



MICRO

The Oral Cavity Microbiome in
Health and Disease – What We
Know

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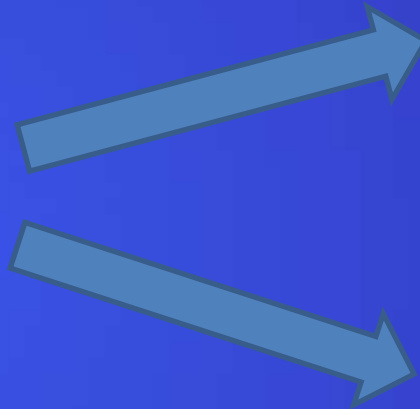
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Learning Objectives:

- Evaluate the timeline of development of human oral microbiome studies.
- Describe the members of the oral microbiome as currently catalogued in the Human Oral Microbiome Database (HOMD) and their role in the establishment of the microbiome at other anatomical sites.
- Evaluate the systemic connections of the oral cavity microbiome to the other parts of the body (in “balance” and “dysbiosis”).

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Presenter Disclaimer and Limitations to What We are About to Review:



Is Not Seeking the
“Overselling the
Microbiome” Award of the
Day

Will Most Likely Need to
Correct Anywhere From
8 – 33% of What is Said in
This Presentation in 6-8
Months

Definitions

- “Microbiome”:
 - Considered to be first coined by 1958 Nobel Prize Laureate Joshua Lederberg in 2001
 - 1988 reference to the term from a plant and fungal association book chapter by UK researchers Whipps, Lewis, and Cook

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- Earliest known use was in a 1949 French dental journal entitled “Paris : Société syndicate odontologique de France”⁵

« On sait, d'autre part, le rôle que joue le PH dans l'évolution du microbiome intestinal. Il est plausible d'admettre qu'à la faveur des lésions intestinales et des modifications du PH intestinal, les migrations parasitaires ou microbiennes peuvent »

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- While maybe not first “coined” by Lederberg, credit should be given to the term first being defined by him, as it relates to the normal flora of the body
- As described in his 2001 publication “ ‘Ome sweet ‘omics – a genealogical treasury of words”, the microbiome is used:
 - “to signify the ecological community of commensal, symbiotic, and pathogenic microorganisms that literally share our body space and have been all but ignored as determinants of health and disease”*

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- Debate has existed as to what “microbiome” actually refers to: “-biome” (as in an ecological niche) or “-ome” (as in genome)
- In 2007, the Committee on Metagenomics published the following statement in an effort to clarify use:

“In the case of the metagenome, a unit derived from the methods of bulk sequencing of environmental samples known as metagenomics, it has been proposed that the roles and identities of individual ecological actors in the community can be bypassed in favor of considering the metagenome itself as a functional unit”

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- This models the “-ome” after the molecular biology correlation such as “genome”, “proteome”, and “transcriptome”
- In contrast, many prominent researchers in the field (e.g., Nicholson, et al.⁷, and Weinstock⁸) have considered the term to refer to the microbial specifics as an ecological niche.
- Perspective: Both are valuable from a research standpoint and one simply needs to clarify usage rather than continue tension over disagreement in definition

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- “Microflora”:
 - Defined as simply “the microscopic wildlife of a given healthy individual”
 - Synonymous with “normal flora” and innately includes all microbial groups as synergistic actors on the stage of a host niche (oral, gut, lung, skin, etc.)
 - Lacking the “-ome”/”-biome” contention of debate, obviously a much less ambiguous term

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- “Dysbiosis”:

- Disruption, disturbance, and perturbation to the structure of resident commensal microbial communities

- What we currently know about dysbiosis inducing dysfunction can be directly related to diagnosis of disease if whole person treatment philosophy is followed:

Dysfunction → Disease → Signs and Symptoms

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- While it is not possible to open various anatomical cavities and organs during a physical exam to grab a snapshot of function/dysfunction
- A primary care PE can open the oral cavity, evaluate a potential dysfunction/dysbiosis, and consider systemic and longitudinal implications
(e.g., gut \leftrightarrow lung axis communication with the oral cavity at a junction)
- Dental issues are signs of dysbiosis or dysfunction

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Moment of Numbers:

- >90% of the world's population will have periodontal disease at some point in their lifetime
- >47% of the US population currently has periodontitis
- The oral microbiome is the only microbiome (according to current knowledge/dogma) that causes disease in the majority of people

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Anton van Leeuwenhoek

1632-1723

- In 1683, Leeuwenhoek wrote to the Royal Society regarding his macroscopic and microscopic observations of his plaque (as well as that of two old men who had never cleaned their teeth):

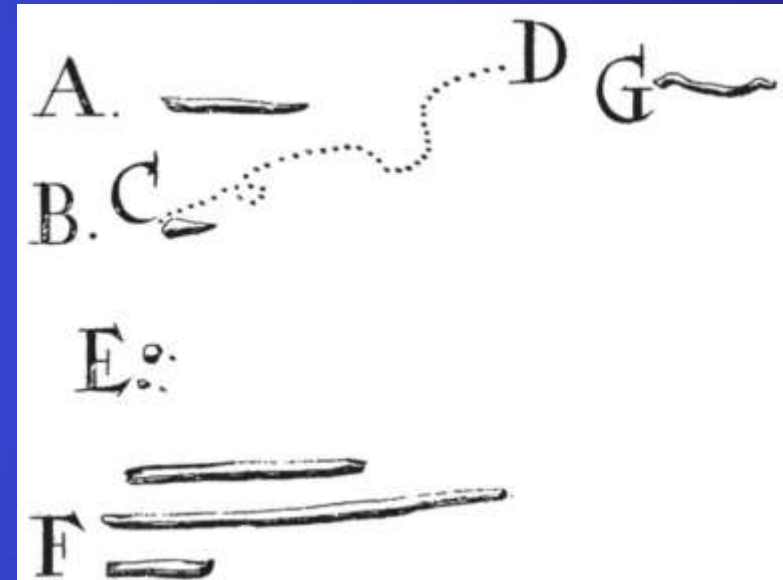
"a little white matter, which is as thick as if 'twere batter."

"I then most always saw, with great wonder, that in the said matter there were many very little living animalcules, very prettily a-moving. The biggest sort. . . had a very strong and swift motion, and shot through the water (or spittle) like a pike does through the water. The second sort. . . oft-times spun round like a top. . . and these were far more in number."

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In the mouth of one of the old men, Leeuwenhoek found:

"an unbelievably great company of living animalcules, a-swimming more nimbly than any I had ever seen up to this time. The biggest sort. . . bent their body into curves in going forwards. . . Moreover, the other animalcules were in such enormous numbers, that all the water. . . seemed to be alive."



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Moment of Numbers:

- Currently, we are thought to have 100 trillion bacterial cells on/in us
 - Each cell is about a micron long
 - Laid end to end and wrapped around the globe, this chorus line of cells would wrap around earth's diameter twice
 - Can be thought of as an additional organ since the bacteria on us weighs about the same as our brain or liver (1.5kg)

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Our “microbial cloud” follows us throughout each day of our lives



Development of the Lung Microbiome

- Influence of the oral microbiome extends to the development and maintenance of the lung microbiome
 - Within the first 5 min following birth, microbiological communities can be detected within the oral cavity and nasopharynx of term newborns
 - The adult lung microbiome appears to have *Streptococcus*, *Veillonella*, and *Prevotella* as the dominant colonizers (80% of bacterial type) followed by most commonly by *Pseudomonas*, *Haemophilus*, and *Neisseria*

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- Lung colonization is influenced most strongly by oral cavity members and least correlated to nasal members
- In healthy adult subjects who underwent microbiome analysis from the oral cavity, nasal cavity, lungs and stomach, the lung microbiome resembled the microbiome of the oral cavity more than other sites tested

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Microbiome Acquisition Overall

- It is currently unclear as to whether there is a low level of colonization of the fetus *in utero*
 - Bacteria has been identified within the placenta, amniotic fluid, and fetal membranes of healthy pregnancies
 - When a microbial community is discovered in what was previously thought to be a sterile tissue/structure, genetic analysis usually reveals a flora that most closely resembles that of the oral cavity

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Meconium counts

- Once thought sterile, bacterial isolates can be detected in low numbers from the first-pass meconium
- The numbers are exceedingly low, but still present, thereby violating the previous “sterile” dogma

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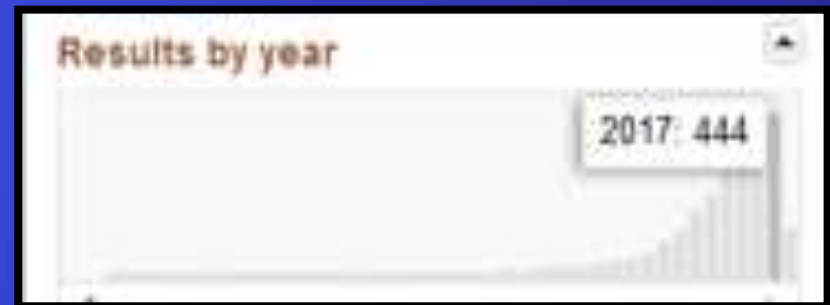
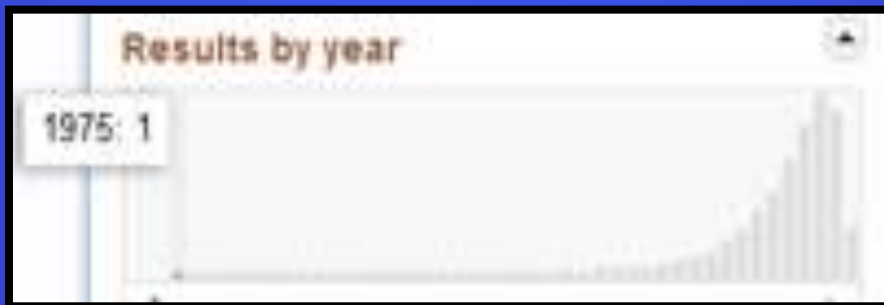
Paleomicrobiological Concepts of the Microbiome

- When studying the ancient microbiome, we are left with a very nice paleological sample: mineralized plaque that transformed into tartar, built up, and provides a well-preserved calculus
- Calculus successively lays down starting in the 20's and by studying the layers, the microbes captured in the mineralized fractions, and conducting genomic studies on those microbes (both 16S rRNA targeted and shotgun), there are also incredibly well-preserved periodontal pathogens from 1,000 years ago (middle ages Germany)

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Development of the Understanding of the Members of the Oral Microbiome Over the Last Three Decades

- “Zinsser Microbiology” in its 20th (1992) edition dedicated almost 3/1,212 text pages to normal flora (inclusive of all microbial groups and body sites)
- A “PubMed” search for the key words of “human oral microbiome” by years/number of publications yields:



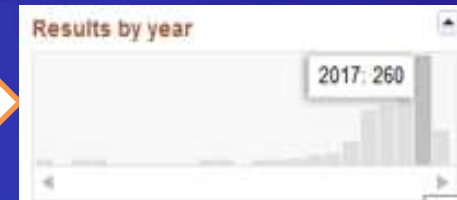
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A “PubMed” search for other microbiome studies, by body site, yields:

Human Lung
Microbiome
(1st Pub, 2004)



Human Brain
Microbiome
(1st Pub, 1996)



Human Gut
Microbiome
(1st Pub, 2002)



Human Eye
Microbiome
(1st Pub, 1995)

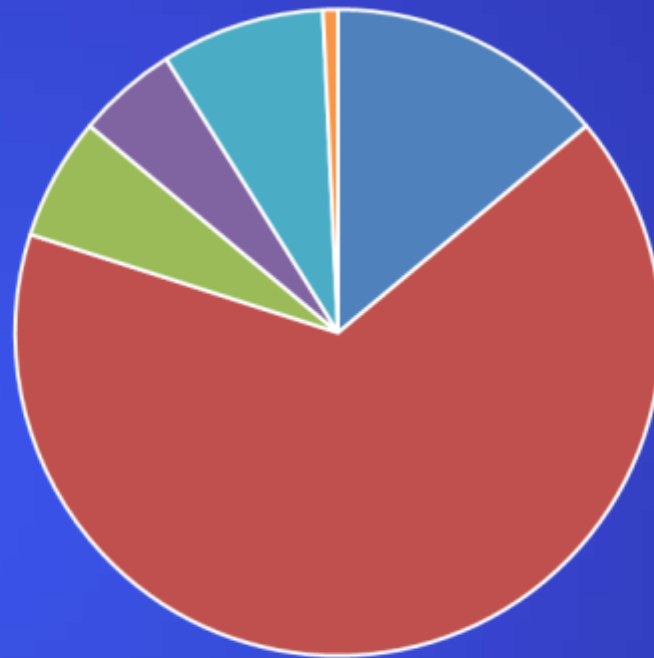


Human Skin
Microbiome
(1st Pub, 1975)



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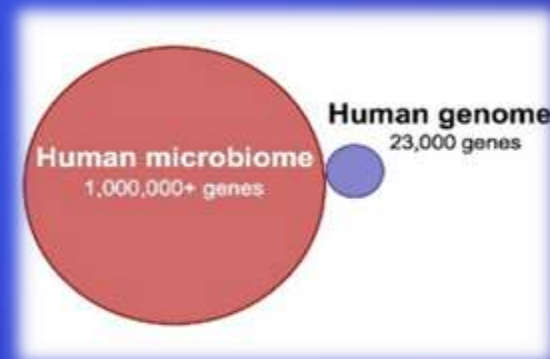
Human Microbiome Publications (By Body Site) in PubMed, 2017



- Human oral microbiome
- Human gut microbiome
- Human skin microbiome
- Human lung microbiome
- Human brain microbiome
- Human eye microbiome

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- In 2008, the Human Microbiome Project was initiated from the NIH Common Fund as what seemed like a natural extension of the 1990 established Human Genome Project (an international project of the US Department of Energy)
 - *The Human Genome Project* was established by Nobel Prize winners Renato Dulbecco and James Watson, the Project reached completion in 2003
 - The Human Microbiome Project sought to qualify the genes of the microbes that associate with the mapped human genes in a ratio of potentially up to 100:1 (= the “superorganism”)



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- Human Microbiome Project goal:

“The Human Microbiome Project (HMP) is an NIH Roadmap project that was initiated to generate resources to enable comprehensive characterization of the human microbiota and analysis of its role in human health and disease. The HMP centers will sequence the genomes of a set of microorganisms that have been previously isolated from the human body. In addition, samples from the digestive tract, mouth, skin, nose, and female urogenital tract of human volunteers will be sequenced for 16S ribosomal RNA analysis and considered for metagenomic analysis.”



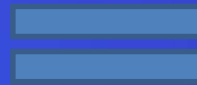
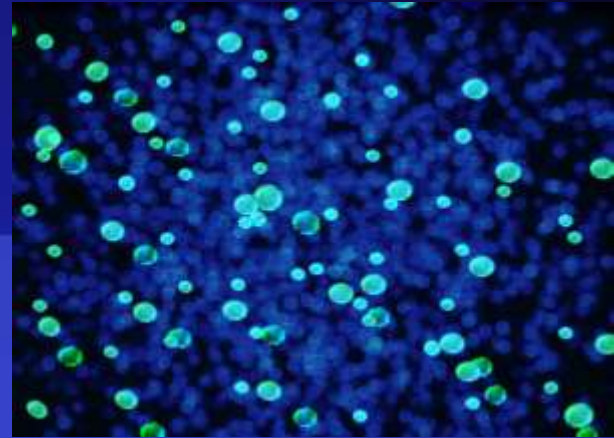
Image Source: NHGRI

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Published as part of the “Roadmap”, these are the body sites sampled from volunteers for the Human Microbiome Project, part of the National Institutes of Health's Roadmap for Medical Research.

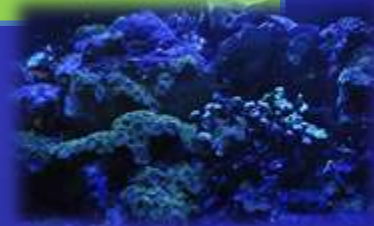
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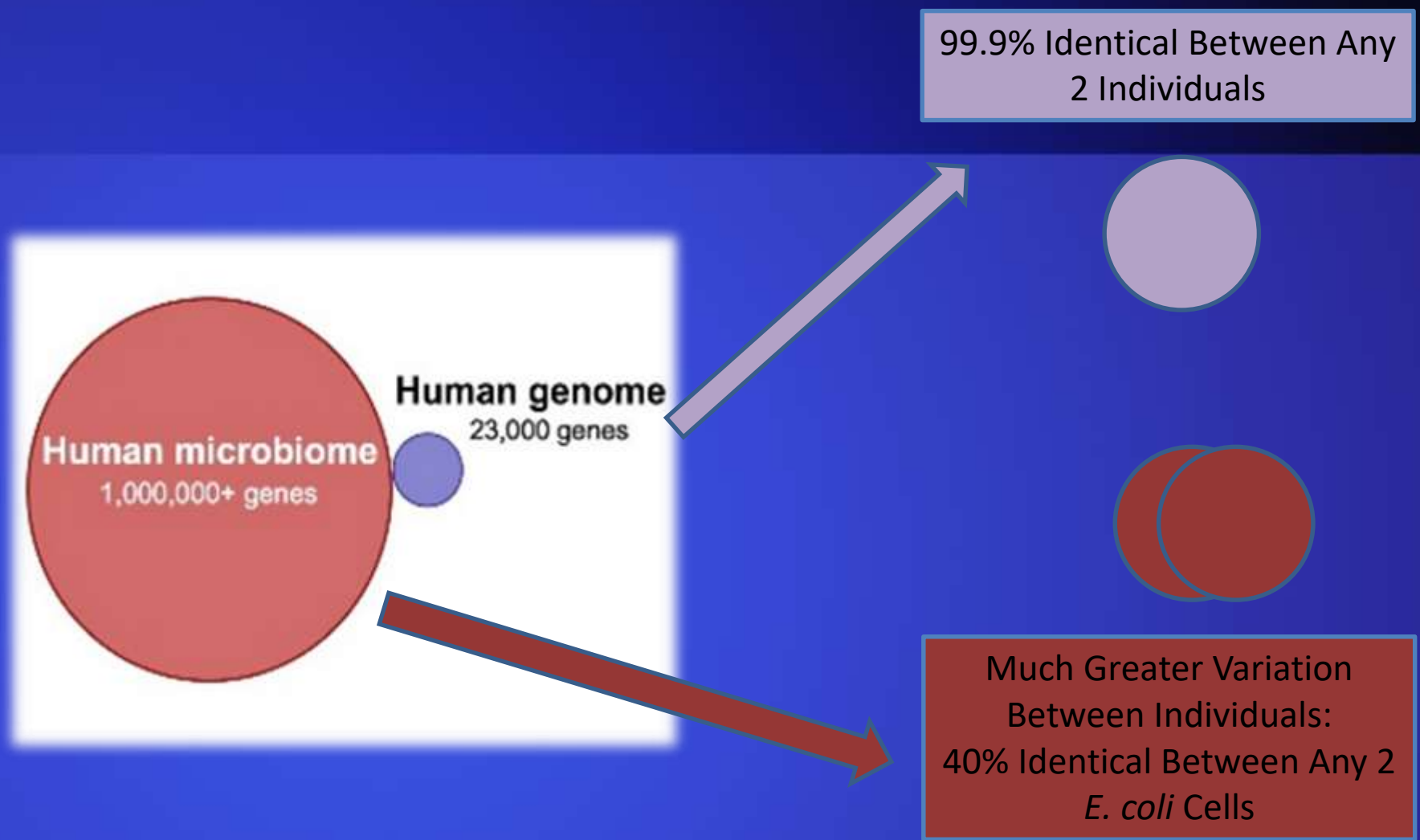
Superorganism

or

Holobiont



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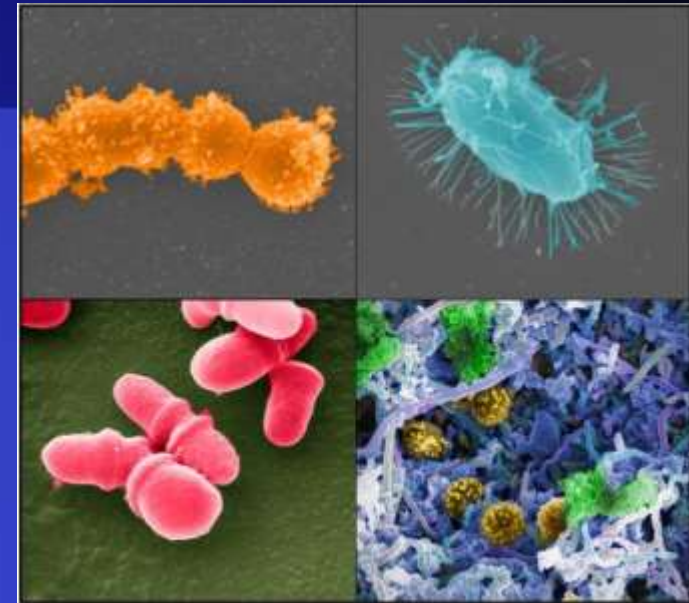
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Genomic Databases

- In addition to contributing another “-ome” to the lexicon of molecular biology, human microbiome research has generated an enormous amount of sequence data
 - All revealing immense variations in microbial diversity at the community, species, and genomic levels
- The oral microbiome is being extensively characterized by cultivation and culture-independent molecular methods such as 16S rRNA sequencing.

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- Online metagenomics database at MSU provides ribosome-related data services to the scientific community
 - over 2.1 million aligned and annotated bacterial and archaeal 16S rRNA sequences
- GenBank Nucleotide Collection (NIH) with over 2,000 bacterial and 100 archaeal full genome sequences



(Credit: Tom Schmidt); microbial biofilm of mixed species, from human body (Credit: A. Earl, Broad Institute/MIT); *Bacillus* (Credit: Tom Schmidt); *Malassezia loophilis* (Credit: J.H. Carr, CDC).

Moment of Numbers:

- One ml of human saliva from a healthy adult contains around 100 million bacterial cells.
- At the normal salivary flow rate (750 ml/day) $\sim 8 \times 10^8$ bacteria are shed from the oral surfaces every 24h

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“Salivaomics”: a merged area of study arising from five major branches of diagnostic components relative to saliva: proteome, transcriptome, micro-RNA, metabolome, and microbiome

- Has been reported that the salivary microbiome could be used in the detection of early resectable pancreatic cancer by means of microbial profiling where two microbial markers (*Neisseria elongata* and *Streptococcus mitis*) were successfully developed with 96.4% sensitivity and 82.1% specificity
- Currently, newer microbiome-based technologies have also become available, such as study of microbial sequences by means of RNA or DNA sequencing

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Human Oral Microbiome Database (HOMD)

- Hosted by the Forsyth Institute and organized in 2009 via "A Foundation for the Oral Microbiome and Metagenome" grant from The National Institute of Dental and Craniofacial Research
- The HOMD is the first curated description of a human-associated microbiome and provides tools for use in understanding the role of the microbiome in health and disease.

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“The goal of creating the Human Oral Microbiome Database (HOMD) is to provide the scientific community with comprehensive information on the approximately 700 prokaryote species that are present in the human oral cavity. Approximately 54% are officially named, 14% unnamed (but cultivated) and 32% are known only as uncultivated phylotypes.”

www.homd.org

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- Beauty of the database: allows for a “provisional naming scheme for the currently unnamed species so that strain, clone, and probe data from any laboratory can be directly linked to a stably named reference scheme.”
- Dynamically links “sequence data with phenotypic, phylogenetic, clinical, and bibliographic information.”

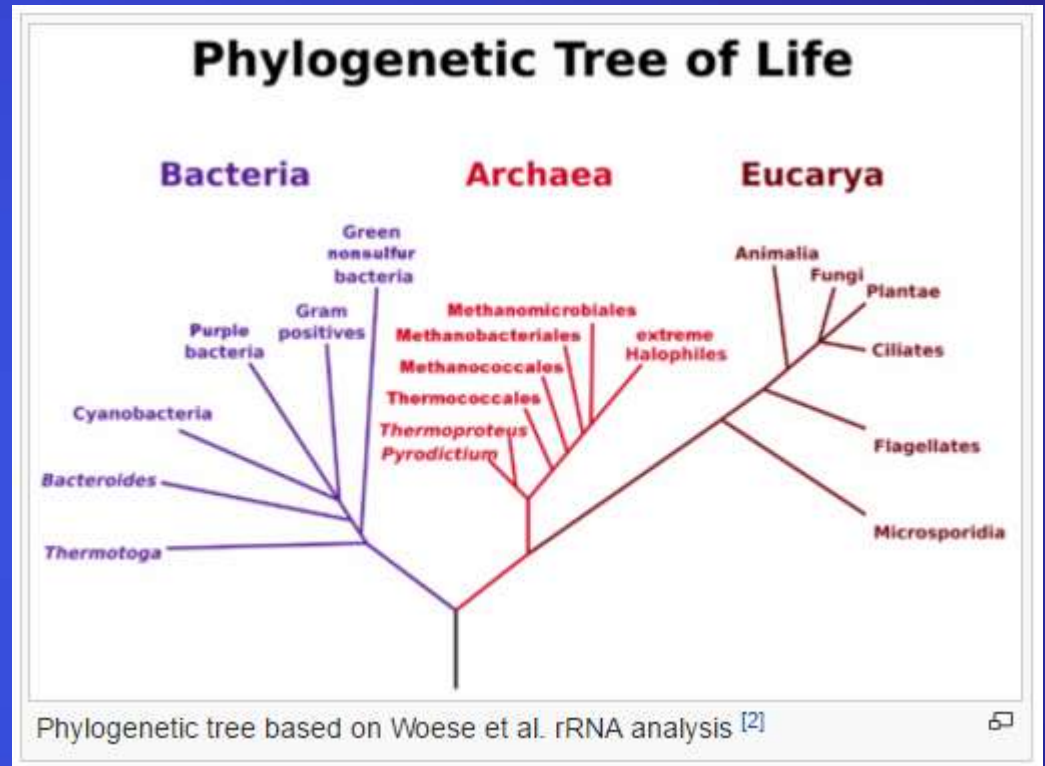
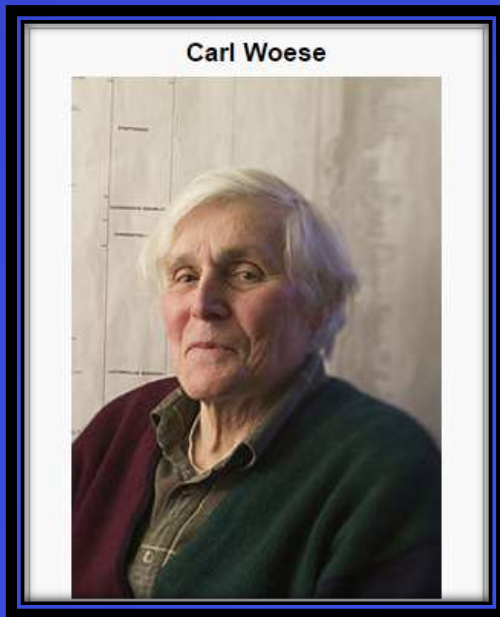
www.homd.org

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- 16S rRNA sequencing?????
- 16S ribosomal RNA sequencing allows for studying the phylogenetic relationships between bacteria.
- Its use in molecular techniques is based on the fact that it is present in all prokaryotic cells taken with the fact that the rDNA encoding the RNA is highly conserved in nature
- Allow for study noncultured/unculturable bacterial cells

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- Developed by Carl Woese in 1977



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70S Ribosomes

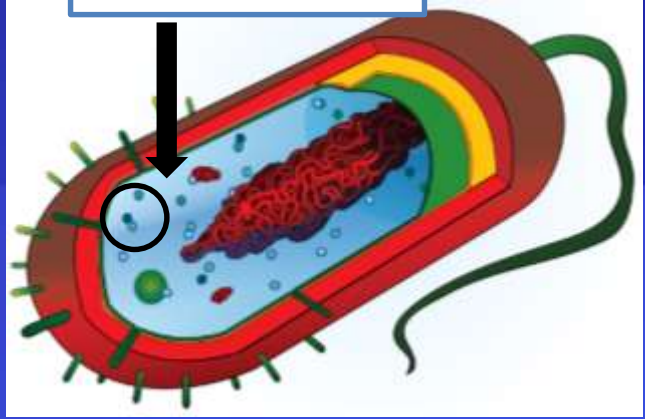


Image Source: Pixabay

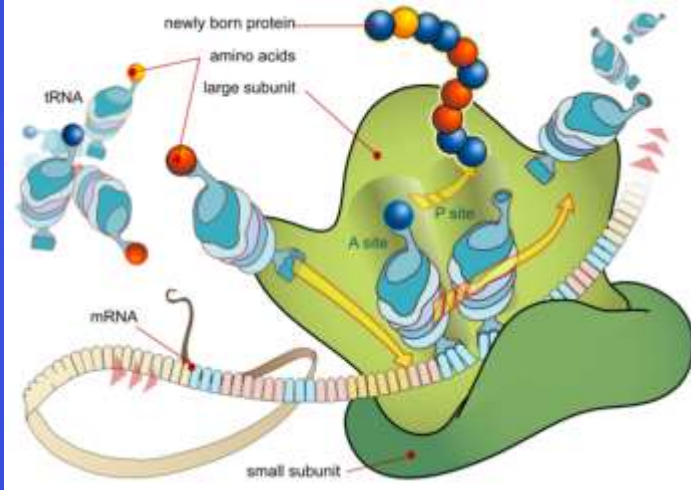
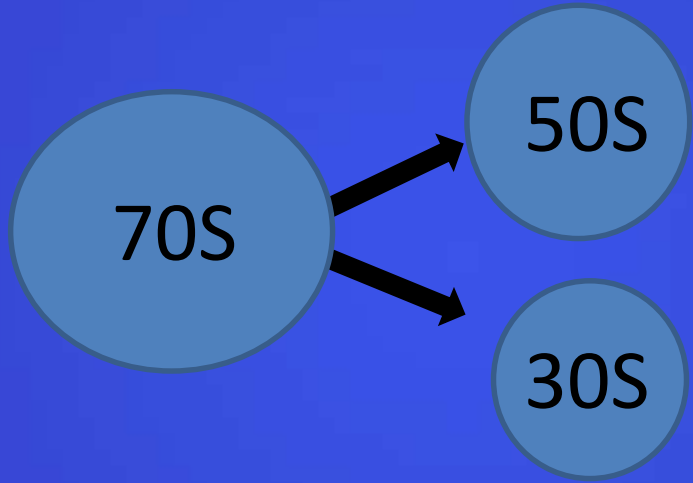
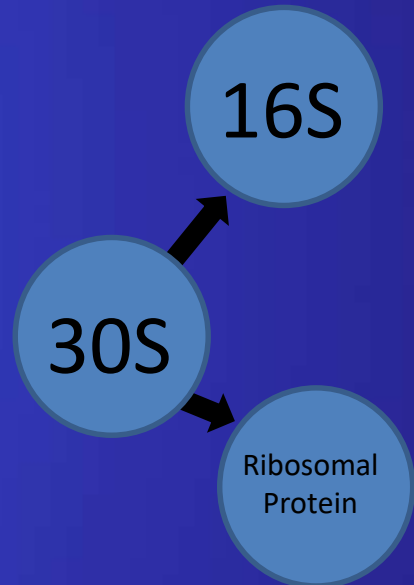


Image Source: Wikipedia



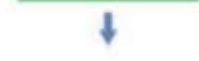
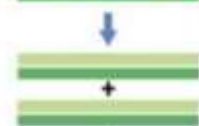
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16S rDNA Sequence Analysis

rRNA gene sequencing



16S rRNA gene



1. Isolate DNA

2. Heat to separate strands;
add specific primers

3. Primer extension with
DNA polymerase

4. Repeat above steps to obtain
many copies of 16S rRNA gene

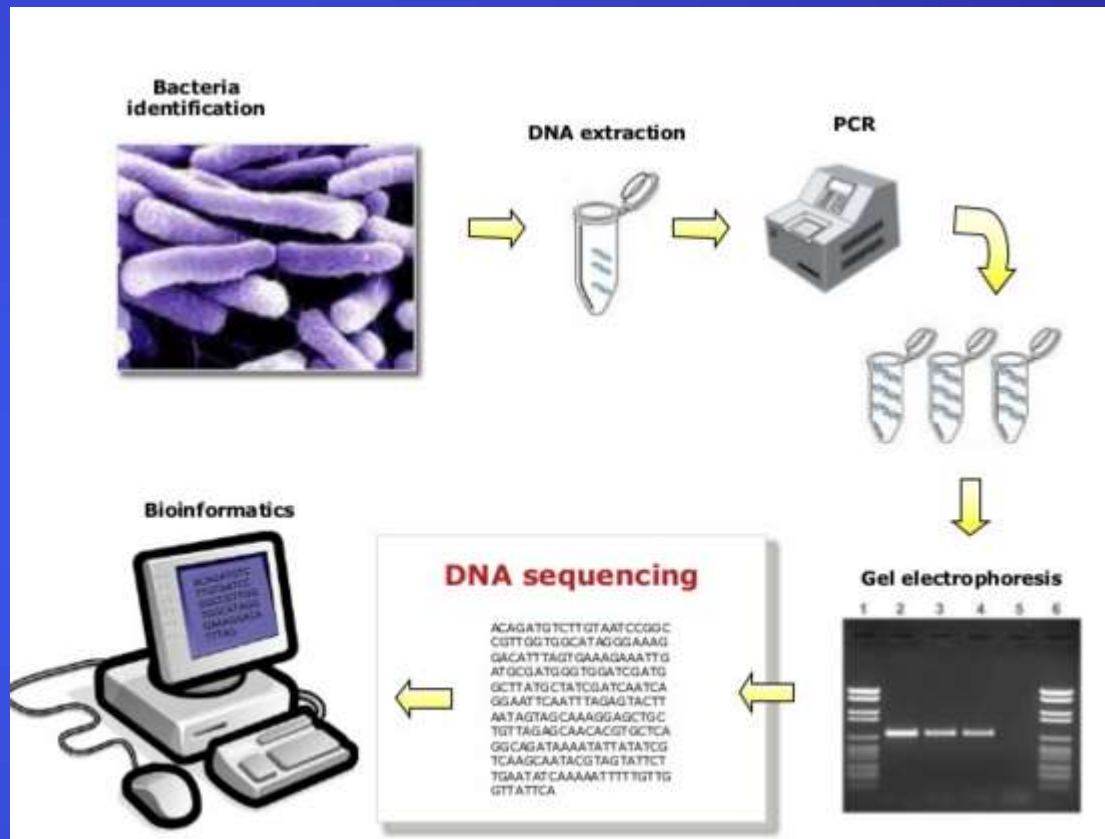
5. Run agarose gel and check
for correct sized product

6. Purify and sequence
PCR product

Figure 11-12 Brock Biology of Microorganisms 11/e
© 2006 Pearson Prentice Hall, Inc.

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16S rDNA Sequence Analysis



Amrita University – Amrita Virtual Laboratories Universalizing Education

The screenshot displays the Amrita Virtual Lab interface for a 16S Ribosomal RNA Sequencing simulation. At the top, the title "16S Ribosomal RNA Sequencing" is shown. Below the title is a navigation bar with icons and labels for "Theory", "Procedure", "Self Evaluation", "Animation", "Assignment", "Reference", and "Feedback". The main content area features the Amrita University logo and the text "AMRITA VIRTUAL LAB". Below this, the simulation title "16 S Ribosomal RNA Sequencing" is displayed with a red control bar containing a home icon, a square icon, and navigation arrows. The central 3D environment is labeled "MICRO BIOLOGY LAB" and shows a laboratory setup with various equipment. The text "16 S Ribosomal RNA Sequencing" is centered at the bottom of the 3D view, with a green "START" button below it.

Virtual Lab Web Address: <http://vlab.amrita.edu/?sub=3&brch=76&sim=1421&cnt=3087>



Taxon Description

- Taxon Table
- Taxonomic Hierarchy
- Taxonomic Level

Identify 16S rRNA Sequence

- BLAST Sequence(s)
- Download RefSeq & Taxonomy

Genomes

- Taxa with Annotated Genomes
- All Oral Genomes
- All Genomes

Proteomes

- Download Protein Sequences

Tools & Download

- HOMD JBrowse Genome Viewer »
- HOMD Genome Viewer »
- View Dynamic Annotation
- BLAST Against HOMD Genomes »
- Dynamic Genome BLAST
- Download HOMD Data
- HOMD FTP Site
- HOMD Posters
- Oralgen »

Welcome to eHOMD

the goal of creating the expanded Human Oral Microbiome Database (eHOMD) is to provide the scientific community with comprehensive curated information on the bacterial species present in the human aerodigestive tract (ADT), which encompasses the upper digestive and upper respiratory tracts, including the oral cavity, pharynx, nasal passages, sinuses and esophagus. eHOMD should also serve well for the lower respiratory tract. Currently, eHOMD includes a total of 770 microbial species, 687 from version 14.51 of HOMD and 83 added in this expansion based on publicly available data on the microbiota of the aerodigestive tract outside of the mouth. Of all the species, 57% are officially named, 13% unnamed but cultivated and 30% are known only as uncultivated phylotypes. one important aspect of the eHOMD, is that it presents a provisional naming scheme for the currently unnamed taxa, based on the 16S rRNA sequence phylogeny, so that strain, clone and probe data from any laboratory can be directly linked to a stably named reference scheme. The eHOMD links sequence data with phenotypic, phylogenetic, clinical and bibliographic information. Genome sequences for aerodigestive tract bacteria determined as part of the HOMD project, the Human Microbiome Project and other sequencing projects are being added to the eHOMD as they become available. Genomes for 482 taxa (63% of all taxa, 89% of cultivated taxa) are currently available on eHOMD. The eHOMD site offers easy to use tools for viewing all publically available ADT bacterial genomes. Welcome!

Primary Investigators: Tsute Chen, Floyd E. Dewhirst, Isabel Fernandez Escapa, Katherine P. Lemon, Bruce J. Paster, Anne Tanner, and William G. Wade

Meta-Database Search

Announcement

- 2018-03-31 07:07:12
Change of taxon ID prefix from HOT to HMT [more]
- 2018-02-02 09:36:22
Announcing the eHOMD - the expanded version of HOMD [more]
- 2015-12-08 11:49:40
Publication: Robust species taxonomy assignment algorithm for 16S rRNA NGS reads:

Database Update

- 2017-11-22 01:11
Genome Annotation Update - *Stenotrophomonas nitritireducens* DSM 12575 [more]
- 2017-02-27 16:02
Genome Annotation Update - [more]
- 2016-02-26 23:02
Genome Annotation Update - *Staphylococcus warneri* L37603 [more]
- 2016-02-26 17:02
Genome Annotation Update - *Streptococcus vestibularis* F0396 [more]

Chen, T., Yu, W-Han, Izard, J., Baranova, O.V., Lakshmanan, A., Dewhirst, F.E. (2010) **The Human Oral Microbiome Database: a web accessible resource for investigating oral microbe taxonomic and genomic information.** *Database*, Vol. 2010, Article ID baq013, doi: 10.1093/database/baq013

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expanded Human Oral Microbiome Database

Forsyth /
Pioneering Discoveries
Profound Change

[Home](#) | [Taxon Description](#) | [Identify 16S rRNA Sequence](#) | [Genomes](#) | [Proteomes](#) | [Tools & Download](#) | [HOMD Information](#) | [How to Use This Page](#) | [Page: HP1](#)



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Human Oral Microbiome Taxonomic Level List

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Taxonomic level:

Domain > Phylum > Class > Order > Family > Genus > Species

Total 2 Domain categories in the database:

Domain List *	Taxon Count in this Domain
Archaea	1
Bacteria	740

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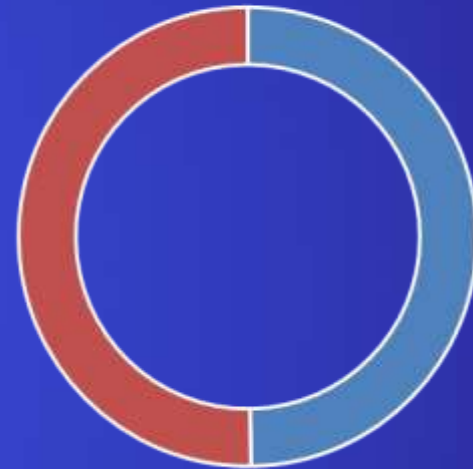
Of The >700 Currently Catalogued Taxa in the HOMD:

Comparison of Gram (+) vs. Gram (-) on Phylum Level



■ Gram (+) Phyla ■ Gram (-) Phyla

Comparison of Gram (+) vs. Gram (-) on Taxon Level



■ Gram (+) ■ Gram (-)

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eHOMD

expanded Human Oral Microbiome Database

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Home | Taxon Description | Identify 16S rRNA Sequence | Genomes | Proteomes | Tools & Download | HOMD Information | How to Use This Page | Page: HP1

Human Oral Microbiome Taxonomic Level List

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Taxonomic level:

Domain > Phylum > **Class** > Order > Family > Genus > Species

Total 66 Class categories in the database:

Up Pointer	Class List*	Taxon Count in this Class
Abconditabacteria (SR1)	Abconditabacteria (SR1) [C-1]	3
Abconditabacteria (SR1)	Abconditabacteria (SR1) [C-2]	1
Abconditabacteria (SR1)	Abconditabacteria (SR1) [C-3]	1
Actinobacteria	Actinobacteria	107
Proteobacteria	Alphaproteobacteria	45
Chloroflexi	Anaerolineae	2
Firmicutes	Bacilli	119
Bacteroidetes	Bacteroidetes [C-1]	13
Bacteroidetes	Bacteroidetes [C-2]	3
Bacteroidetes	Bacteroidia	85
Proteobacteria	Betaproteobacteria	72
Chloroflexi	Caldilineae	1
Bacteroidetes	Chitinophagia	3
Chlamydiae	Chlamydia	1
Chlorobi	Chlorobia	1
Firmicutes	Clostridia	109
Actinobacteria	Coriobacteria	44
Proteobacteria	Deltaproteobacteria	32
Proteobacteria	Epsilonproteobacteria	36
Firmicutes	Erysipelotrichia	26
Bacteroidetes	Flavobacteria	30
Fusobacteria	Fusobacteria	41
Proteobacteria	Gammaproteobacteria	71
Gracilibacteria (GN02)	Gracilibacteria (GN02) [C-1]	4
Gracilibacteria (GN02)	Gracilibacteria (GN02) [C-2]	1
Chlorobi	Ignimbacteria	2
Euryarchaeota	Methanobacteria	1
Firmicutes	Mollicutes	31
Firmicutes	Negativicutes	77
Cyanobacteria	Oscillatoriophyceae	1
Saccharibacteria (TM7)	Saccharibacteria (TM7) [C-1]	21
Bacteroidetes	Sphingobacteria	5
Spirochaetes	Spirochaetia	51
Synergistetes	Synergistia	10
WPS-2	WPS-2 [C-1]	1

List of Human Microbial Taxa

[Previous page](#)

Navigate Taxa by Alphabet:

A|B|C|D|E|F|G|H|I|J|K|L|M|N|O|P|Q|R|S|T|U|V|W|X|Y|Z|All Entries

Search: All fields Matching ANY words Partial field

Total: **770 taxa** (Note: Change from HOT to HMT)

Status: Named Unnamed Phylotypes Lost Dropped

All Valid Taxa All

Showing 1 - 770 Sort/toggle table order by

Body Site: Oral Nasal Skin Vaginal Unassigned NonOralRef

Taxon ID	Genus ▲	Species	Status	Body Site	Flag	Taxon Link	Genome Link	Genome Size
HMT-389	<i>Abiotrophia</i>	<i>defectiva</i>	Named	Oral		Taxon Description	1 Genome	3.48 Mbps
HMT-345	<i>Abconditabacteria (SR1) [G-1]</i>	<i>bacterium HMT 345</i>	Phylotype	Oral		Taxon Description	0 Genome	
HMT-874	<i>Abconditabacteria (SR1) [G-1]</i>	<i>bacterium HMT 874</i>	Phylotype	Oral		Taxon Description	1 Genome	1.11 Mbps
HMT-875	<i>Abconditabacteria (SR1) [G-1]</i>	<i>bacterium HMT 875</i>	Phylotype	Oral		Taxon Description	0 Genome	
HMT-343	<i>Achromobacter</i>	<i>xylooxidans</i>	Named	Unassigned		Taxon Description	5 Genomes	6.29 - 7.36 Mbps
HMT-191	<i>Acidipropionibacterium</i>	<i>acidifaciens</i>	Named	Oral		Taxon Description	2 Genomes	3.02 - 3.04 Mbps
HMT-211	<i>Acidovorax</i>	<i>caeni</i>	Named	Unassigned		Taxon Description	0 Genome	
HMT-209	<i>Acidovorax</i>	<i>ebreus</i>	Named	Unassigned		Taxon Description	1 Genome	3.80 Mbps
HMT-216	<i>Acidovorax</i>	<i>temperans</i>	Named	Unassigned		Taxon Description	1 Genome	4.48 Mbps
HMT-554	<i>Acinetobacter</i>	<i>baumannii</i>	Named	Unassigned		Taxon Description	7 Genomes	3.48 - 4.06 Mbps
HMT-297	<i>Acinetobacter</i>	<i>johnsonii</i>	Named	Unassigned		Taxon Description	1 Genome	4.08 Mbps
HMT-282	<i>Acinetobacter</i>	<i>junii</i>	Named	Unassigned		Taxon Description	1 Genome	3.38 Mbps
HMT-005	<i>Acinetobacter</i>	<i>lwoffii</i>	Named	Unassigned		Taxon Description	1 Genome	3.38 Mbps
HMT-010	<i>Acinetobacter</i>	<i>radioresistens</i>	Named	Unassigned		Taxon Description	1 Genome	3.21 Mbps
HMT-408	<i>Acinetobacter</i>	<i>sp. HMT 408</i>	Phylotype	Unassigned		Taxon Description	0 Genome	
HMT-850	<i>Actinomyces</i>	<i>cardiffensis</i>	Named	Oral		Taxon Description	1 Genome	2.19 Mbps
HMT-888	<i>Actinomyces</i>	<i>dentalis</i>	Named	Oral		Taxon Description	1 Genome	3.53 Mbps

MICRO

HACEK Group Taxonomy Changes Relative to Diagnosis and Expansion of Strain Analysis:

Haemophilus aphrophilus --> *Aggregatibacter aphrophilus*

Haemophilus paraphrophilus --> *Aggregatibacter paraphrophilus*

Actinobacillus actinomycescomitans --> *Aggregatibacter actinomycescomitans*

Spring
2016

531	<i>Aggregatibacter</i>	<i>actinomycescomitans</i>	Named	Taxon Description	20 Genomes	1.99 - 2.40 Mbps
545	<i>Aggregatibacter</i>	<i>aphrophilus</i>	Named	Taxon Description	4 Genomes	2.25 - 2.41 Mbps
720	<i>Aggregatibacter</i>	<i>paraphrophilus</i>	Named	Taxon Description	1 Genome	

Spring
2018

HMT-531	<i>Aggregatibacter</i>	<i>actinomycescomitans</i>	Named	Oral	Taxon Description	36 Genomes	1.86 - 2.40 Mbps
HMT-545	<i>Aggregatibacter</i>	<i>aphrophilus</i>	Named	Oral	Taxon Description	3 Genomes	2.25 - 2.31 Mbps
HMT-720	<i>Aggregatibacter</i>	<i>paraphrophilus</i>	Named	Oral	Taxon Description	1 Genome	2.41 Mbps

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eHOMD *expanded* Human Oral Microbiome Database

Forsyth / Pioneering Discoveries
Profound Change

Home | Taxon Description | Identify 16S rRNA Sequence | Genomes | Proteomes | Tools & Download | HOMD Information | How to Use This Page | Page: HP1

Too Many, Too Long At The Order >
Family > Genus > Species Levels

[Going To The Site.....](#)

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Current Learning Objectives:

1. Every participant in the room will identify sensations of blurring eyes, overwhelming respect, and a feeling of exhilaration for what is currently known about the microbiome of the oral cavity.
2. Participants in the room will manage the excitement internally building by the nanosecond at the anticipation of where microbiome knowledge will be at in one week, one month, or at the scientific knowledge normal doubling rate of less than two years!

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Systemic Connections, Diagnosis, and Clinical Trials

- Salivaomics: non-invasive diagnostic tool with a point-of-care goal utilizing scientific rationale and mechanisms that convey systemic diseases to saliva
- The microbiome as an “endocrine organ”
- Untreated or ineffectively treated periodontitis is a known independent predictor of, and comorbid contributor to, preterm birth, cardiovascular disease, pulmonary disorders, diabetes, and obesity.
 - Microbiome and atherosclerosis: exclusively bacterially-derived serine dipeptide lipids isolated from plaques

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- Role of oral microbiome in pancreatic cancer
- A significant association between preterm birth and periodontitis at 21 to 24 weeks' gestation exists
- Microbiota biomarker utilization in the pursuit of anti-cancer personalized medicine

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Cause or Effect?

- Microbiome analysis in humans has been largely observational, associating disease phenotypes with specific microbial presence/absence/dysbiosis
- Sir Austin Bradford Hill's criteria for causation has great value to clinical applications of microbiome studies: "In what circumstances can we pass from this observed association to a verdict of causation? Upon what basis should we proceed to do so?"

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- Strength of association - consistency, biologic/basic science plausibility, specificity, and temporality
- The presence of biologic gradients
- Existence of experimental support
- Extrapolation from known causal relationships
- Applicable to understanding either causal roles of environmental or genetic (including metagenomics and other “-omics” fields) elements

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Therapeutic Manipulation of the Microbiome

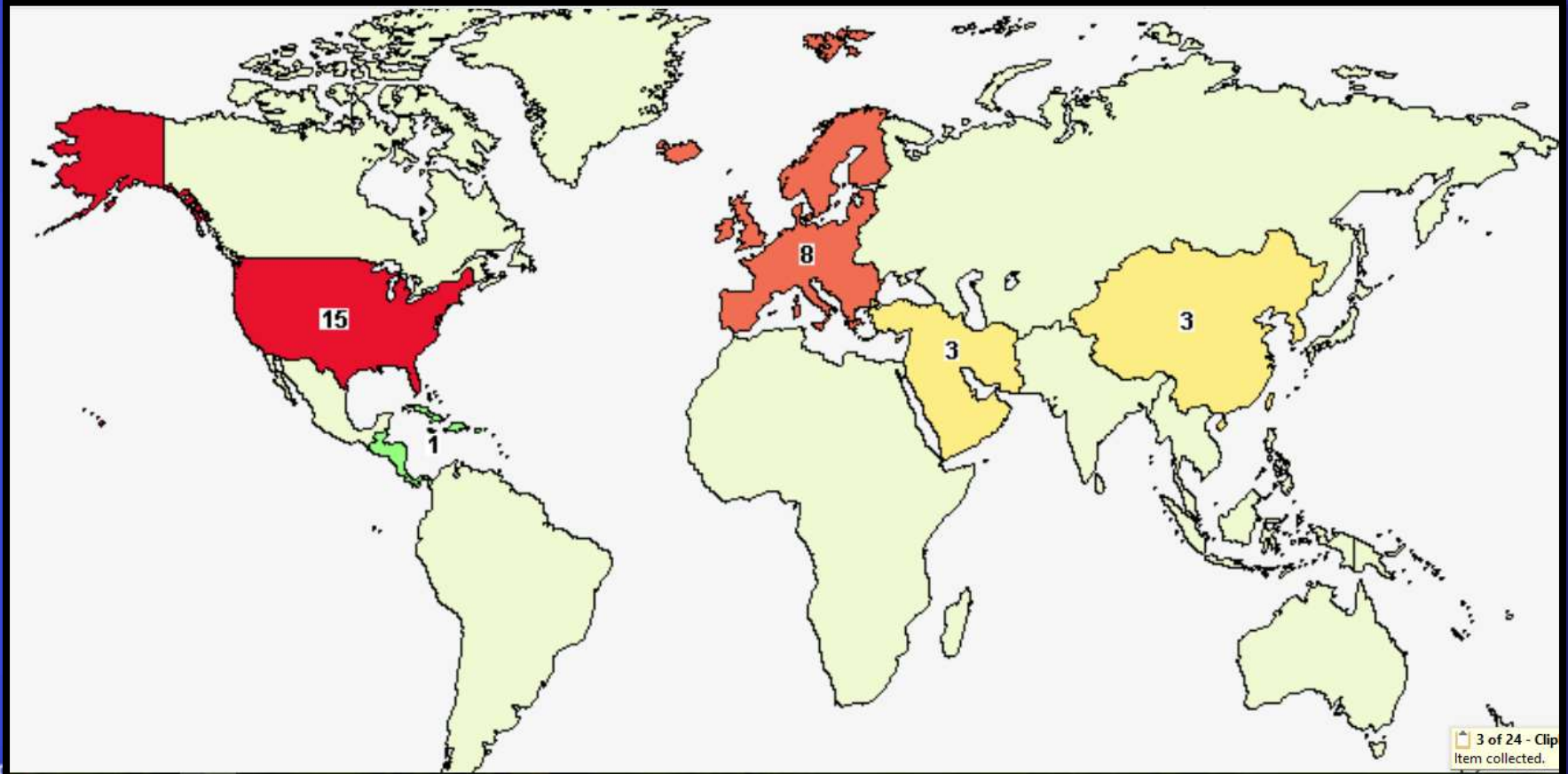
- Prebiotics: nondigestible food components that beneficially affect the host by selectively stimulating the growth and/or activity of 1 or a limited number of bacteria in the colon and thereby improving host health
- Probiotics: viable (mainly isolates from the human microbiota) organisms that possess health benefits following administration; commonly administered bacterial genera include bifidobacteria, lactobacilli, streptococci, enterococci, and *E. coli*

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As of Summer 2018, there are 273,931 clinical trials research studies in 50 states and 204 countries catalogued in the NIH → U.S. National Library of Medicine as can be viewed at [Clinicaltrials.gov](https://clinicaltrials.gov)

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37 Studies found for: oral microflora | oral microbiota with the following geographic distribution



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- In summary, “the microbiome-minded clinician scientist will consider the stability of oral microbiome composition as a hallmark of human health.” *(Taken from a Clinical Key© Book Chapter “The Human Microbiome of Local Body Sites and Their Unique Biology” of “Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Updated Edition” (8th edition, 2015)*
- Smiles for Life©: National, interprofessional oral health curriculum aimed at the integration of oral health and primary care

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Final Thoughts on the Oral Cavity Microbiome:

- In general, it is estimated that 99% of the bacteria on earth has yet to be grown in the lab
- Intra- and inter-species communication by bacteria (known as “quorum sensing”) using auto inducers as their language has yet to be extensively or translationally studied in the oral microbiome
- “Bacteriome” should be the term used for all we are discussing today because where are the others???

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- It is estimated that there are 10^{31} bacteriophages on earth
- It is estimated that viruses outnumber bacteria 10:1
- Virally-infected bacterial cells can release anywhere from 100 – 1000 bacteriophage virions
- “Virome”
- “Fungome”



Image Source: Wikipedia

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Research in the Taylor Lab

SUMMER 2012 – PNWU Division of Microbiology as a partner with a Heritage University National Science Foundation – REU 2012-15 Grant began undergraduate:professional student intercollegiate work:

- Evaluating the prevalence of ECC in Yakima County both on and off Yakama Nation
 - Evaluated a small 2 year sample (2010-12) to establish somewhat of a statistical/epidemiological baseline in the area
 - 37% prevalence in Yakima City (28% nationally)
 - 98% prevalence on Yakama Nation

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Research in the Taylor Lab

- Began development of educational bilingual materials that could be distributed at health fairs and other community events:

Caries de la primera infancia
Caries de la primera infancia (ECI) es una enfermedad que causa caries dentales en los niños pequeños, desde los bebés hasta niños de aproximadamente 6 años de edad.

0-6 meses: Limpieza sus encías de su bebé.
✓ Limpie suavemente las encías de su bebé con un paño limpio.
✓ Enjuague la boca alrededor de su bebé y hable que su bebé desde las primeras semanas.

6-12 meses: Las Primeras Dientes.
✓ Continúe limpiando las encías de su bebé.
✓ Limpie regularmente las mordeduras y chupón.
✓ Consciencia e limpiar los dientes y cepillo de bristles suaves.
✓ Limpie los dientes de su bebé cada mañana y noche.
✓ Dese a su bebé agua en vez de jugo o leche en la noche.

12-24 meses: Teething Time.
✓ Continúe a limpiar su bebé's gums.
✓ Regularly clean teething rings and pacifiers.
✓ Start to clean teeth with a soft toothbrush.
✓ Clean your baby's teeth every night.
✓ Give your baby wear teether at night.


24-30 Months: Teeth are visible.
✓ Continue using a soft toothbrush with non-fluoride toothpaste.
✓ Use gentle circular motions.

30-36 Months: Introducing.
✓ Use pacifiers for short periods.
✓ Avoid sugary drinks with enough water.
✓ Continue to clean your child's teeth.

36-48 Months: Introducing.
✓ Durante el día, evite los jugos de frutas que tienen gran cantidad de azúcar o considere diluirlos en agua.
✓ Durante la noche, dé a su hijo agua en vez de jugo.
✓ Reemplace el cepillo de dientes de su niño cada 3 meses.
✓ Utilice pasta dental sin fluoruro hasta que su hijo pueda escupir.
✓ Utilizar aproximadamente una cantidad del tamaño de un guisante (concentra de pasta de dientes).

Consejos útiles para dientes sanos
✓ Durante el día, evite los jugos de frutas que tienen gran cantidad de azúcar o considere diluirlos en agua.
✓ Durante la noche, dé a su hijo agua en vez de jugo.
✓ Reemplace el cepillo de dientes de su niño cada 3 meses.
✓ Utilice pasta dental sin fluoruro hasta que su hijo pueda escupir.
✓ Utilizar aproximadamente una cantidad del tamaño de un guisante (concentra de pasta de dientes).

✓ During the day, avoid sugary drinks with high amounts of sugar or consider diluting them in water.
✓ During the night, give your child water instead of juice.
✓ Replace your child's toothbrush every 3 months.
✓ Use non-fluoride toothpaste until your child can spit.
✓ Use about a pea size amount of toothpaste.

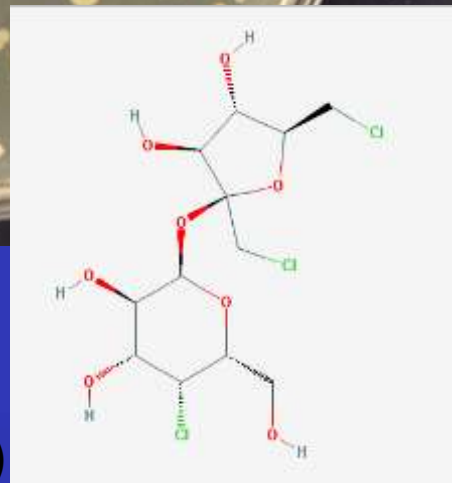
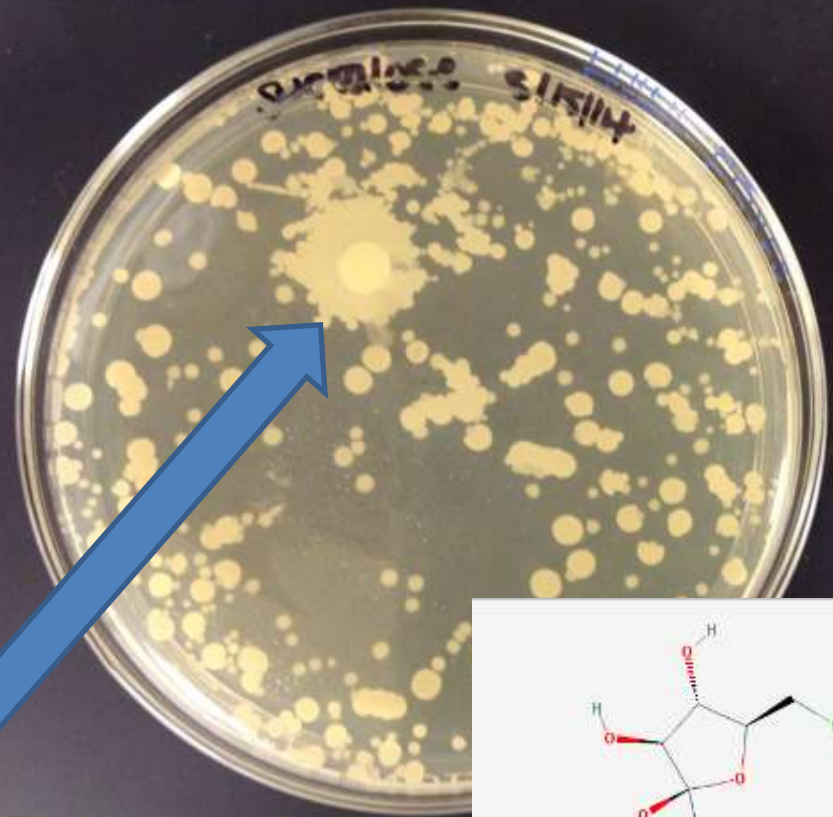


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Research in the Taylor Lab

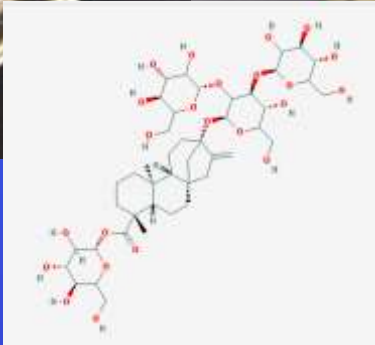
- Based on the addition of *Streptococcus salivarius* to oral probiotic formulations and its key role in the matrix of viridans streptococci colonization of the oral cavity, plate studies were conducted evaluating the effects of non-sucrose based sweeteners commonly used in both oral health products and in the American food supply in general

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Sucralose
(Trichlorosucrose)

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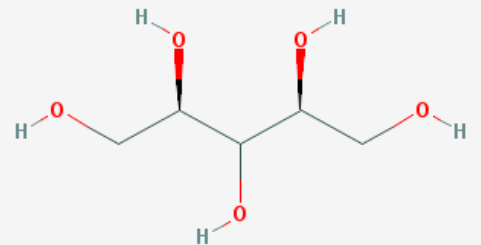


Stevia

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Xylitol

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Research in the Taylor Lab

- Ultimately we would like to evaluate the presence of *Scardovia wiggisiae* in ECC/SECC lesions in Yakima County with and without the presence of *Streptococcus mutans* in the cavitous lesion
 - Evaluations to be conducted by both culturing and nonculturing (16S rRNA and whole genome sequencing) techniques



Image Source: NHGRI

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Thank You!

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REFERENCES

1. Lederberg J, and Mccray AT. 'Ome sweet 'omics—a genealogical treasury of words. *Scientist* 2001; 15:8-10.
2. <http://www.columbia.edu/itc/hs/pubhealth/p8475/readings/lederberg.pdf>
3. "Joshua Lederberg - Facts". *Nobelprize.org*. Nobel Media AB 2014.
http://www.nobelprize.org/nobel_prizes/medicine/laureates/1958/lederberg-facts.html

MICRO

4. Whipps JM, Lewis K, and Cook RC, *Fungi in Biological Control Systems* (M.N. Burge, ed.) Manchester University Press, Manchester, 1988.
5. Revue odontologique v.71:1949. Part of the Hathi Trust Digital Library.
6. Committee on Metagenomics (2007). The new science of metagenomics: revealing the secrets of our microbial planet. National Academies Press, Washington, DC

MICRO

7. Nicholson JK, Holmes E, and Wilson ID. Gut microorganisms, mammalian metabolism and personalized health care. *Nat Rev Microbiol* (2005) 3:431–438
8. Weinstock G. Genomic approaches to studying the human microbiota. *Nature* (2012) 489:251–256
9. Gallacher DJ and Kotecha S. “Respiratory microbiome of newborn infants” Review in *Frontiers in Pediatrics* (February 2016).

MICRO

10. Aagaard K, Ma J, Anthony KM, Ganu R, Petrossino J, Versalovic J, The placenta harbors a unique microbiome. *Sci Transl Med* (2014) 6(237) ra65. doi: 10.1126/scitranslmed.3008599.
11. DiGiulio DB, Romero R, Amogan HP, Kusanovic JP, Bik EM, Gotsch F, Kim CJ, Erez O, Edwin S, Relman DA. Microbial prevalence, diversity and abundance in amniotic fluid during preterm labor: a molecular and culture-based investigation. *PLoS One*. (2008) Aug 26;3(8):e3056. doi: 10.1371/journal.pone.0003056.

MICRO

12. Jones HE, Harris KA, Azizia M, Bank L, Carpenter B, Hartley JC, Klein N, Peebles D. Differing prevalence and diversity of bacterial species in fetal membranes from very preterm and term labor. *PLoS One*. (2009) Dec 8;4(12):e8205. doi: 10.1371/journal.pone.0008205.
13. Hansen R, Scott KP, Khan S, Martin JC, Berry SH, Stevenson M, Okpapi A, Munro MJ, Hold GL. First-Pass Meconium Samples from Healthy Term Vaginally-Delivered Neonates: An Analysis of the Microbiota. *PLoS One*. (2015) Jul 28;10(7):e0133320. doi: 10.1371/journal.pone.0133320. eCollection 2015.

MICRO

14. Rogers GB, Shaw D, Marsh RL, Carroll MP, Serisier DJ, Bruce KD. Respiratory microbiota: addressing clinical questions, informing clinical practice.

Thorax. (2015) Jan;70(1):74-81. doi: 10.1136/thoraxjnl-2014-205826. Epub 2014 Jul 17.

15. Ziesemer KA, Mann AE, Sankaranarayanan K, Schroeder H, Ozga AT, Brandt BW, Zaura E, Waters-Rist A, Hoogland M, Salazar-García DC, Aldenderfer M, Speller C, Hendy J, Weston DA, MacDonald SJ, Thomas GH, Collins M, Lewis CM, Hofman C, Warinner C. Intrinsic challenges in ancient microbiome reconstruction using 16S rRNA gene amplification. *Sci Rep*. (2015) Nov 13;5:16498. doi: 10.1038/srep16498.

MICRO

16. Warinner C, Speller C, Collins MJ. A new era in palaeomicrobiology: prospects for ancient dental calculus as a long-term record of the human oral microbiome. *Philosophical Transactions of the Royal Society B*. 8 December 2014.
DOI:10.1098/rstb.2013.0376
17. Turnbaugh PJ, Ley RE, Hamady M, Fraser-Liggett C, Knight R, Gordon JI. The human microbiome project: exploring the microbial part of ourselves in a changing world. *Nature*. (2007) ;449(7164):804-810.
doi:10.1038/nature06244.

MICRO

18. Human Microbiome Project: <http://hmpdacc.org/>
19. Shade A and Handelsman J. Beyond the Venn diagram: the hunt for a core microbiome. *Environ Microbiol* (2012) 14:4–12.
20. Segal LN, Rom WN, Weiden MD. Lung microbiome for clinicians. New discoveries about bugs in healthy and diseased lungs. *Ann Am Thorac*. (2014) Jan;11(1):108-16. doi: 10. 1513/Annals ATS.201310-339FR.

MICRO

21. Beck, JM, Young VB, and Huffnagle GB. The microbiome of the lung. *Transl Res.* (2012) Oct;160(4):258-66. doi: 10.1016/j.trsl. 2012.02.005.
22. Dickson RP, Erb-Downward JR, and Huffnagle GB. The role of the bacterial microbiome in lung disease. *Expert Rev Respir Med.* (2013) Jun;7(3):245-57. doi: 10.1586/ers. 13.24.

MICRO

23. Huang YJ, Lynch SV. The emerging relationship between the airway microbiota and chronic respiratory disease: clinical implications *Expert Rev Respir Med.* (2011) Dec;5(6):809-21. doi: 10.1586/ers.11.76.
24. Jiménez E, Fernández L, Marín ML, Martín R, Odriozola JM, Nueno-Palop C, Narbad A, Olivares M, Xaus J, Rodríguez JM. Isolation of commensal bacteria from umbilical cord blood of healthy neonates born by cesarean section. *Curr Microbiol.* (2005) Oct;51(4):270-4.