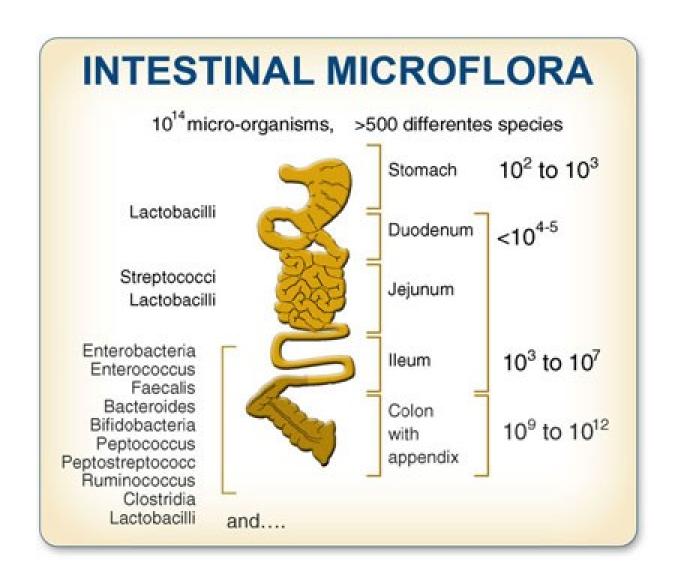


DTU Health Technology Bioinformatics

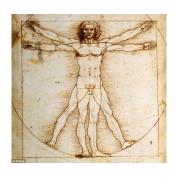
Human microbiome

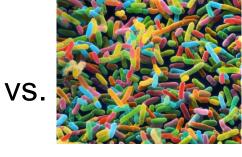
Gisle Vestergaard Associate Professor Section of Bioinformatics Technical University of Denmark gisves@dtu.dk

Human microbiome



Human microbiome in numbers

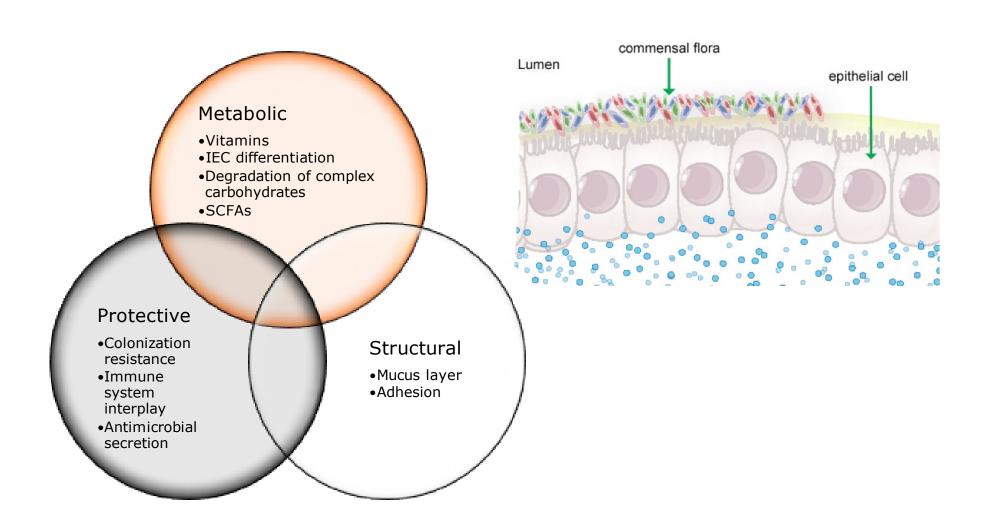




	Human (isolated)	Microbiota
weight	~ 50-100 kg	~ 2 kg
species	1	1000-5000
cells	~ 1012	10 ¹³ - 10 ¹⁴
genes	25.000	>4.000.000

IGC catalogue (non-redundant genes found in gut microbes): >9.800.000 genes

Human microbiome: Functions



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nature

ARTICLES

A human gut microbial gene catalogue established by metagenomic sequencing

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To understand the impact of gut microbes on human health and well-being it is crucial to assess their genetic potential. Here we describe the Illumina-based metagenomic sequencing, assembly and characterization of 3.3 million non-redundant microbial genes, derived from 576.7 gigabases of sequence, from faecal samples of 124 European individuals. The gene set, ~150 times larger than the human gene complement, contains an overwhelming majority of the prevalent (more frequent) microbial genes of the cohort and probably includes a large proportion of the prevalent human intestinal microbial genes. The genes are largely shared among individuals of the cohort. Over 99% of the genes are bacterial, indicating that the entire cohort harbours between 1,000 and 1,150 prevalent bacterial species and each individual at least 160 such species, which are also largely shared. We define and describe the minimal gut metagenome and the minimal gut bacterial genome in terms of functions present in all individuals and most bacteria, respectively.

- Sequence (Illumina) based metagenomic study
- 3.3 million microbial genes
- 124 samples from a European cohort
- Large overlap between the individuals
- ~ 1000 1.150 prevalent bacterial species
- ~160 prevalent species per individual
- · Minimal gut bacterial genome and metagenome

Aim/hypothesis:

"To get a broader overview of the human gut microbial genes we used the Illumina Genome Analyser (GA) technology to carry out deep sequencing of total DNA from faecal samples of 124 European adults."

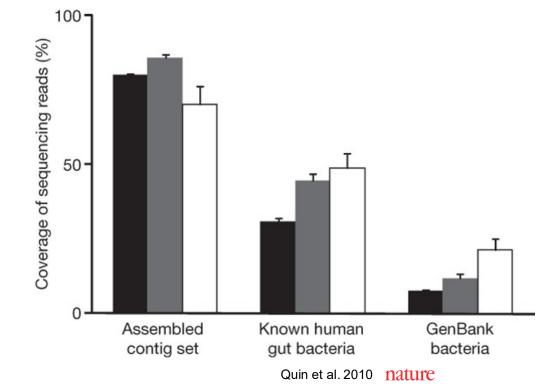
- Sequence (Illumina) based metagenomic study
- •3.3 million microbial genes
- •124 samples from a European cohort
- Large overlap between the individuals (>86%)
- Large majority of prevalent intestinal microbial genes
 - over 70% of the metagenomic reads American and Japanese individuals can be mapped
 - about 80% of the microbial genes from 89 common gut reference genomes are present in our set.

•80% of reads could be mapped to assembly at 90% identity

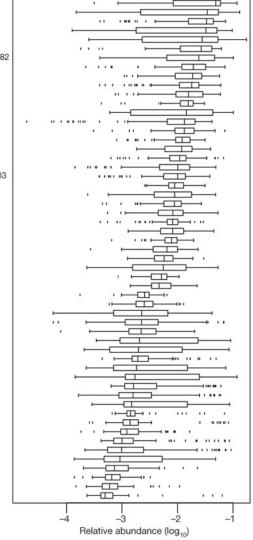
·Less than 50% of reads could be mapped to known gut bacteria

Interestingly, the majority of reads from two other larger studies

could also be mapped to assembly

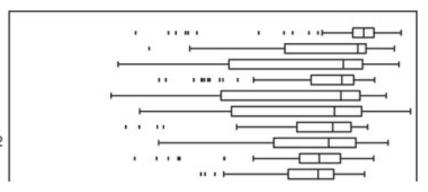


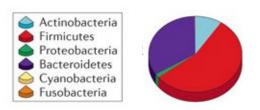
Bacteroides uniformis Alistipes putredinis Parabacteroides merdae Dorea longicatena Ruminococcus bromii L2-63 Bacteroides caccae Clostridium sp. SS2-1 Bacteroides thetaiotaomicron VPI-5482 Eubacterium hallii Ruminococcus torques L2-14 Unknown sp. SS3 4 Ruminococcus sp. SR1 5 Faecalibacterium prausnitzii SL3 3 Ruminococcus lactaris Collinsella aerofaciens Dorea formicigenerans Bacteroides vulgatus ATCC 8482 Roseburia intestinalis M50 1 Bacteroides sp. 2 1 7 Eubacterium siraeum 70 3 Parabacteroides distasonis ATCC 8503 Bacteroides sp. 9_1_42FAA Bacteroides ovatus Bacteroides sp. 4_3_47FAA Bacteroides sp. 2 2 4 Eubacterium rectale M104 Bacteriodes xylanisolvens XB1A Coprococcus comes SL7 1 Bacteroides sp. D1 Bacteroides sp. D4 Eubacterium ventriosum Bacteroides dorei Ruminococcus obeum A2-162 Subdoligranulum variabile Bacteroides capillosus Streptococcus thermophilus LMD-9 Clostridium leptum Holdemania filiformis Bacteroides stercoris Coprococcus eutactus Clostridium sp. M62 1 Bacteroides eggerthii Butyrivibrio crossotus Bacteroides finegoldii \vdash Parabacteroides johnsonii Clostridium sp. L2-50 Clostridium nexile Bacteroides pectinophilus Anaerotruncus colihominis Ruminococcus anavus Bacteroides intestinalis Bacteroides fragilis 3_1_12 Clostridium asparagiforme -Enterococcus faecalis TX0104 Clostridium scindens . —— Blautia hansenii



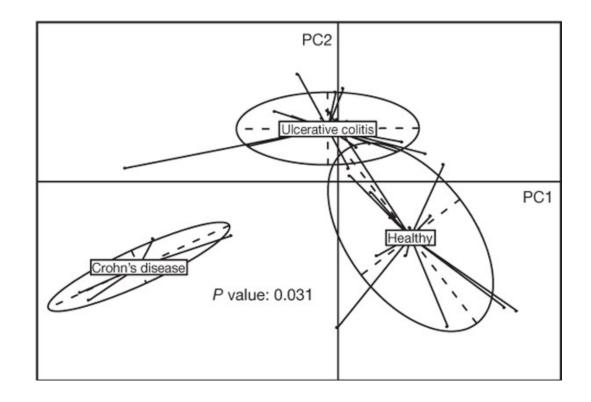
Relative abundance of 57 frequent microbial genomes among individuals in cohort

Bacteroides uniformis
Alistipes putredinis
Parabacteroides merdae
Dorea longicatena
Ruminococcus bromii L2–63
Bacteroides caccae
Clostridium sp. SS2–1
Bacteroides thetaiotaomicron VPI–5482
Eubacterium hallii
Ruminococcus torques L2–14



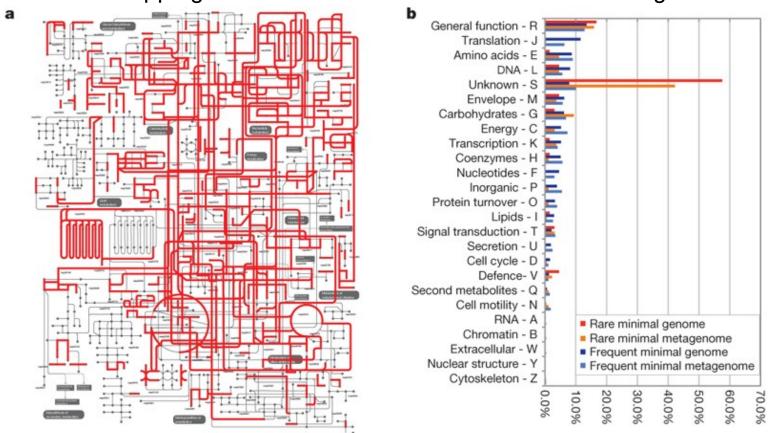


Bacterial species abundance: Differentiation of IBD patients and healthy individual



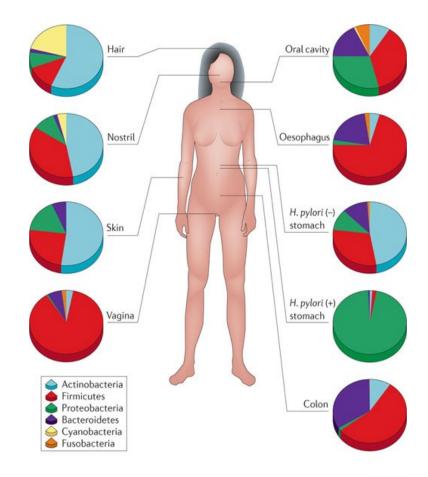
Minimal gut genome and metagenome

KEGG mapping indicates +6000 functions in the minimal gut microbiome



Human microbiome: overview

- Substantial microbiome differences between anatomical sites
- Substantial microbiome differences individuals at each anatomical site
- Healthy microbiomes are longitudinally stable



Paper exercise time!