

Human Gut Microbiome Viewed Across Age and Geography

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What is a microbiome?

- ▶ general
 - ▶ entirety of microorganisms normally living on a creature
 - ▶ distinct biomes on surface & inside of skin, saline and mucosa
 - ▶ includes bacteria, fungi, archaea
 - ▶ about 10x as many as cells on the human
- ▶ functions
 - ▶ digestive enzyme activity
 - ▶ synthesis of vitamins
 - ▶ interaction with immune system
 - ▶ protection from pathogens

What to learn from microbiomes

- ▶ taxonomic diversity
 - ▶ number and composition of microbial communities
 - ▶ Operational Taxonomic Units (OTUs)
 - ▶ population diversity
- ▶ functional metagenomics
 - ▶ functions of communities
 - ▶ proteins
 - ▶ enzymes

Human Gut Microbiome Viewed Across Age and Geography

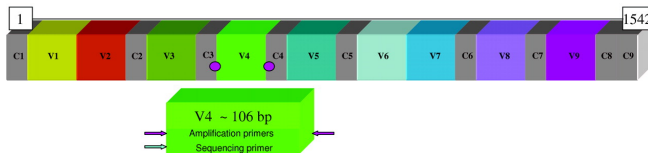
- ▶ part of the Human Microbiome Project

Origin	individuals	families	age 0-17	age 18-70
Malawi	115	34	83	31
Venezuela	100	19	65	35
USA	316	98	178	136
total	531	151	326	202

Impact

- ▶ demonstration project to search for patterns related to locations and lifestyles
- ▶ understand how westernization changes microbiomes
- ▶ understand nutritional needs
- ▶ increase sustainability of agriculture

Methods: 16s rRNA



- ▶ component of the 30S small subunit of prokaryotic ribosomes
- ▶ constant (C_n) regions → location
- ▶ “hypervariable” (V_n) regions: → identify
 - ▶ molecular clock → phylogeny
 - ▶ analyze taxonomy

Methods: Whole genome sequencing

- ▶ shotgun sequencing & reassembly
- ▶ subset of samples used
- ▶ functional analysis

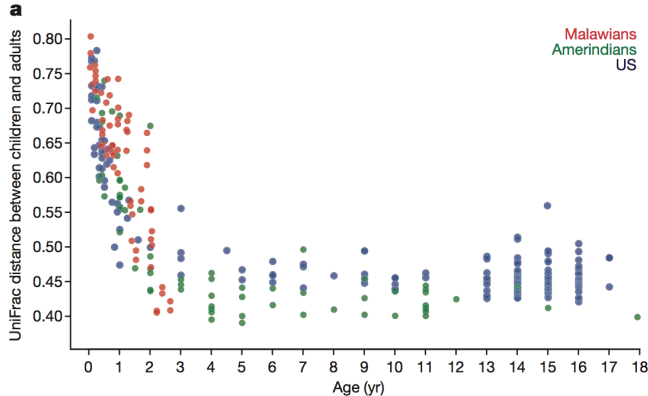
Analysis of 16s rRNA

- ▶ UniFrac distance
 - ▶ shared phylogeny branch fraction
 - ▶ → phylogenetic distance
- ▶ clustered into OTUs (by genetic similarity)
 - ▶ Greengenes database
 - ▶ OTU measure: 97% similarity
- ▶ diversities of OTUs compared

Analysis of whole genome sequences

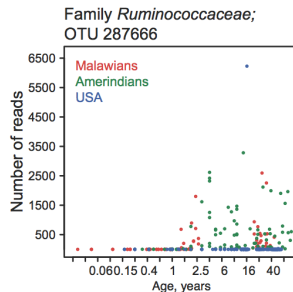
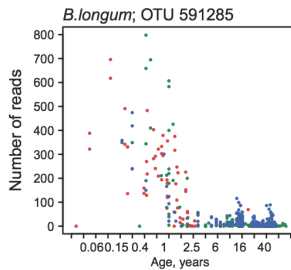
- ▶ BLAST against KEGG and COG databases
 - ▶ mapped with 95% similarity
- ▶ Random Forest analysis (OTU abundances → US/non US)

Evolution of phylogenetic composition



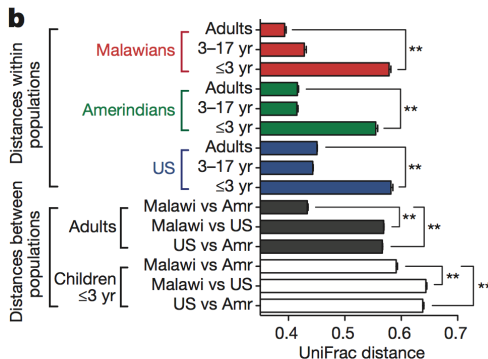
⇒ Child- to adult-composition within first three years

Evolution of phylogenetic composition



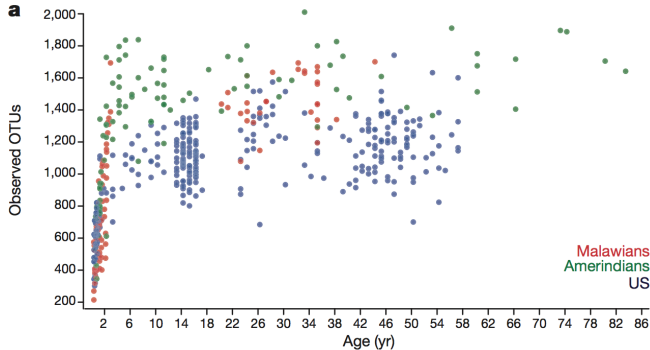
- ▶ *Bifidobacterium longum*: sugar → lactic acid, acetic acid
- ▶ Ruminococcaceae: butyrate productions

Comparison of compositions



- ▶ interpersonal variation greater among children
- ▶ significant differences between countries (esp. USA)
- ▶ no significance between villages/regions inside countries

Comparison of compositions



⇒ diversity increases with age

Clustering analysis

- ▶ Random Forest analysis
 - ▶ younger: *Bifidobacterium longum*
 - ▶ strong predictors for US \leftrightarrow non-US
 - ▶ weaker predictors Malawia \leftrightarrow Venezuela

Shared functional changes over time

- ▶ no unique ECs (Enzyme Commission id)
- ▶ total num of ECs constant
- ▶ assignable ECs decline with age - increasing complexity?
- ▶ differences in vitamine synthesis, fermentation pathways

Shared functional changes over time

young	old
folate de novo	dietary folate
lactic acid	methanogenesis
cis	arg, glu, asp, lys

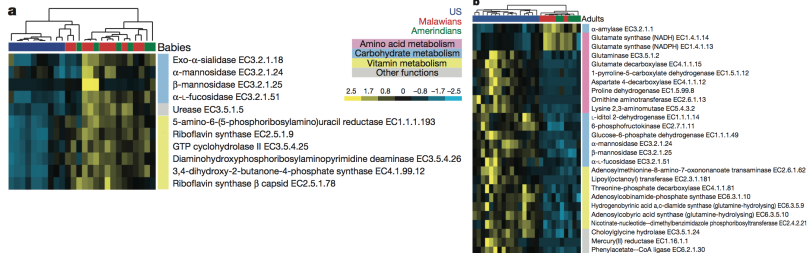
⇒ confirms other researchers' findings

Population- and age-specific differences

US	Δt	non-US	Δt
		B2 biosynthesis	-
α -fucosidase	+	specific glycans	-
urease	low	urease	-

- ▶ urease: nitrogen recycling
- ▶ α -fucosidase, glycans: oligosaccharide metabolism

Population- and age-specific differences

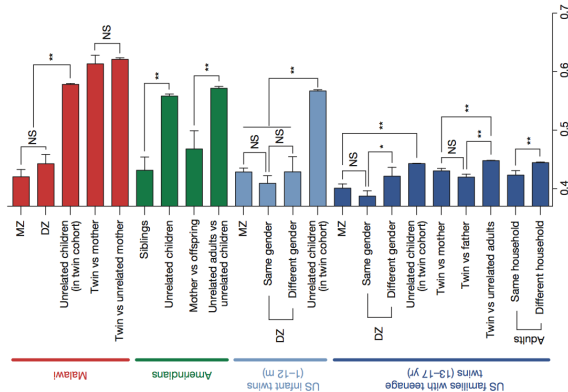


Differences in adult fecal microbiomes

- ▶ differential ECs:
 - ▶ US \leftrightarrow non-US: 893
 - ▶ Malawian \leftrightarrow Amerindian 445
- ▶ non-US:
 - ▶ glu-synthase
 - ▶ starch degradation
- ▶ US:
 - ▶ degradation of asp, pro, lys, gln, ornithin, simple sugars, sugar-substitutes, host glycans
 - ▶ biosynthesis of vitamins, biotin, lipoic acid
 - ▶ metabolism of xenobiotics (aromatic compounds, mercury), bile salts

⇒ parallels to difference carnivorous/herbivorous mammals

Effects of kinship across countries



- ▶ twin studies (*almost exclusively US twins*)
 - ▶ microbiome heritability is low
 - ▶ monozygotic twins no different from dizygotic twins

Effects of kinship across countries

- ▶ mother's microbiomes not more similar to child's than father's
- ▶ co-habiting non-biological fathers more similar than other families
- ▶ similarities among families consistent across populations

⇒ environmental exposure shapes gut microbiome

Conclusion

- ▶ nutrition and lifestyle affect microbiome composition
- ▶ inter-personal variances \gg functional variances
- ▶ different needs for ages / cultural backgrounds
 - ▶ health
 - ▶ nutrition

The end

- ▶ 16s rRNA image from *www.clinchem.org*
- ▶ additional information: Phillip E. Melton: *Bioinformatic and statistical analysis of microbiome sequence data* In: *www.academia.edu*