Gut microbial strategies for harvesting glycan

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Joint Graduate seminar
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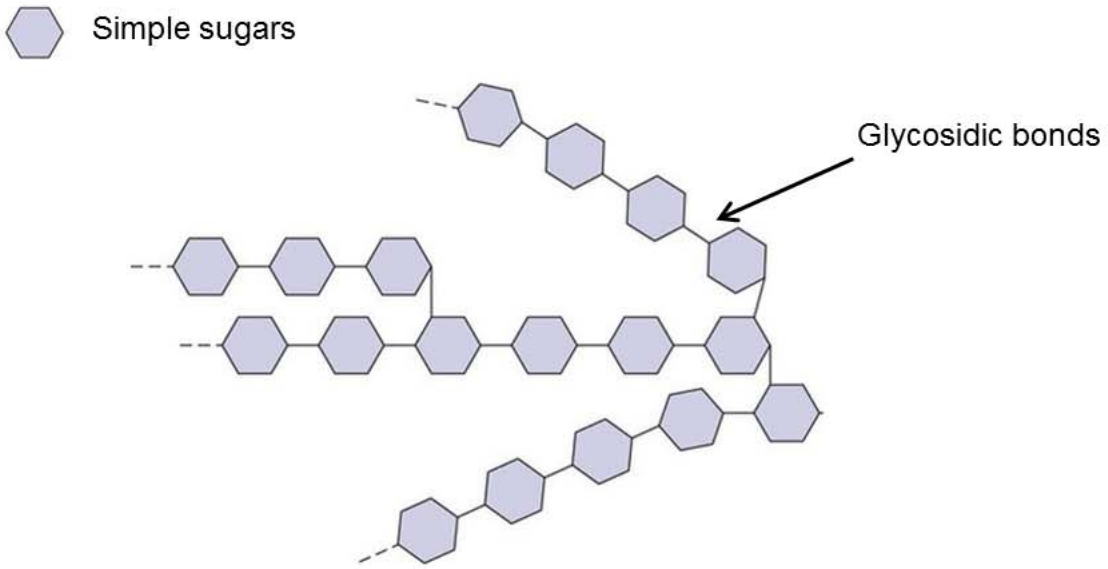
Outline

- What is glycan
- Carbohydrate-active enzymes
- Three examples: glycan harvesting strategies
- The impact of glycan degradation
- Insights and challenges

What is glycan

- The terms **glycan** and **polysaccharide** are synonyms meaning “polymers of multiple simple sugars connected by glycosidic bonds”.

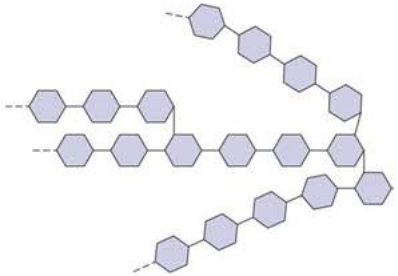


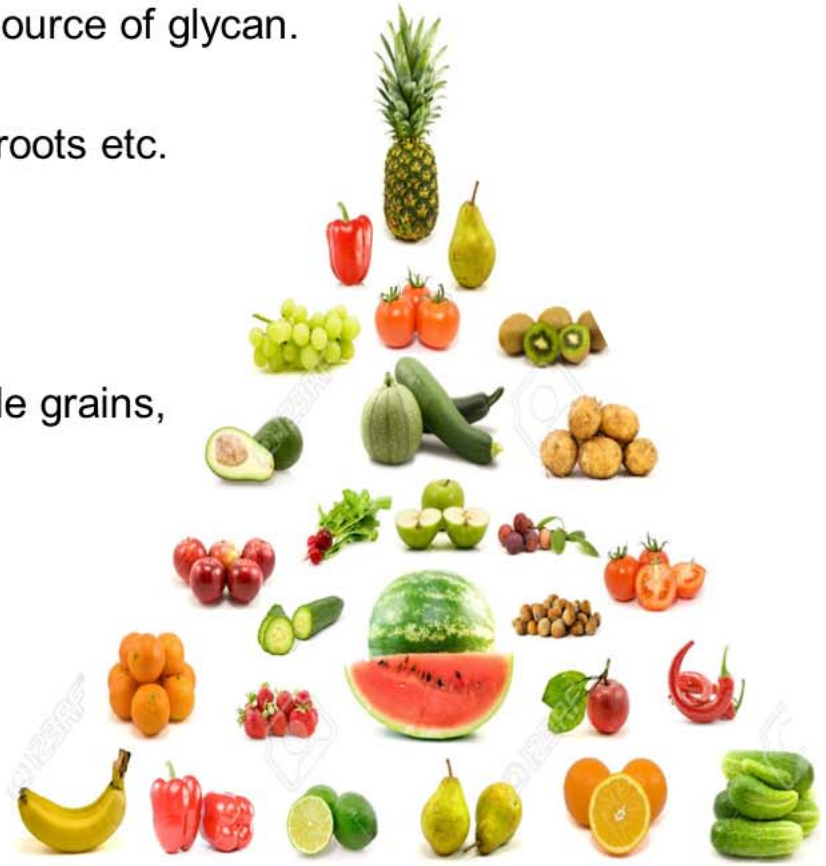
Glycan in food

Plant foods are by far the commonest and major source of glycan.

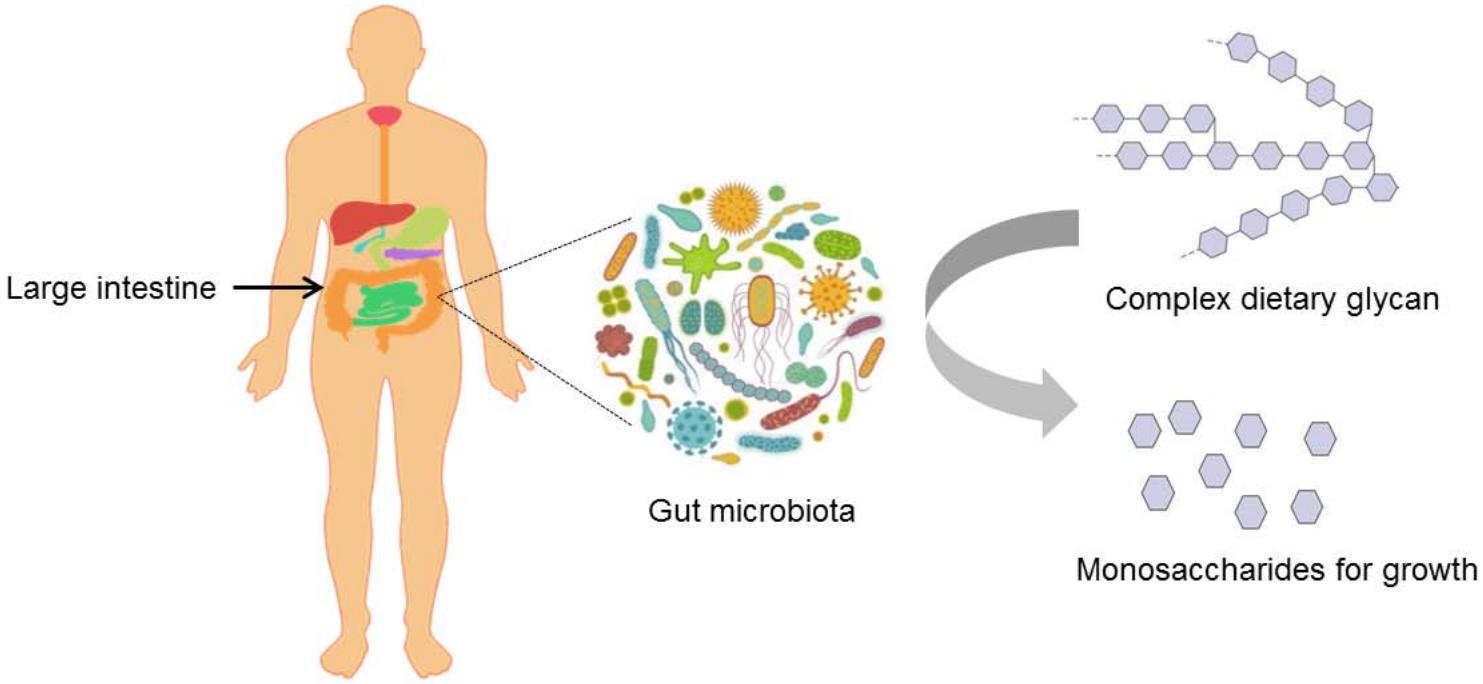
- **Digestible**: sucrose, starch …in potatoes and roots etc.

- **Non-digestible**: pectin, hemicellulose…in whole grains, legumes, vegetables and fruits etc.





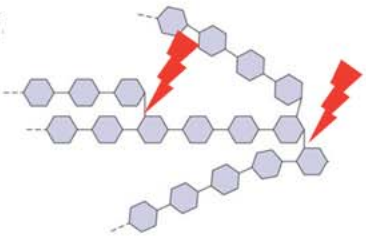
Glycan in gut



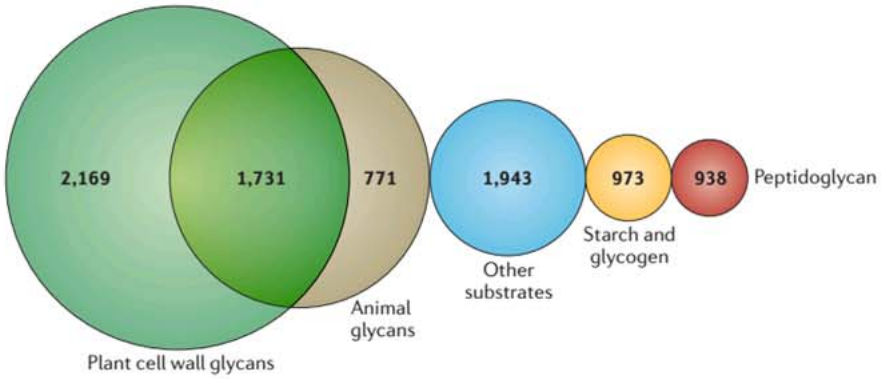
Why gut bacteria can degrade these complex and various glycan?

Enzymatic machinery for glycan degradation

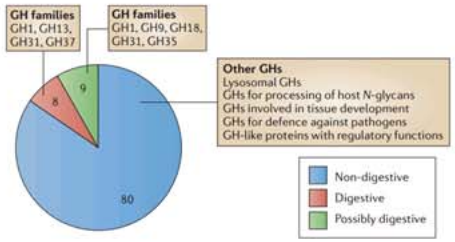
- Carbohydrate-active enzymes (CAZymes) can catalysing the breakd of various complex glycan to the fermentable monosaccharides.



Human gut microbiome (9412)

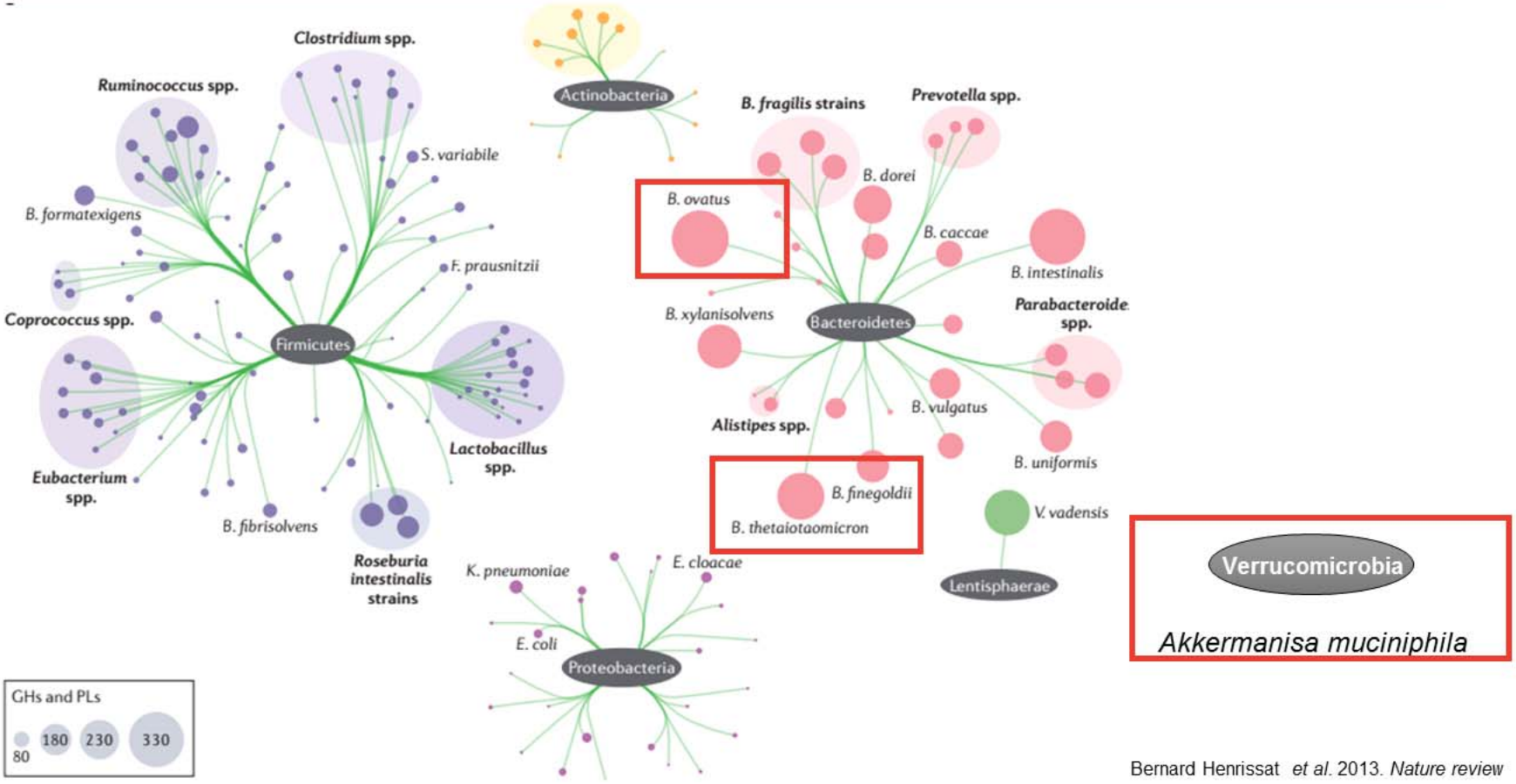


Human genome (~17)



Bernard Henrissat et al. 2013. *Nature review*

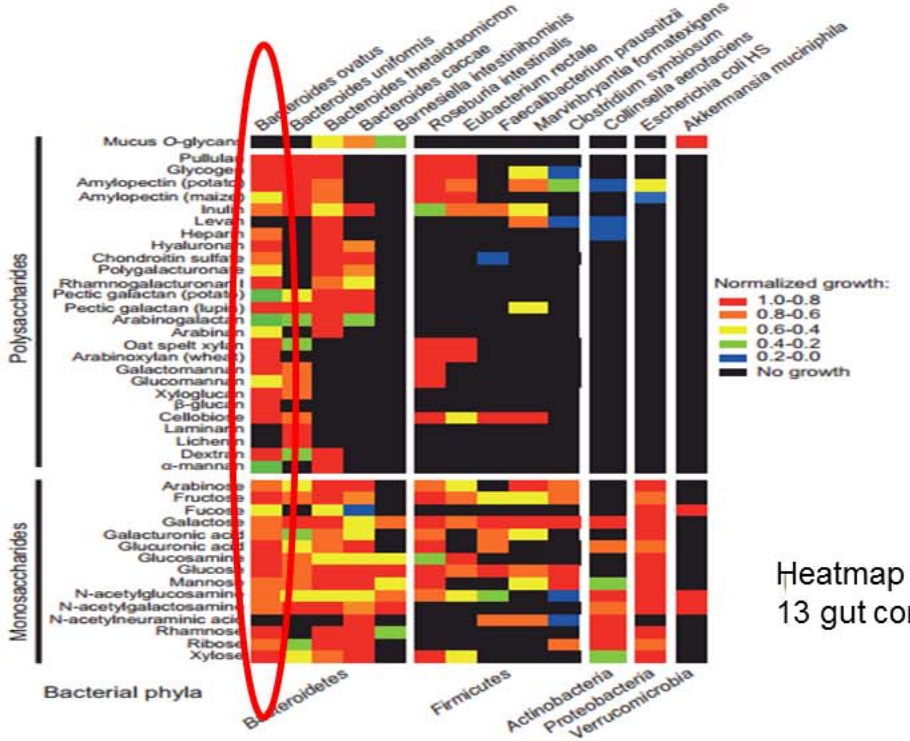
Distribution of CAZymes in human gut microbiota



Bernard Henrissat *et al*. 2013. *Nature review*

Generalist: *Bacteroides ovatus (B. ovatus)*

- *B. ovatus* is a common commensals in the gut microbiota.
- Broad glycan-degrading abilities.



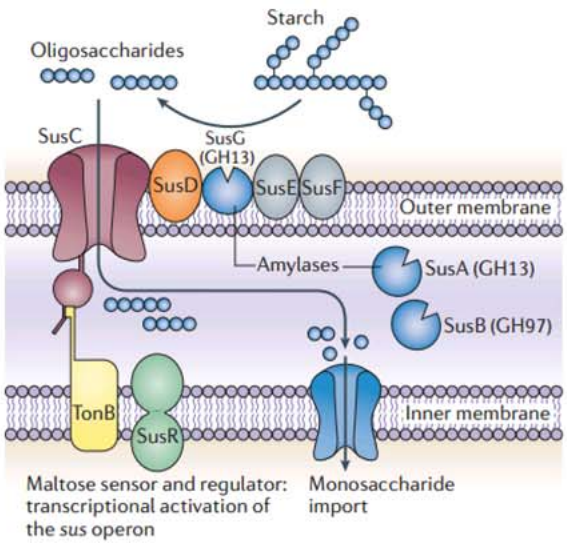
Heatmap showing growth values of 13 gut commensals.

Eric C. Martens *et al.* 2016. *Cell.*

Generalist: *Bacteroides ovatus (B. ovatus)*

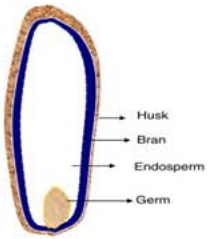
- B. ovatus dedicates ~20% to encode Starch utilization (Sus)-like systems.

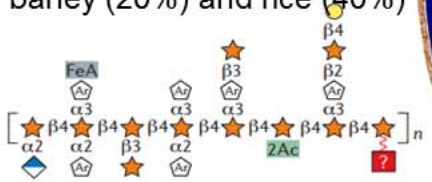
Starch utilization system



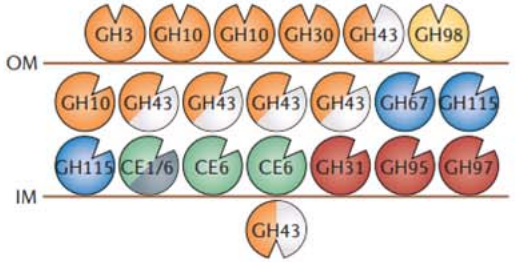
Arabinoxylan (AX):

Endosperm cell walls of barley (20%) and rice (40%)



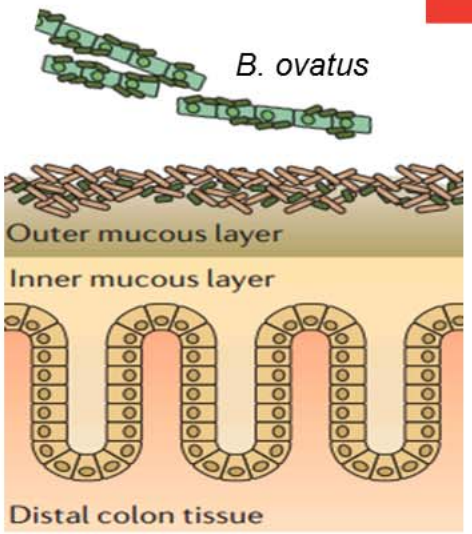


AX-degrading enzymes



Eric C. Martens *et al.* 2016. *Cell*.

Challenge: how to response to rapid diet change?



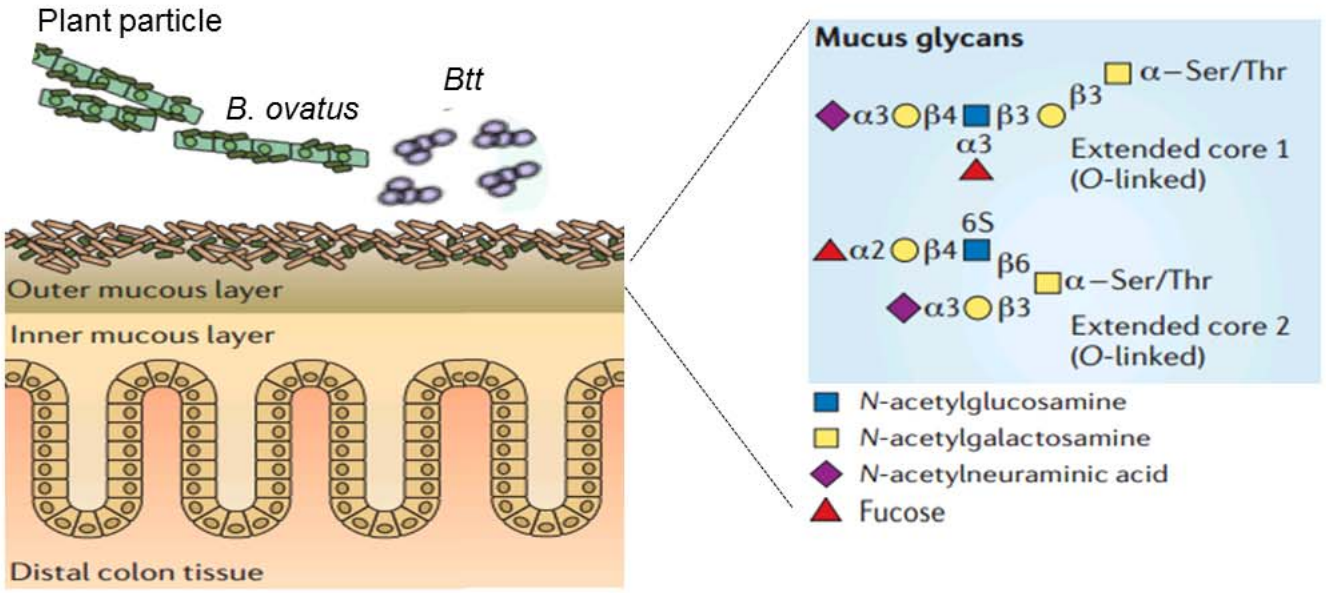
High plant glycan diet

Low plant glycan diet

Rely on dietary glycan may not a best strategy for survive!

Mucin degrader: *Bacteroides thetaiotaomicron*(Btt)

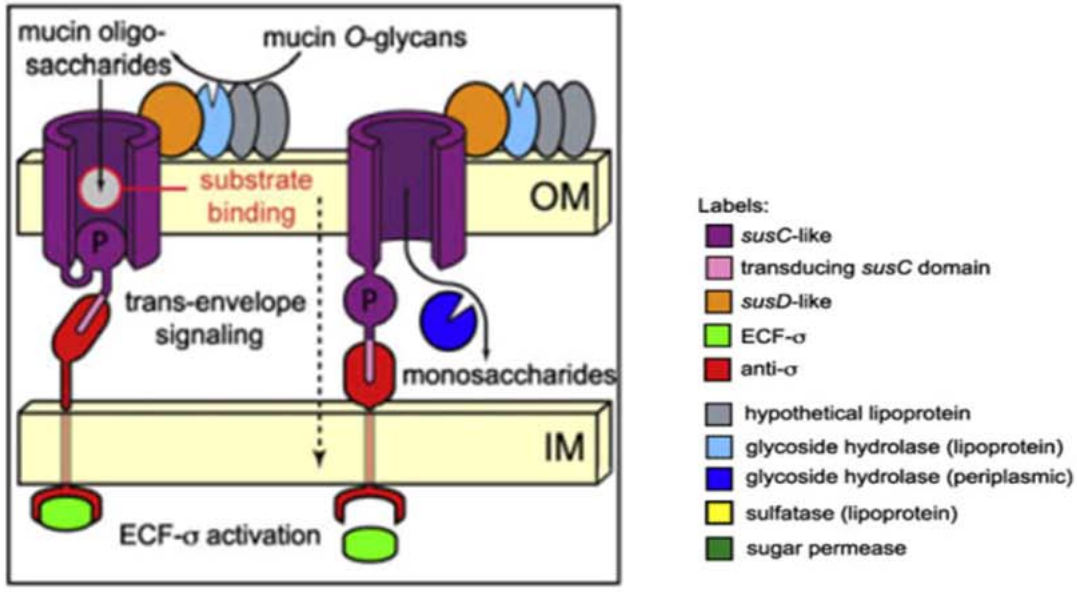
- Host mucus glycan is a stable nutritional sources.
- Btt has evolved to harvest the glycan from host mucus.



Mahesh S. Desai *et al.* 2018. *Nature reviews.*

Unique mucin glycan utilization system

- Largest repertoire of genes: 236 glycoside hydrolase and 15 polysaccharidase lyase genes.
- Unique mucin glycan utilization system.



Jeffrey I. Gordon *et al.* 2008. *Cell*

Mucin glycan degradation: fitness advantage

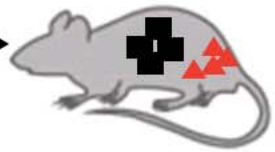
Cell Host & Microbe
Article

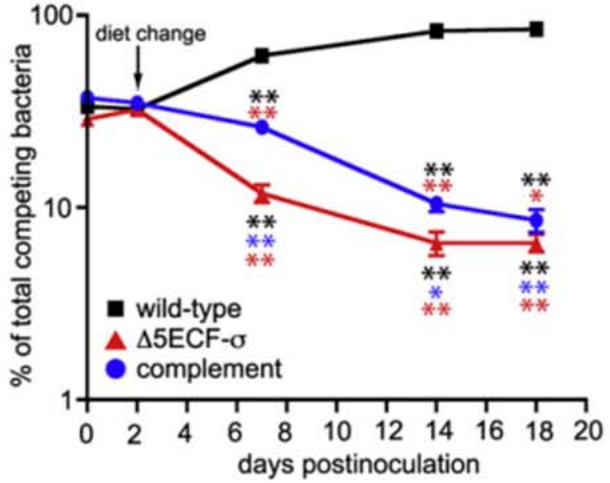
Mucosal Glycan Foraging Enhances Fitness and Transmission of a Saccharolytic Human Gut Bacterial Symbiont

B. thetaiotaomicron

■ wild-type
▲ Δ5ECF-σ

Plant glycan →
Simple sugar →



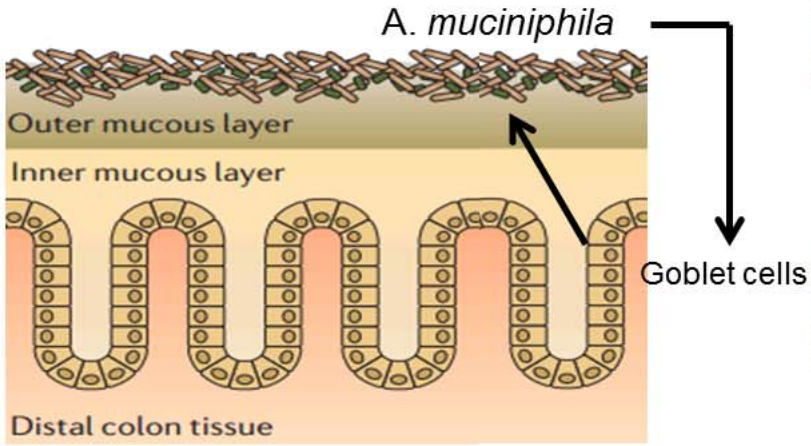


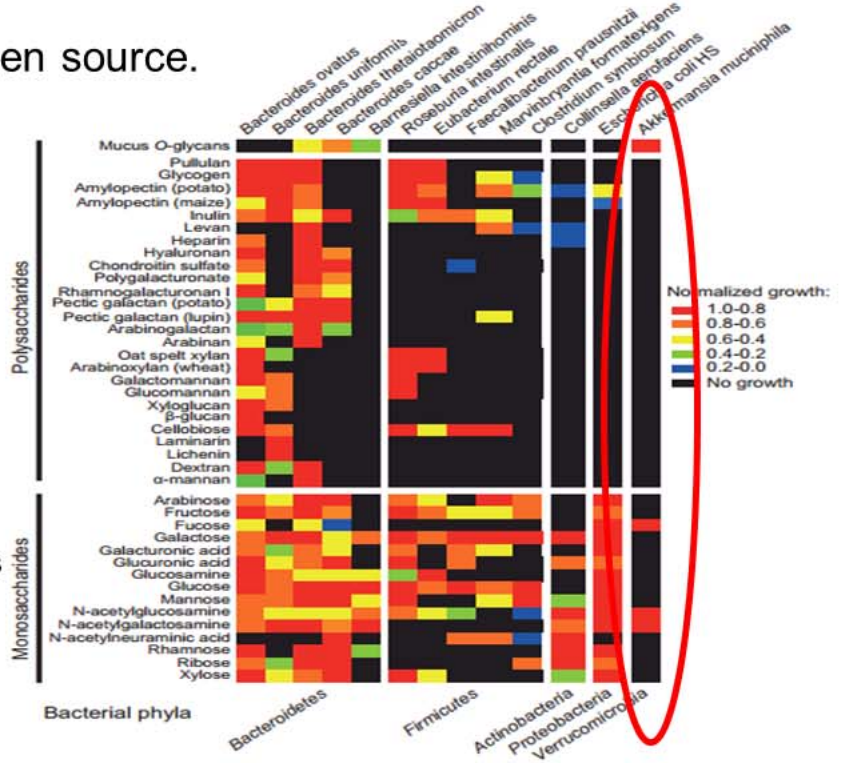
- Host mucin glycan degrading is induced in the absence of dietary glycan and in presence of host mucin glycan.

Jeffrey I. Gordon *et al.* 2008. *Cell*

Specialist: *Akkermansia muciniphila* (Akk)

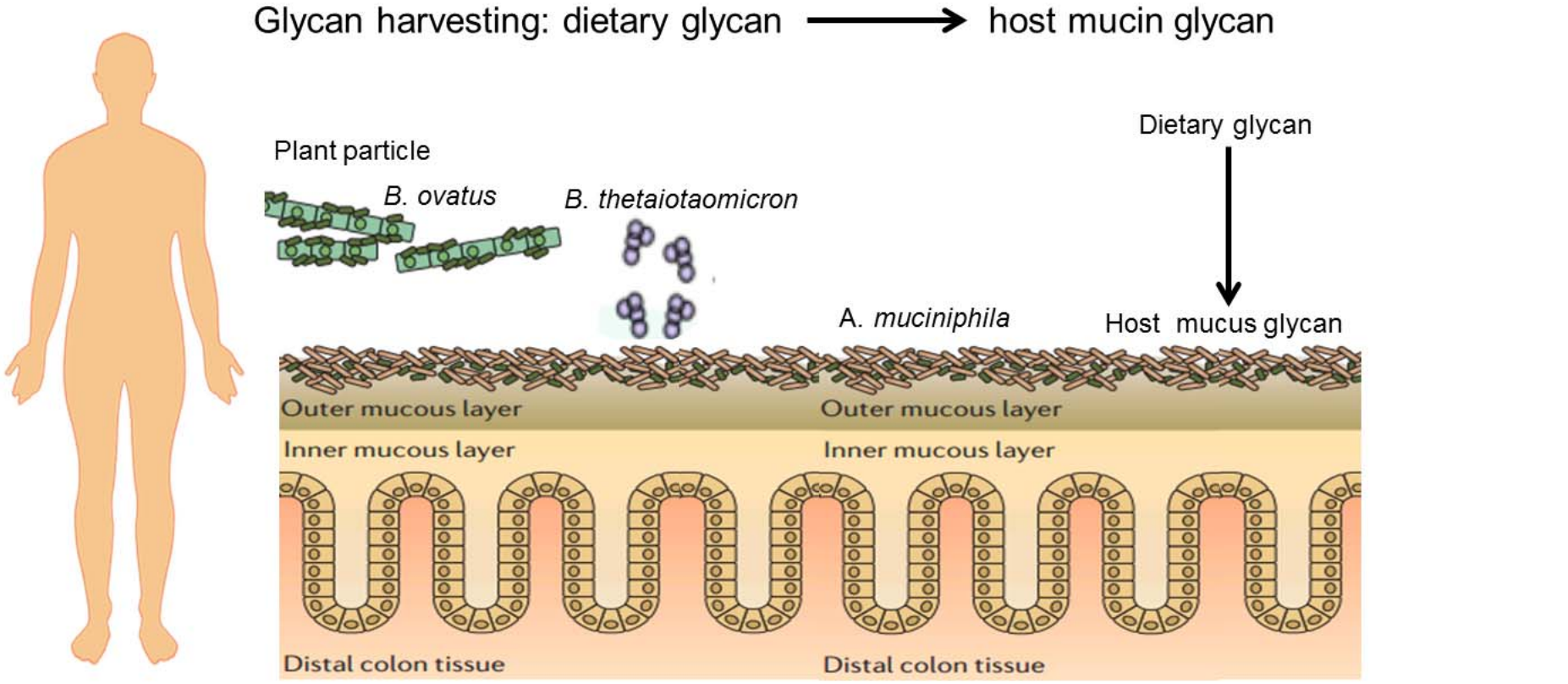
- Anaerobic Gram-negative bacterial species in Verrucomicrobia phylum.
- Utilizing mucins as sole carbon and nitrogen source.
- Stimulate the host secretion of mucus by increasing the goblet cell.





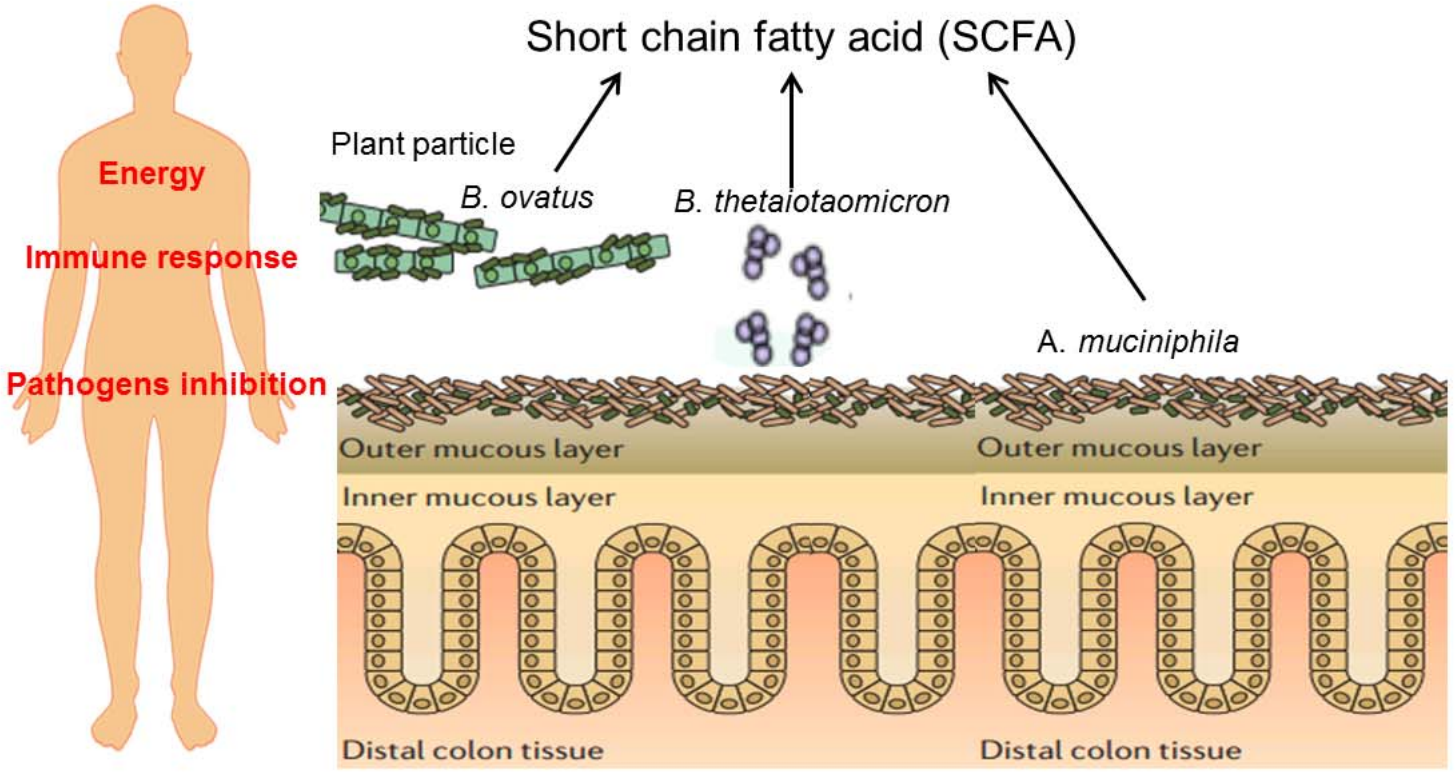
Eric C. Martens *et al.* 2012. Nature review.

Impact of glycan degradation



Mahesh S. Desai *et al.* 2018. *Nature reviews.*

Positive: short chain fatty acid (SCFA)



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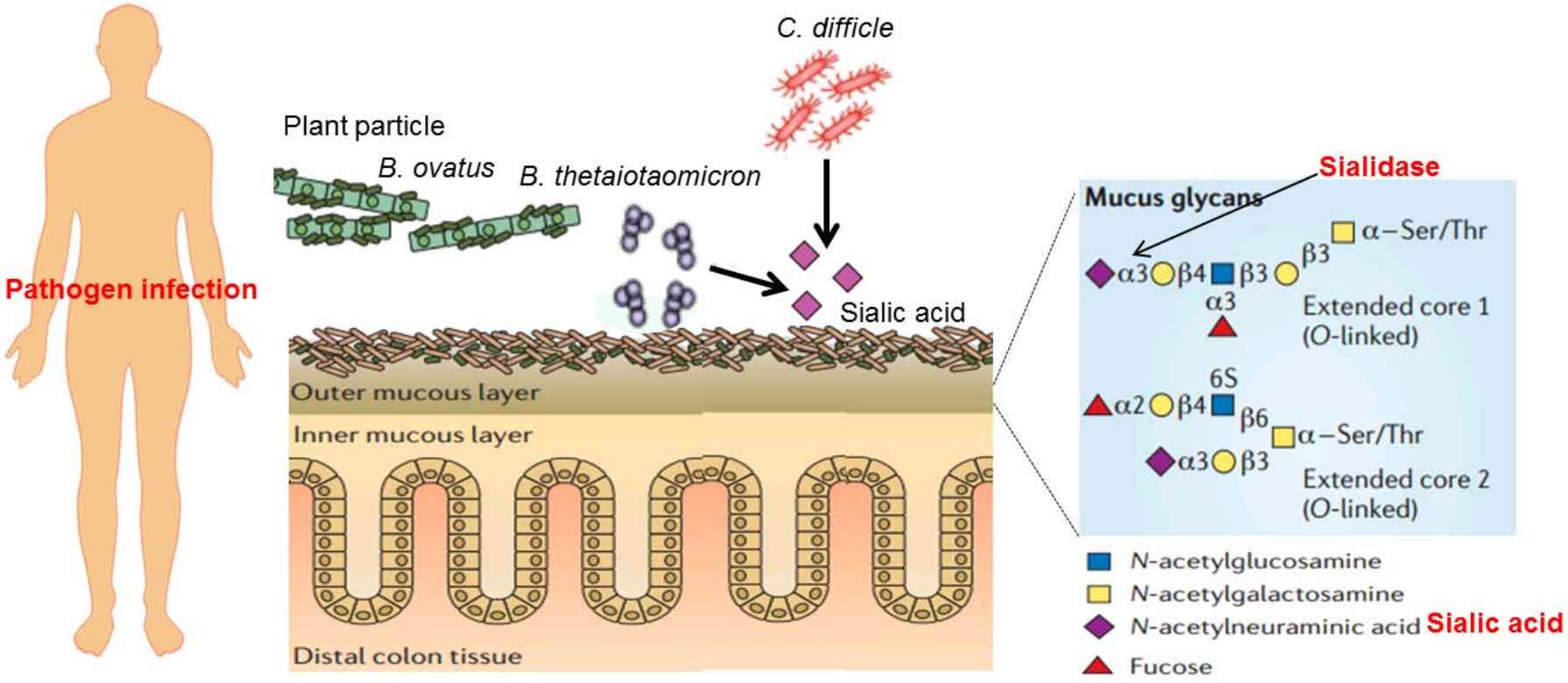
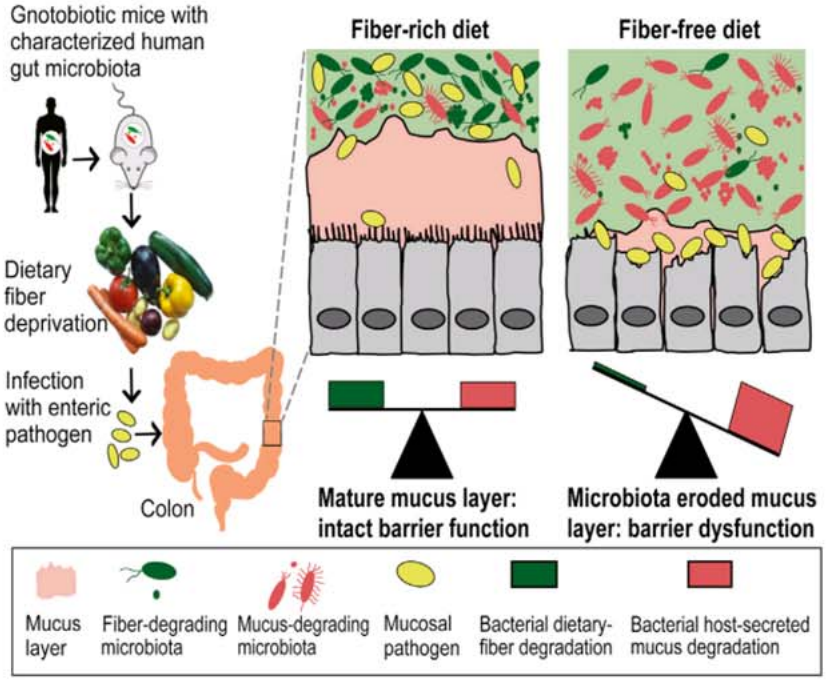
Negative: sialic acid-pathogens



Mahesh S. Desai *et al.* 2018. *Nature reviews.*

Cell **A Dietary Fiber-Deprived Gut Microbiota Degrades the Colonic Mucus Barrier and Enhances Pathogen Susceptibility**



- Fiber-rich diet can keep a balance between fibre degradation and mucus degradation.
- Fiber-deprived gut microbiota promotes aggressive colitis by an enteric pathogen.

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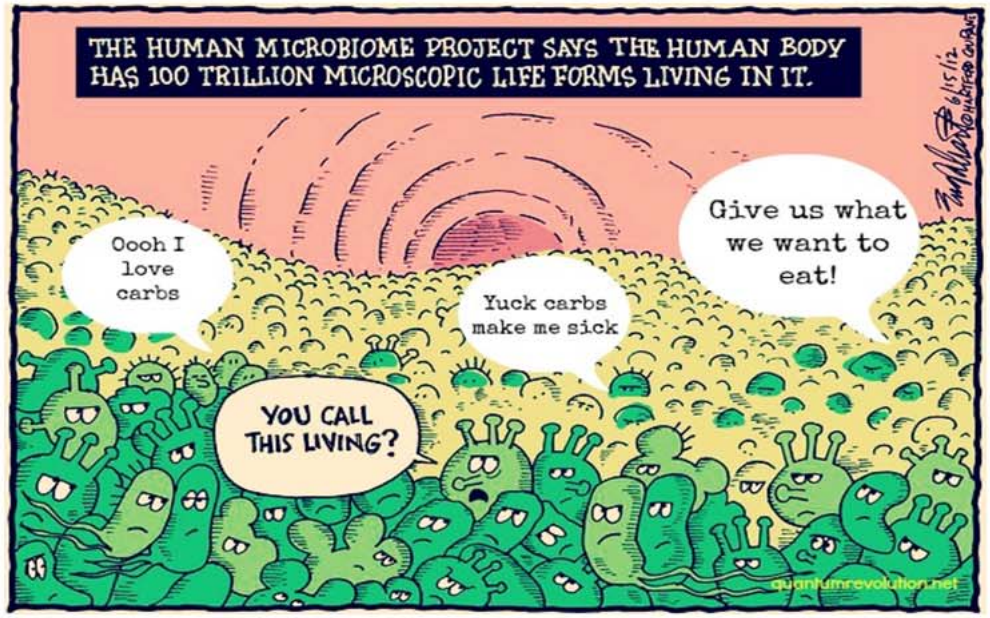
Eric C. Martens *et al*. 2016. *Cell*

Treat or trick



Feed me glycan or eat your gut!

Insights and challenges

- Plant-derived glycan is important for keep health.
- Dietary fiber or prebiotics may be promising non-invasive avenues to intentionally manipulate the gut community.
- Understanding of the precise connections between the many different dietary and endogenous mucosal carbohydrates and the microorganisms that directly degrade them.

Thank you