Capturing One of the Human Gut Microbiome's Most Wanted - DTU Orbit (17/03/2019)

Capturing One of the Human Gut Microbiome's Most Wanted: Reconstructing the Genome of a Novel Butyrate-Producing, Clostridial Scavenger from Metagenomic Sequence Data

The role of the microbiome in health and disease is attracting great attention, yet we still know little about some of the most prevalent microorganisms inside our bodies. Several years ago, Human Microbiome Project (HMP) researchers generated a list of "most wanted" taxa: bacteria both prevalent among healthy volunteers and distantly related to any sequenced organisms. Unfortunately, the challenge of assembling high quality genomes from a tangle of metagenomic reads has slowed progress in learning about these uncultured bacteria. Here, we describe how recent advances in sequencing and analysis allowed us to assemble "most wanted" genomes from metagenomic data collected from four stool samples. Using a combination of both de novo and guided assembly methods, we assembled and binned over 100 genomes from an initial data set of over 1,300 Gbp. One of these genome bins, which met HMP's criteria for a "most wanted" taxa, contained three essentially complete genomes belonging to a previously uncultivated species. This species is most closely related to Eubacterium desmolans and the clostridial cluster IV/Clostridium leptum subgroup species Butyncicoccus pullicaecorum (71-76% average nucleotide identity). Gene function analysis indicates that the species is an obligate anaerobe, forms spores, and produces the antiinflammatory short-chain fatty acids acetate and butyrate. It also appears to take up metabolically costly molecules such as cobalamin, methionine, and branch-chained amino acids from the environment, and to lack virulence genes. Thus, the evidence is consistent with a secondary degrader that occupies a host-dependent, nutrient scavenging niche within the gut; its ability to produce butyrate, which is thought to play an anti-inflammatory role, makes it intriguing for the study of diseases such as colon cancer and inflammatory bowel disease. In conclusion, we have assembled essentially complete genomes from stool metagenomic data, yielding valuable information about uncultured organisms' metabolic and ecologic niches, factors that may be required to successfully culture these bacteria, and their role in maintaining health and causing disease.

General information
State: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Mayo Clinic, University of Illinois at Urbana-Champaign
Number of pages: 13
Publication date: 2016
Peer-reviewed: Yes

Publication information
Journal: Frontiers in Microbiology
Volume: 7
Article number: 783
ISSN (Print): 1664-302X
Ratings:
BFI (2019): BFI-level 1
Web of Science (2019): Indexed yes
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 4.19 SJR 1.699 SNIP 1.174
Web of Science (2017): Impact factor 4.019
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 4.16 SJR 1.759 SNIP 1.161
Web of Science (2016): Impact factor 4.076
Web of Science (2016): Indexed yes
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 4.15 SJR 1.869 SNIP 1.193
Web of Science (2015): Impact factor 4.165
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 3.76 SJR 1.879 SNIP 1.148
Web of Science (2014): Impact factor 3.989
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 3.56 SJR 1.776 SNIP 0.949
Web of Science (2013): Impact factor 3.941
ISI indexed (2013): ISI indexed no
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 2.78 SJR 1.46 SNIP 0.722
ISI indexed (2012): ISI indexed no
Scopus rating (2011): SJR 0.642 SNIP 0.192
Web of Science (2011): Indexed yes
Original language: English
Keywords: Binning, Butyricicoccus, Genome assembly, Metagenomics, Microbiome
Electronic versions:
Capturing_One_of_the_Human_Gut_Microbiome_s_Most_Wanted.pdf
DOIs:
10.3389/fmicb.2016.00783

Bibliographical note
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Source: FindIt
Source-ID: 2304701396
Research output: Research - peer-review › Journal article – Annual report year: 2016