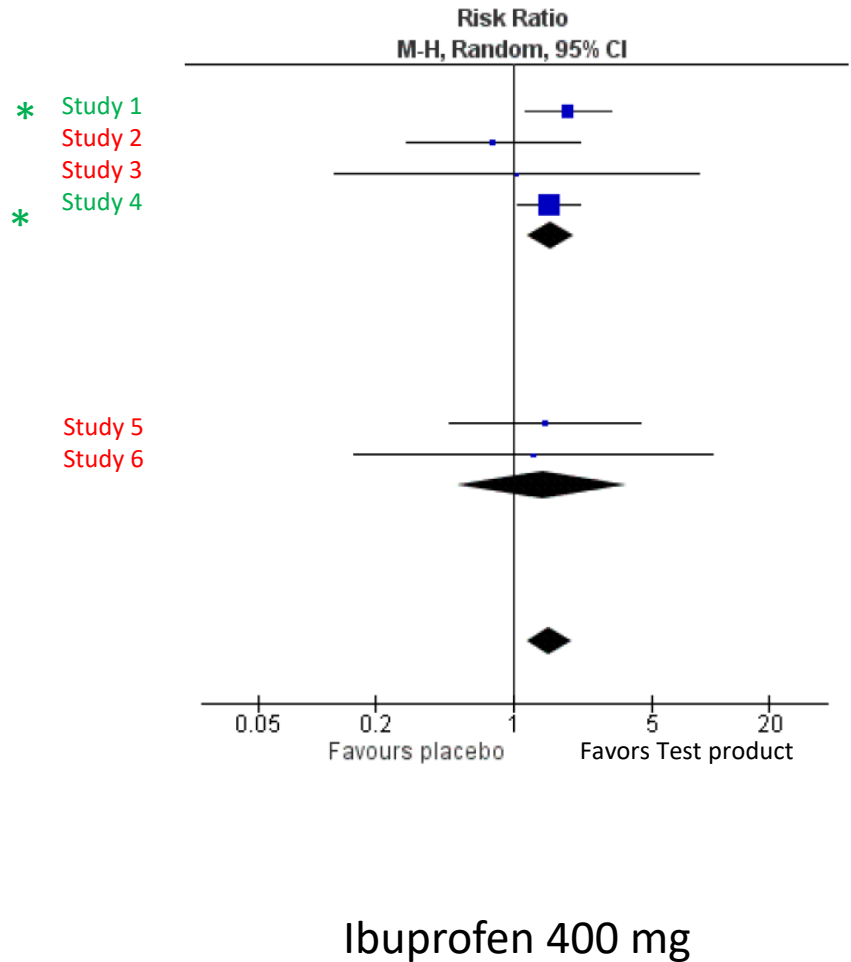
Although certain bacteria help treat some gut disorders, they have no known benefits for healthy people

By Ferris Jabr | Scientific American July 2017 Issue



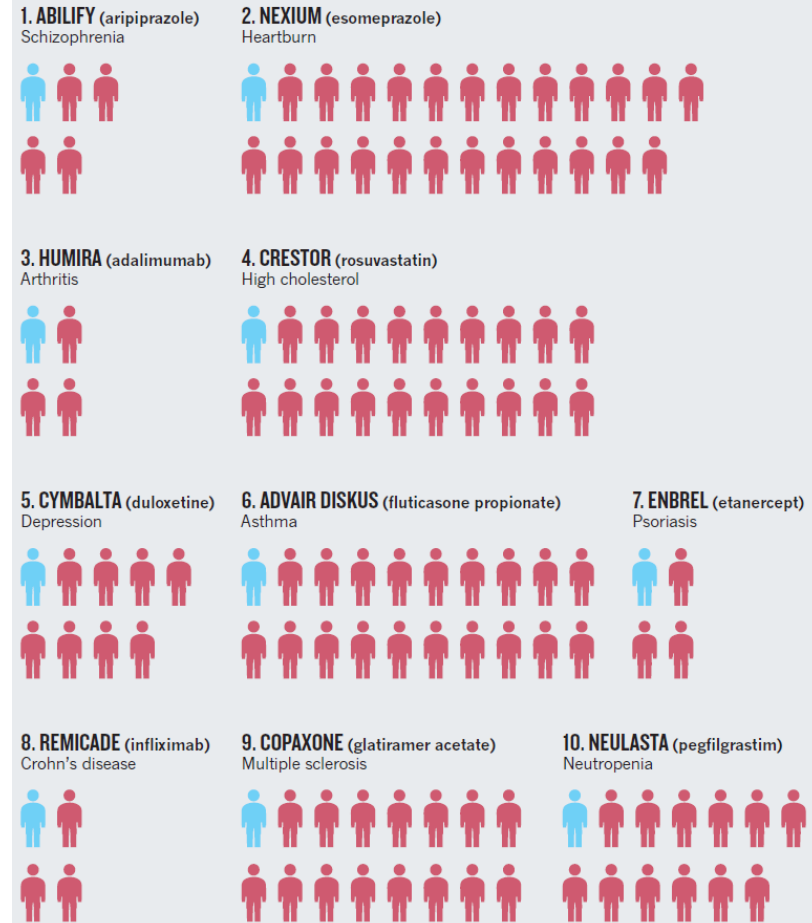
**DO PROBIOTICS ACTUALLY DO ANYTHING?**  
*Probiotics, manufactured mixtures of "good bacteria" that help digest food, have become a growing multibillion-dollar industry. But do they work?*

# Need for precision in medicine



## IMPRECISION MEDICINE

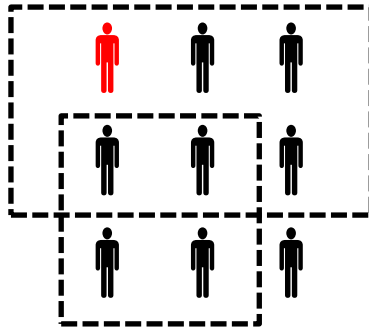
For every person they do help (blue), the ten highest-grossing drugs in the United States fail to improve the conditions of between 3 and 24 people (red).



Based on published number needed to treat (NNT) figures. For a full list of references, see Supplementary Information at [go.nature.com/4dr78f](http://go.nature.com/4dr78f).

# Need for a precision approach in probiotic research

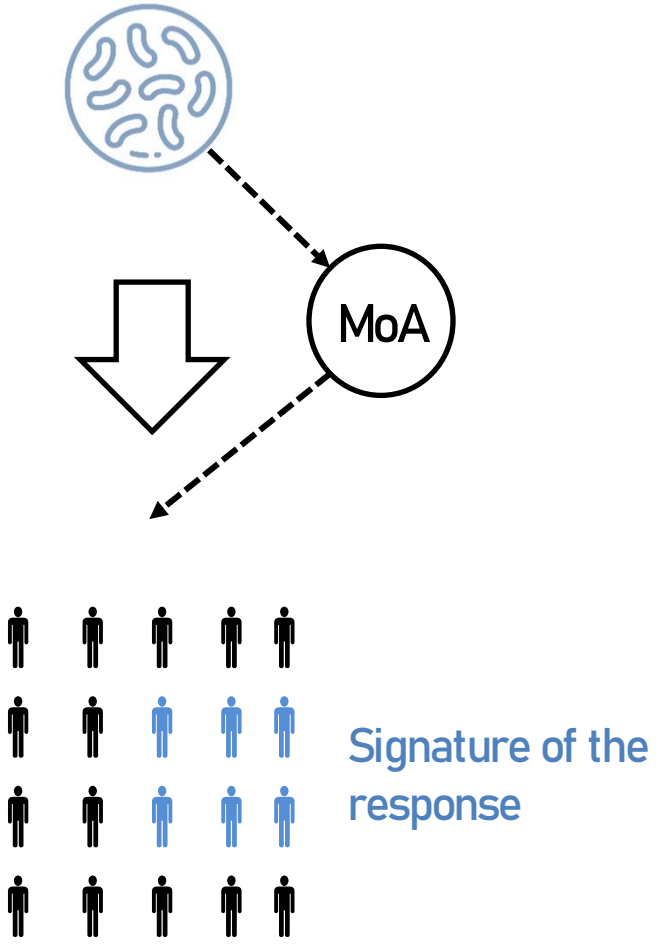
Probiotic  
NNT : 9



NNT	Probiotic	Benefit	study
10	<i>Saccharomyces boulardii</i> CNCM I-745	Antibiotic associated diarrhea	Dinleyici <i>et al.</i> , 2014
14	<i>L. casei</i> Shirota	Acute diarrhoea in children	Sur <i>et al.</i> 2011
10	<i>Bifidobacterium lactis</i> CNCM I-2494 + lactic acid bacteria	Overall gastrointestinal discomfort	Eales <i>et al.</i> , 2017
7	<i>Lactobacillus rhamnosus</i> GG	Abdominal pain in children with IBS	A. Horvath <i>et al.</i> , 2011
5	<i>L. casei</i> CNCM I-1518	Antibiotic associated diarrhea in <i>C. dif</i> patients	Hickson <i>et al.</i> , 2007

# Precision approaches to probiotics

## TOP-DOWN



# A fermented milk containing *B. lactis* CNCM I-2494 improves gastrointestinal well being

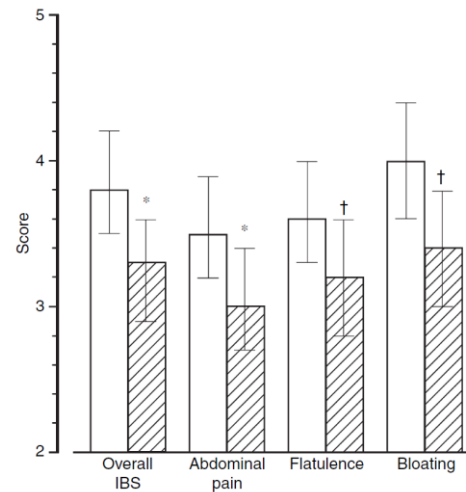
## The Fermented Product



*Bifidobacterium lactis* CNCM I-2494  
*Lactococcus lactis* CNCM I-1631  
*Lactobacillus bulgaricus* CNCM I-1632  
*Lactobacillus bulgaricus* CNCM I-1519  
*Streptococcus thermophilus* CNCM I-1630

## Decreases gas-related symptoms

### IBS with constipation

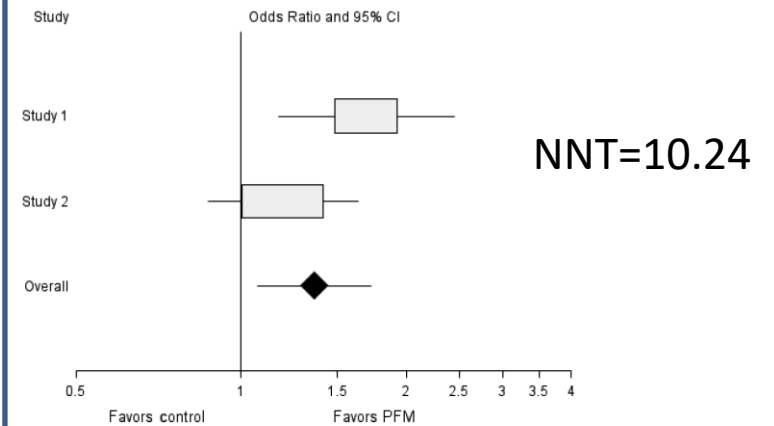


Agrawal *et al.*, Aliment Pharmacol Ther. 2009 (n=34)

Guyonnet *et al.*, Aliment Pharmacol Ther. 2007 (n=267)

## Improves gastro-intestinal well being

### General Population



Marteau *et al.*, 2013, Neurogastroenterol Motil. (n=335)

Guyonnet *et al.*, 2009, Br J Nutr (n=199)

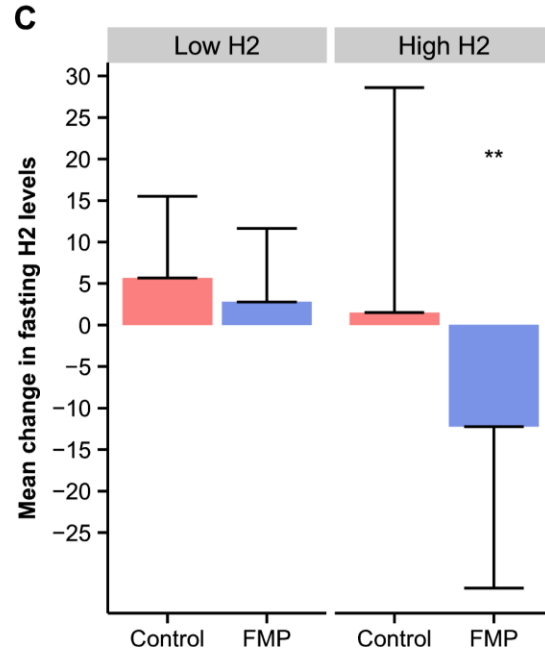
Eales *et al.*, 2017

# Gut microbiota may dictate the response to the *B. lactis* CNCM I-2494 fermented milk

FMP reduces fasting H<sub>2</sub> production in high H<sub>2</sub> producers in IBS subjects



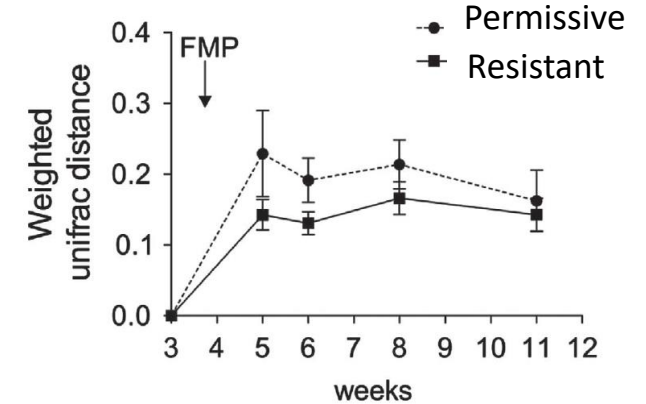
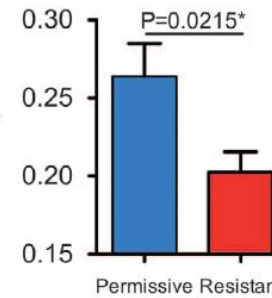
UNIVERSITY OF  
GOTHENBURG



Le Nevé *et al.*, 2019, Plos One

Not all microbiota respond the same to the  
*B. lactis* CNCM I-2494 fermented milk

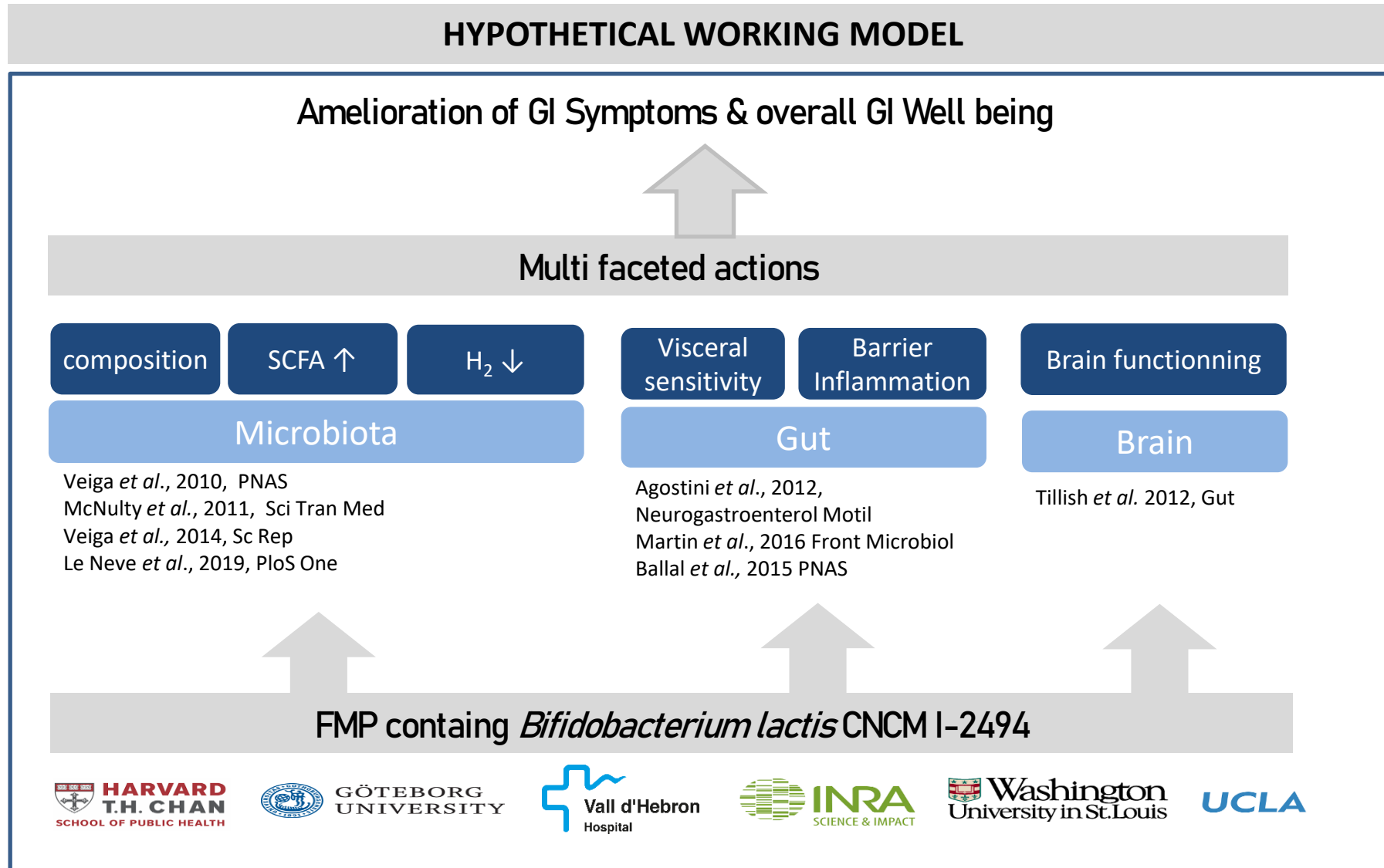
Weighted Unifrac Distance  
between Day 0 and 15



Zhang *et al.*, 2016, ISME J



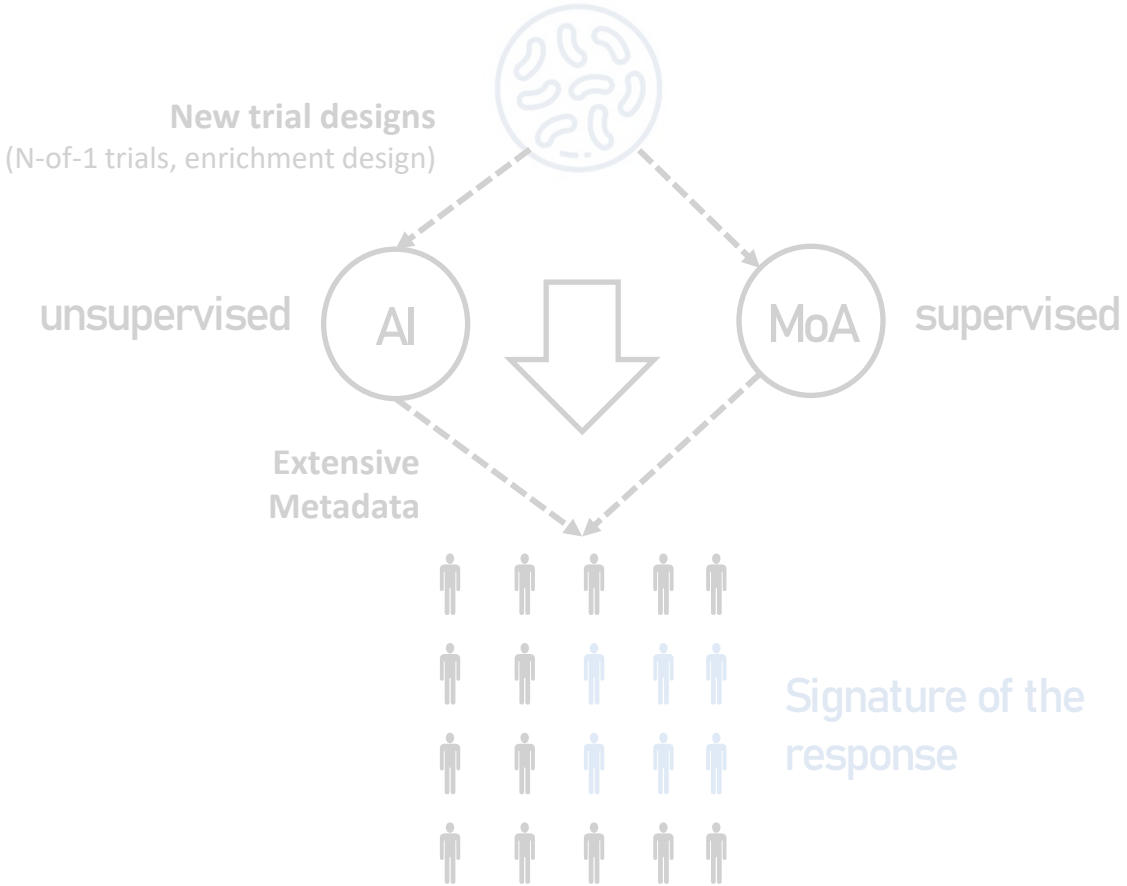
# Digging into inter-individual response for each possible MoA would be endless...





# Precision approach to probiotics

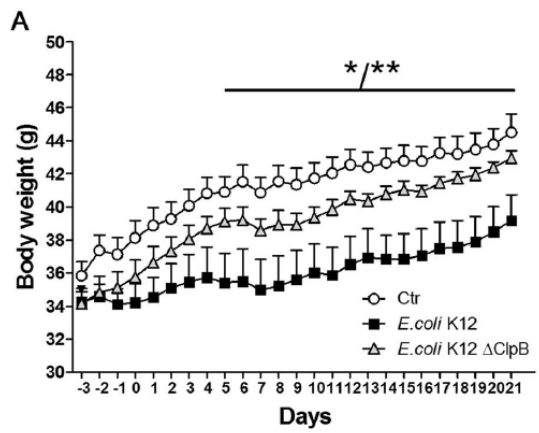
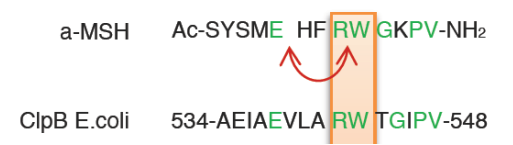
## TOP-DOWN



← Mechanisms of Action

# From a protein of interest to *Hafnia alvei* 4597™

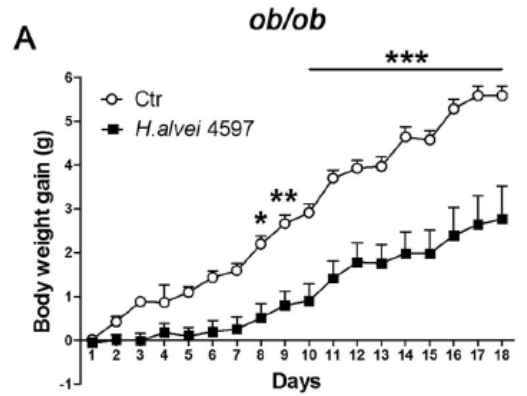
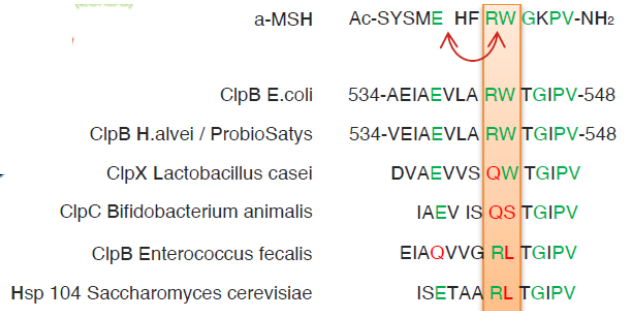
## *E. coli* ClpB is an antigen mimetic of the $\alpha$ -MSH



Legrand\*, Lucas\* et al., Int J Obes 2020

Courtesy of G. Lambert, Targedys

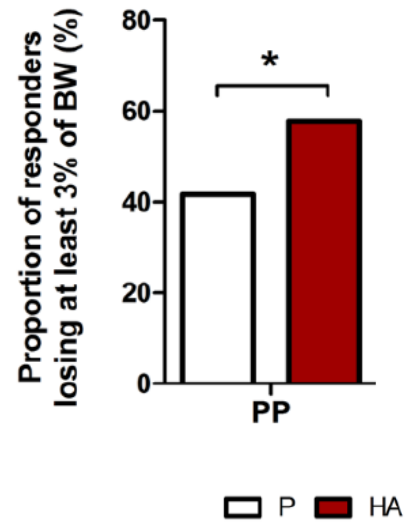
## *Hafnia alvei* prevents weight gain in *Ob/Ob* mouse



Legrand\*, Lucas\* et al., Int J Obes 2020

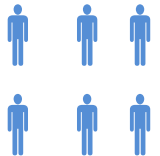
Courtesy of G. Lambert, Targedys

## *Hafnia alvei* improve weight loss in Human under caloric restriction



Déchelotte et al., 2021

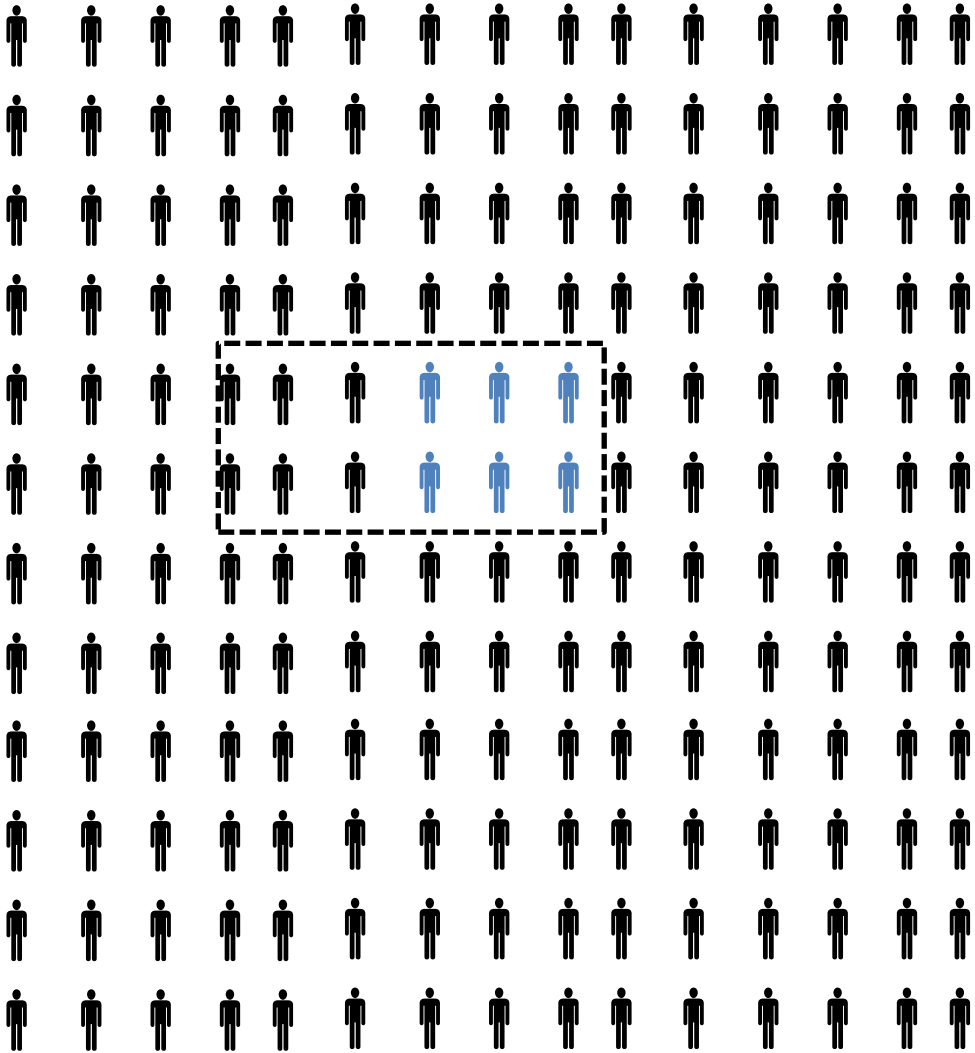
# Precision approach to probiotics



Markers of the Response to a Probiotic

Socio-demographic  
Anthropometrics  
Health Biomarkers

Microbiota.....



# Mapping the variations of the Human Microbiota & Diets : THDMI



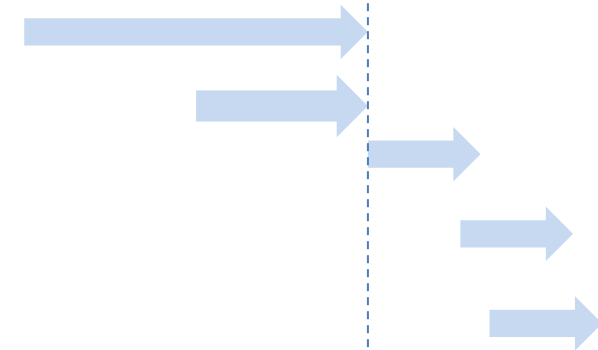
With Rob Knight & Daniel McDonald groups

- Map diets & microbiome accros different countries by
  - Collecting 2500-3000 stool samples
  - Collecting DIET through FFQ
  - Sequencing 16S & whole DNA
  - 5 countries
  - Offering citizen scientists



Launch  
World Microbiome Day  
2019, June

World Microbiome Day  
2021, June 27th



Thdmi.org

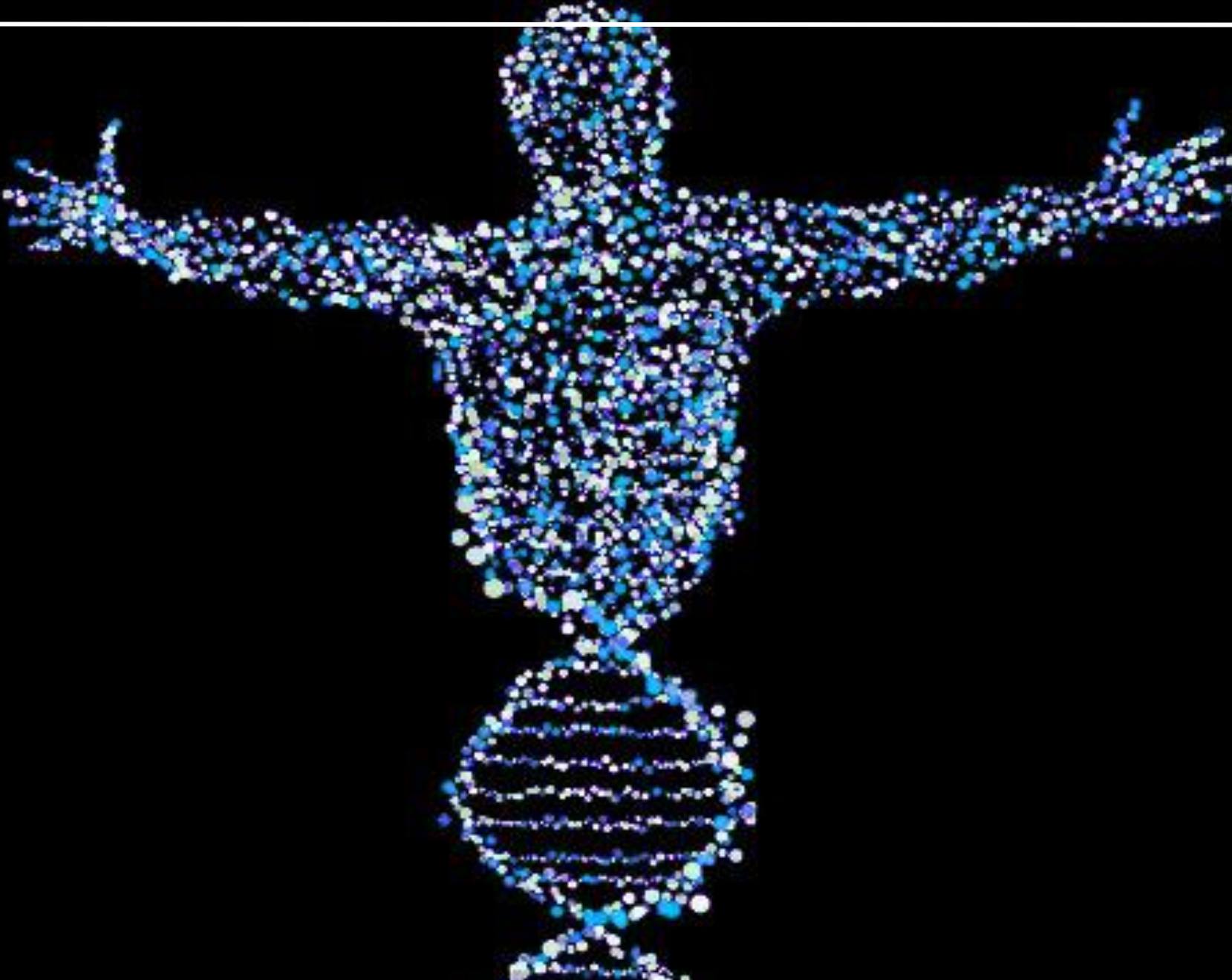


@DanoneResearch



A precision approach will prepare the future

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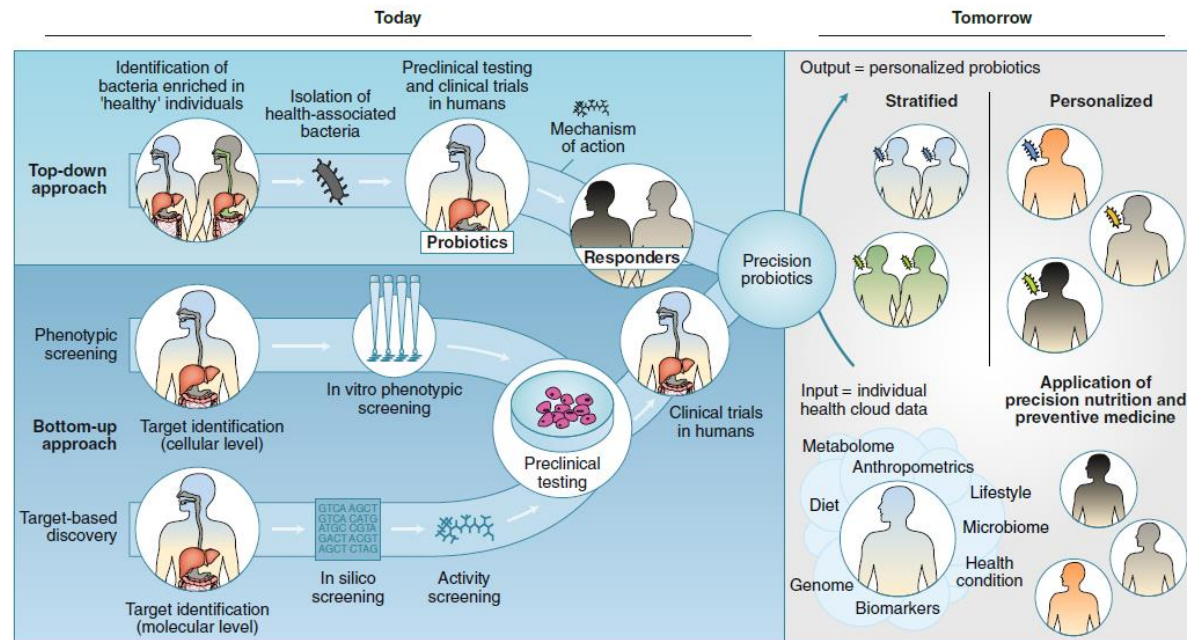
Which probiotic works for me &  
my microbiota?



# Moving from probiotics to precision probiotics

A precision approach to probiotics could address the heterogeneity inherent to probiotic strains, the hosts and their microbiomes. Here, we discuss the steps required to develop precision probiotics: mechanistic studies, phenotypic and target-based discovery strategies, and person-centric trials.

Patrick Veiga, Jotham Suez, Muriel Derrien and Eran Elinav



# Conclusions

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- A precision approach to probiotics has the potential to
  - make probiotic research more convincing & more efficient
  - help in preparing the future of precision probiotics



THANK YOU  
FOR YOUR ATTENTION



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