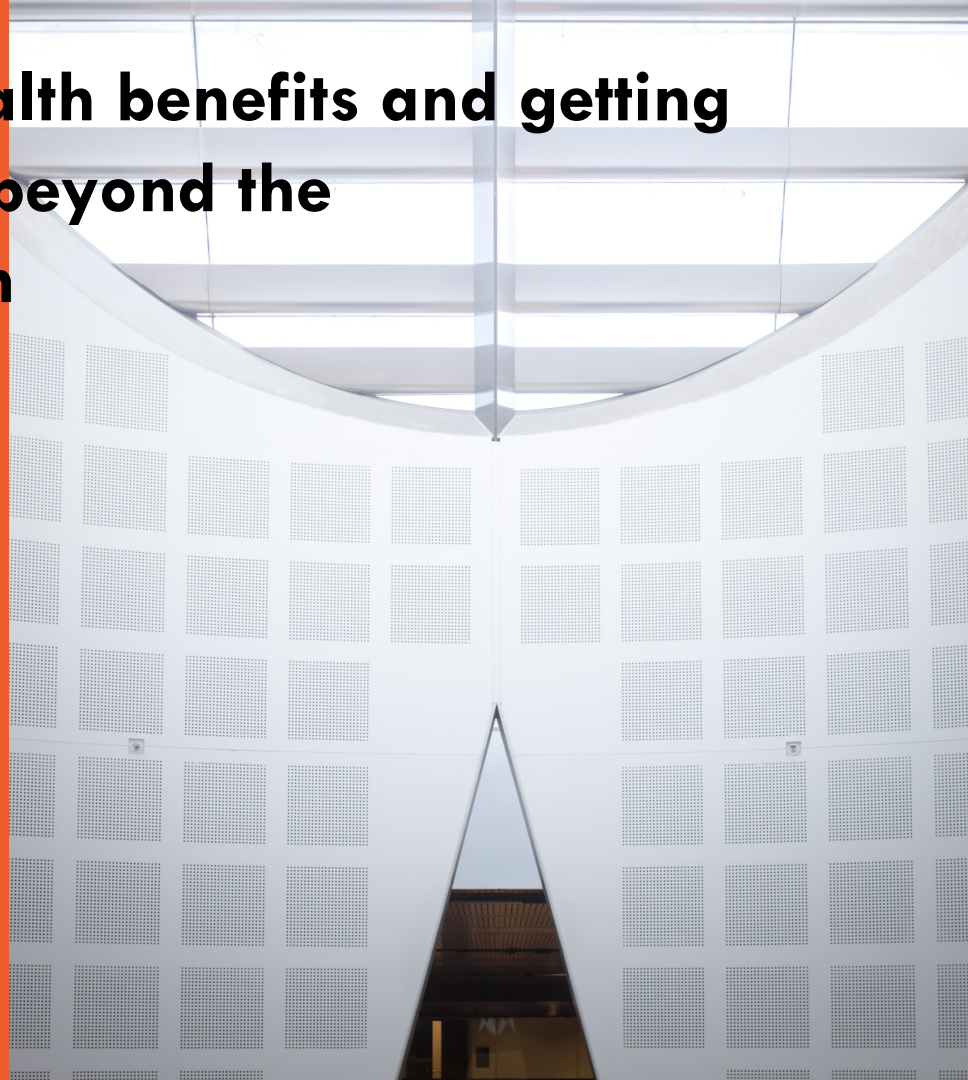
Delivering pre/probiotic health benefits and getting them to market by moving beyond the 'One Size Fits All' paradigm

Presented by
Dr. Mark Read
School of Computer Science
The Charles Perkins Centre

THE UNIVERSITY OF SYDNEY



Probiotics (bugs) & Prebiotics (food for bugs)

"products that contain an adequate dose of live microbes that have been documented in target-host studies to **confer a health benefit**"

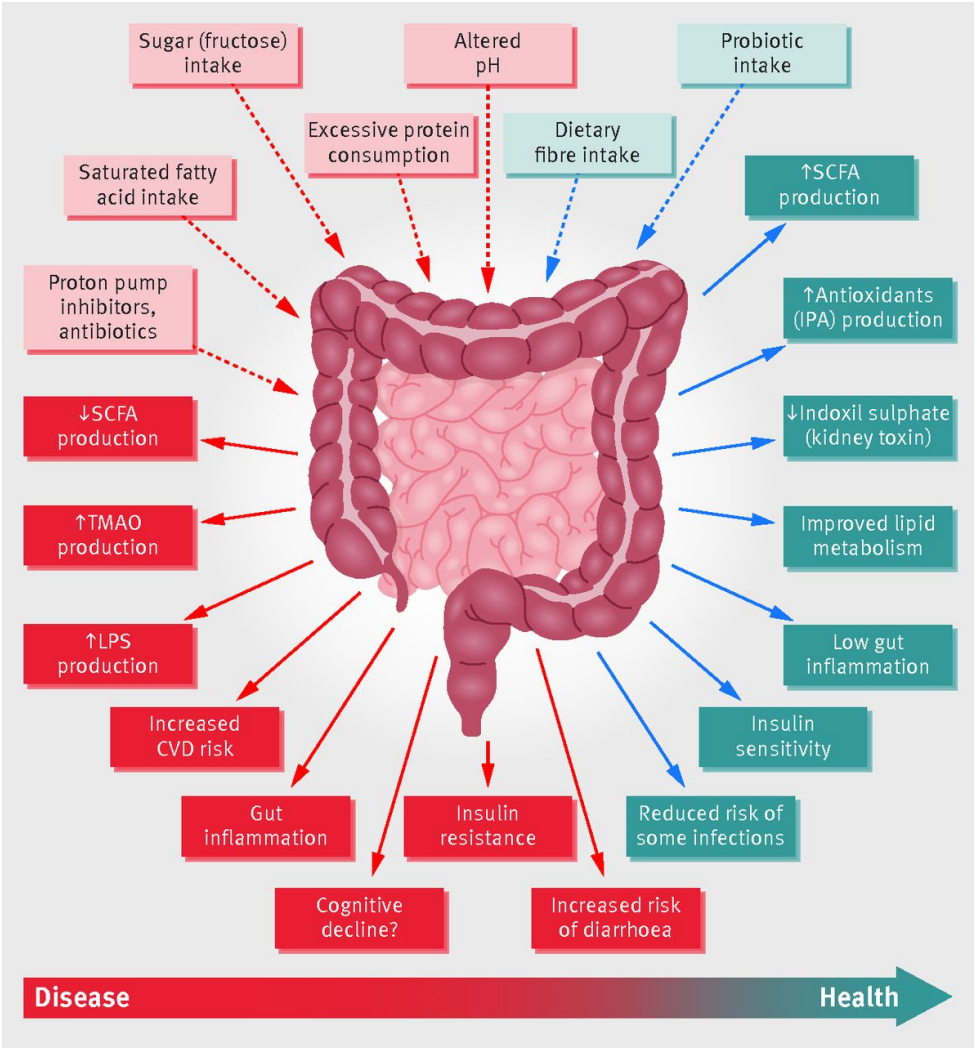
[Sanders. Clinical Infectious Diseases 46, 2008]

"a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microbiota that confers **benefits upon host wellbeing and health**"

[Gibson et al. Nutrition Research Reviews 17, 2004]

Gut microbiome in health and disease

Inflammatory bowel disease
Cancer
Metabolic disorders
Obesity
Diabetes
Cardiovascular disease
Psoriatic arthritis



[Valdes et al. BMJ 361, 2018]

Non-communicable disease (NCD) epidemic

- 60% of deaths worldwide
- 44% of premature deaths
- “In the next 10 years, China, India and the United Kingdom are projected to lose $558 billion, $237 billion and $33 billion, respectively [from NCD]”

[Daar et al. Nature 450, 2007]

Pre/Pro-biotics getting to market

- Consumers **want** health-promoting products
- However, regulators are **rejecting probiotic health claims**
- Limited evidence for probiotic health impacts, e.g.:
  - Reducing diarrhoea duration
  - Reducing constipation
  - Resisting respiratory or genito-urinary infections
  - Allergic rhinitis and asthma
- "So far, EFSA has rejected all submitted health claims for probiotics" [de Simone. Clinical Gastroenterology and Hepatology 17, 2019]; European Food Safety Authority

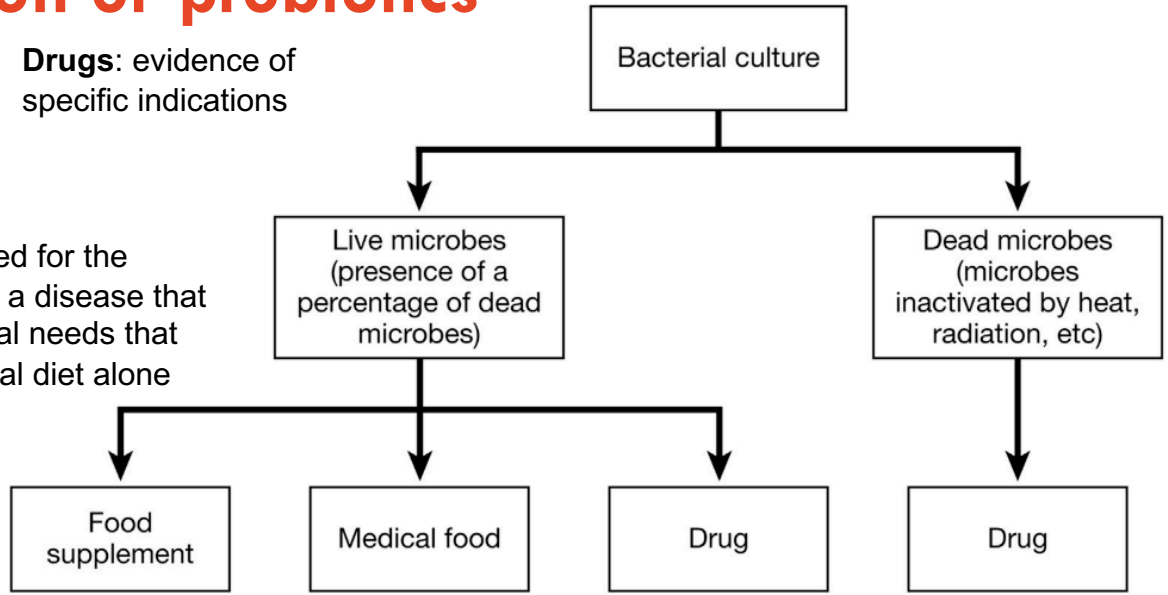
[Katan. Beneficial Microbes 3(2), 2012]

Regulation of probiotics

Supplements: evidence of general beneficial effects

Drugs: evidence of specific indications

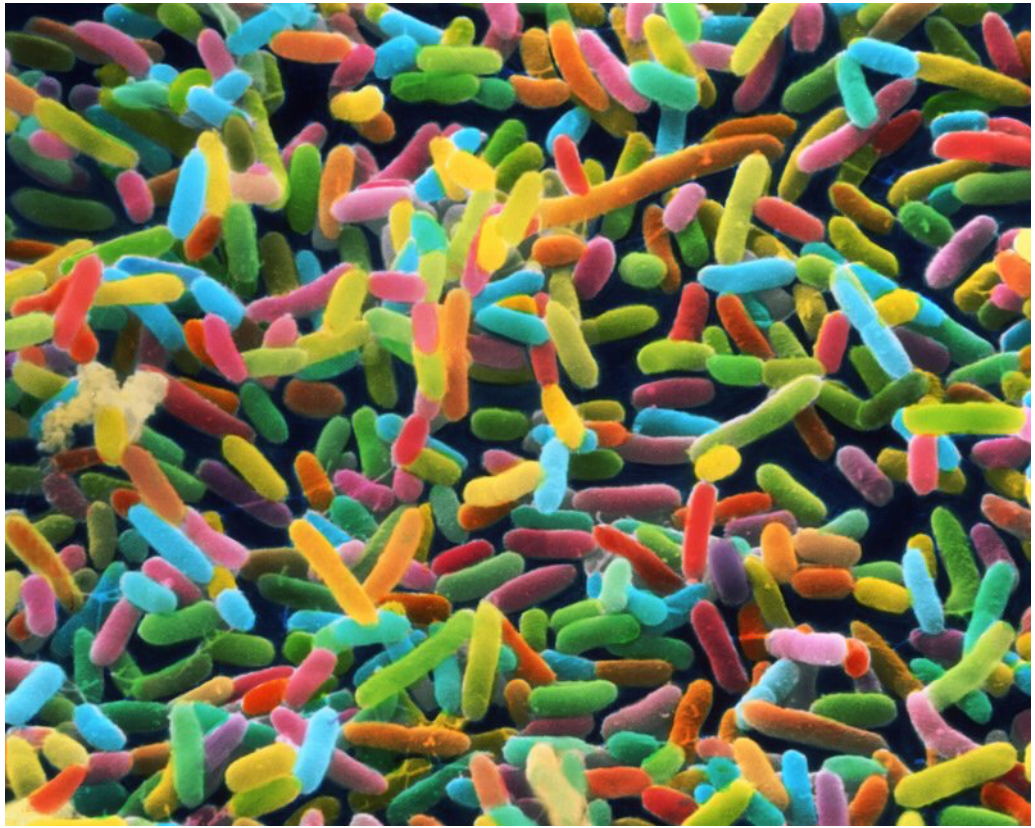
Medical food: supported for the dietary management of a disease that has distinctive nutritional needs that cannot be met by normal diet alone



General health claims
Low consumer interest
Low evidence burden

Specific health claims
High consumer interest
High evidence burden

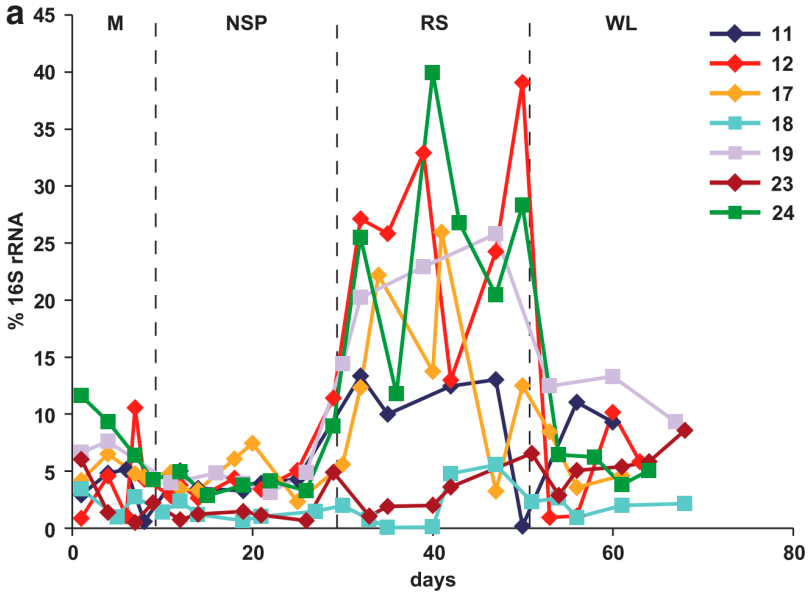
[de Simone. Clinical Gastroenterology and Hepatology 17, 2019]



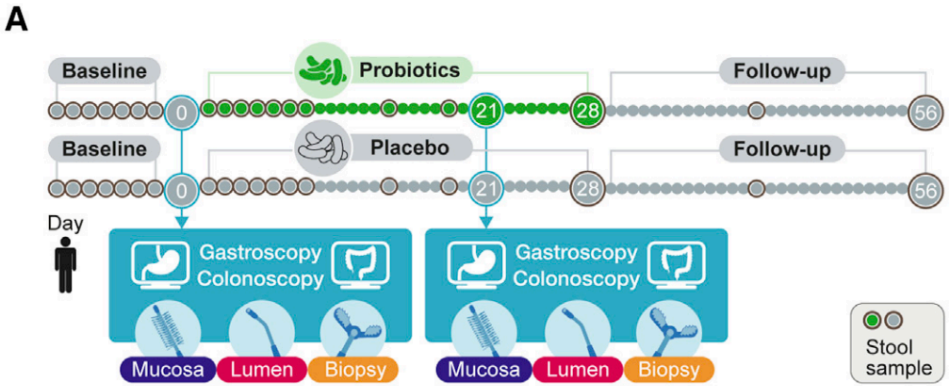
Divergent responses to the same interventions

% *Ruminococcus* in whole community in overweight patients

Maintenance | Non-Starch Polysaccharide | Resistant Starch | Weight Loss

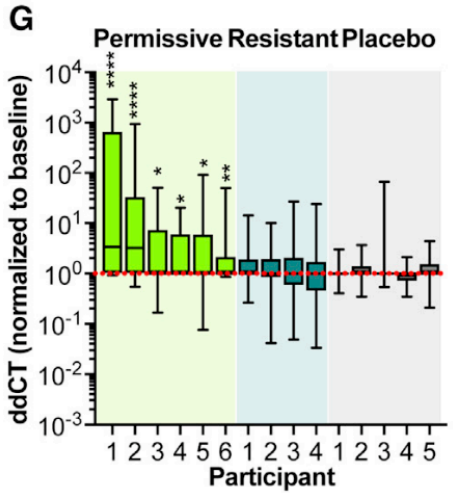


[Walker et al. ISME 5(2), 2011]



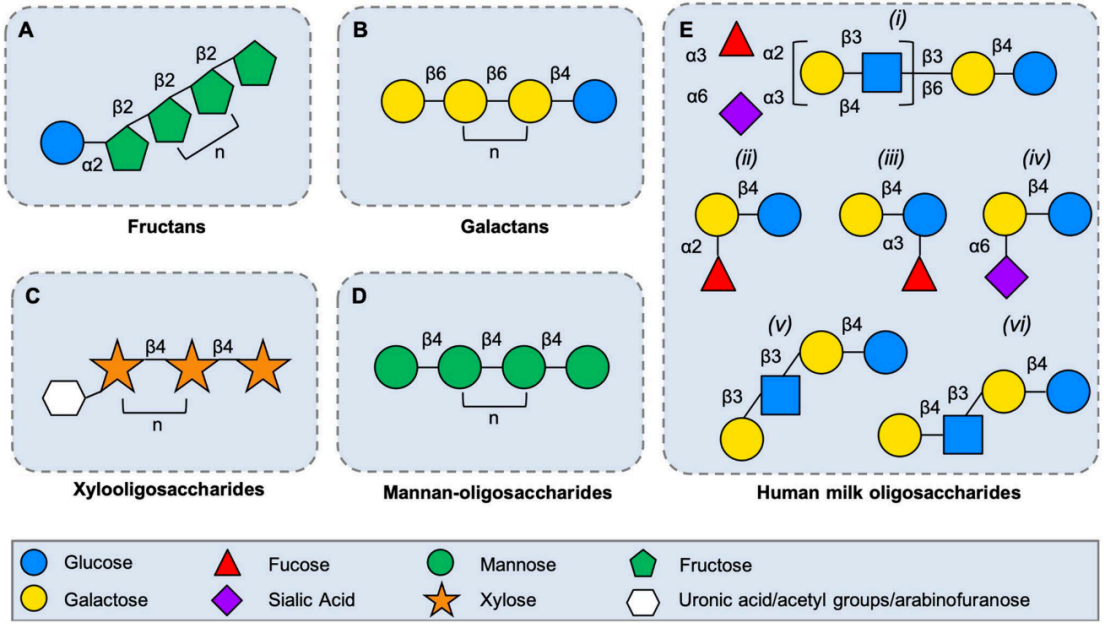
Participants vary in probiotic mucosal colonization during supplementation

(11 strains pooled)



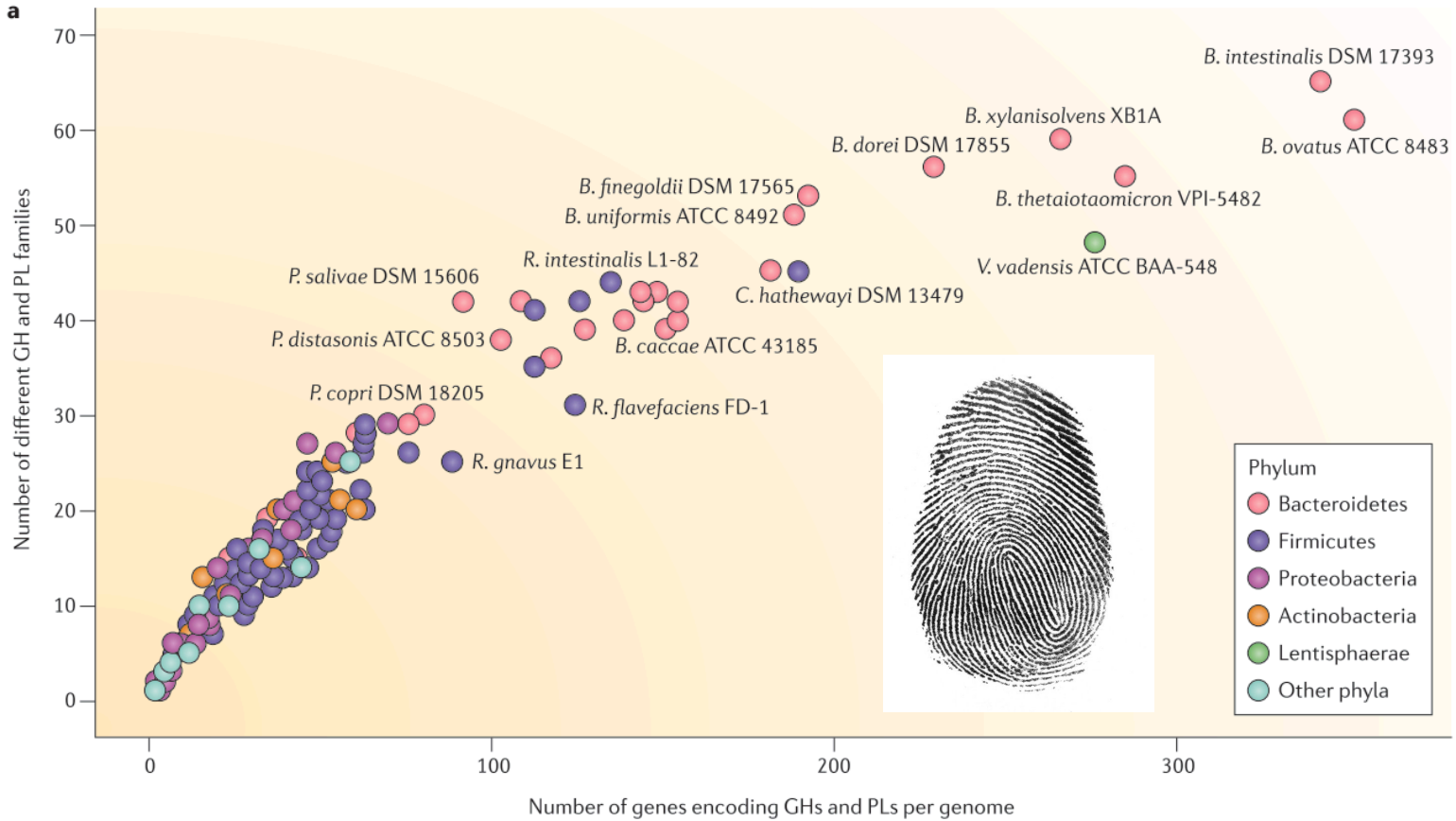
[Zmora et al. Cell 174, 2018]

Prebiotics



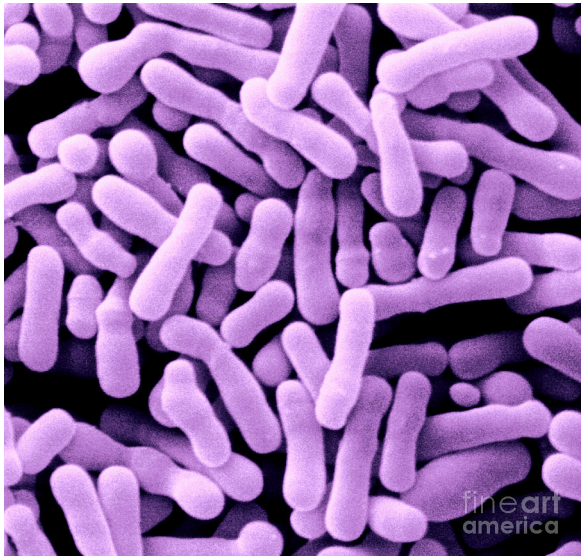
[Enam, Mansell. J. Ind. Micro. and Biotech. 2019]

Diversity in strain carbohydrate degradation capacity

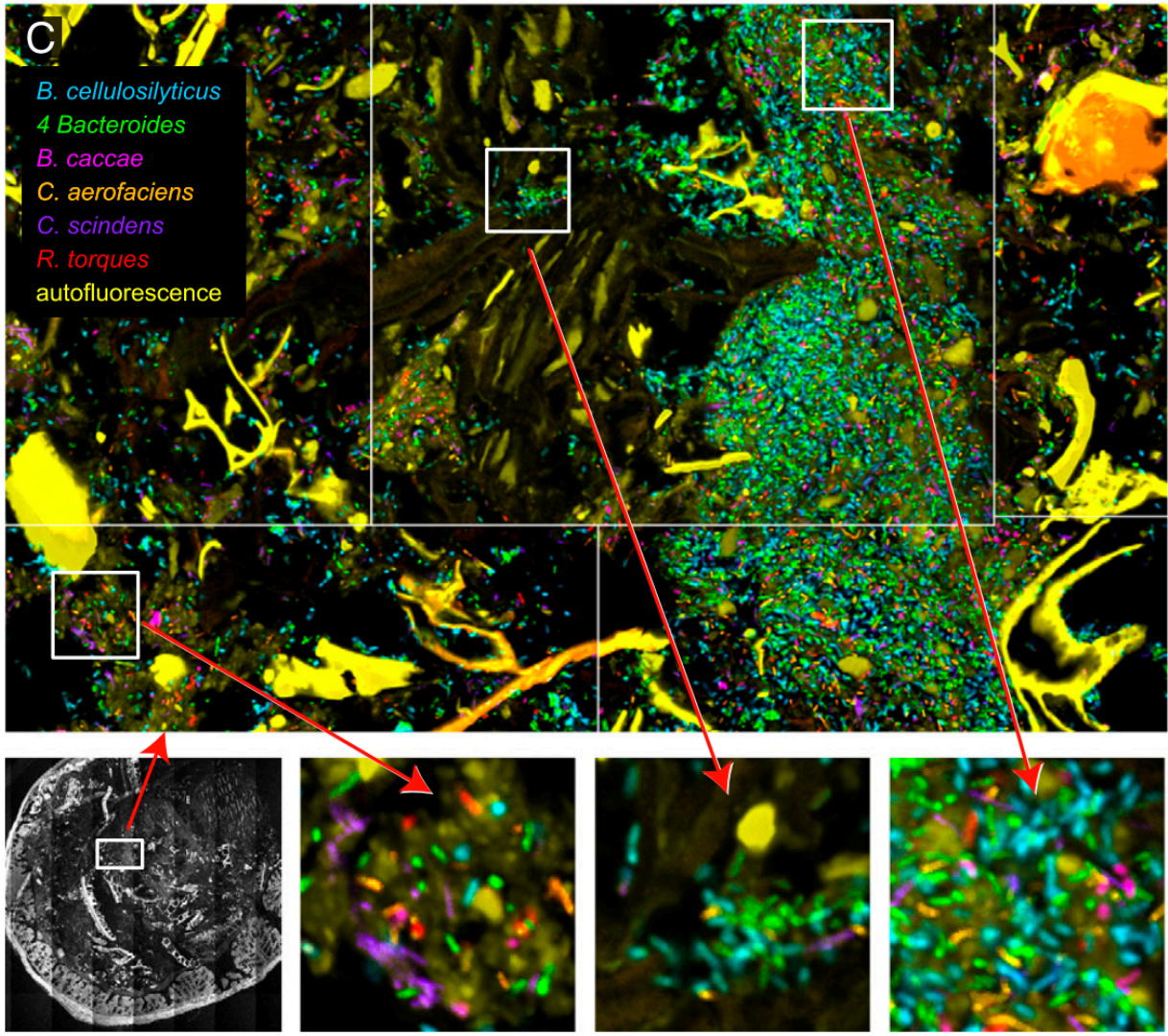


[El Kaoutari et al. Nature Rev. Micro. 11(7), 2013]

Microbial systems are complex



[*Bifidobacteirum Animalis*]



[Welch et al. PNAS 2017]

It’s not that pre/pro-biotics ***can’t*** work,

It’s that they ***don’t work the same way in all people.***

So how do we characterize those individuals who would benefit?

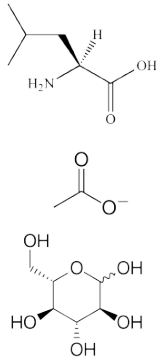
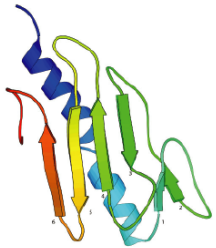
In CAFE:

1. Harness clinical data to identify **who.**
2. Employ mechanism-level modelling to identify **why.**

[Slides containing unpublished data have been removed.]

Outlook



- Pre- & pro-biotics can benefit health
  - **But not the same way for all people**
- Regulatory impasse
  - General public/patients lose
  - Companies lose
- Can we (**cheaply**) identify who **will** benefit, and market to **them?**
- Requires input of clinical data (identify **who**)
- Requires input of experimental data (identify **why**)