Microbioom & mentaal welzijn: inzichten van populatiestudies



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KU LEUVEN

VIB

The Economist

AUGUST 18TH–24TH 2012

Economist.com

The Catholic church's unholy mess

Paul Ryan: the man with the plan

Generation Xhausted

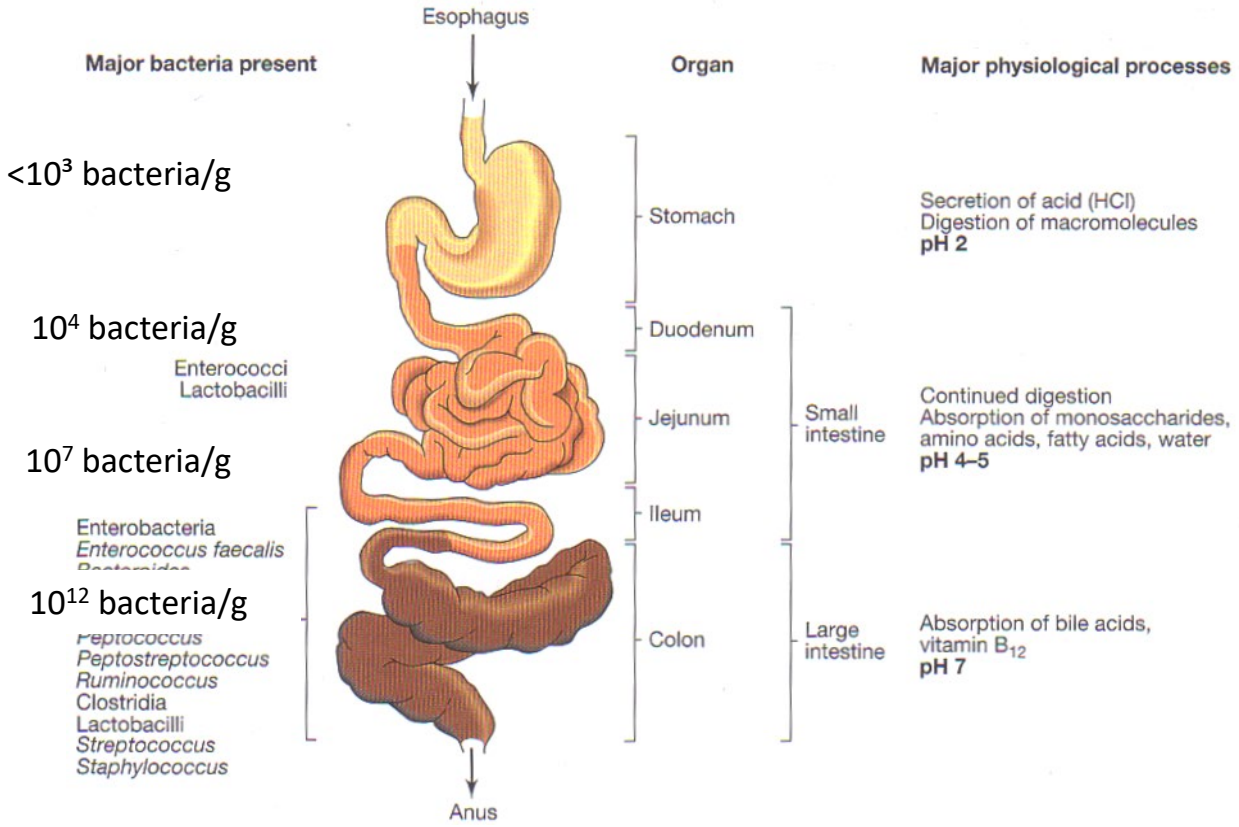
China, victim of the Olympics?

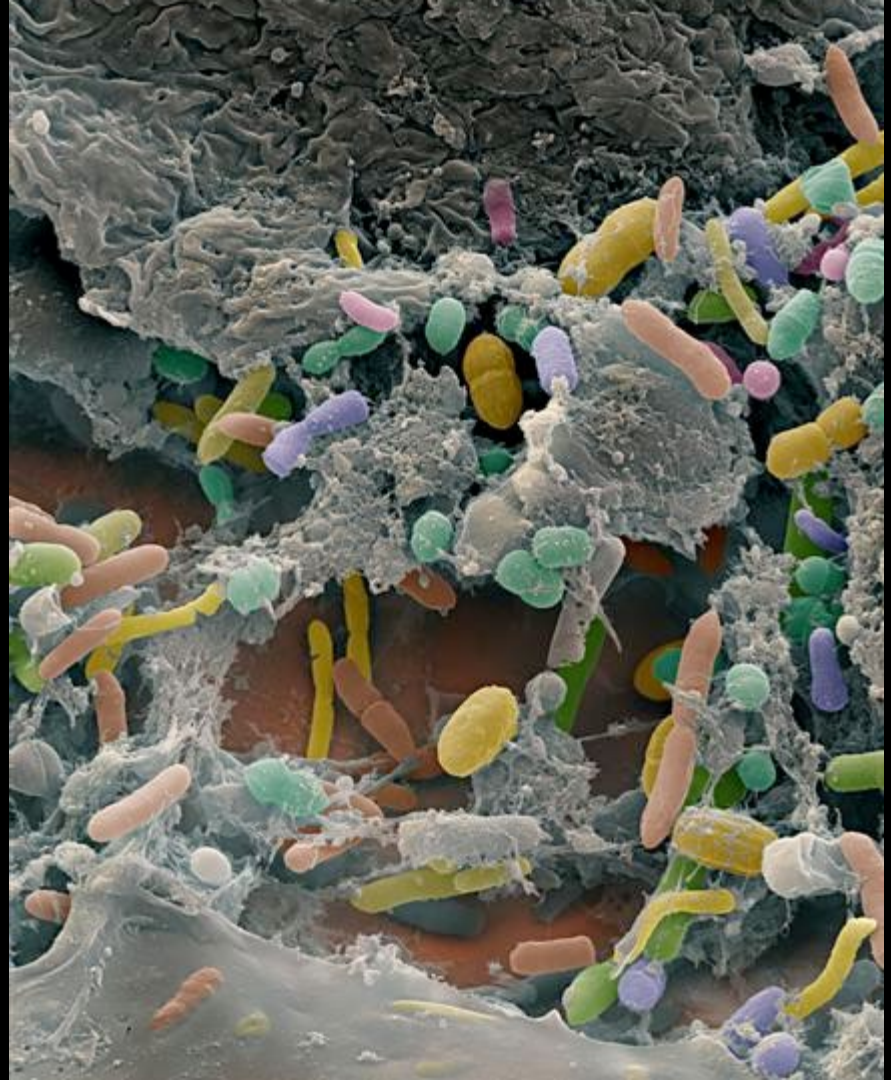
On the origin of specie

Microbes maketh man



Gut microbiota: distribution





Your flora is your friend

- Food digestion
- Protection against pathogens
- Provides essential nutrients (e.g. vitamins)
- ‘Trains’ your immune system
- *Disturbance* of flora is linked to major diseases

The promise of the microbiome field:
diagnostics & cure for all major diseases on the planet



Reality check:
We *don't* even know what a *healthy* flora means!

Microbiome sequencing state-of-the-art:

MetaHIT, HMP + specific lab studies combined have sequenced ±3000 healthy individuals world-wide, still biased cut of the population

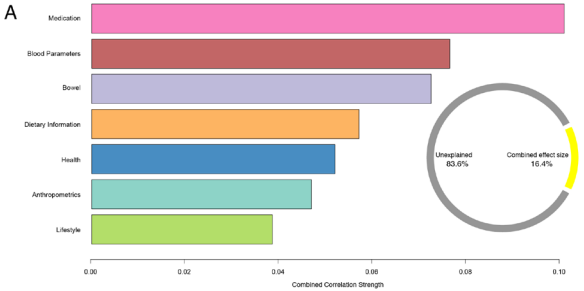


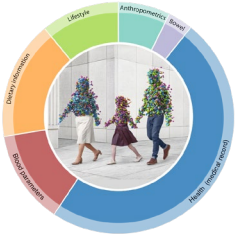
Genetics: 10-100.000s individuals

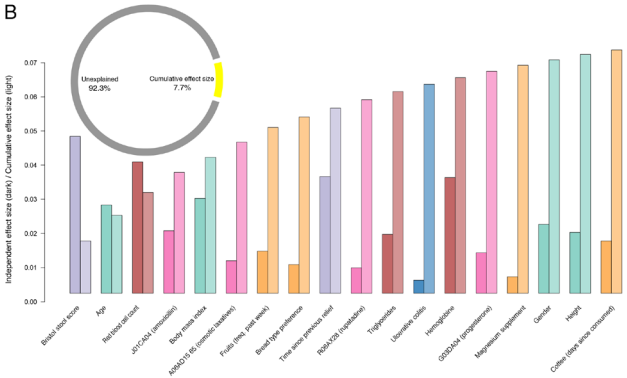
Variation in clinically relevant population = largely unknown
Temporal variation & stability of biomarkers = largely unknown
Factors influencing gut flora composition = largely unknown
Effect environment = largely unknown

Clinical end points for functional foods, pre-/pro/synbiotics, pharma-/nutriceutical interventions etc are *unknown*

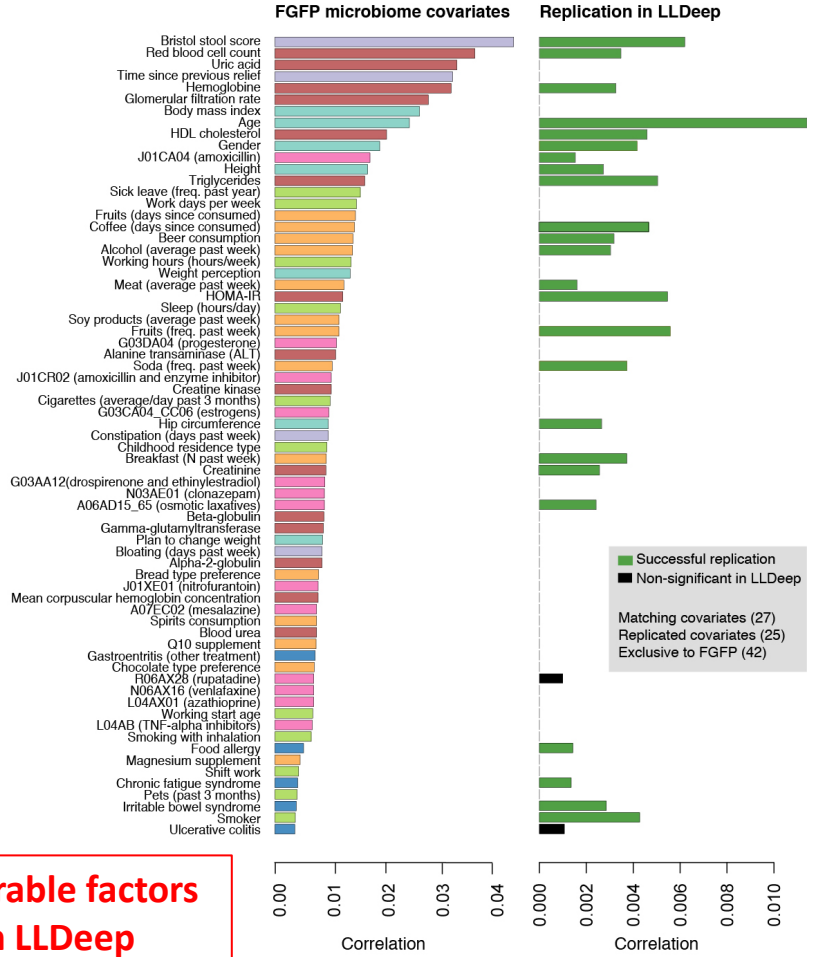
Flemish Gut Flora Project (n=3400) enables identification 69 factors associated with microbiota variation











92% of comparable factors replicate in LLDeep

Falony et al. **Science**, 2016

Quality of life and depression in the FGFP dataset



Falony *et al*, *Science* (2016)

The RAND HRQoL questionnaire

- **Mental health indicators:**
  - Social functioning (SF)
  - Mental health (MH)
  - Vitality (VT)
  - Role limitations caused by emotional health (RE)

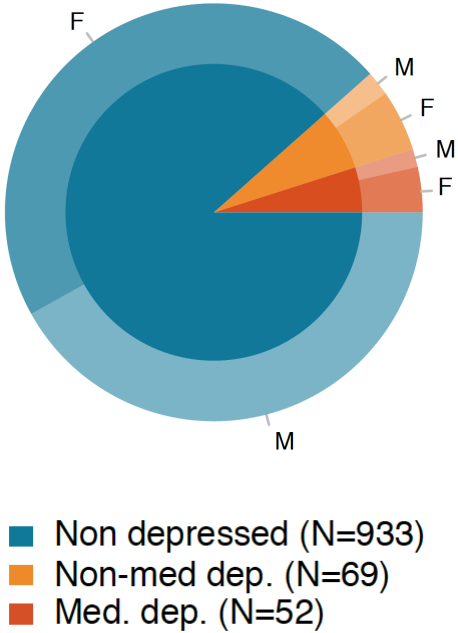
Mental component summary (MCS)

- **Physical health indicators:**
  - Physical functioning (PF)
  - Bodily pain (BP)
  - General health (GH)
  - Role limitations caused by physical health (RP)

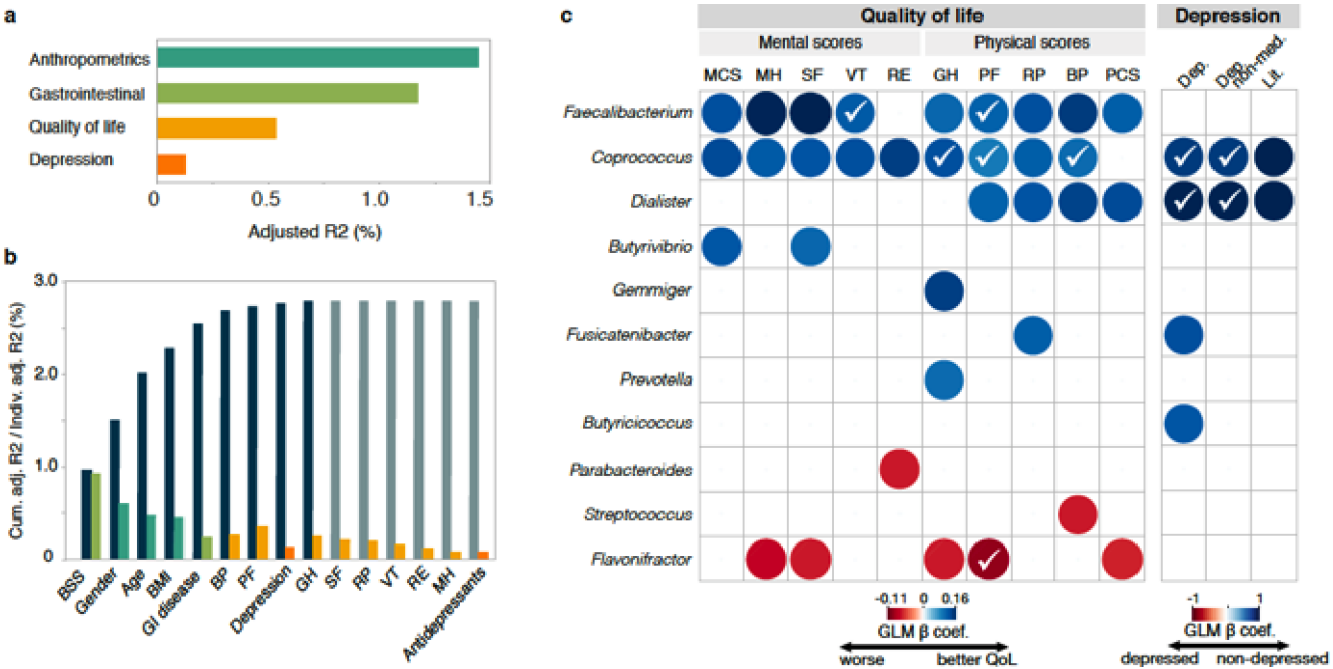
Physical component summary (PCS)

Hays, R. D. & Morales, L. S. *Ann. Med.* (2001).

Depression



Population-level analysis (discovery n=1054; replication n=1070) identifies microbiota markers for quality of life (RAND) and depression



Faecalibacterium, Coprococcus (butyrate producers): increased with higher QoL

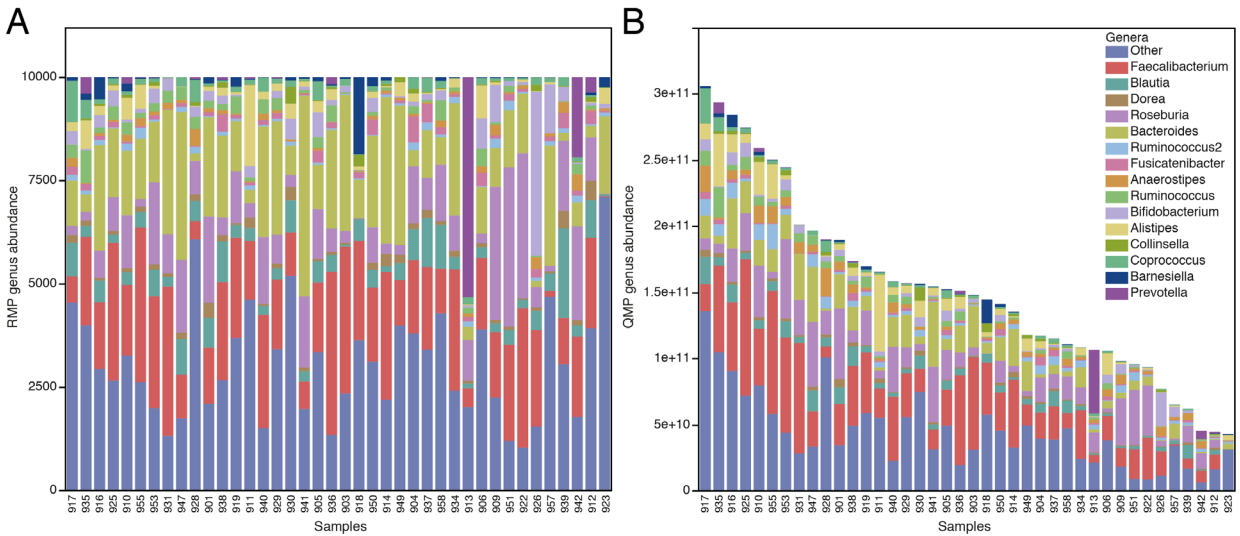
Coprococcus, Dialister: decreased in depression

Antidepressants = important confounder!

Valles-Colomer et al **Nature Microbiology** *2019*

From Relative to Quantitative profiling



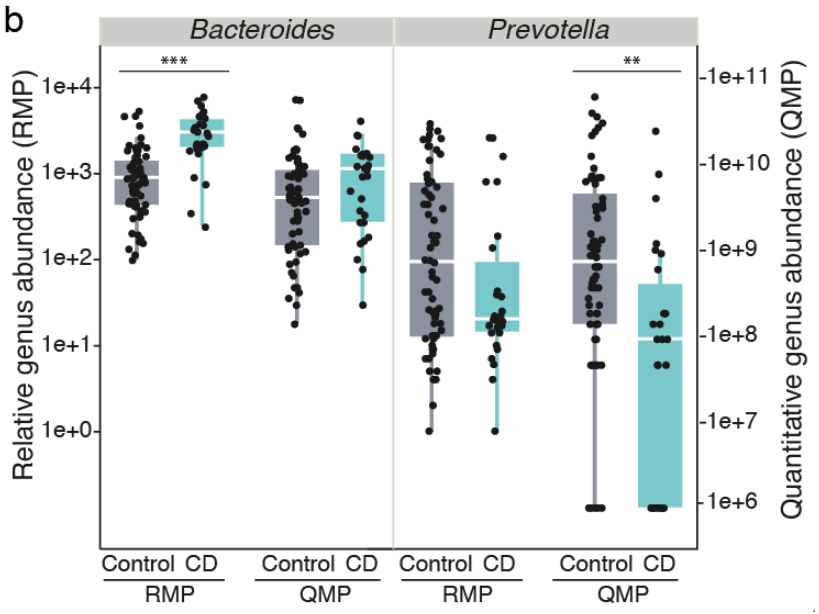


Relative Microbiome Profiling (RMP)
(current standard)

Quantitative Microbiome Profiling (QMP)
(new approach)

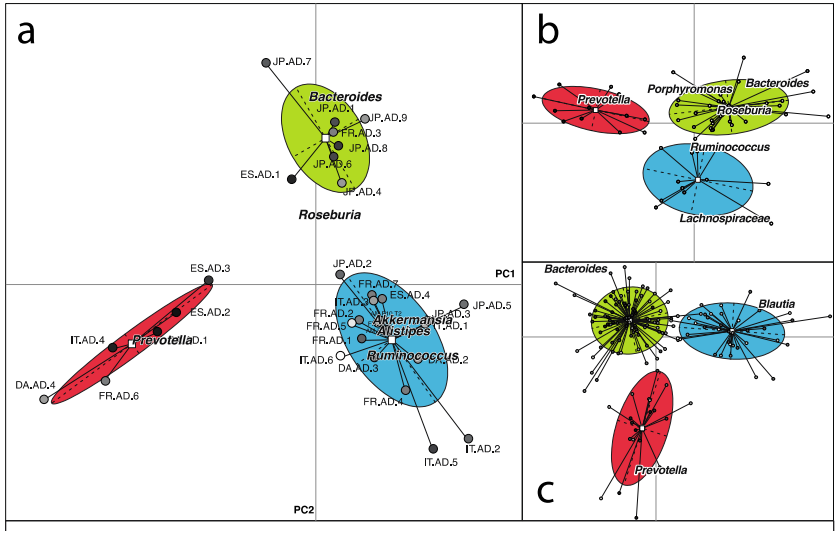
Vandeputte et al., **Nature** 2017

Clinical relevance (i): Strong effect on biomarker discovery in Crohn's Disease

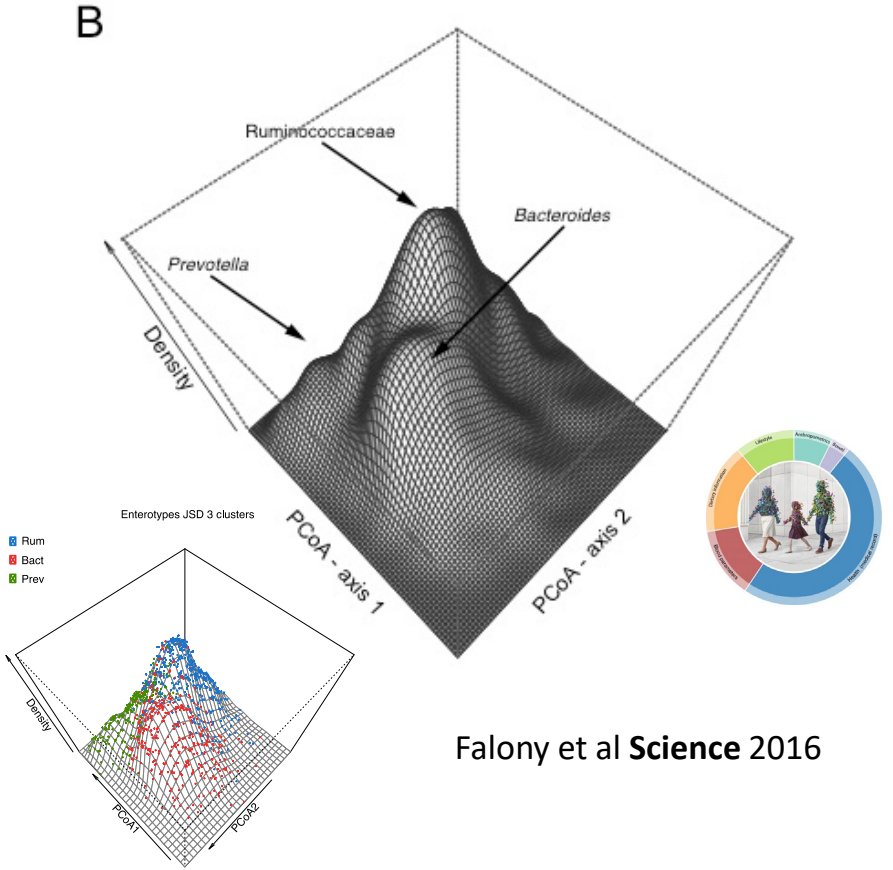


Vandeputte et al., **Nature** 2017

Enterotypes: density peaks representing ‘preferred’ ecosystem constellations

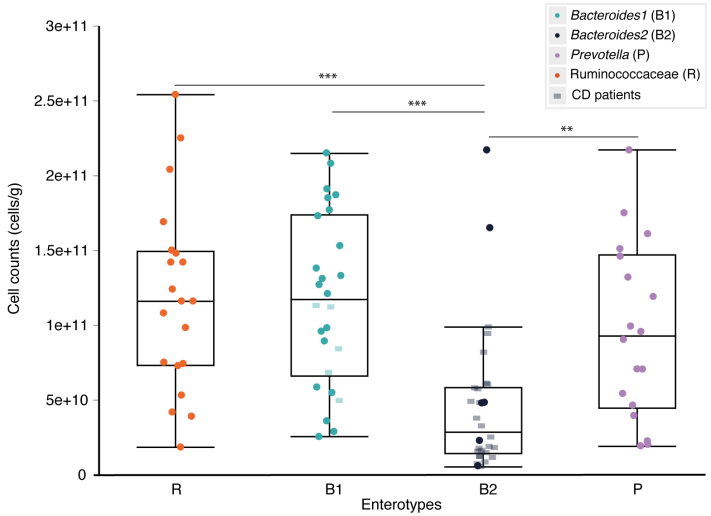


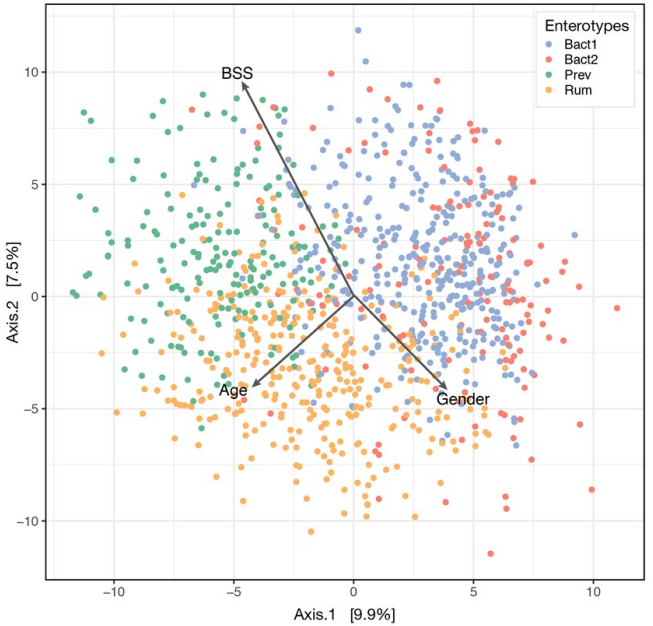
Arumugam*, Raes* et al. **Nature** 2011



Falony et al **Science** 2016

Clinical relevance (ii): Discovery of a 4th low-microbial load enterotype associated with Crohn's disease

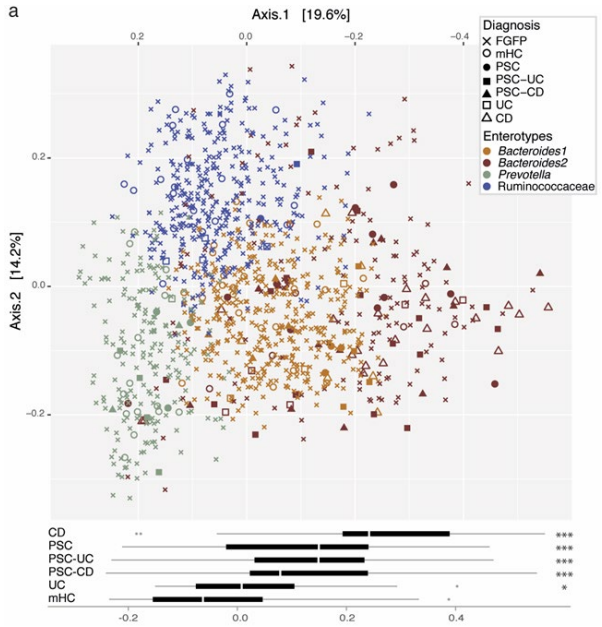


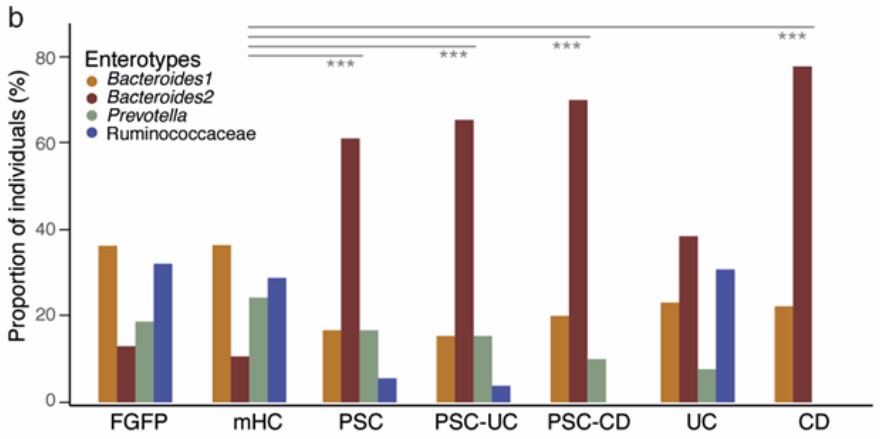


Vandeputte et al., **Nature** 2017

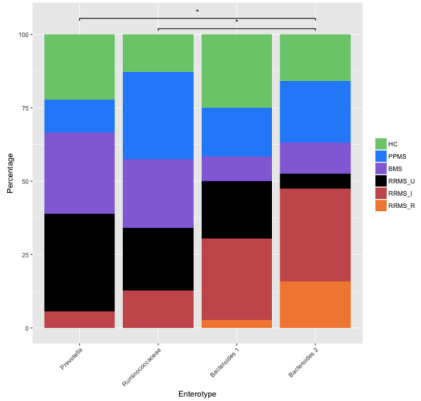
B2: a cross-disease, low cell count enterotype

Increased prevalence of B2 across multiple pathologies





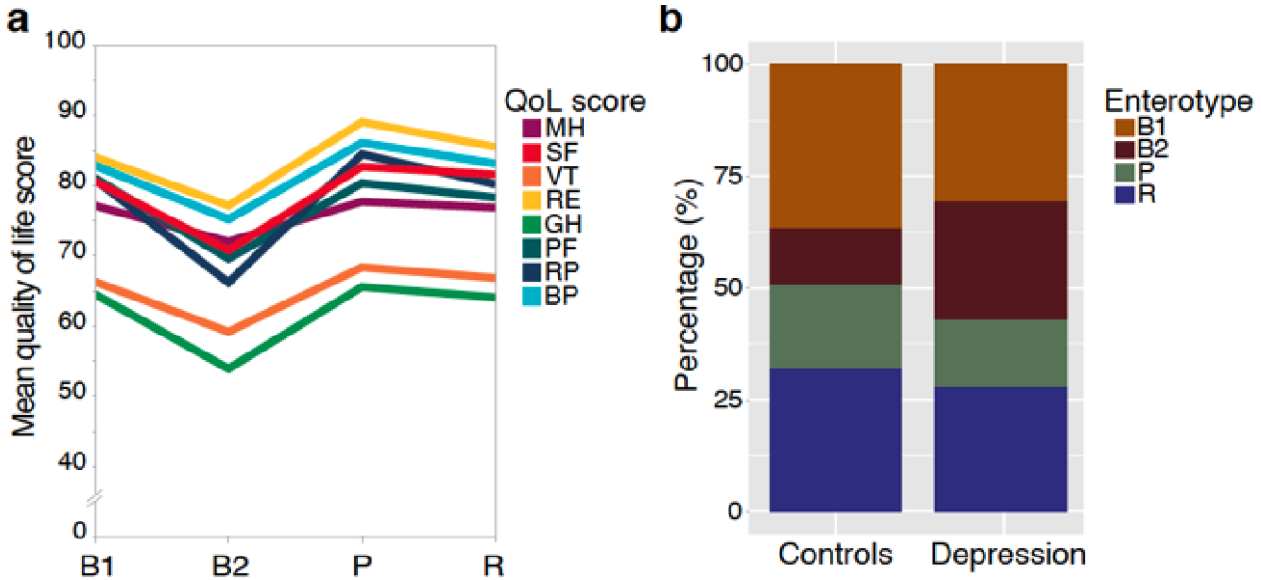
Vieira-Silva *et al.,* **Nature Microbiology** *2019*



Multiple Sclerosis subtypes
Reynders et al **Ann Clin Transl Neur** *2020*

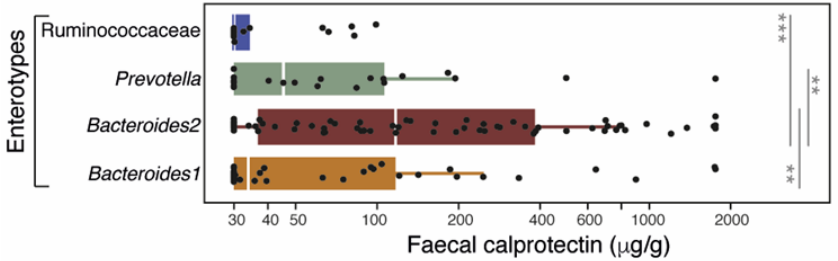
CD: Crohn's Disease; PSC: Primary Sclerosing Cholangitis; UC: Ulcerative Colitis

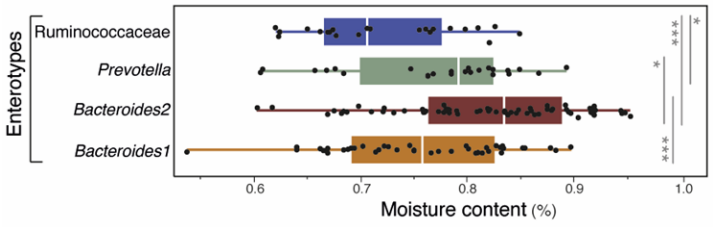
B2 enterotype associated to lowered QoL and depression

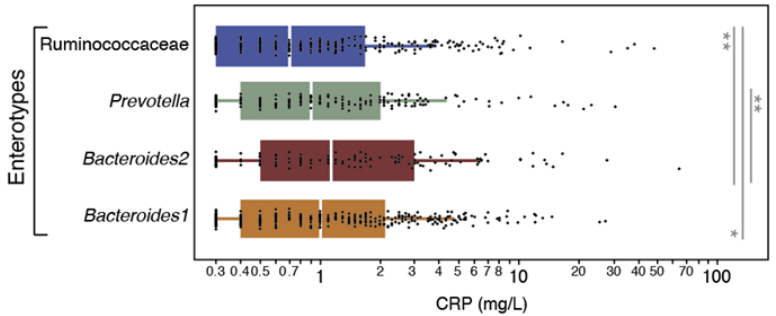


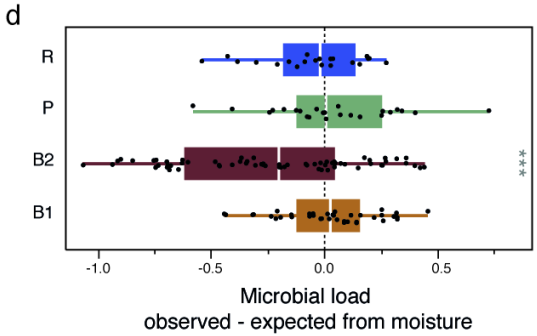
Valles-Colomer et al **Nature Microbiology** *2019*

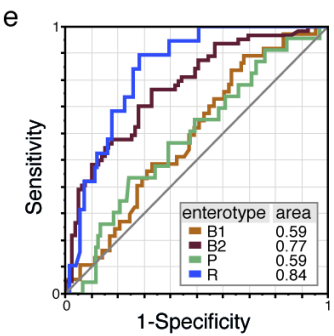
B2 hallmarks: inflammation and fast transit

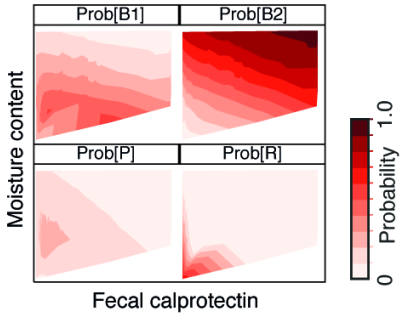












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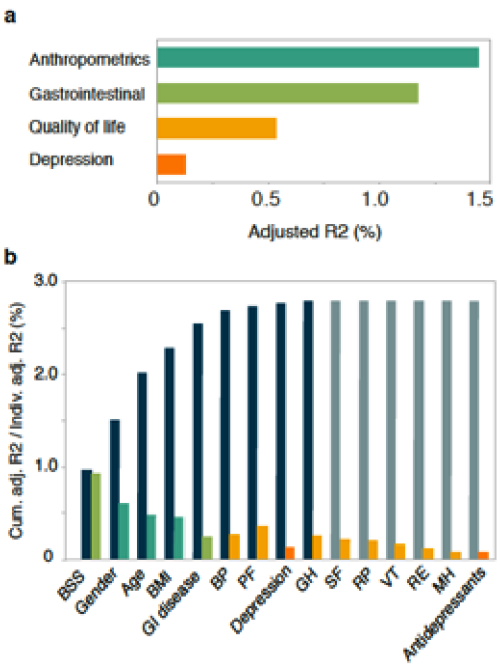

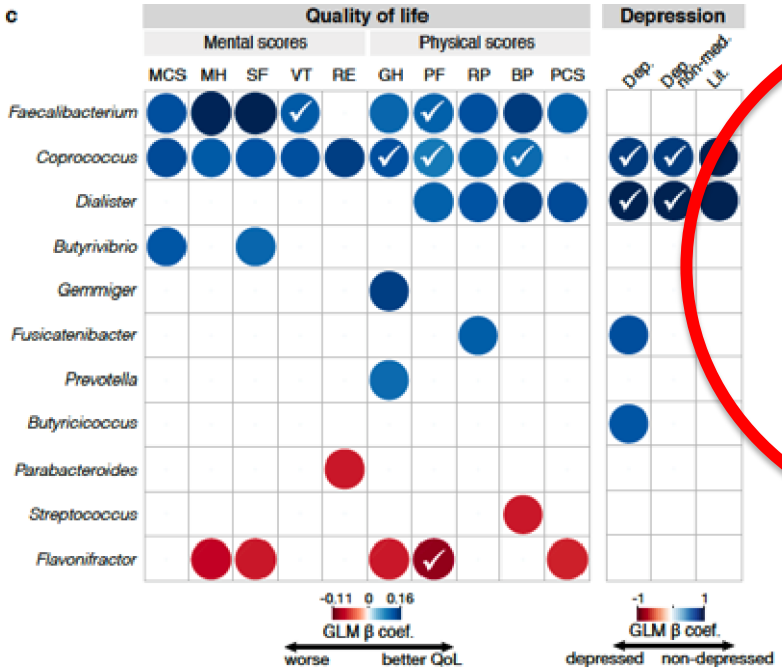

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Butyrate producers!

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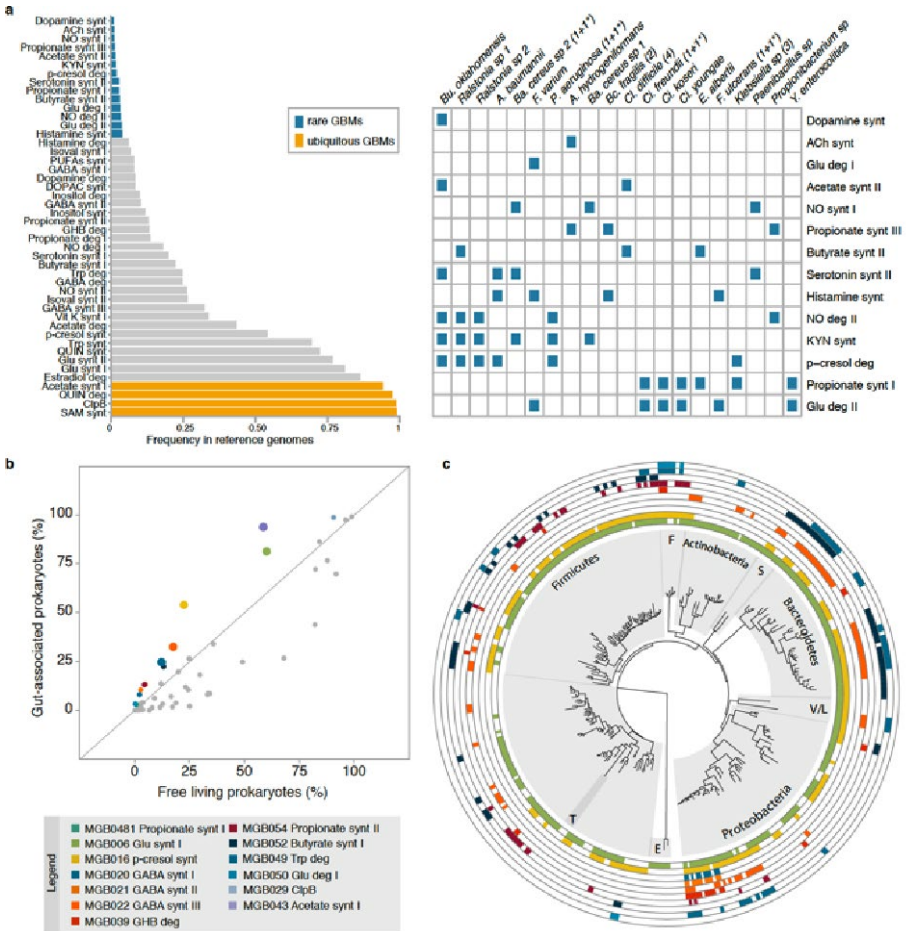
Valles-Colomer et al **Nature Microbiology** *2019*



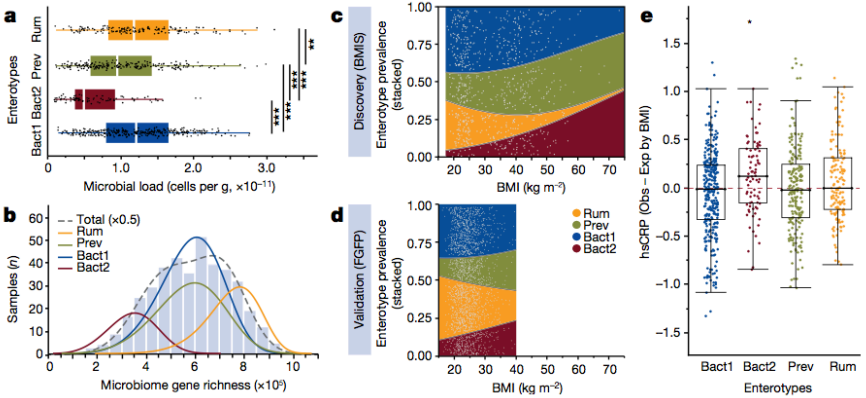
Catalog of gut microbiota neuroactive potential using novel gut-brain-axis analysis platform

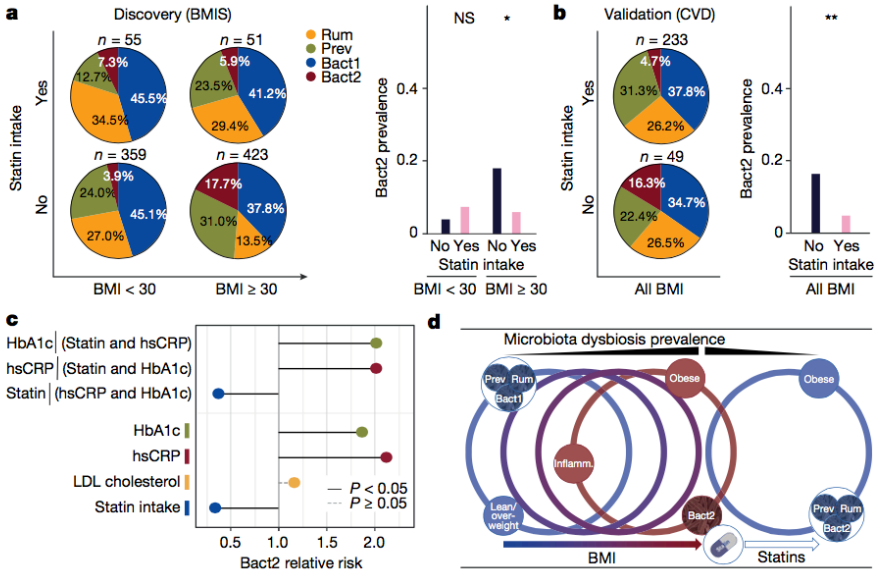
- Some functionalities restricted to specific taxa (“rare” e.g. dopamine synthesis)
- Histamine synthesis overrepresented in Fusobacterium phylum
- 2 pathways for serotonin, one rare (<5%), one more common (>20%; eg Akkermansia)
- Neuroactive pathways overrepresented in gut organisms vs free living
- No pathways on plasmids

Valles-Colomer et al **Nature Microbiology** *2019*

From diagnostics to treatments?

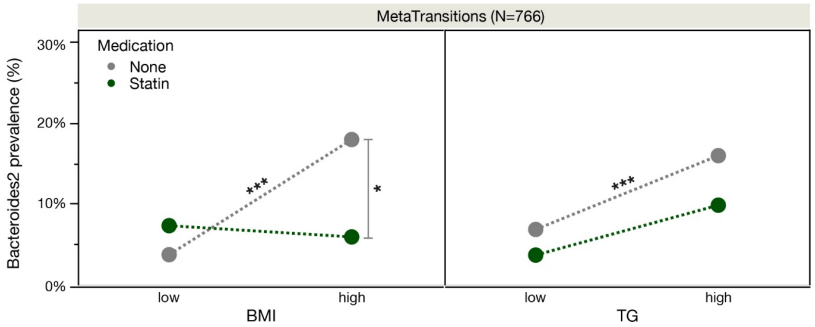
B2 prevalence increases with BMI



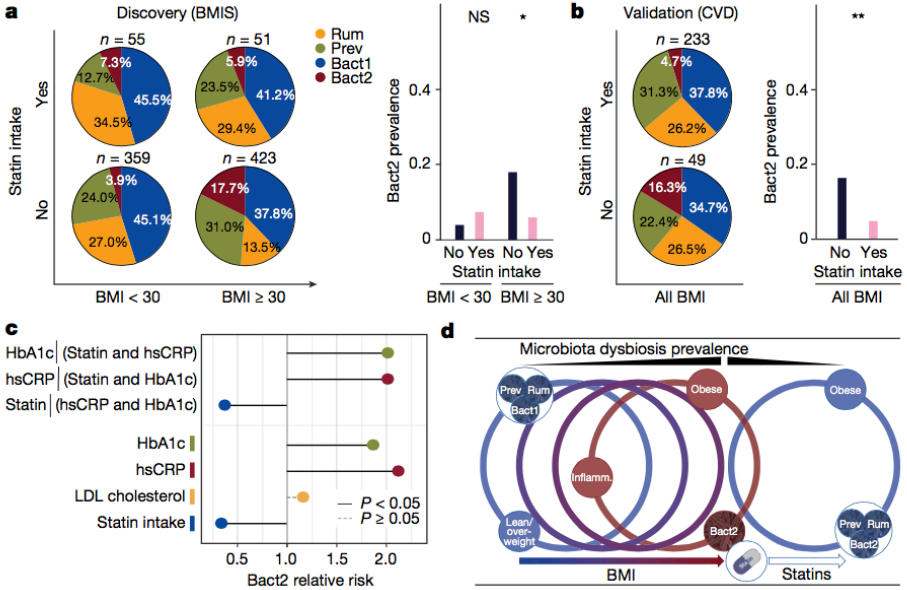


Vieira-Silva *et al.*, **Nature** *2020*

…except when using statins!

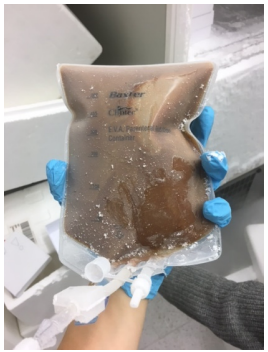


-> Statins potential microbiota modulator?



Vieira-Silva *et al.*, **Nature** *2020*

Probiotics 2.0







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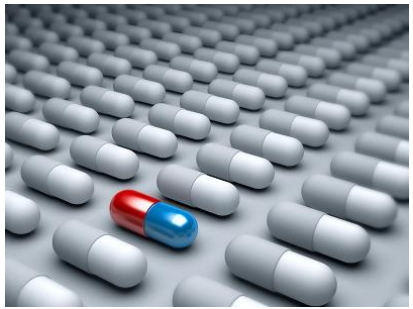
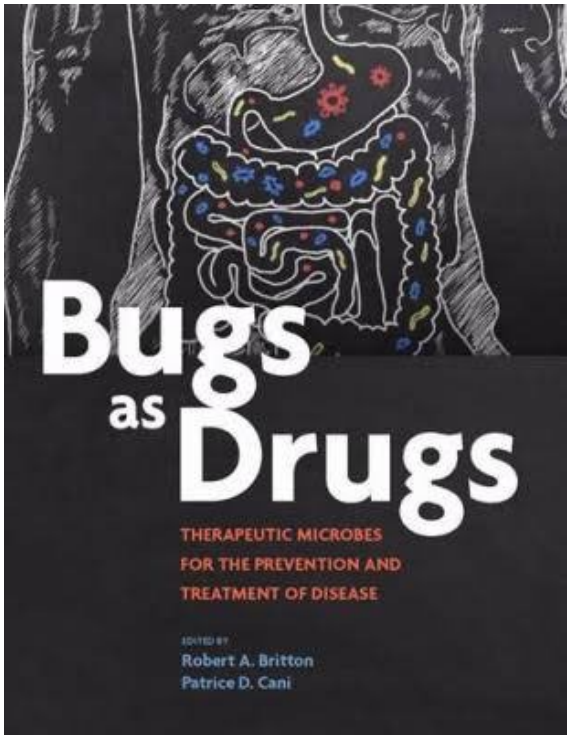
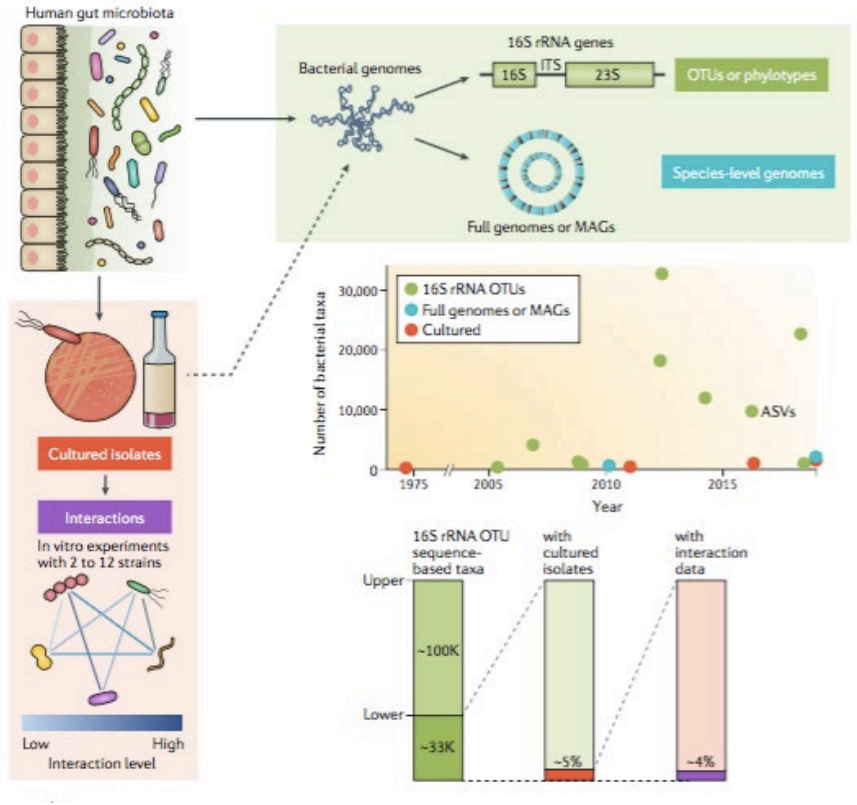




Vázquez-Castellanos et al **Curr Opin Pharm** 2019

Closing the gap: gut microbiology in the post-sequencing age



REVIEWS

Synthetic ecology of the human gut microbiota

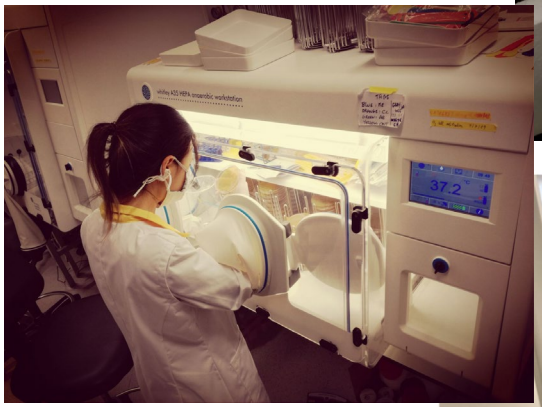
*Gino Vrancken[1,2,3], Ann C. Gregory[1,2,3], Geert R. B. Huys[1,2], Karoline Faust[1] and Jeroen Raes[1,2]**

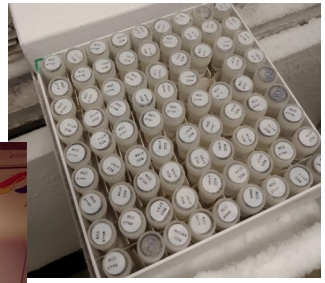
We have the data,
we miss the bugs
(and their interactions)!

Vranken*, Gregory* et al **Nat Rev Microbiol** 2019

The ingredients: novel strategies for high-throughput isolation & screening

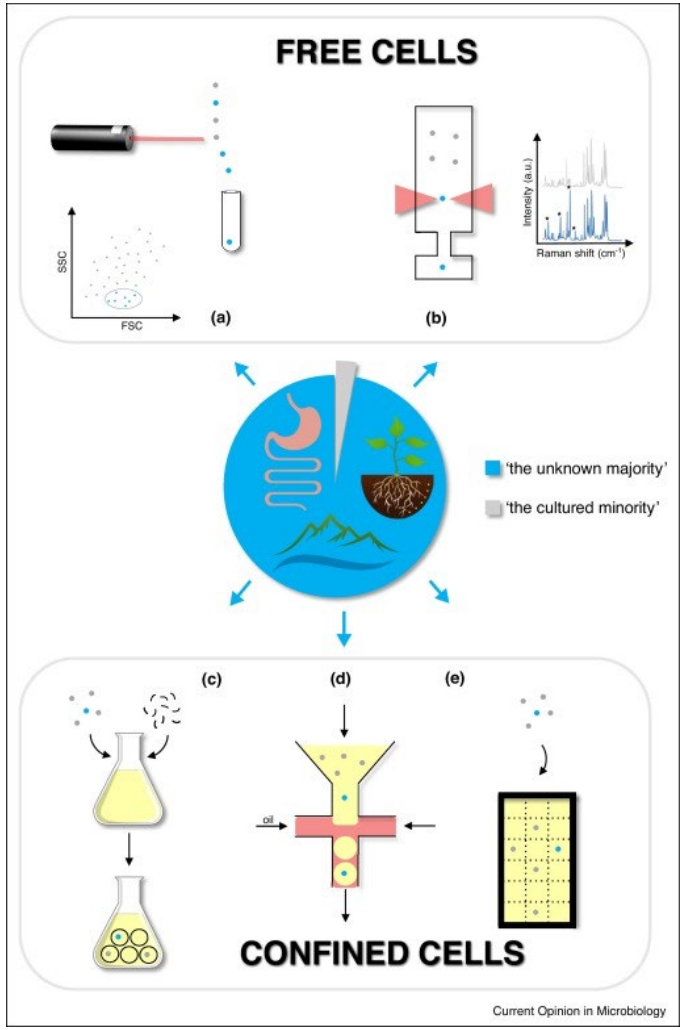
Raes lab culture collection
>3000 strains



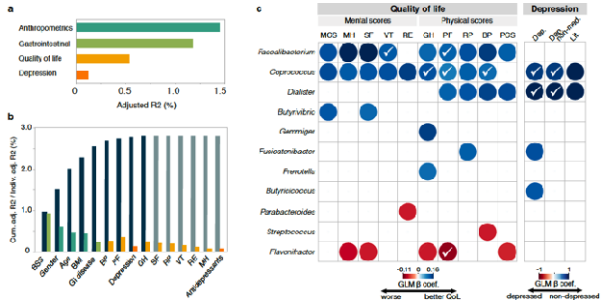


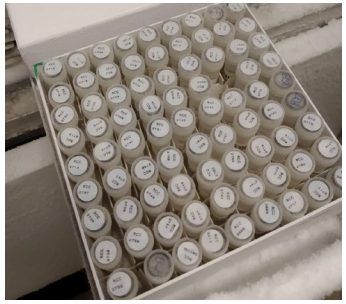


Huys & Raes, **Curr Opin Micro** 2018

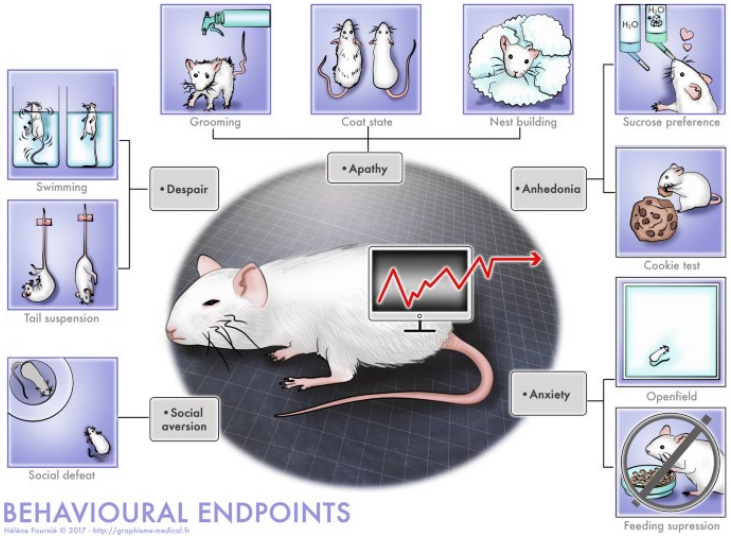


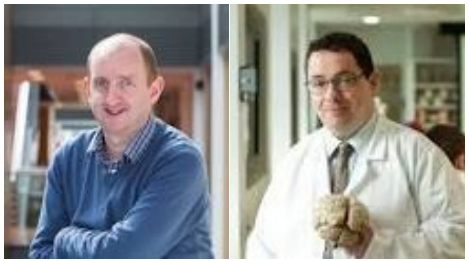
Towards probiotics for depression? Establishing causality first…





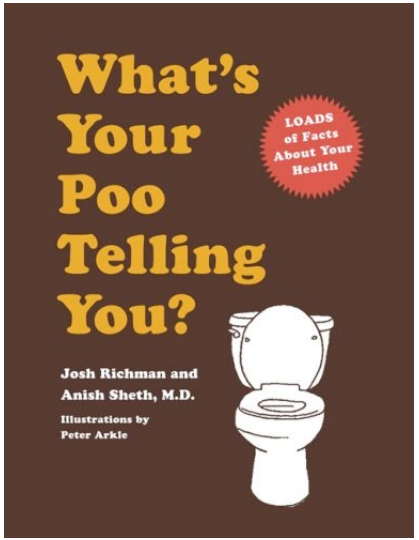
DISCOVERIE





Collab G. Clarke, J. Cryan UCC

Conclusions



- Population cohorts important for confounders but also source of targets for clinical work
- Quantitative profiling necessary for pathomechanism understanding
- Depression & microbiome: reproducible signals in human, but regarding causality and mechanisms still work to do

Acknowledgments & collaborators

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Asiye Kazeroonian
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Sara Deleu
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Severine Vermeire
Danny Delooze
Sasha Zhernakova
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Patrice Cani
Sabine Tejpar
Kristin Verbeke
Gigi Veereman



Lucas Van Oudenhove
Stephan Claes
Luc De Vuyst
Didier Gonze
Jan Danckaert
Tom Van de Wiele
Griet Glorieux
Sofie Goormachtig

Dirk Elewaut
Lars Vereecke
Kristin Verbeke
Guy Boeckxtaens
Philip Rosenstiel
Andre Franke
Jan Tack
Ronny Bruffaerts

Karine Clement
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Peer Bork
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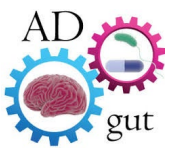
Funding & collaborations















Thanks for your attention

Open postdoc positions (wet/dry)

Contact:
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