



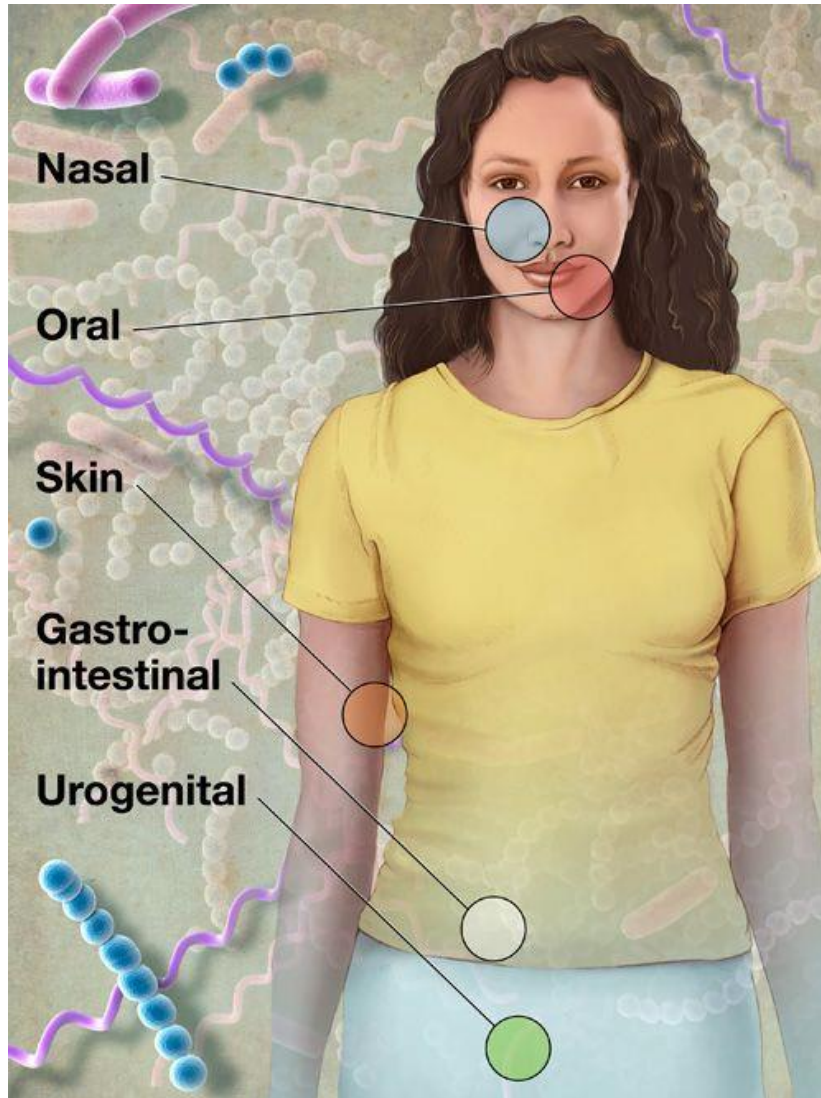
Early-Life Microbiota

Connecting Nutrition and Health, EI
January 26th, 2017

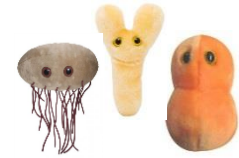
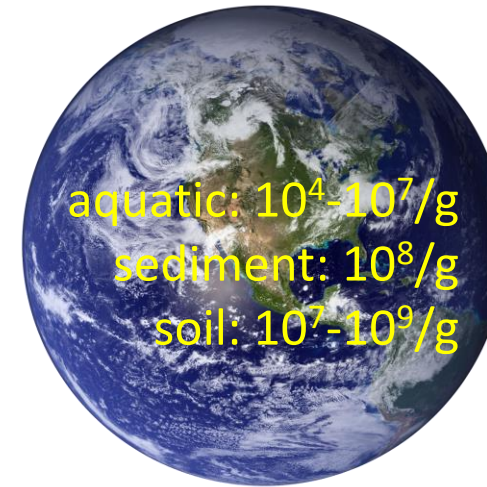
Dr Melissa Lawson
Research fellow
Hall laboratories

Our microbial ecosystem: the *Microbiota*

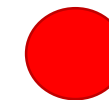
We are home to highly diverse and dynamic microbial communities



100 % Human ?



Laid end to end our body's microbiota would circle the earth **2.5 times**



blood cell

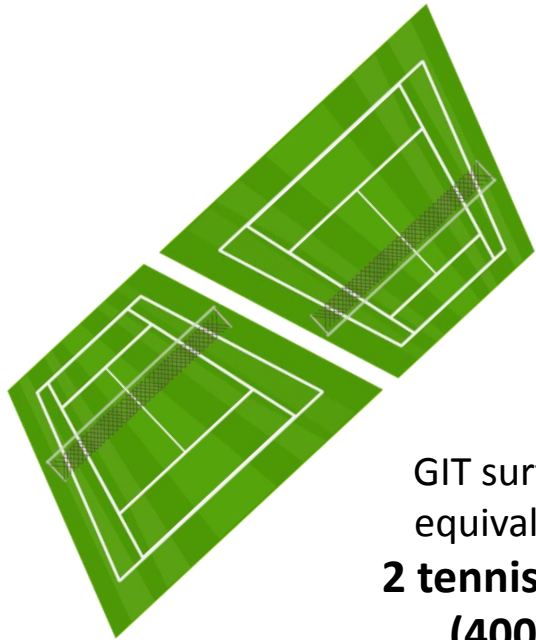


bacterial cell

Bacteria are **10 to 50 times smaller** than human cells

The gut microbiota

~**90%** of our own
bacteria found in
gastrointestinal tract
(GIT)

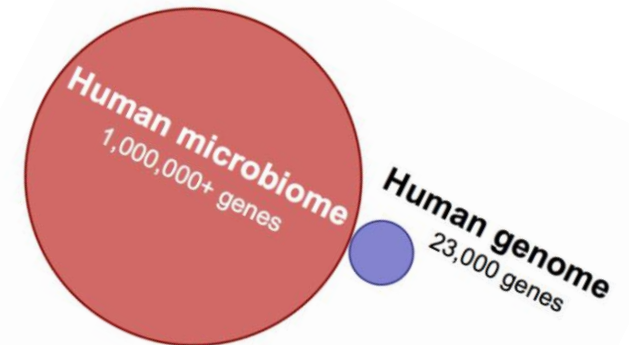


GIT surface is
equivalent to
2 tennis courts
(400m²)

Mammalian intestine
most densely
colonised habitat
found in nature



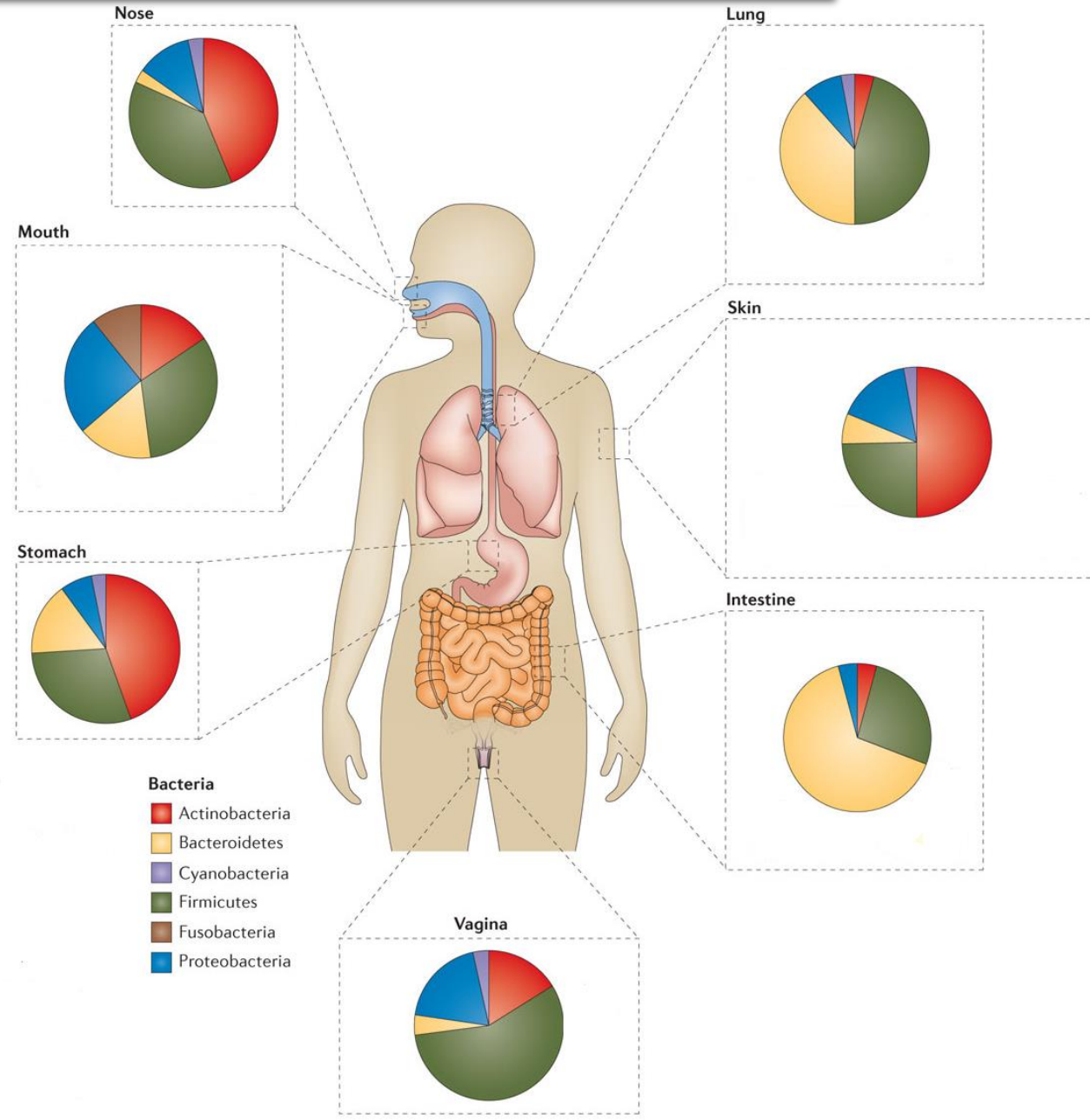
contains **100s of trillions**
of bacteria



Microbiome contains **150 times** more
unique genes than human genome

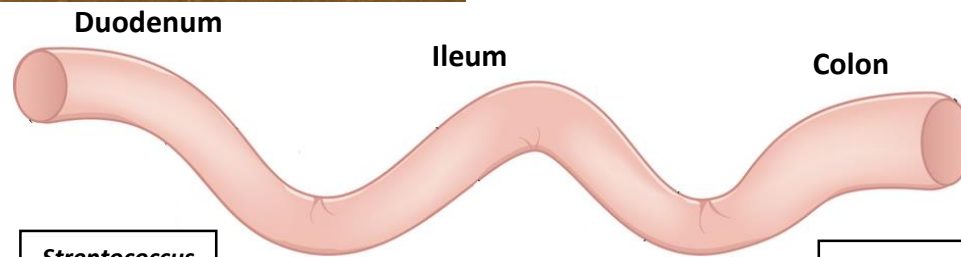
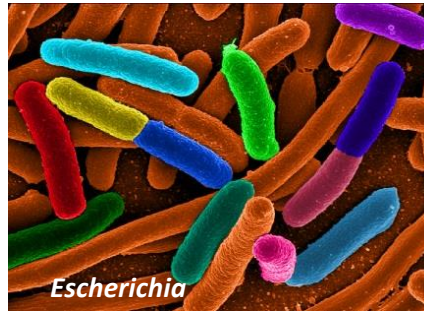
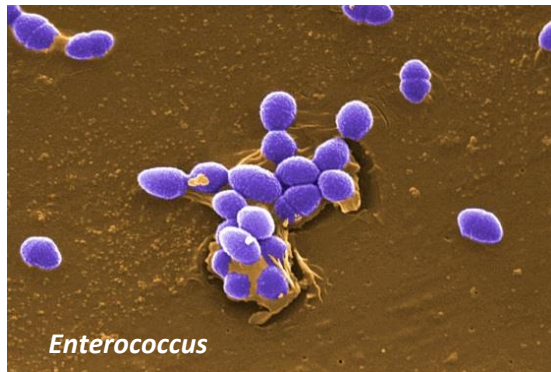
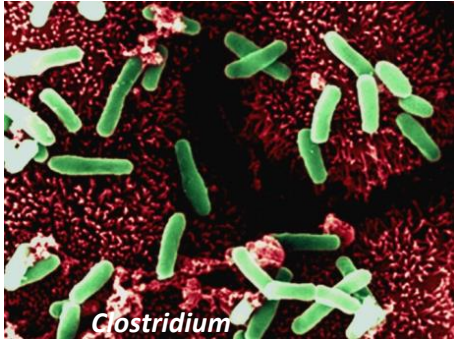
Detecting who's there ?

DNA sequencing



Who's in the gut microbiota?

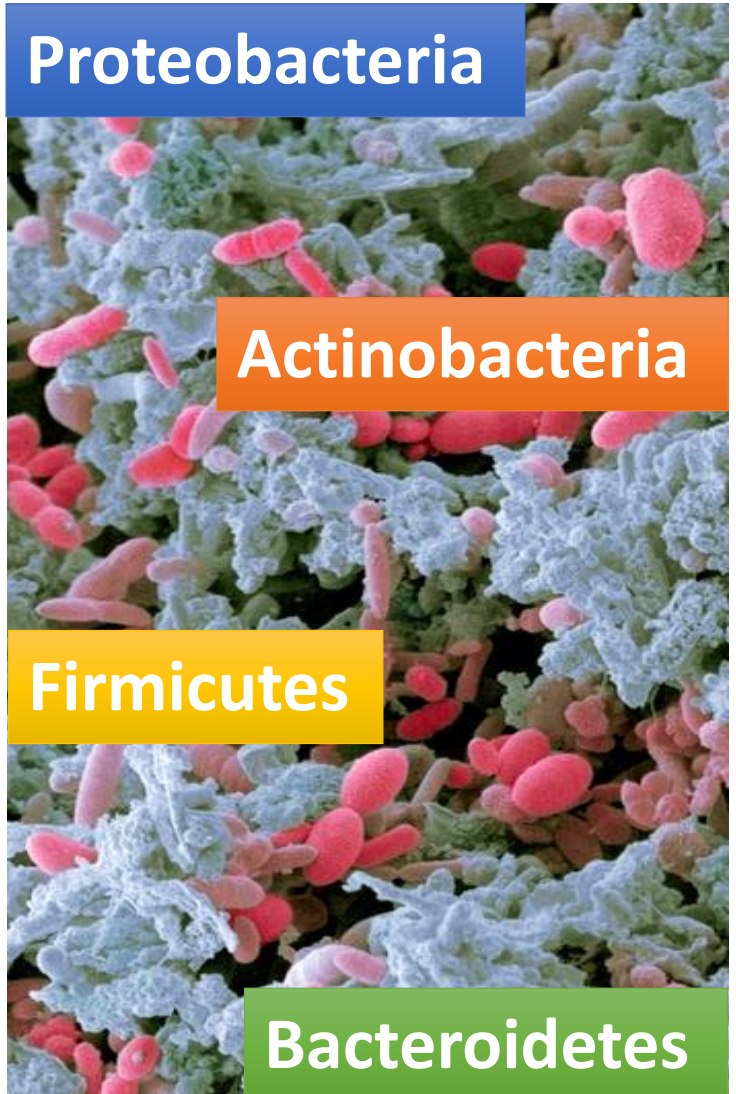
>500 species of bacteria comprise the 10^{13} bacteria in the GIT



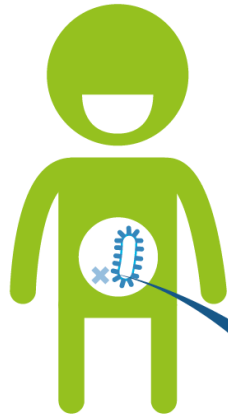
Streptococcus
Lactobacillus
Enterococcus
Yeast species

Enterobacteriaceae
Bacteroides
Clostridium

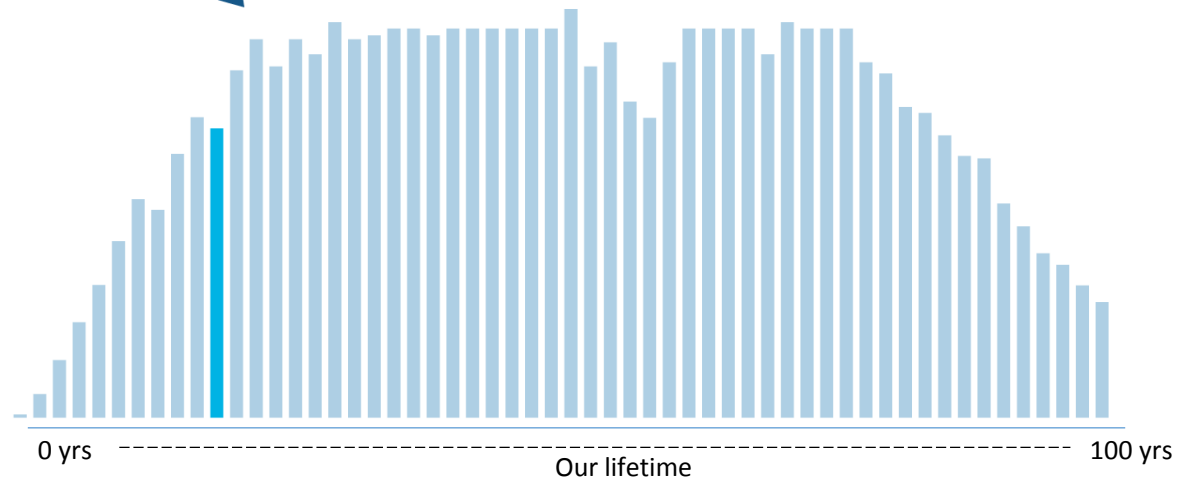
Prevotellaceae
Proteobacteria
Bifidobacterium
Fusobacteriia
Lachnospiraceae



How does it evolve?



The composition of our microbiota evolves throughout our entire life, from birth to old age, and is the result of different external influences

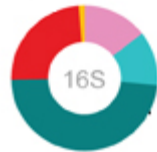


How does it evolve?



Unborn

- sterile

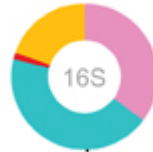


Baby

- Initial gut bacteria
- Low diversity
- High instability

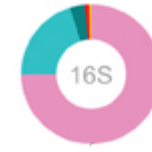
Bacterial groups:

- Firmicutes
- Bacteroidetes
- Actinobacteria
- Proteobacteria
- others



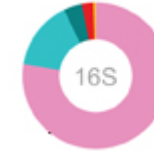
Toddler

- New species, out compete early ones
- Rapid increase in diversity
- High instability
- Changes in response to e.g. diet



Adult

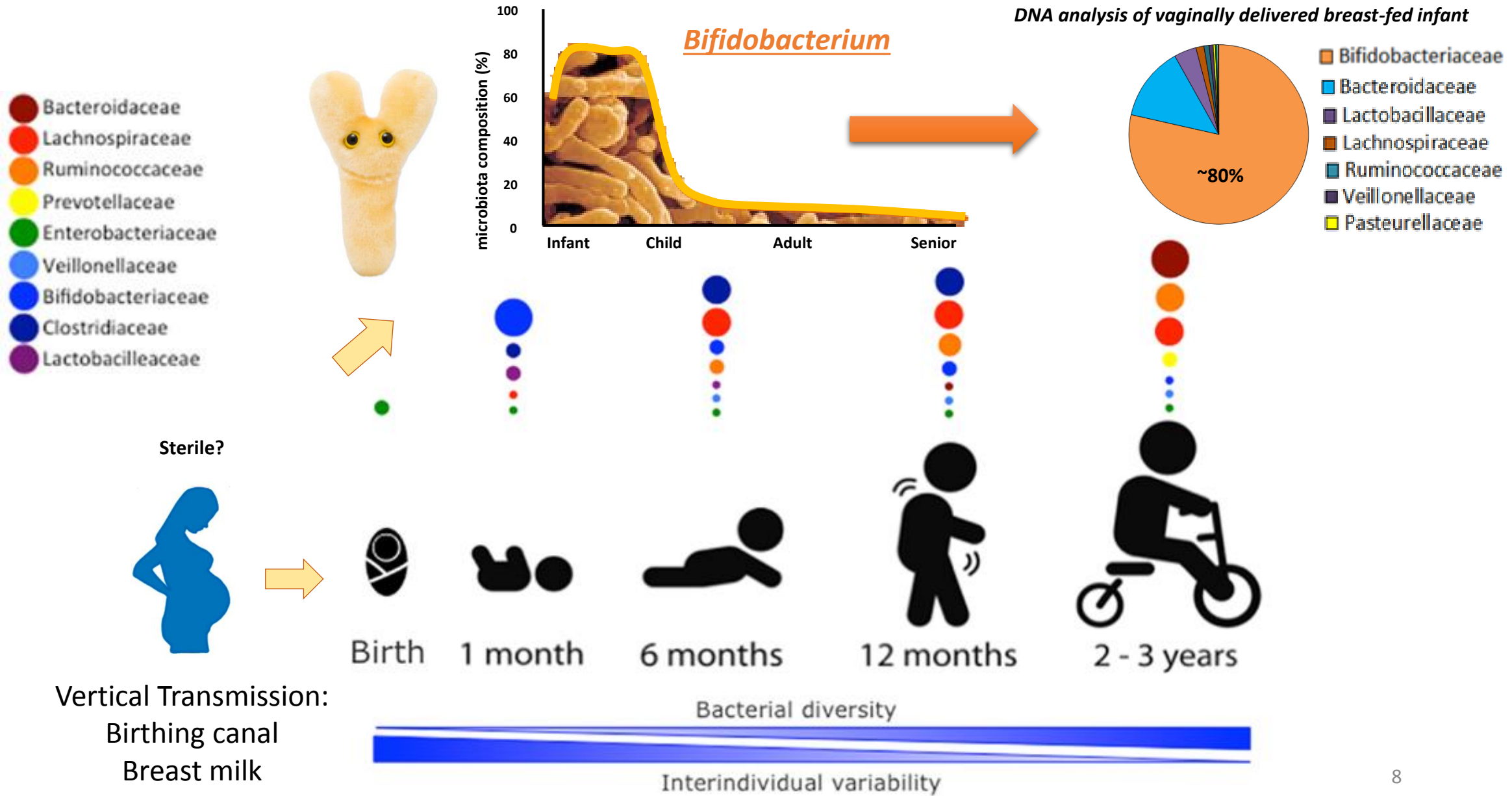
- Highly distinct, diverse microbiota
- Microbial community may continue to change, but at a slower rate than childhood



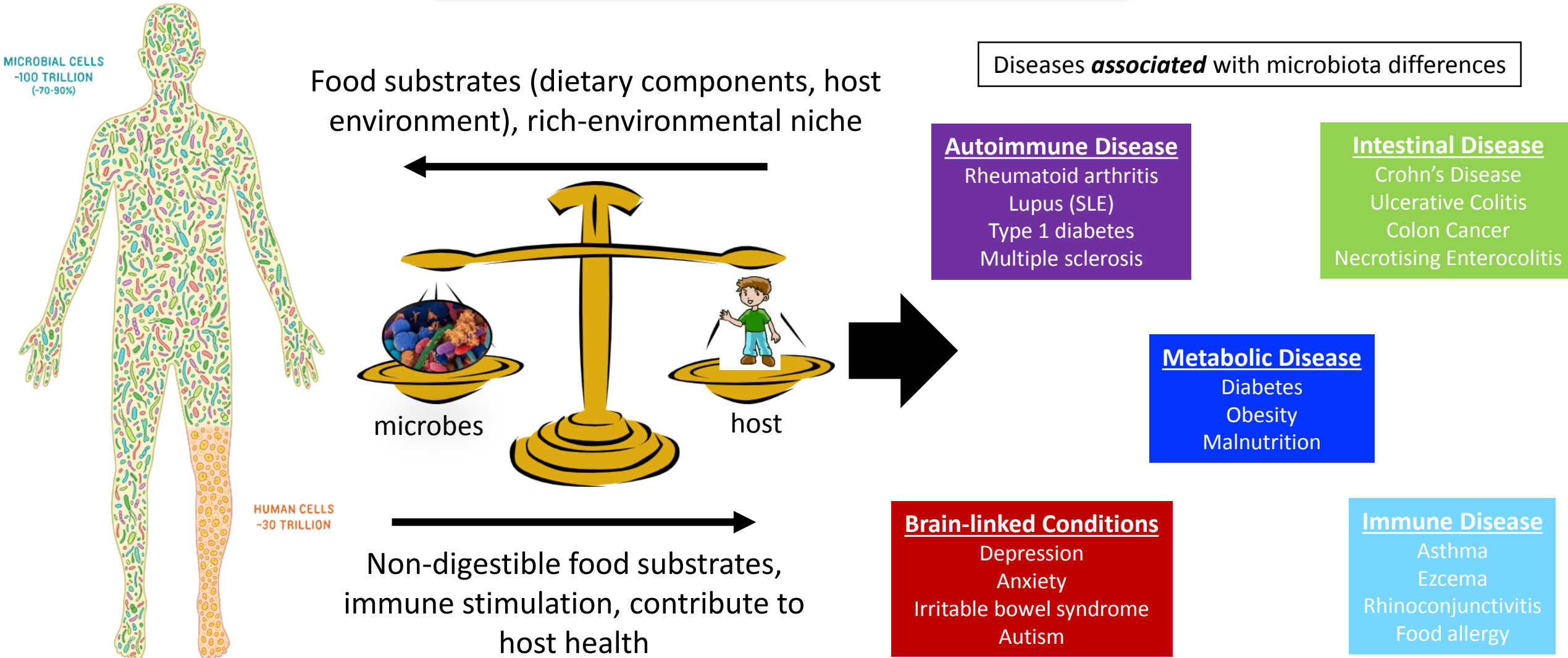
Elderly

- Substantially different microbiota than younger adults
- Lower diversity

Early life development



Host-microbial crosstalk



Microbiota disturbances

Causes

Genetic Factors

Antibiotics

Infections

Childbirth method

Environment

Diet

Stress

Antibiotics



- microbiota resilience decreases with each course of antibiotics
- once disrupted, normal microbiota may never completely recover
- may be replaced by resistant organisms

**Microbial
CONSEQUENCES**



- Natural delivery helps to 'seed' infant with first microbiota
- C-section often results in 'skin-like' microbiota in the infant gut

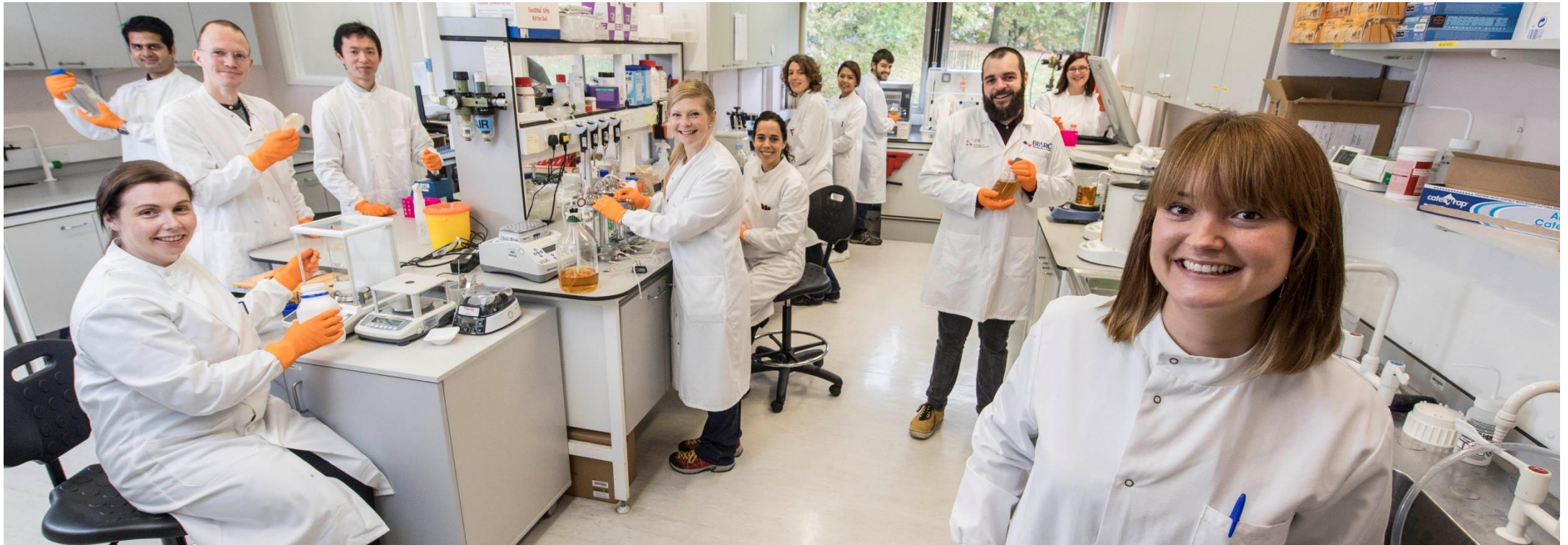
Delivery method



Milk diet



- Breast milk contains compounds that 'feed' specific bacteria (e.g. *Bifidobacterium*)
- Breast-milk also contains compounds that inhibit pathogens
- Breast milk may also contain live bacteria



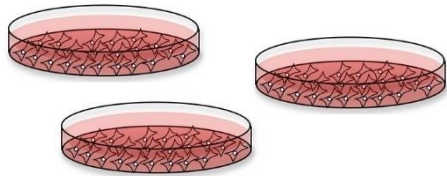
Which members of the microbiota are important to maintain homeostasis?

What is their function?

Are these functions specific to one bacterial species ?

Experimental model systems to study the microbiota

In vitro systems:



Immortal cell lines
(1 host cell type + microbial cell/compound)



Bacterial monocultures
(single microbial community + host compounds)

Increase complexity



Chemostat systems
(continuous influx/efflux of nutrients
Combination of host components and
diverse microbial community)

In vivo systems:



Outbred Germ-free Colonised (SPF)

Mouse (animal) models
(clonally similar individuals, immune deficient models)



Human samples/clinical trials
(highly variability in individuals,
trends, personalised medicine)

Why is this important?

- Early-life is a critical window of opportunity to change how the gut microbiota develop
- Developing novel tools to improve infant gut microbiota development
 - BAMBI food study to improve infant health
 - Personalized nutrition for infants
- Our gut microbiota is imprinted in early-life, and has long-term effects on adult health
 - autoimmune diseases
 - inflammatory diseases
 - metabolic diseases



Stronger, healthy babies



Stronger, healthy adults

Tools used

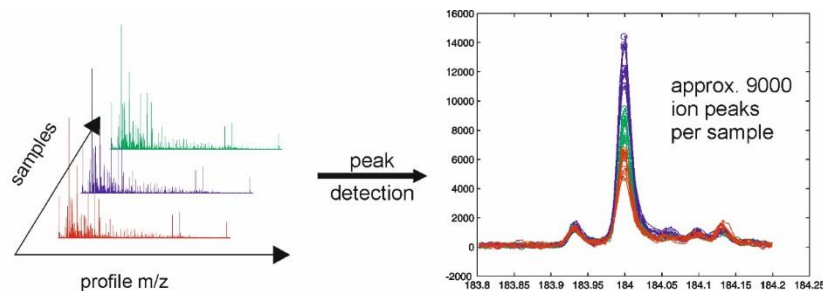
- Monitoring changes in metabolite production can identify novel compounds to be used as prebiotics
- Combining metabolomic and metagenomics outputs to answer biological questions
- Two-way correspondence analysis that shows potential associations between metabolite data (NMR) and microbiota (16S rRNA analysis)
 - Illustrates similar trends in metabolites and microbiota composition across all infants
- Important to examine each sample on its' own to understand individual relationships between metabolomic, metagenomics and immune data

Lessons and Challenges

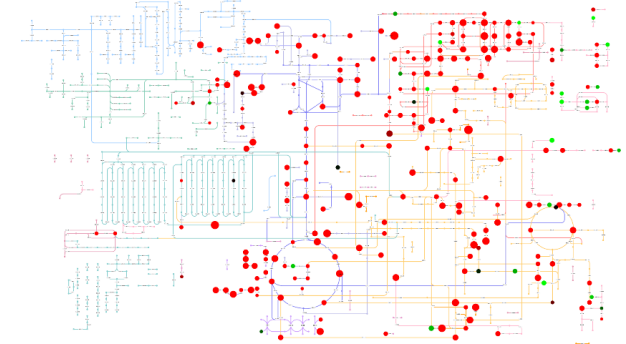
A microbiologist's perspective

- Proper preparation of control samples is the key!
- 1000's of signals (MS data) from metabolic extracts of biological samples whose masses don't match conventional charts/pipeline
- Large integrative datasets require biological interpretation & manual annotation
- Realistic expectations of what is possible (both in yield and annotation)

Metabolomics platform



Annotation coverage



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Helena Adjei
Charlotte Leclaire
ChoZin Soe
Ian O'Neill
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Shab Caim

Sanger Institute

Trevor Lawley
Gordon Dougan

Stratagem IPM Ltd:

Isla Furlong
Nicola Baker-Munton

Milk Support:

Barcelona BioBank
IFR Metabolomics Team:
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Emma Allen-Vercoe (UofG)
Albert Koulman (MRC)
Larissa Richardson (MRC)

EM imaging:

Kathryn Cross

Earlham Institute:

Matt Clark
Richard Leggett

Acknowledgements

Norfolk and Norwich
University Hospitals

NHS Foundation Trust

Paul Clarke
Karen Few
Kate Lloyd



IFR

Institute of
Food Research



Cambridge University Hospitals



NHS Foundation Trust

Gusztav Belteki



wellcometrust
New Investigator Award to LJH 11000974/Z/13/Z



MSCA-IF-EF-2014 Project 661594