

Human Microbiome through the Lens of Global Environmental Ecosystems

Rekha Seshadri, PhD

13th Microbiome & Probiotics Forum USA

San Diego, CA

Oct 13, 2025

Joint Genome Institute is a U.S. Dept of Energy User Facility



Mission: Enable large-scale, multi-omic studies of plants, fungi, algae, bacteria, archaea & microbial communities



DoE **Focus** :
energy & environmental
challenges



Enabling high quality User Science since 2004



Genome Targets:

- Plant
- Fungal & Algal
- Metagenome
- Microbial

Infrastructure/ Capabilities



DNA Sequencing Platforms

- Illumina NovaSeq X
- PacBio Revio
- Oxford Nanopore PromethION



Advanced Genomic Technologies

- Single-cell Sequencing
- Stable Isotope Labeling
- Methylation/Epigenomics
- Transcriptomics



Metabolomics

- Polar-/non-polar LC/MS metabolite profiling
- Targeted and untargeted metabolite analysis



DNA Synthesis

- Design & Pathway Assembly
- Host Engineering



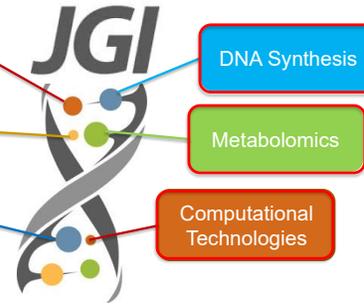
Secondary Metabolites

- Large-scale bioinformatic mining
- Integrated workflows
- BGC exploration

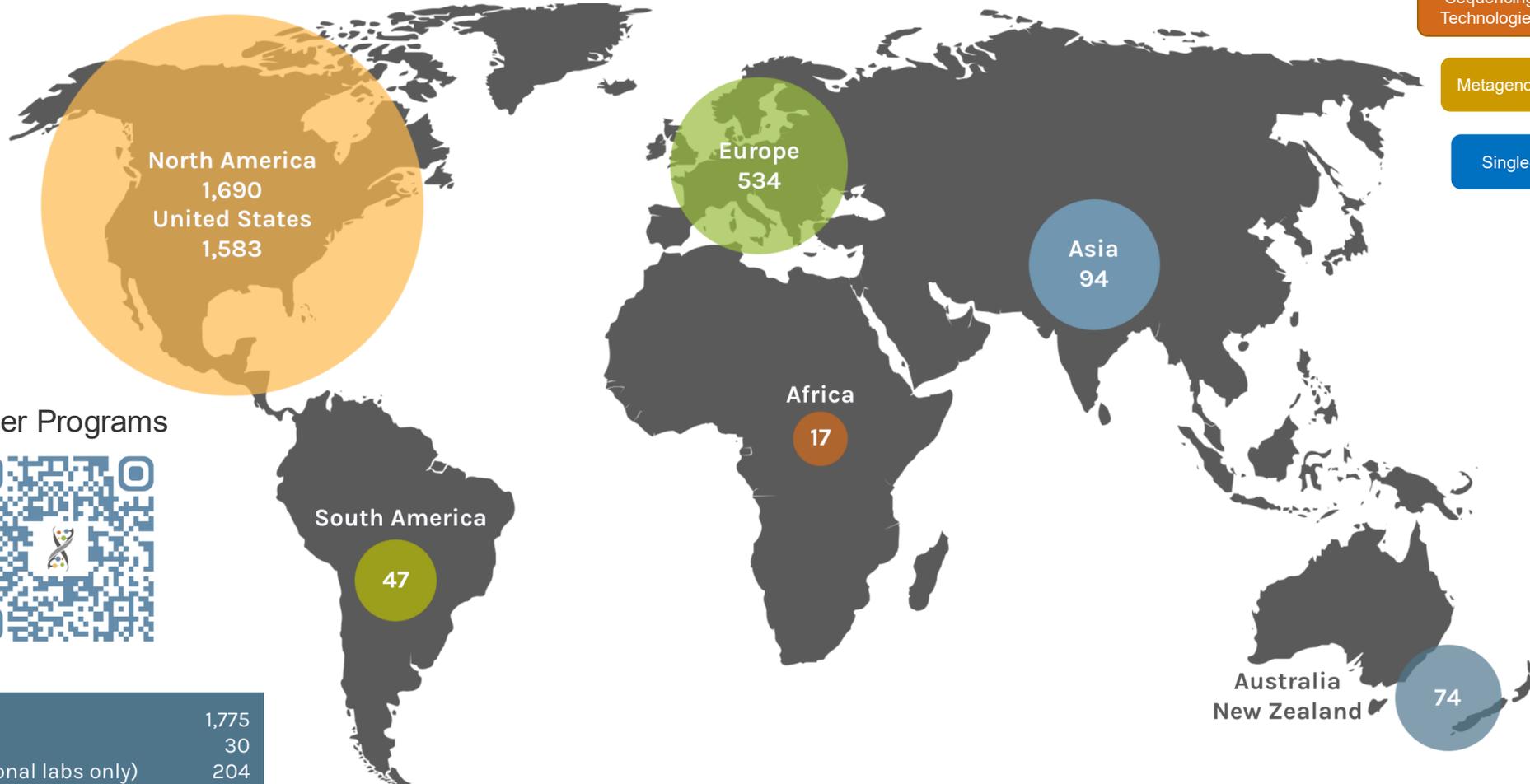
Data Science & Informatics



JGI Worldwide Users



JGI "services"



User Programs



Academic	1,775
Industry	30
DOE (national labs only)	204
Government	154
Other	293
Total Users	2,456

Community Science Program (CSP): Genomic Encyclopedia of Bacteria & Archaea



GEBA-pilot (56)

nature
A phylogeny-driven genomic encyclopaedia of Bacteria and Archaea
Donohue W, Pridmore P, Karpman A, et al. (2012) *Nature* 486: 255-262

2007

PNAS
Improving the coverage of the cyanobacterial phylum using diversity-driven genome sequencing
Wang S, et al. (2012) *PNAS* 109: 1058-1063

2012

GEBA-I Diversity



nature biotechnology
1,003 reference genomes of bacterial and archaeal isolates expand coverage of the tree of life
Suzart M, et al. (2012) *Nature Biotechnology* 30: 1003-1010

2013

GEBA-II Genus coverage

GEBA-III Soil & Rhizosphere



nature genetics
Genomic features of bacterial adaptation to plants
Frost L, et al. (2013) *Nature Genetics* 45: 115-122

2014

GEBA-IV Ubiquitous OTUs
GEBA-V Pangenomes

2015

GEBA Actinos



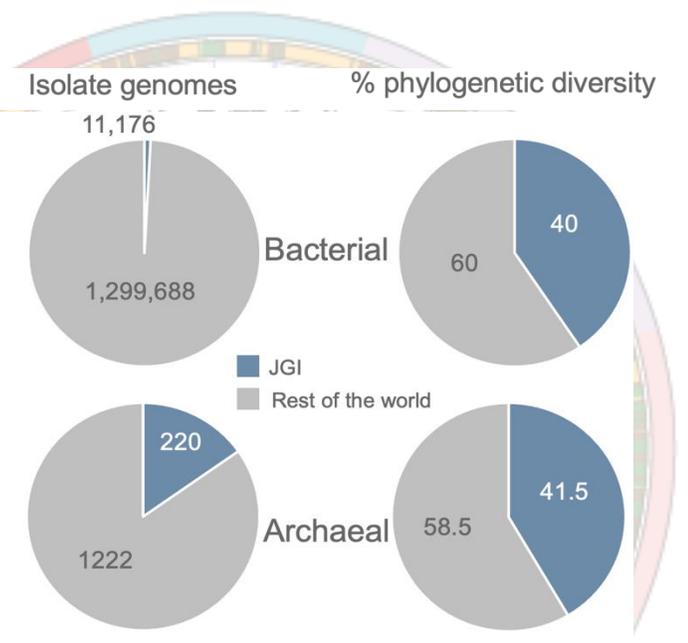
Cell Genomics
Expanding the genomic encyclopedia of Actinobacteria with 824 isolate reference genomes
Baker S, et al. (2015) *Cell Genomics* 1: 1-10

2017

nature biotechnology
Cultivation and sequencing of rumen members from the Hungate1000 Collection
Meyer R, et al. (2017) *Nature Biotechnology* 35: 100-108

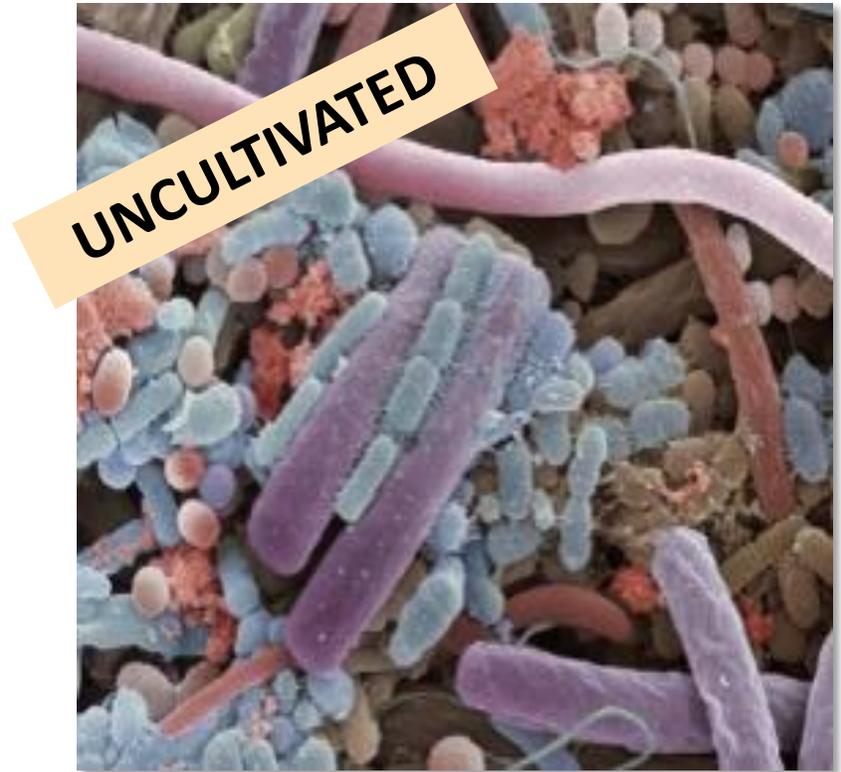
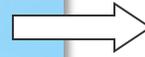
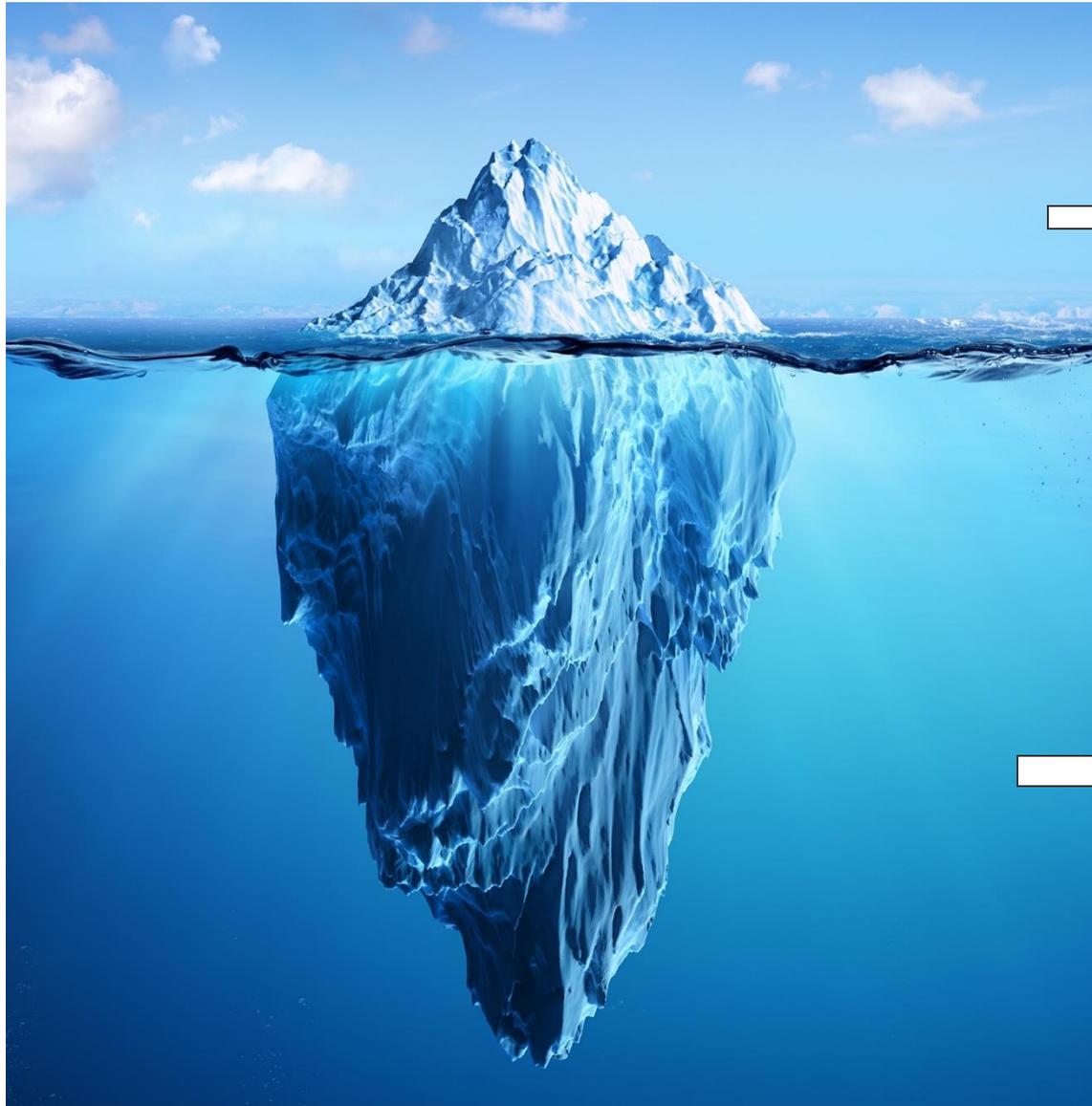
2019

GEBA-10K



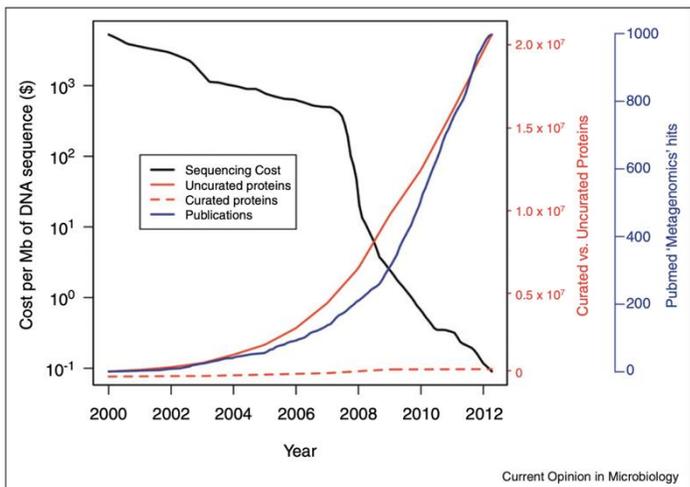
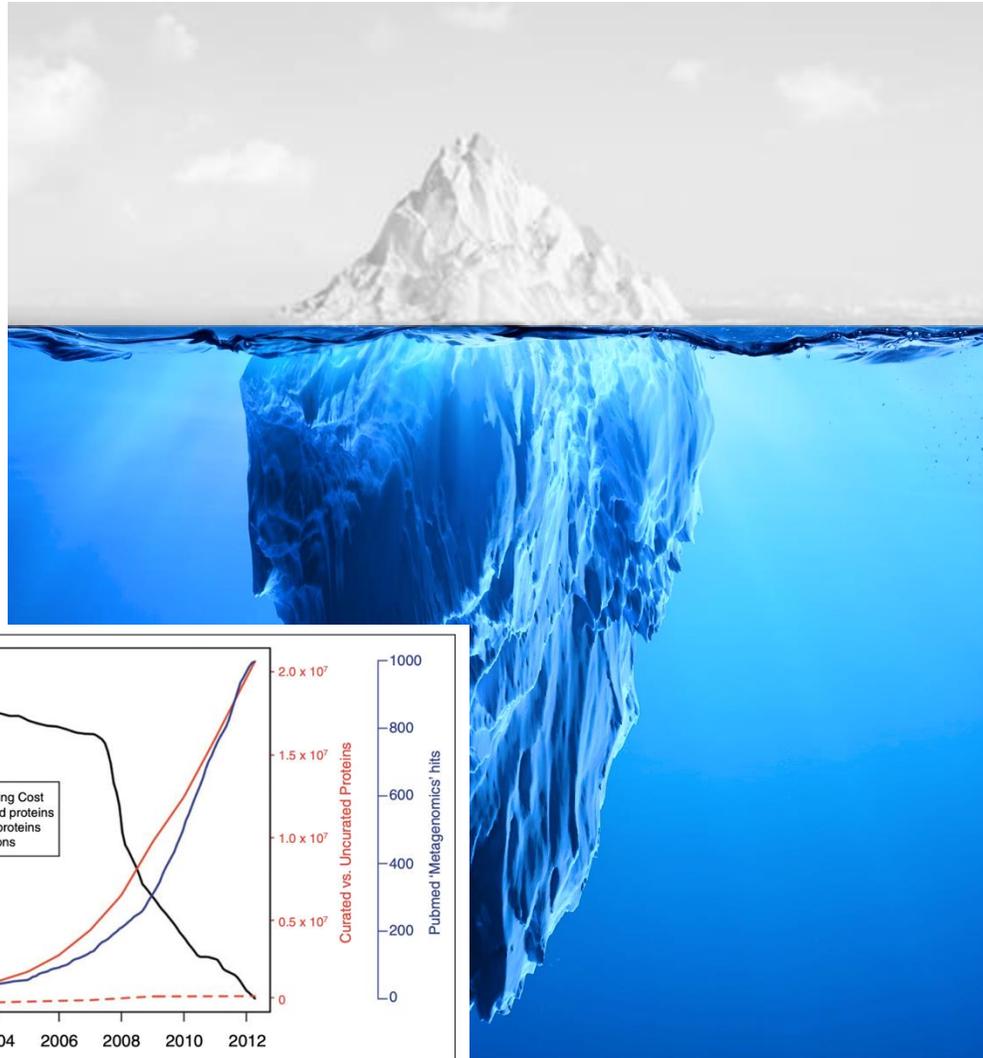
Just 11,000 JGI genomes account for >40% of total diversity from >2 million genomes in GenBank

Microbial Dark Matter



Pioneering metagenomic studies at the JGI

- No cultivation, no prior knowledge required



2004 **nature** **Community structure and metabolism through reconstruction of microbial genomes from the environment**
 Gene W. Tyson¹, Jarrod Chapman^{1,2}, Philip Hugenholtz¹, Eric E. Allen¹, Rachna J. Ram¹, Paul M. Richardson¹, Victor V. Solovyev¹, Edward M. Rubin¹, Daniel S. Rokhsar^{1,2} & Jillian F. Banfield^{1,2}



SAGs

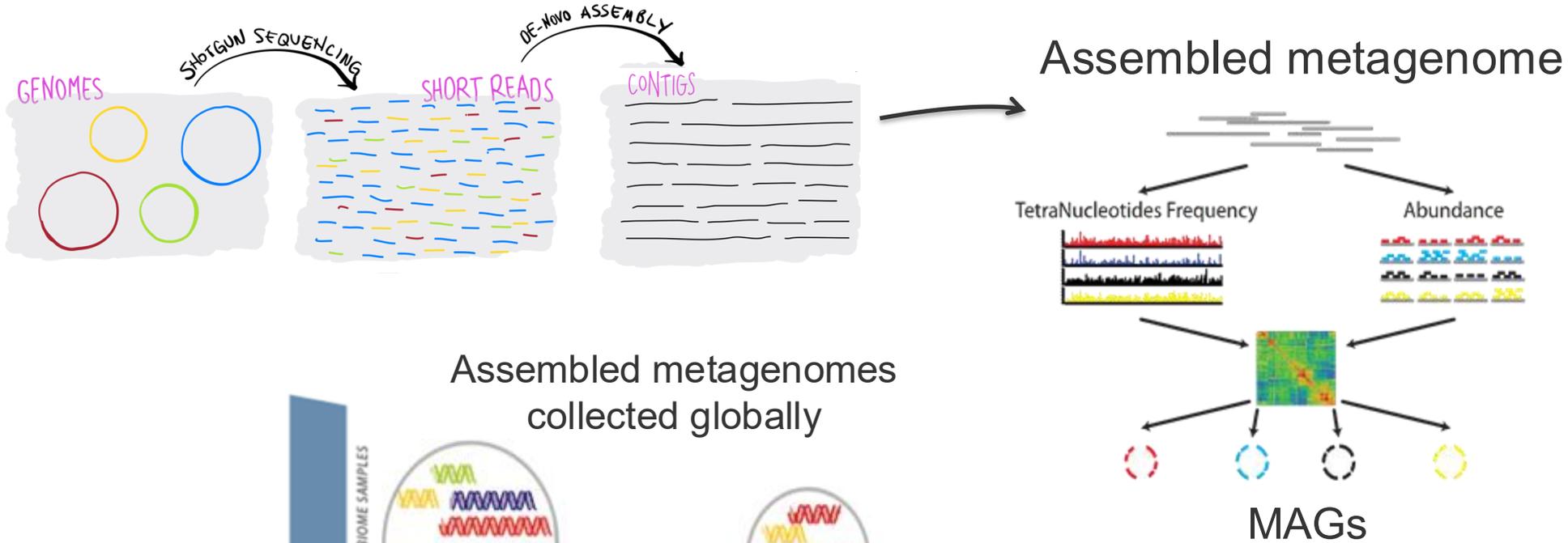
 SINGLE CELL GENOMICS
 Single Amplified Genomes

MAGs

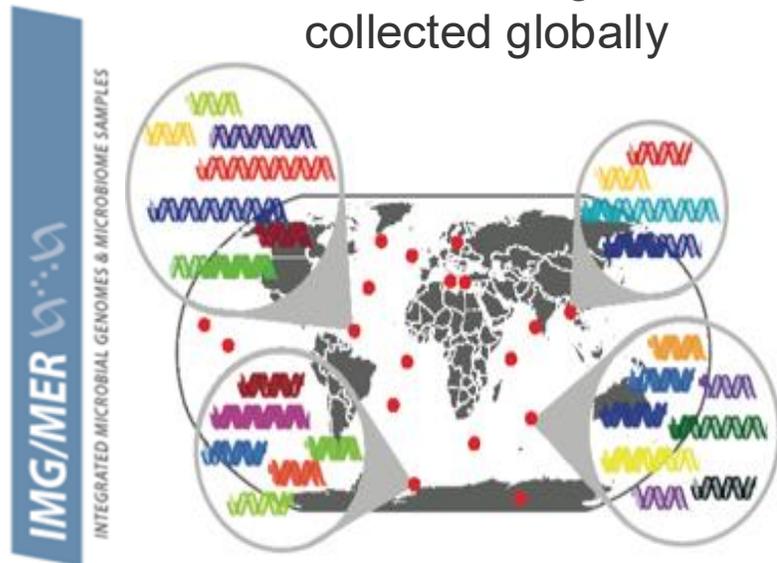
 Metagenome Assembled Genomes

Recovering MAGs AT SCALE

“Binning” exploits similarities in “coverage” & nucleotide composition to pull together discrete contigs into a MAG



Assembled metagenomes collected globally



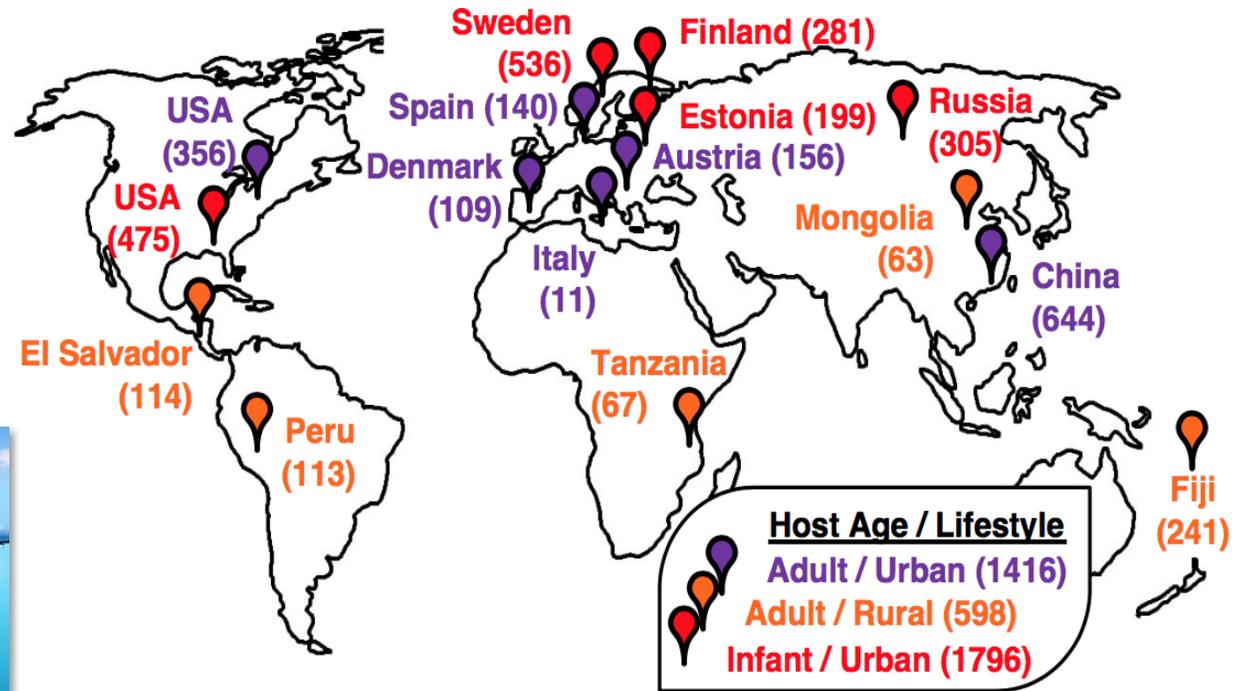
nature

Article | [Open access](#) | Published: 13 March 2019

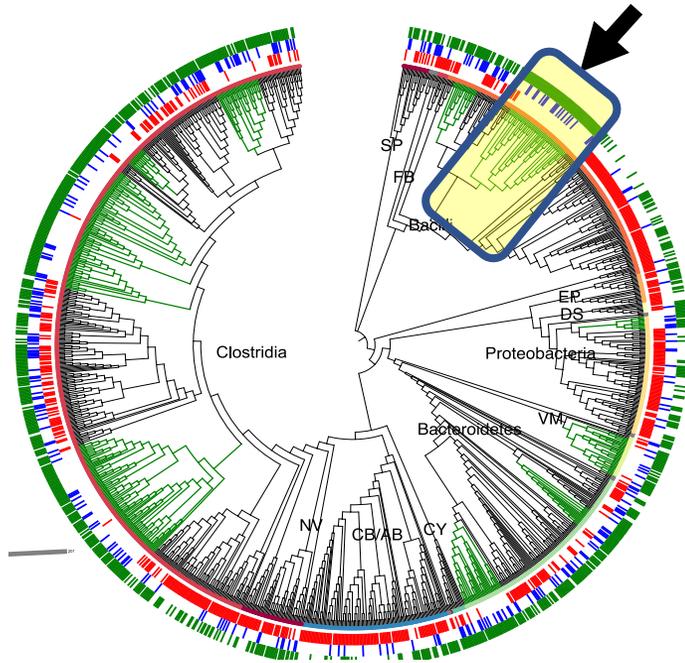
New insights from uncultivated genomes of the global human gut microbiome

[Stephen Nayfach](#) ✉, [Zhou Jason Shi](#), [Rekha Seshadri](#), [Katherine S. Pollard](#) & [Nikos C. Kyrpides](#) ✉

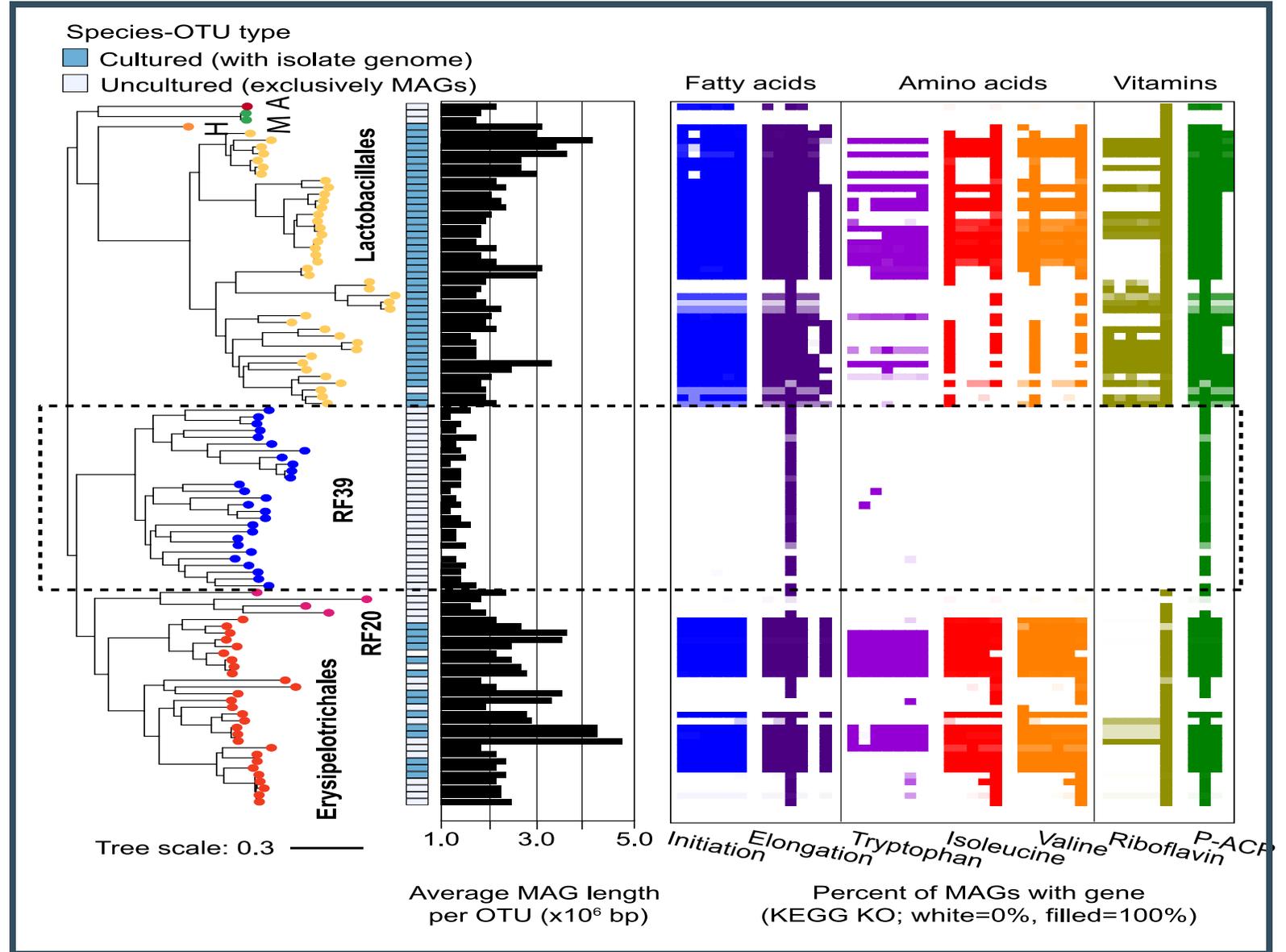
- 3,810 samples from 2,444 individuals
 - multiple geo regions, age groups, lifestyles, and disease states
- 60,664 MAGs reconstructed
 - 4,558 microbial species
 - 80% new



Large Lineages don't have cultured representatives



- RF39 is found in 49% of healthy adults
- Numerous MAGs, (no isolates)
- genome deficits – metabolic dependencies



Unified Human Gastrointestinal Genome Catalog

ARTICLE JGI OPEN
<https://doi.org/10.1038/s41586-019-1058-x>

New insights from uncultivated genomes of the global human gut microbiome

Stephen Nayfach^{1,2*}, Zhou Jason Shi^{3,4}, Rekha Seshadri^{1,2}, Katherine S. Pollard^{3,4,5,6,7,8} & Nikos C. Kyrpides^{1,2*}

ARTICLE EBI OPEN
<https://doi.org/10.1038/s41586-019-0965-1>

A new genomic blueprint of the human gut microbiota

Alexandre Almeida^{1,2*}, Alex L. Mitchell¹, Miguel Boland¹, Samuel C. Forster^{2,3,4}, Gregory B. Gloor⁵, Aleksandra Tarkowska¹, Trevor D. Lawley² & Robert D. Finn^{1*}

Cell CIBIO Resource

Extensive Unexplored Human Microbiome Diversity Revealed by Over 150,000 Genomes from Metagenomes Spanning Age, Geography, and Lifestyle

Three Parallel Studies

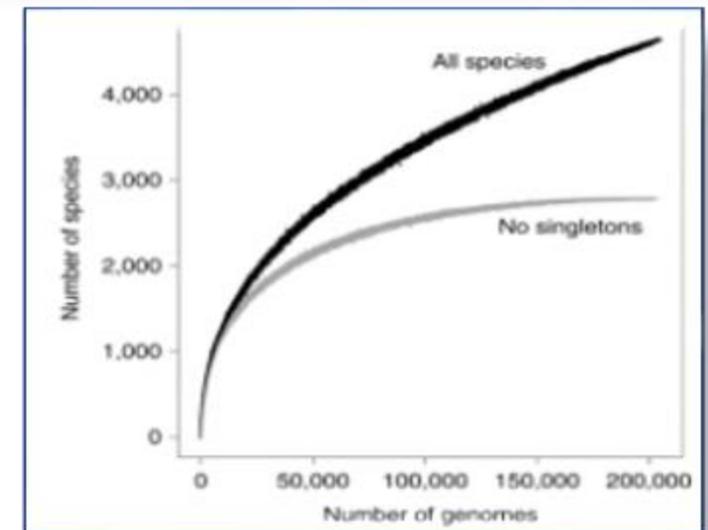
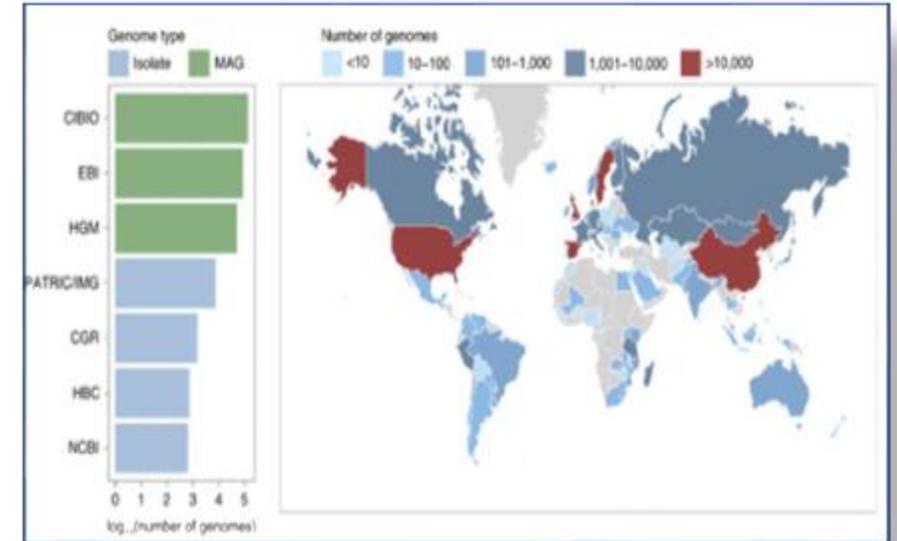


nature biotechnology A unified catalog of 204,938 reference genomes from the human gut microbiome

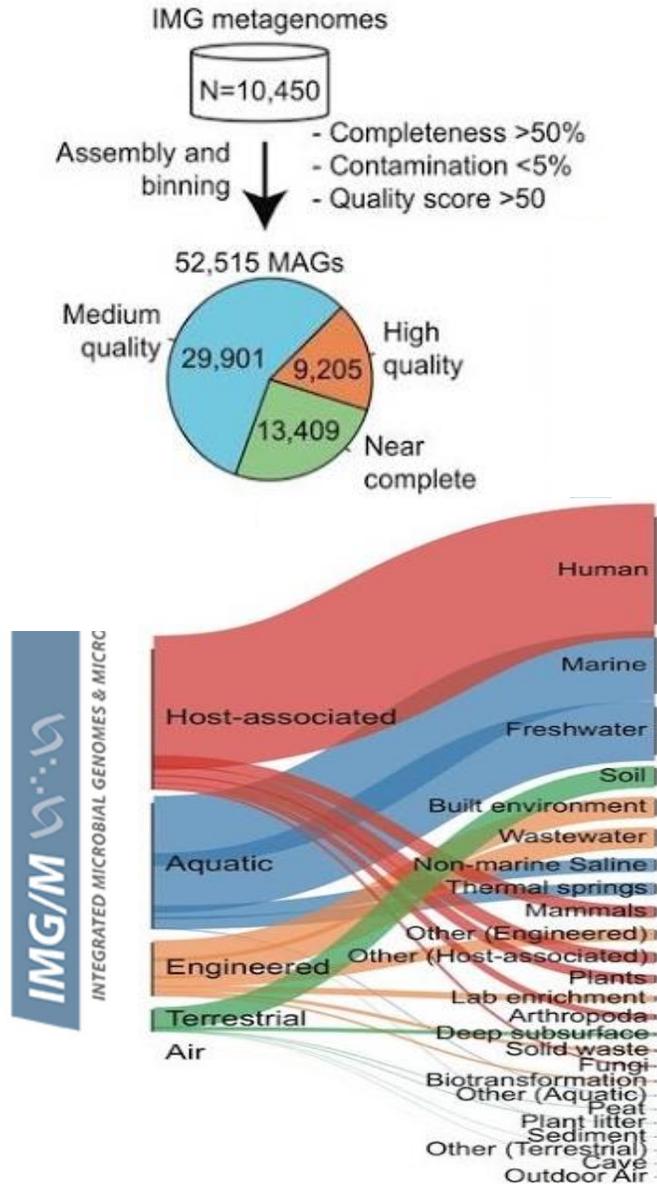
Alexandre Almeida^{1,2,5}, Stephen Nayfach^{3,4}, Miguel Boland¹, Francesco Strozzi⁵, Martin Beracochea¹, Zhou Jason Shi^{6,7}, Katherine S. Pollard^{6,7,8,9,10,11}, Ekaterina Sakharova¹, Donovan H. Parks¹², Philip Hugenholtz¹², Nicola Segata¹³, Nikos C. Kyrpides^{3,4} and Robert D. Finn^{1,5}

- 11,831 unique samples
- 204,938 NR Genomes
 - 4,644 species
 - 3,750 (81%)
Uncultured species

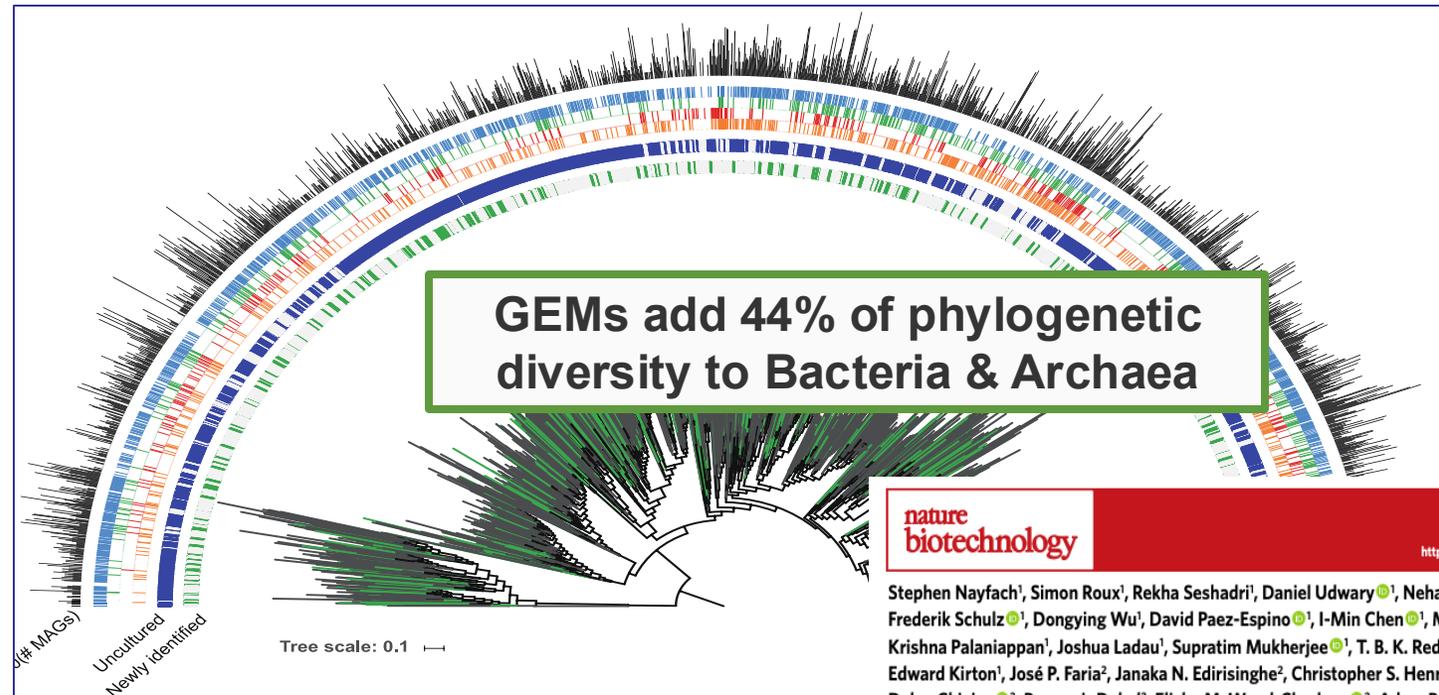
- 625,255,473 proteins
 - 14M clusters



A Genomic Catalog of Earth's microbiomes (GEMs)



- 10,450 metagenomes from diverse habitats (IMG/M database)
- 52,515 MAGs reconstructed
 - Grouped into 18,028 species-level OTUs
 - 12,556 were novel species from 135 phyla
- 3x more diversity compared to previous studies

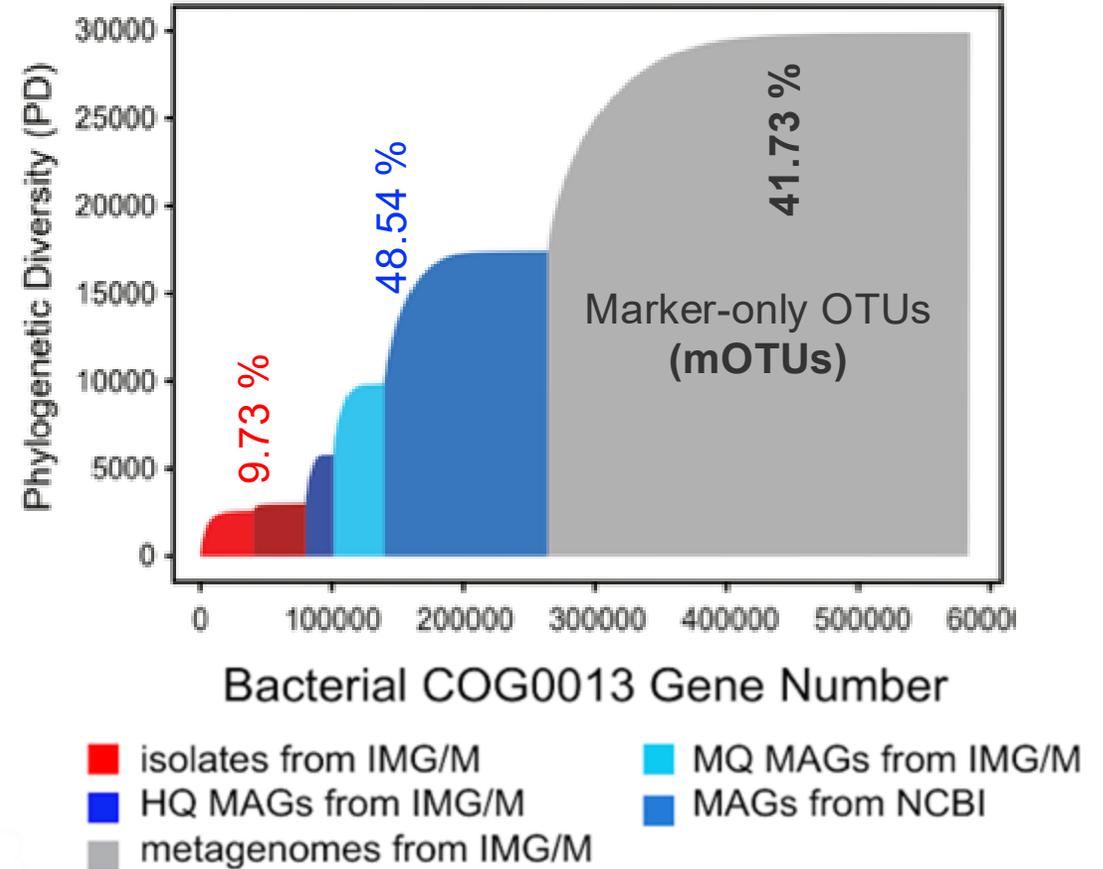
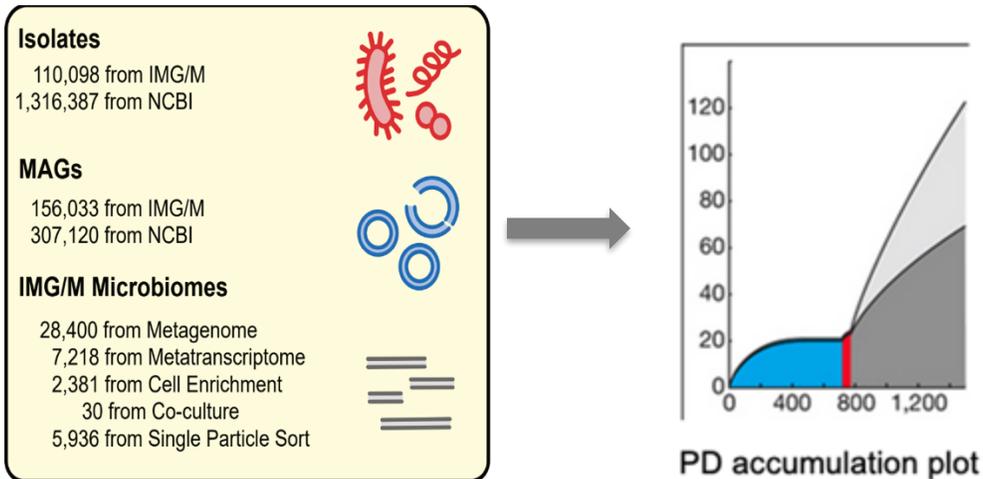


SCIENCE ADVANCES | RESEARCH ARTICLE

MICROBIOLOGY

A metagenomic perspective on the microbial prokaryotic genome census

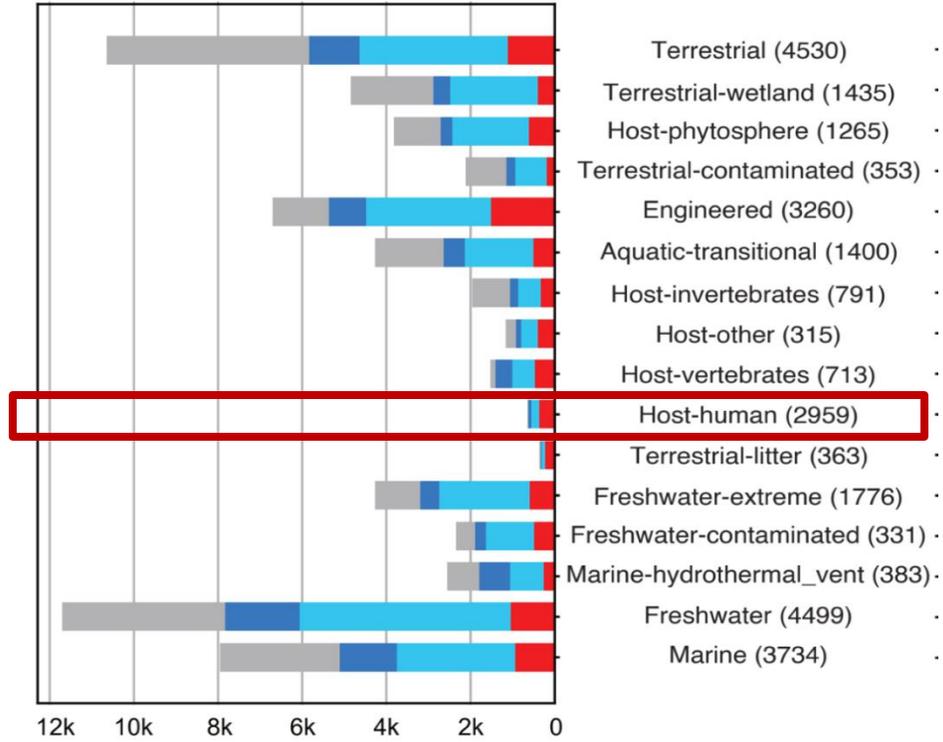
Dongying Wu, Rekha Seshadri, Nikos C. Kyrpides, Natalia N. Ivanova*



- 41.73% “unrepresented” diversity at lower taxonomic ranks
- mOTUs ~134,966 species in 18,087 metagenomic samples.

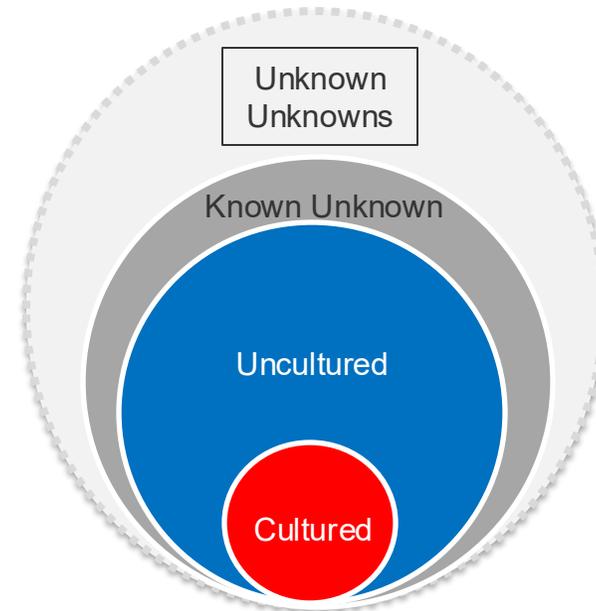
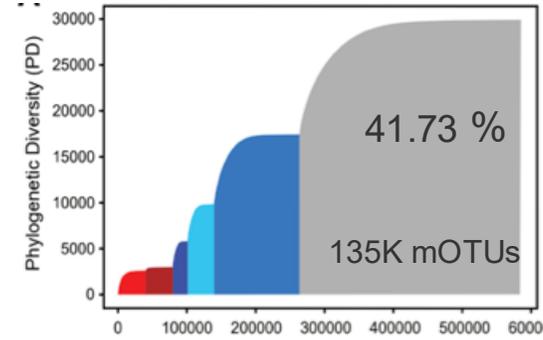
Marker-only OTUs by Habitat & Taxonomy

- Diversity hotspots - sediment, soil, freshwater, marine subsurface



Number of Bacterial Genus Level COG0013 OTUs in Metagenomes from IMG/M

- OTUs Include Isolates
- OTUs Include IMG/M MAGs (with No Isolates)
- OTUs Include NCBI MAGs (with neither Isolates nor IMG/M MAGs)
- OTUs Include Only IMG/M Metagenome Genes



#Genus mOTUs

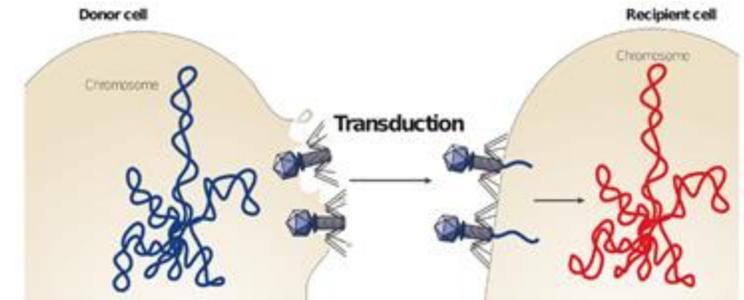
Genome Catalogs of Uncultivated Viruses

But first, why viruses?

Viruses have multi-level impacts

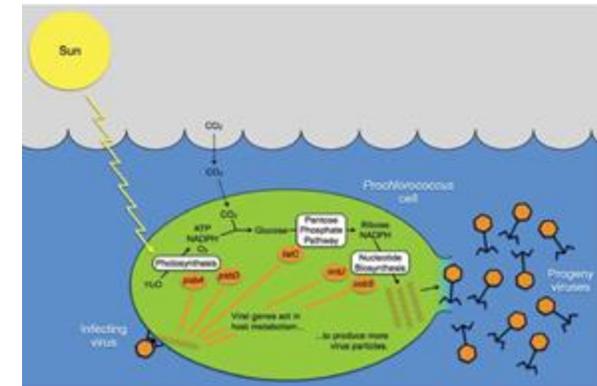
- The most abundant biological entities on earth (estim. $>10^{31}$)
- Parasitize all cellular life forms
- Co-evolution of viruses and host defense systems is key aspect in evolution of both viruses and cells
- Influence microbiome processes

Genetic transfer



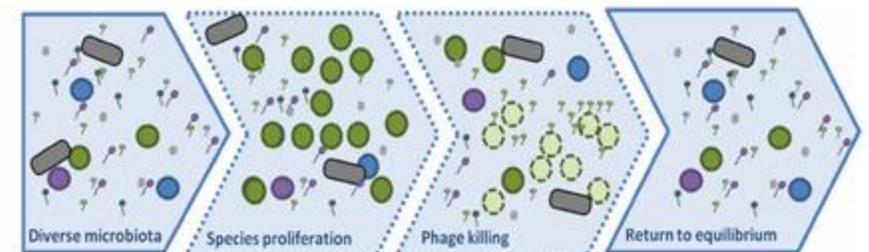
Frost et al., 2005

Alter host metabolism



Breitbart et al., 2007

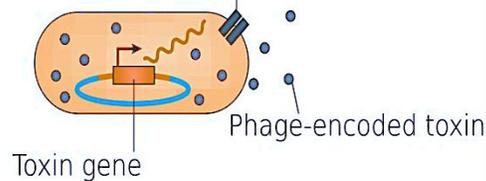
Maintain diversity



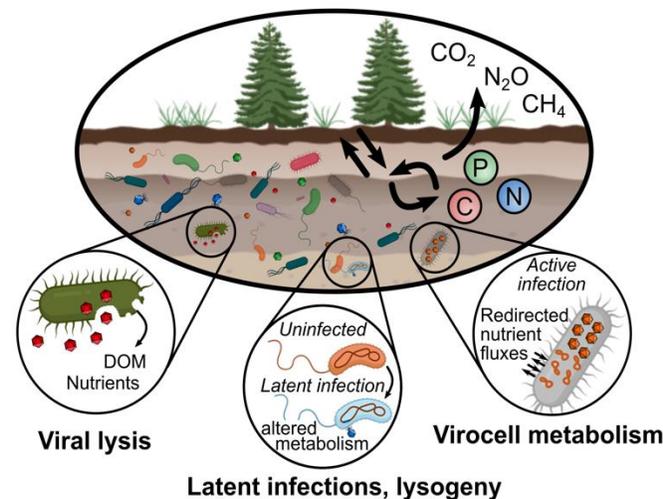
De Paepe et al., 2014

Expression during lysogeny

Bacterial secretion system



Feiner et al., 2015

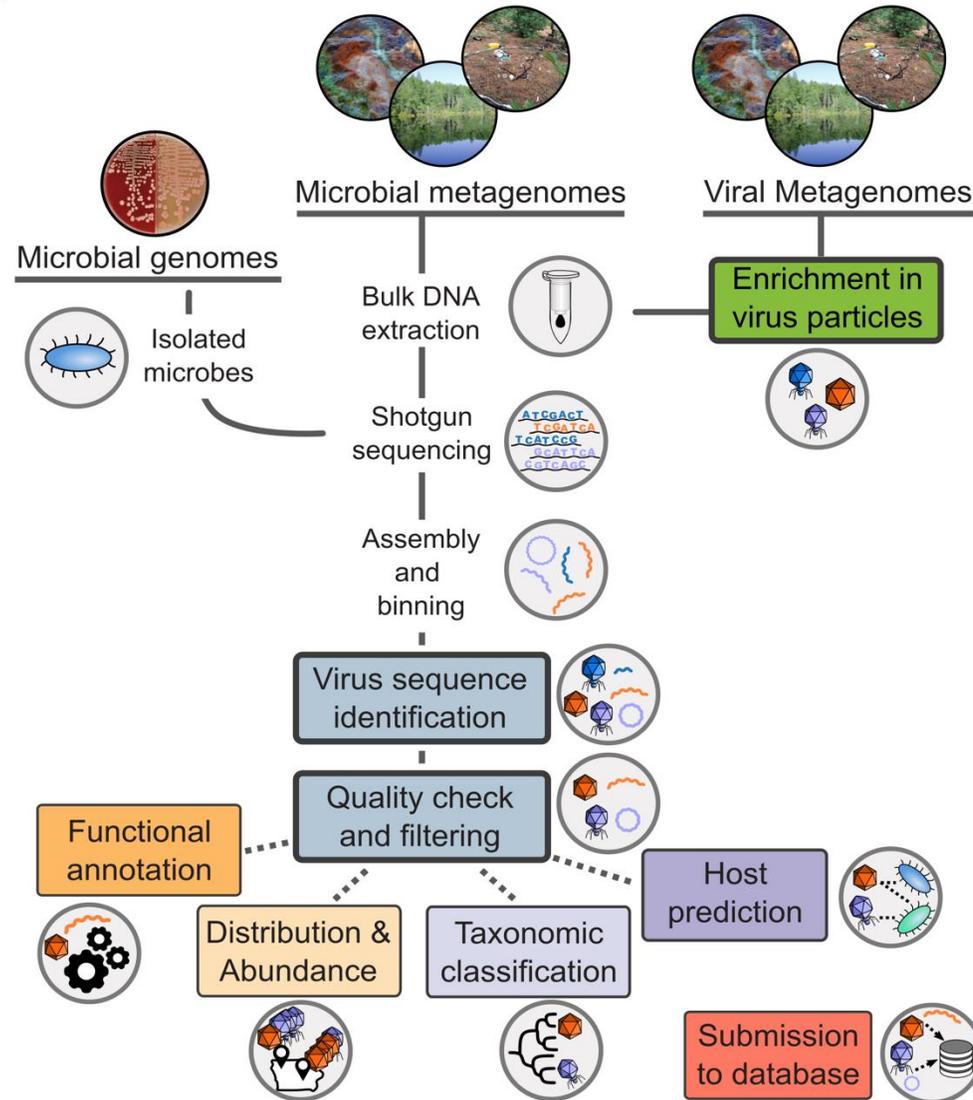


Latent infections, lysogeny

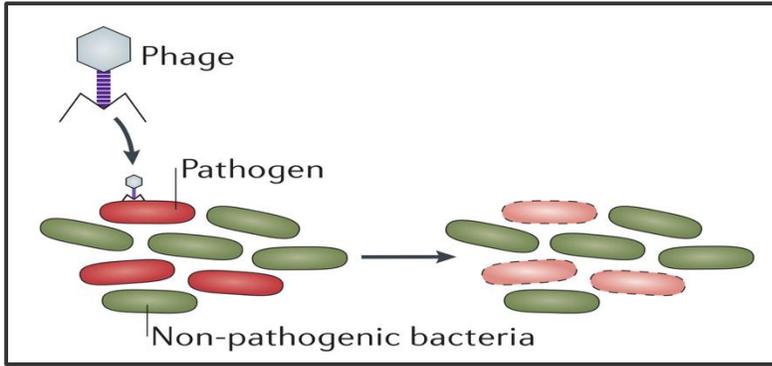
The main approach for exploring viral diversity at scale

LIMITATIONS for DISCOVERY

- ✗ No available cultures
- ✗ No universal viral marker genes
- ✗ Applications – phage therapy



Host specificity can be leveraged for phage therapy



Phage Therapies Clinical Trial Pipeline Shows Potential with Active Contributions from 20+ Key Companies | DelveInsight

The phage therapy market is experiencing significant growth due to the increasing prevalence of antibiotic-resistant infections and the growing interest in alternative treatments. Advances in biotechnology and ongoing research are driving innovation in phage-based therapeutics, offering a promising solution to combat multidrug-resistant pathogens. Additionally, regulatory support and rising investments in the development of phage therapies are further fueling market expansion. This market is expected to continue growing as healthcare providers seek effective alternatives to traditional antibiotics.

January 23, 2025 13:00 ET | Source: [DelveInsight Business Research LLP](#)

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DECEMBER 31, 2024 | 7 MIN READ



Nearly Forgotten 'Phage Therapy' Fights Antibiotic Resistance

In a new book, a science journalist recounts the story of a lifesaving treatment for infection that scientists broadly dismissed until recently

BY SAIMA S. IQBAL | EDITED BY TANYA LEWIS



Health topics ▾

Our work ▾

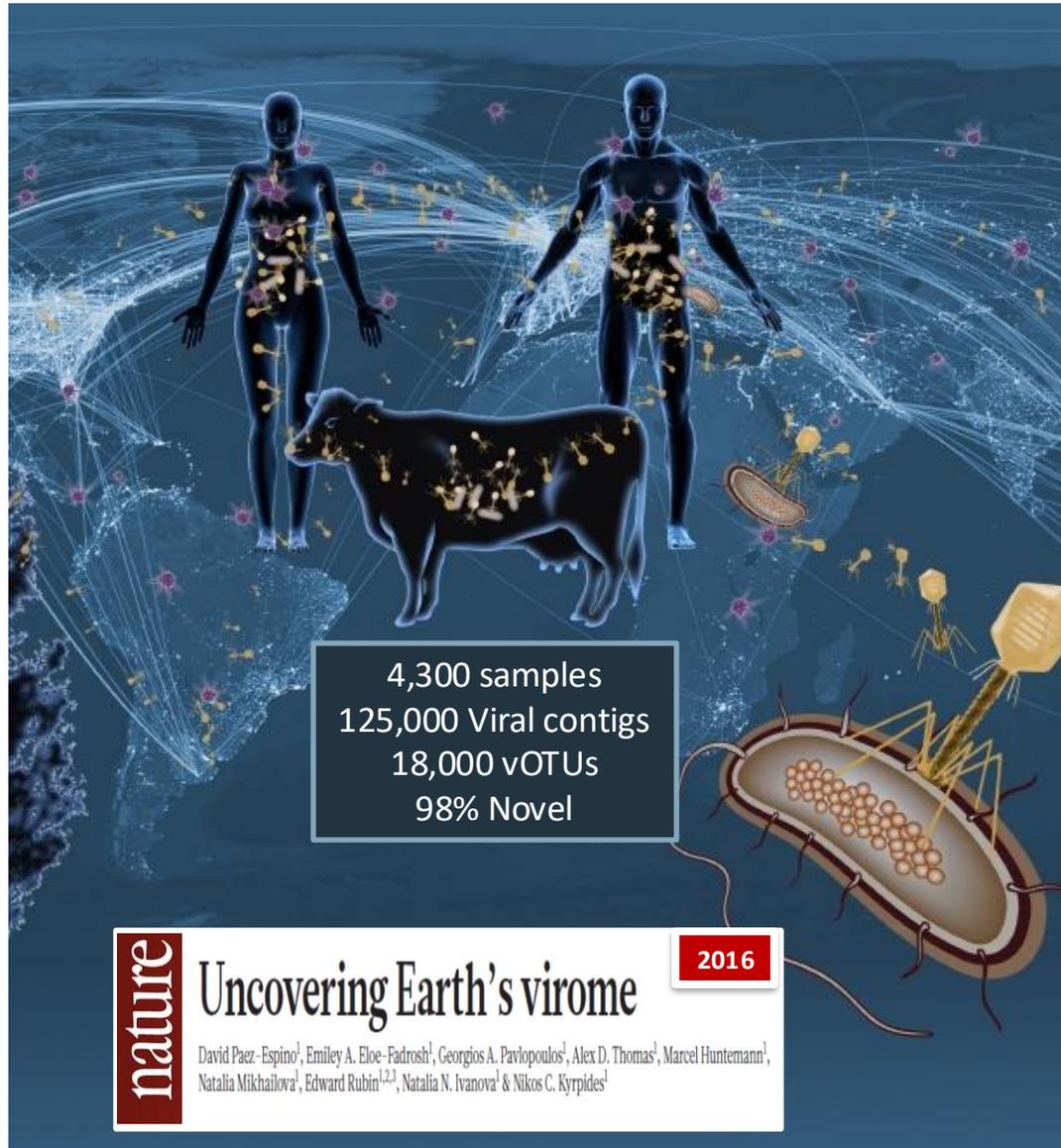
Newsroom

Latest news

Building evidence for the use of bacteriophages against antimicrobial resistance

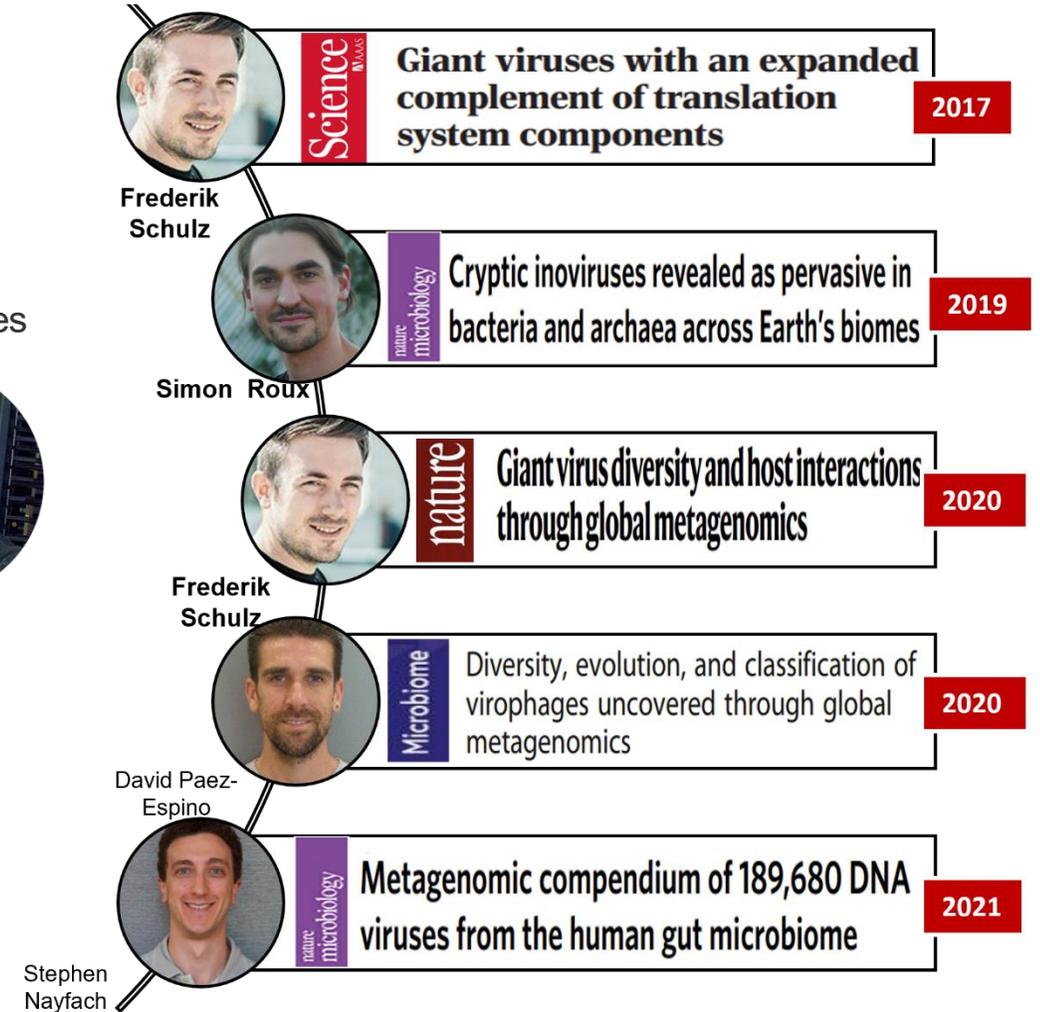
Jun 25, 2024, 13:33 PM

Virus Discovery from metagenomes

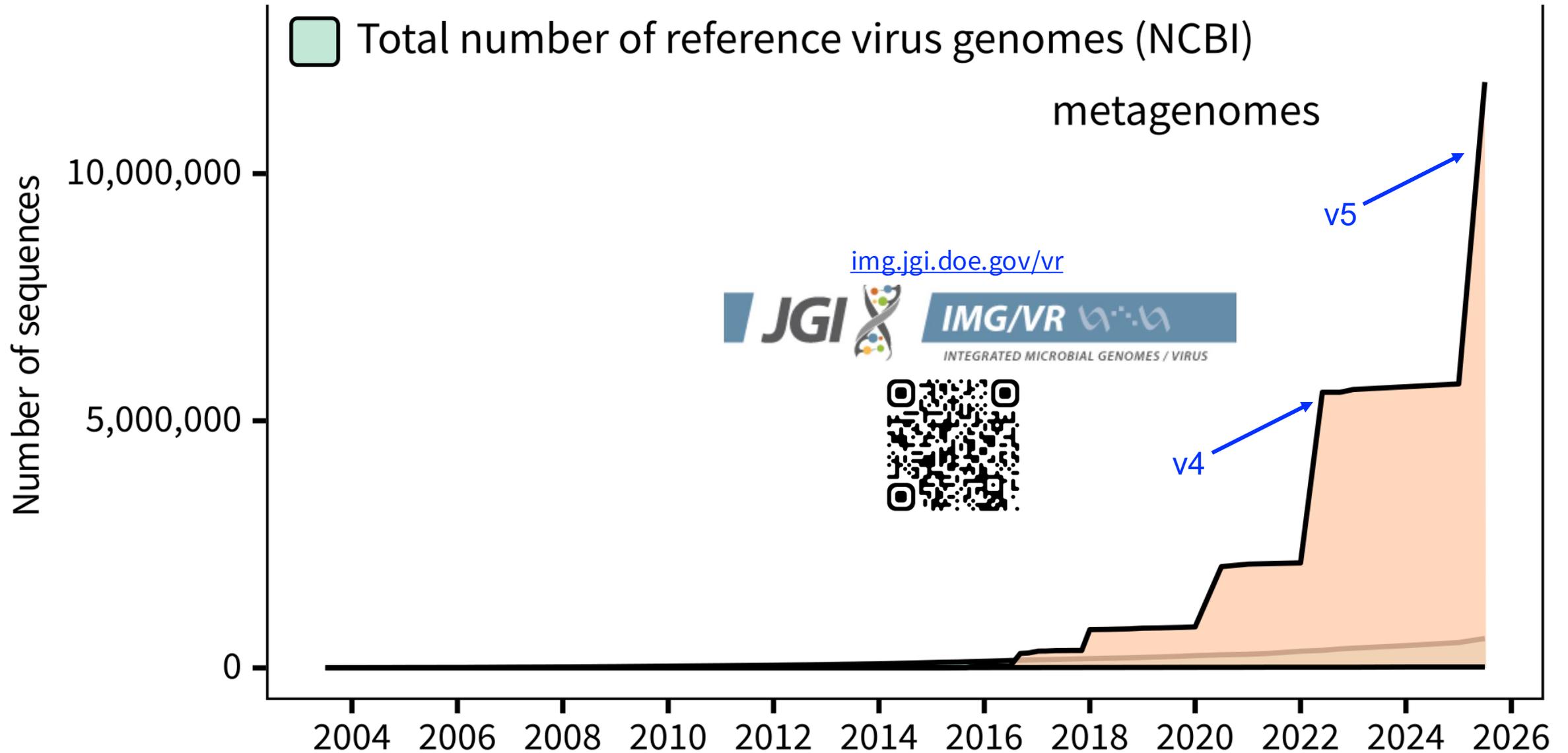


Uncultivated genomes massively expand the known diversity of viruses

Nikos Kyrpides



Aggregating global viral genome catalogs



Computational Tools



Tools & Standards for Metagenomics

PeerJ
MetaBAT, an efficient tool for accurately reconstructing single genomes from complex microbial communities

Bioinformatics Computational Biology Genomics

Dongwan D. Kang^{1,2}, Jeff Froula^{1,2}, Rob Egan^{1,2}, Zhong Wang^{1,2,3}
Published August 27, 2015

nature biotechnology
Minimum information about a single amplified genome (MISAG) and a metagenome-assembled genome (MIMAG) of bacteria and archaea

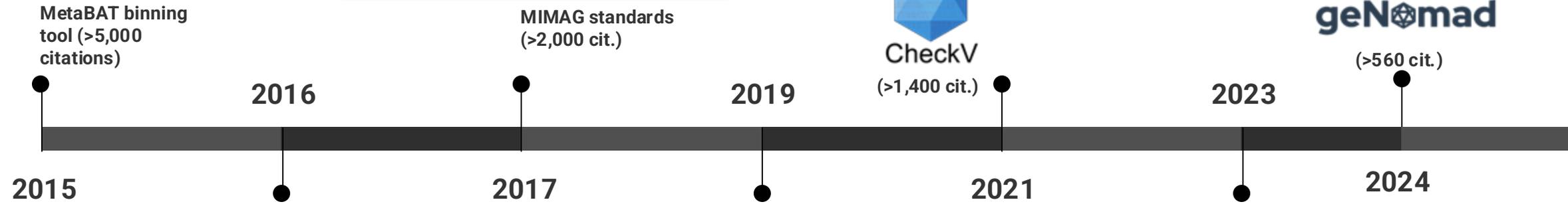
Robert M Bowen¹, Nikos C Kyrpides¹, Ramona Stapanian², Miranda Harmon-Smith³, Devita Doud⁴, Y B K Sodhi⁵, Frederik Schulz⁶, Jessica Savel⁷, Adam B Kover⁸, Emily A Elze-Fadness⁹, Susannah G Tringe¹⁰, Natalie N Ivanova¹¹, Alex Copeland¹², Alexis Chou¹³, Eric D Brevick¹⁴, Ben B Malhotra¹⁵, Steven Brereton¹⁶, Mircea Podar¹⁷, Paul Book¹⁸, George M Weinstock¹⁹, George M Garrity²⁰, Jeremy A Dodson²¹, Shiba Sengupta²², Grainger Sutton²³, Frank O Glockner²⁴, Jack A Gilbert²⁵, William C Nelson²⁶, Steven J Hallam²⁷, Sean P Longbrake²⁸, Thilo J G Eitner²⁹, Scott Taylor³⁰, Konstantinos T Konstantinidis³¹, Wai-Tai Liu³², Brent E Baker³³, Thomas Ratten³⁴, Jonathan A Eisen³⁵, Brian Hattfield³⁶, Katherine D McManus³⁷, Noah Fierer³⁸, Rob Knight³⁹, Rob Finn⁴⁰, Guy Cochrane⁴¹, Bence Kercs Mészáros⁴², Gene W Tyson⁴³, Christian Rindler⁴⁴, The Genome Standards Consortium⁴⁵, Ali Lapidis⁴⁶, Jøller Merer⁴⁷, Polina Yilmaz⁴⁸, Doreen H Parks⁴⁹, A M Egan⁵⁰, Lynn Schranz⁵¹, Silvan F Bandelt⁵², Philip Hugenholtz⁵³ & Tanja Woyke⁵⁴

nature biotechnology
CheckV assesses the quality and completeness of metagenome-assembled viral genomes

Stephen Nayfach^{1,2}, Antonio Pedro Camargo³, Frederik Schulz⁴, Emiley Elze-Fadness⁵, Simon Roux⁶ and Nikos C. Kyrpides⁷

nature biotechnology
Identification of mobile genetic elements with geNomad

Antonio Pedro Camargo^{1,2}, Simon Roux³, Frederik Schulz⁴, Michal Babinski⁵, Yan Xu⁶, Bin Hu⁷, Patrick S. G. Chain⁸, Stephen Nayfach⁹ & Nikos C. Kyrpides¹⁰



nature
ARTICLE
Uncovering Earth's virome

World Peer-Editor, Lindsey A. Elze-Fadness¹, George A. Parkes², Alex D. Thomas³, Nikos Kyrpides⁴, Nicole Mitchell⁵, Howard Ochsen⁶, Nicola W. Brown⁷ & Wai-Tai Liu⁸

nature biotechnology
Minimum Information about an Uncultivated Virus Genome (MIUViG)

Simon Roux¹, Evlaine M. Adriaenssens², Ben E. Dutilleul³, Eugene V. Koonin⁴, Andrew M. Krupnik⁵, Marc Kropinski⁶, Sun H. Kwon⁷, Bob Langen⁸, J. Rodney Brister⁹, Arvind Varma¹⁰, Clara Amal¹¹, Rany K. Aziz¹², Seth B. Bordenstein¹³, Paul Book¹⁴, Mya Breitbart¹⁵, Guy B. Cochrane¹⁶, Rebecca A. Daly¹⁷, Charlotte Desnues¹⁸, Melissa B. Dufosse¹⁹, Joana B. Emerson²⁰, François Enault²¹, Inel A. Fahrenius²², Pascal Honggang²³, Philip Hugenholtz²⁴, Bonnie L. Harwitz²⁵, Natalia N. Ivanova²⁶, Inesica M. Labadie²⁷, Kyung-Bum Lee²⁸, Ben B. Malhotra²⁹, Manuel Martinez Garcia³⁰, Bence Kercs Mészáros³¹, Shiroki Ogata³², David Price-Evans³³, ...

PeerJ
MetaBAT 2: an adaptive binning algorithm for robust and efficient genome reconstruction from metagenome assemblies

Dongwan D. Kang¹, Feng Li², Edward Kirton¹, Ashleigh Thomas¹, Rob Egan¹, Hong An³ and Zhong Wang^{1,3,4}

MetaBAT2 (>3,200 cit.)

iPHoP: An integrated machine learning framework to maximize host prediction for metagenome-derived viruses of archaea and bacteria

PLOS Biology

Portals for Microbiome Research



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Phytozome 13
THE PLANT GENOMICS RESOURCE



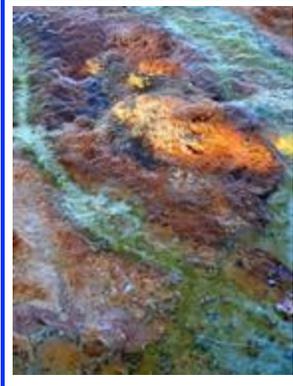
MycoCosm
THE FUNGAL GENOMICS RESOURCE



PhycoCosm
THE ALGAL GENOMICS RESOURCE



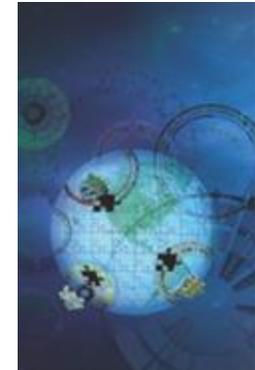
IMG/M 
INTEGRATED MICROBIAL GENOMES & MICROBIOMES



Data Portal



GOLD
GENOMES ONLINE DATABASE



JGI  **IMG/MER** 
INTEGRATED MICROBIAL GENOMES & MICROBIOMES

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IMG Systems
(>8600 cit.)

IMG/M Integrated Microbial Genomes & Microbiomes

Bridging the Gap from Sequence to Biology



Viral Resource



IMG/VR 

Plasmid Resource



IMG/PR 

scientific **data**

OPEN

DATA DESCRIPTOR

Coassembly and binning of a twenty-year metagenomic time-series from Lake Mendota

Tiffany Oliver^{1,2,3}, Neha Varghese¹, Simon Roux¹, Frederik Schulz¹, Marcel Huntemann¹, Alicia Clum³, Brian Foster¹, Bryce Foster¹, Robert Riley¹, Kurt LaButti¹, Robert Egan¹, Patrick Hajek¹, Supratim Mukherjee³, Galina Ovchinnikova¹, T. B. K. Reddy¹, Sara Calhoun¹, Richard D. Hayes¹, Robin R. Rohwer^{1,10}, Zhichao Zhou⁴, Chris Daum¹, Alex Copeland¹, I-Min A. Chen¹, Natalia N. Ivanova¹, Nikos C. Kyrpides¹, Nigel J. Mouncey¹, Tijana Glavina del Rio¹, Igor V. Grigoriev^{1,3,5}, Steven Hofmeyr⁶, Leonid Olikier⁵, Katherine Yelick^{6,7}, Karthik Anantharaman⁴, Katherine D. McMahon^{4,8}, Tanja Woyke^{1,9} & Emiley A. Eloë-Fadrosch^{1,3}

- Twenty-year time series from Lake Mendota
- Better recovery of low-abundance organisms; longer contigs.

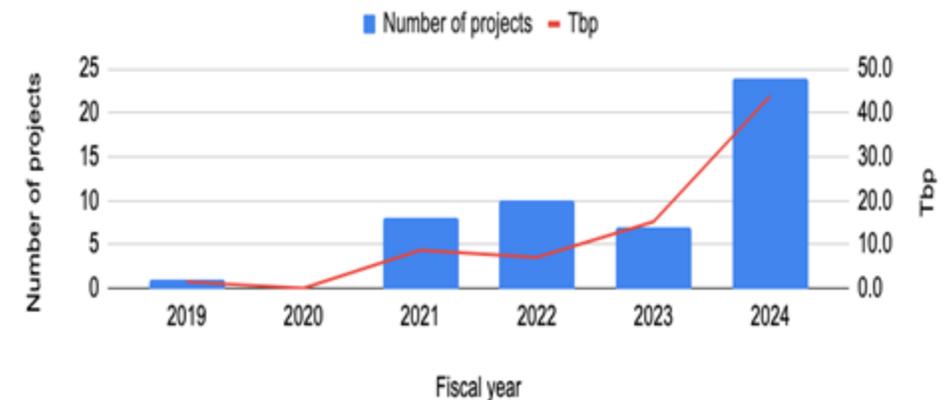
MetaHipMer scales to run on supercomputers



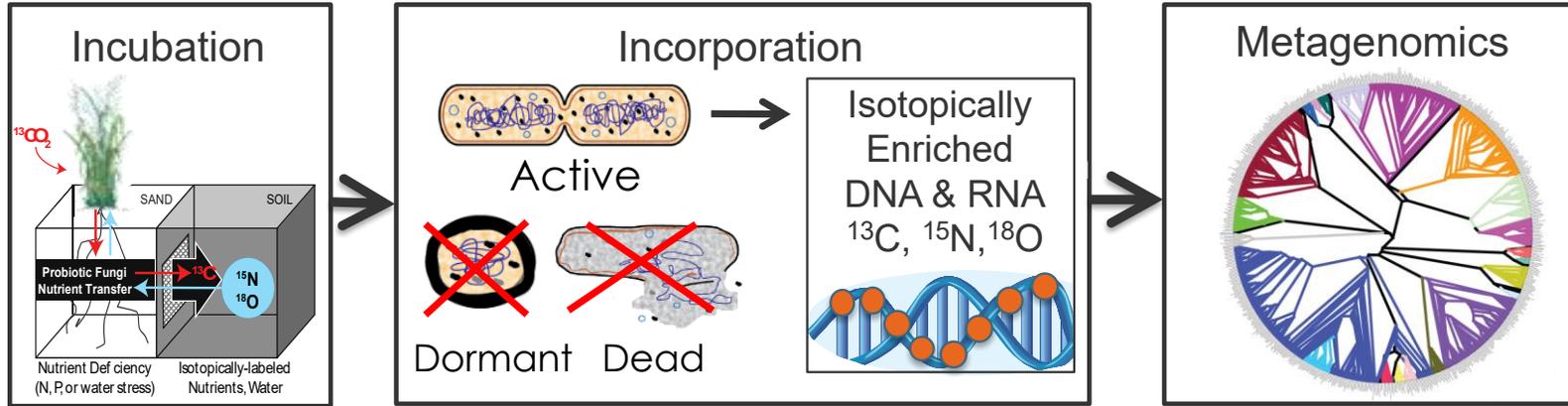
Emiley
Eloë-Fadrosch

- Input Data: >10 Tbp from 471 individual metagenome samples
- Largest environmental metagenome assembly
 - Staggering 95,523,664 contigs assembled
- 1,894 non-redundant prok MAGs, 9 euk MAGs, 6,350 HQ viruses

Number of large combined assemblies and Tbp by fiscal year



Accessing active populations with qSIP-Metagenomics



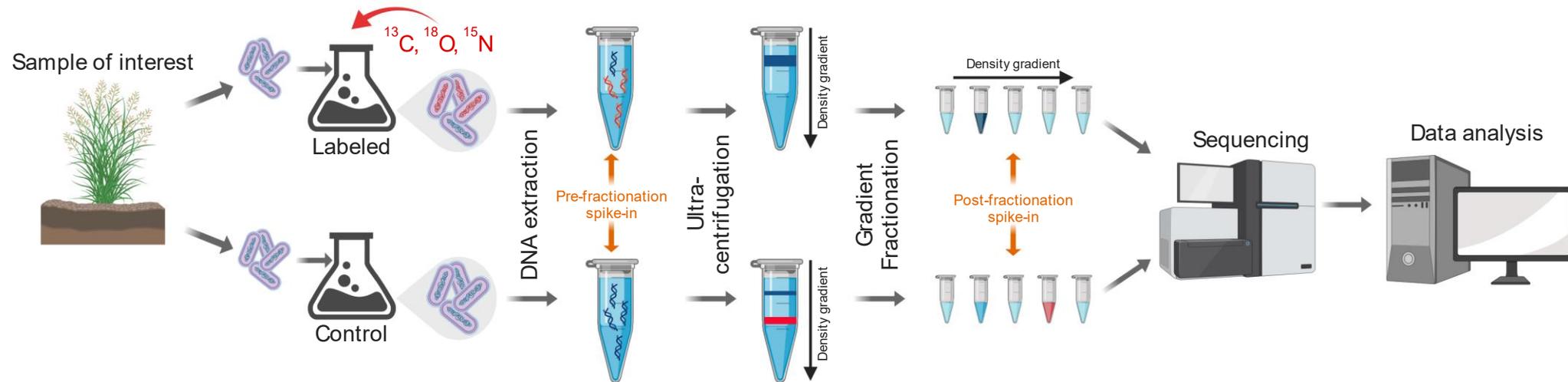
AMERICAN SOCIETY FOR MICROBIOLOGY | **mSystems** | Check for updates

Computational Biology | Methods and Protocols

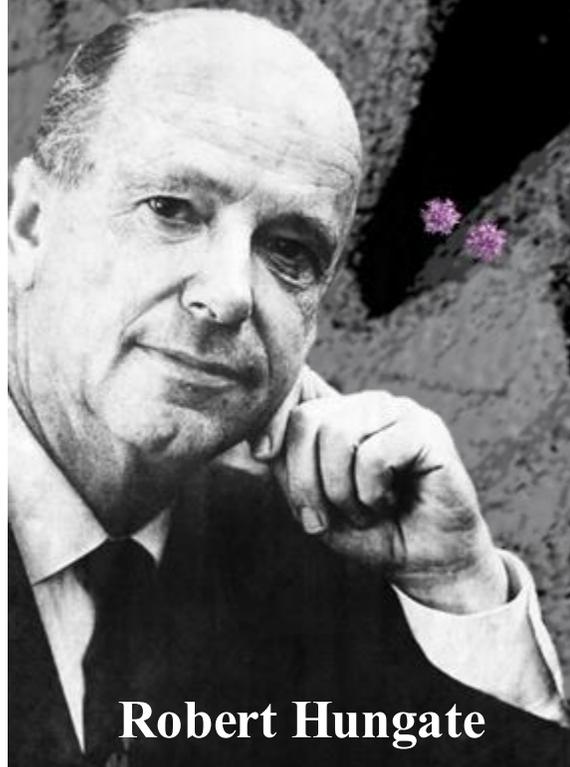
A standardized quantitative analysis strategy for stable isotope probing metagenomics

Daria Vyshenska,¹ Pranav Sampara,² Kanwar Singh,¹ Andy Tomatsu,¹ W. Berkeley Kauffman,¹ Erin E. Nuccio,¹ Steven J. Blazewicz,¹ Jennifer Pett-Ridge,^{1,4} Katherine B. Louis,¹ Neha Varghese,¹ Matthew Kellom,¹ Alicia Clum,¹ Robert Riley,¹ Simon Roux,¹ Emily A. Elze-Fadrosch,¹ Ryan M. Ziels,² Rex R. Malmstrom¹

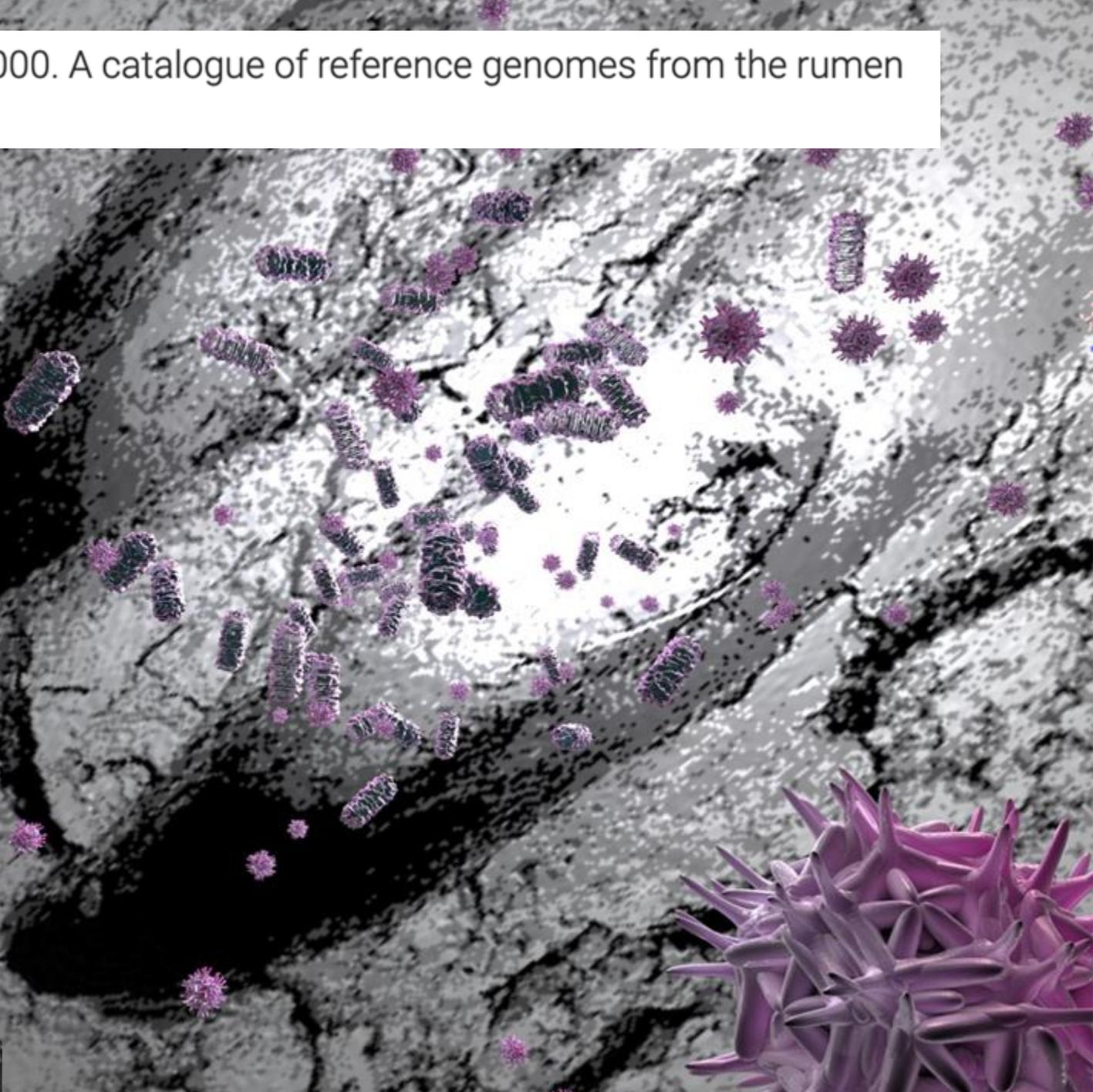
Rex Malmstrom



The Hungate 1000. A catalogue of reference genomes from the rumen microbiome.

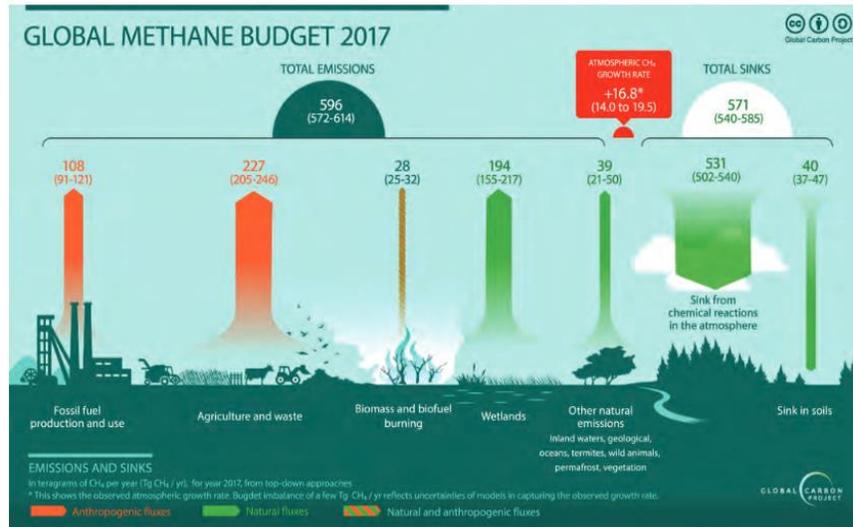
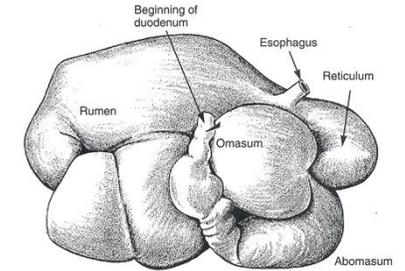


Robert Hungate



Why the Rumen

- World's largest commercial fermentation chamber
- Dense microbial habitat - **symbiotic** bacteria, archaea, fungi, protozoa & viruses
- 2-12% feed energy loss from via CO₂ and CH₄ - 1/3rd of human-made emission
- Goal - Modify rumen microbiome to reduce CH₄, improve animal health and nutrient utilization!



Jackson et al, 2020

Figure 4. The global CH₄ budget for year 2017 based on natural sources and sinks (green), anthropogenic sources (orange), and mixed natural and anthropogenic sources (hatched orange-green). Image from Jackson et al. 2020.



Rumen Model System
Direct access to site (cannula)
Large (liters), allows comprehensive multi-omics.
High control over diet, environ; isolate variables
Low; use of specific breeds
Can ethically induce and study states of dysbiosis (e.g., acidosis).

Monensin and Nisin Affect Rumen Fermentation and Microbiota Differently *In Vitro*

Junshi Shen^{1,2}, Zhuang Liu¹, Zhongtang Yu^{2*}, Weiyun Zhu^{1*}

> [Appl Environ Microbiol.](#) 2009 Apr;75(7):1860-6. doi: 10.1128/AEM.02453-08. Epub 2009 Feb 6.

A vaccine against rumen methanogens can alter the composition of archaeal populations

Yvette J Williams¹, Sam Popovski, Suzanne M Rea, Lucy C Skillman, Andrew F Toovey,

Effects of active dry yeasts on the rumen microbial ecosystem: Past, present and future ☆

Application of Bacteriophages To Control Intestinal *Escherichia coli* O157:H7 Levels in Ruminants

Authors: Haiqing Sheng, Hannah J. Knecht, Indira T. Kudva, Carolyn J. Hovde ✉ | [AUTHORS INFO & AFFILIATIONS](#)

Meta-analysis on Methane Mitigating Properties of Saponin-rich Sources in the Rumen: Influence of Addition Levels and Plant Sources

Anuraga Jayanegara^{1*}, Elizabeth Wina², and Junichi Takahashi^{1,3}

An inhibitor persistently decreased enteric methane emission from dairy cows with no negative effect on milk production

Alexander N. Hristov ✉, Ioanvo Oh, Fabio Giallongo, Tyler W. Frederick, Michael T. Harner, Hollev I. Weeks, Antonio F.

Epub 2015 May 23.

Effect of Probiotics/Prebiotics on Cattle Health and Productivity

Yutaka Uyeno¹, Suguru Shigemori, Takeshi Shimosato

208 Effects of bacteriophages, their bacterial hosts, and combined phage-bacteria inoculations on *in vitro* ruminal fermentation and methane production

Gabriela Magossi, Godson Aryee, Kendall C Swanson, Samat Amat

Journal of Animal Science, Volume 103, Issue Supplement_1, May 2025, Pages 43-44,

The role of probiotics, prebiotics and synbiotics in animal nutrition

Paulina Markowiak¹, Katarzyna Śliżewska¹

J. Dairy Sci. 92:2118-2127

doi:10.3168/jds.2008-1903

© American Dairy Science Association, 2009.

Crushed sunflower, flax, or canola seeds in lactating dairy cow diets: Effects on methane production, rumen fermentation, and milk production

K. A. Beauchemin,^{*1} S. M. McGinn,^{*} C. Benchaar,[†] and L. Holtshausen^{*}

^{*}Agriculture and Agri-Food Canada, Lethbridge, Alberta, T1J 4B1, Canada

[†]Dairy and Swine Research and Development Centre, Sherbrooke, Quebec, J1M 1Z3, Canada

Red seaweed (*Asparagopsis taxiformis*) supplementation reduces enteric methane by over 80 percent in beef steers

Breanna M. Roque  , Marielena Venegas , Robert D. Kinley , Rocky de Nys , Toni L. Duarte , Xiang Yang , Ermias Kebreab 

Ruminal Fluid Transplantation Accelerates Rumen Microbial Remodeling and Improves Feed Efficiency in Yaks

Yan Li^{1,2,3}, Yingkui Yang^{1,2,3}, Shatuo Chai^{1,2,3}, Kaiyue Pang^{1,2,3}, Xun Wang^{1,2,3}, Linpeng Xu^{1,2,3}, Zheng Chen^{1,2,3},

Methane production and digestion of different physical forms of rapeseed as fat supplements in dairy cows

M. Brask^{*}, P. Lund^{*}  , M.R. Weisbjerg^{*}, A.L. F. Hellwing^{*}, M. Poulsen^{*}, M.K. Larsen[†], T. Hvelplund^{*}

> [PLoS One.](#) 2017 Aug 16;12(8):e0182235. doi: 10.1371/journal.pone.0182235. eCollection 2017.

Natural and artificial feeding management before weaning promote different rumen microbial colonization but not differences in gene expression levels at the rumen epithelium of newborn goats

Exploitation of dietary tannins to improve rumen metabolism and ruminant nutrition

Amlan K Patra , Jyotisna Saxena

First published: 02 September 2010 | <https://doi.org/10.1002/jsfa.4152> | Citations: 558

Strategy/Intervention	Primary Objective(s)	Mechanism & Description	Status & Practicality	Key References
Dietary & Feed Additive Strategies				
Seaweed (<i>Asparagopsis</i>)	Methane Mitigation	bromoform, potently inhibits key enzyme in the final step of methanogenesis.	Highly effective (>80% reduction). Commercially available	Roque, B. M. et al. (2021). <i>PLOS ONE</i>
Chemical Inhibitors (3-NOP)	Methane Mitigation	A synthetic molecule that directly inhibits methyl-coenzyme M reductase	Highly effective and commercially approved in many regions. A leading practical solution.	Dijkstra, J. et al. (2018). <i>PNAS</i> .
Lipid Supplementation	Methane Mitigation	Adds fats/oils to diet, toxic to methanogens and protozoa, and also acts as a sink for hydrogen.	Moderately effective, widely practical. Can impact feed costs and other production aspects	Beauchemin, K. A. et al. (2008). <i>Journal of Dairy Sci.</i>
Ionophores (e.g., Monensin)	Production Efficiency, Methane Mitigation	Antibiotics that select against certain bacteria, shifting fermentation to propionate production, using up hydrogen.	Widely used for decades. Regulatory approval varies globally (banned as a feed additive in the EU).	Russell J.B. Strobel H.J. (1989). <i>Appl. Environ. Microbiol.</i> 55, 1–6.
Plant Bioactives (Tannins, etc.)	Methane Mitigation, Improved Protein Utilization	Natural plant compounds with antimicrobial properties that suppress protozoa and methanogens. (also protect protein)	Variable effectiveness. An active area of research for natural, sustainable solutions.	Patra, A. K., & Saxena, J. (2011). <i>Advances in Agronomy</i> .
Probiotics (Direct-Fed Microbials)	Animal Health, Production Efficiency	Beneficial microbes (e.g., <i>Saccharomyces cerevisiae</i> , <i>Lactobacillus</i>) to stabilize rumen, improve digestion, and outcompete less desirables	Commonly used to improve gut health and feed digestion. Effects on methane are generally minor and inconsistent.	Chaucheyras-Durand, F. et al. (2008). <i>Animal Feed Science and Tech.</i> Uyeno, Y. et al. (2015). <i>Animal Sci.</i>
Prebiotics	Animal Health (e.g., pH stability), Production Efficiency	Provides fermentable substrates (e.g., Fructo-oligosaccharides [FOS], Galacto-oligosaccharides [GOS], Xylo-oligosaccharides [XOS]) to selectively stimulate beneficial microbes.	Used to promote a healthy microbial balance. Effectiveness can be variable due to the complexity of the rumen ecosystem.	Markowiak, P., & Śliżewska, K. (2018). <i>Animals</i> .
Host & Advanced Strategies				
Early-Life Programming	All Three (Long-Term)	Manipulating diet, environment of young to establish beneficial biome that persists in adult.	Experimental but promising. set a permanent beneficial trajectory for the animal's life.	Yáñez-Ruiz, D. R. et al. (2015). <i>Front in Microbiology</i> .
Rumen Transfaunation	All Three (Corrective)	Transferring rumen fluid from a "donor" animal with a desirable microbiome to a "recipient" animal.	Highly effective for research and treating digestive upset. Long-term stability for production traits is still being studied.	Weimer, P. J. (2015). <i>Front. Microbiol.</i>
Vaccines & Phage Therapy	Methane Mitigation (Highly Targeted)	Developing vaccines to target methanogens or using viruses (phages) to specifically kill them.	Highly experimental early research stages. Significant technical, immunological challenge.	Magossi G (2025) <i>J Anim Sci.</i> Gilbert, R. (2020). <i>Front in Microbiol.</i>

Hungate Isolates & Reference Genomes

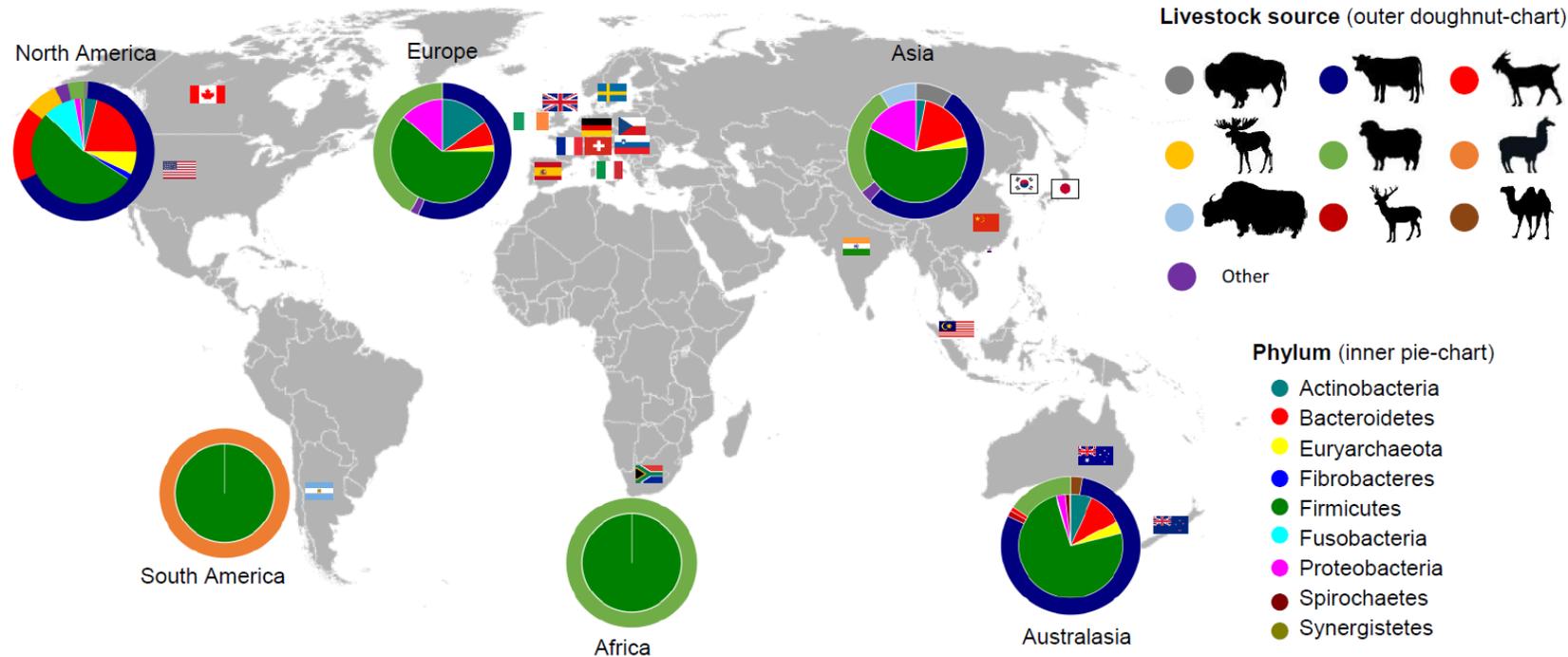
nature biotechnology

Cultivation and sequencing of rumen microbiome members from the Hungate1000 Collection

[Rekha Seshadri](#), [Sinead C Leahy](#), [Graeme T Attwood](#), [Koon Hoong Teh](#), [Suzanne C Lambie](#), [Adrian L Cookson](#), [Emiley A Eloie-Fadros](#), [Georgios A Pavlopoulos](#), [Michalis Hadjithomas](#), [Neha J Varghese](#), [David Paez-Espino](#), [Hungate1000 project collaborators](#), [Rechelle Perry](#), [Gemma Henderson](#), [Christopher J Creevey](#), [Nicolas Terrapon](#), [Pascal Lapebie](#), [Elodie Drula](#), [Vincent Lombard](#), [Edward Rubin](#), [Nikos C Kyrpides](#), [Bernard Henrissat](#), [Tanja Woyke](#), [Natalia N Ivanova](#) & [William J Kelly](#)

Nature Biotechnology 36, 359–367 (2018) | [Cite this article](#)

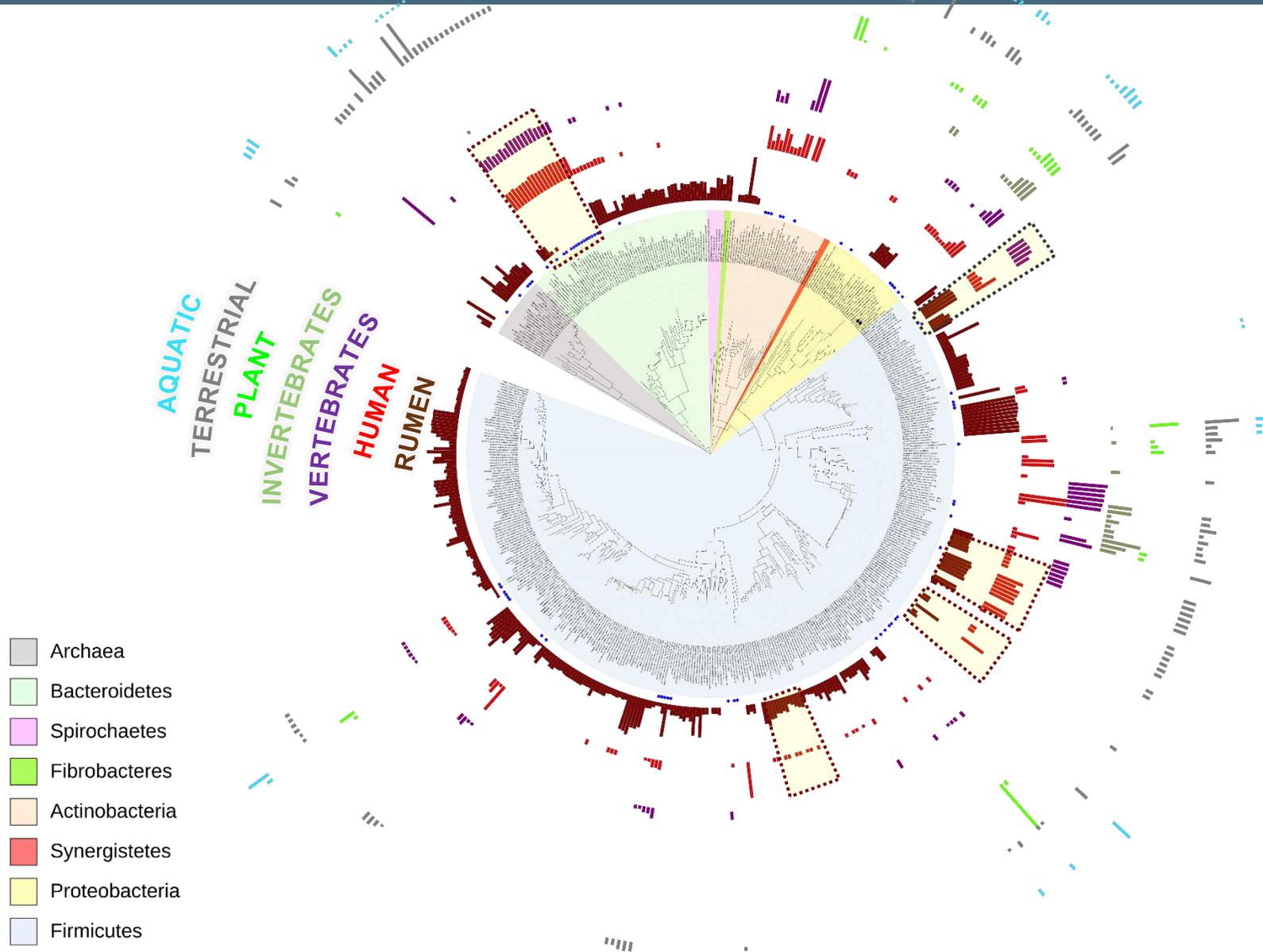
- 410 genomes contributed (15 at inception)
- Study total - 481 Bacteria & 21 Archaea



William Kelly



Hungate Isolates “in the wild”



- Comparing 500 ISOLATES against >8,200 metagenomes in IMG/M
- 400 isolates in **only 40** rumen samples
- 130 overlapping species with human G.I., e.g.,
 - *Megasphaera elsdenii*
 - *Prevotella bryantii*
 - *Streptococcus gallolyticus*, *S. equinus*
 - *Ruminococcus flavefaciens*
 - *Dorea* spp.
 - *Blautia* spp.

2025 NeLLi Symposium

Nov 4-7, 2025 @
UNLV & DRI

Hosted by the JGI, University of Nevada, Las Vegas, and the Desert Research Institute



Take part in the "Sequences to Cultures" Jamboree!

Immediately following the NeLLi Symposium, join us for a 1.5-day jamboree on November 6–7 focused on improving cultivation and genomic coverage. Experts in cultivation and environmental genomics will work together to develop recommendations for cultivating new bacteria and archaea revealed by a recent [genome census](#). A key outcome will be a compelling position paper, and we are pleased to have *Nature Microbiology* editor Kyle Frischkorn joining us to contribute to discussions and provide an editorial perspective.