The Microbiota Vault

A global non-profit initiative to conserve long-term health for humanity

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Agenda

- Why biobanking the microbiota?
- What is the Microbiota Vault?
- What do we currently do?
  - Experience from the pilot phase

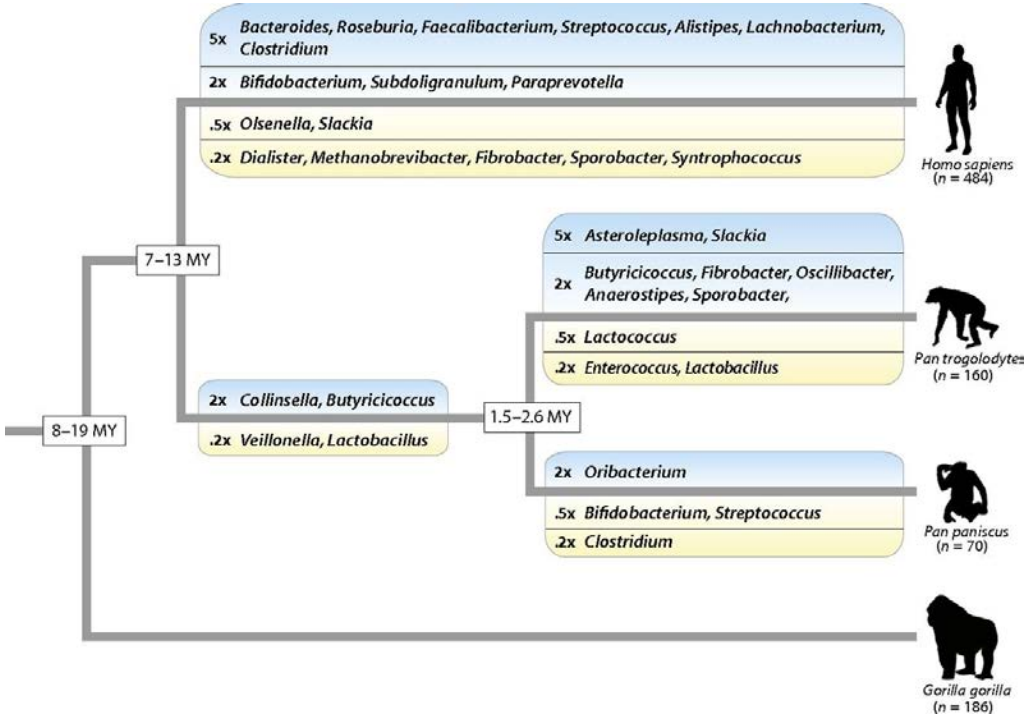
Why is a biobanking system for the microbiota necessary?

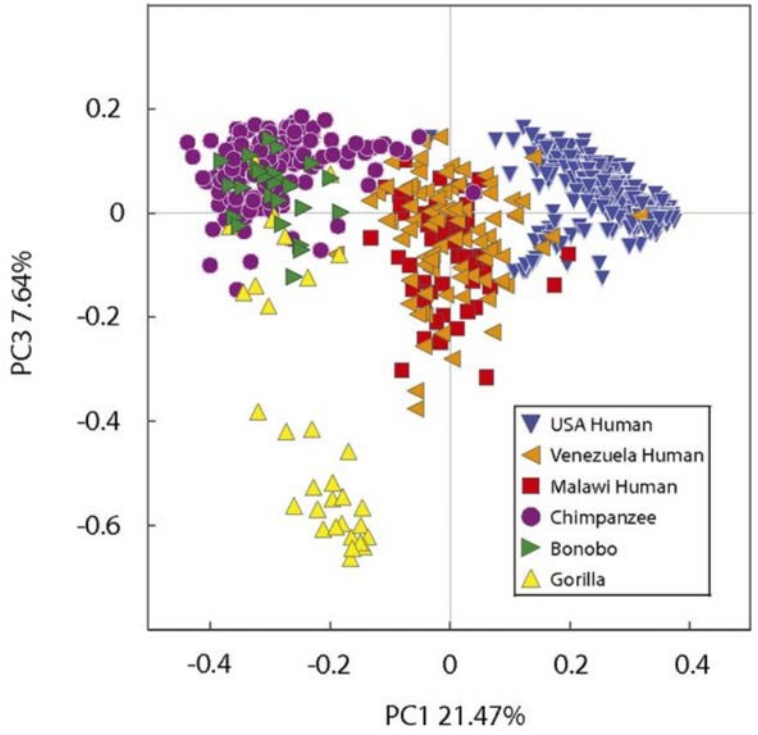
- **Decreasing biodiversity** at microscopic levels (ongoing silent extinction)
  - Preservation for the future
  - Multiple applications of microbes in health and industry

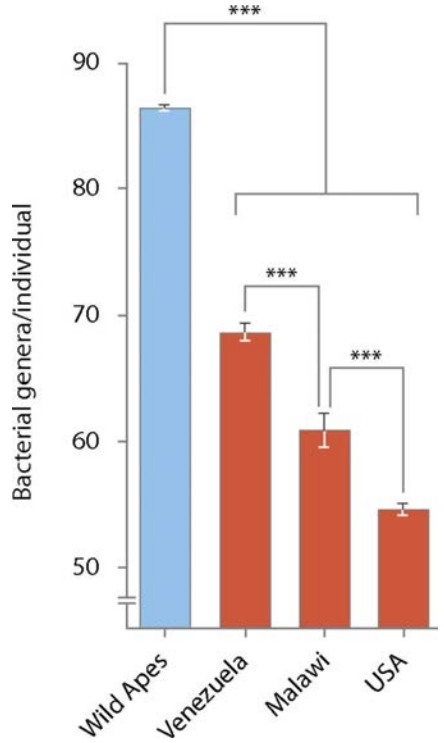
- **Reproducibility crisis** of science (including microbiome research)
  - Lack of standardized processes (collection, storage, sequencing, analysis)
  - Metadata is key!

- **Infrastructure** for low- and middle income countries

Diversity among species and rural impact



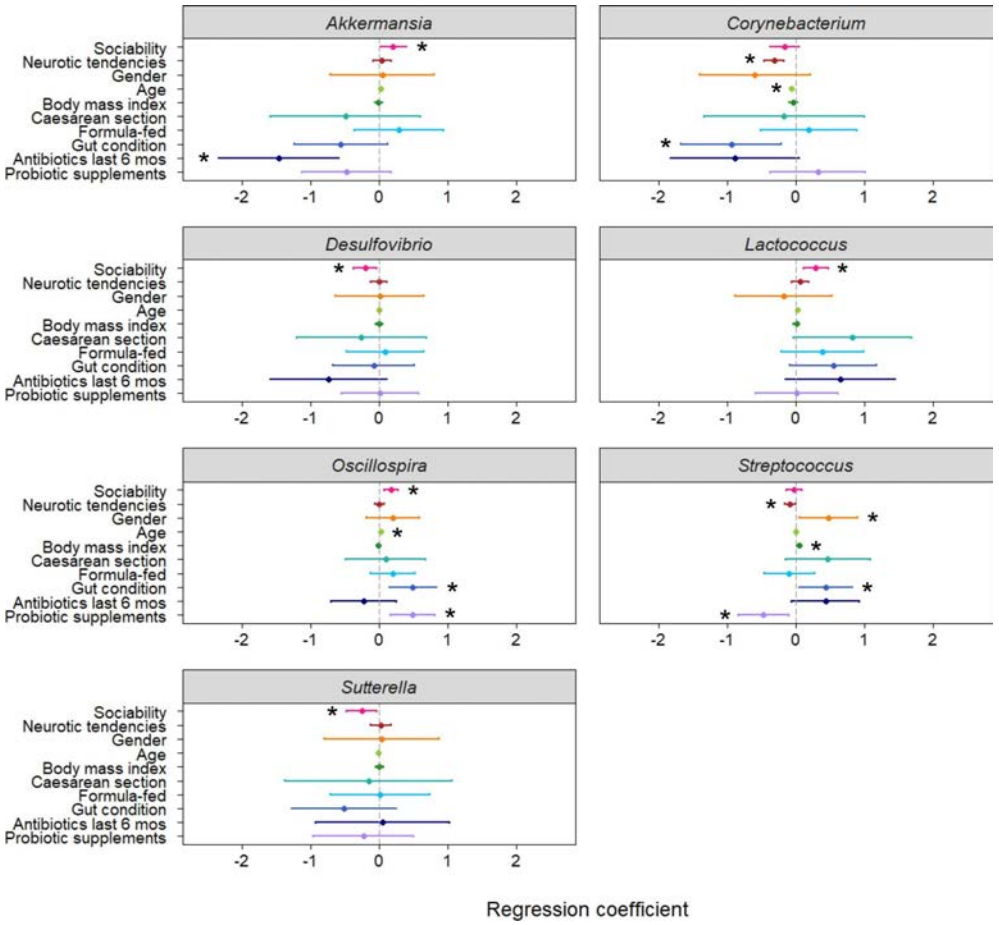




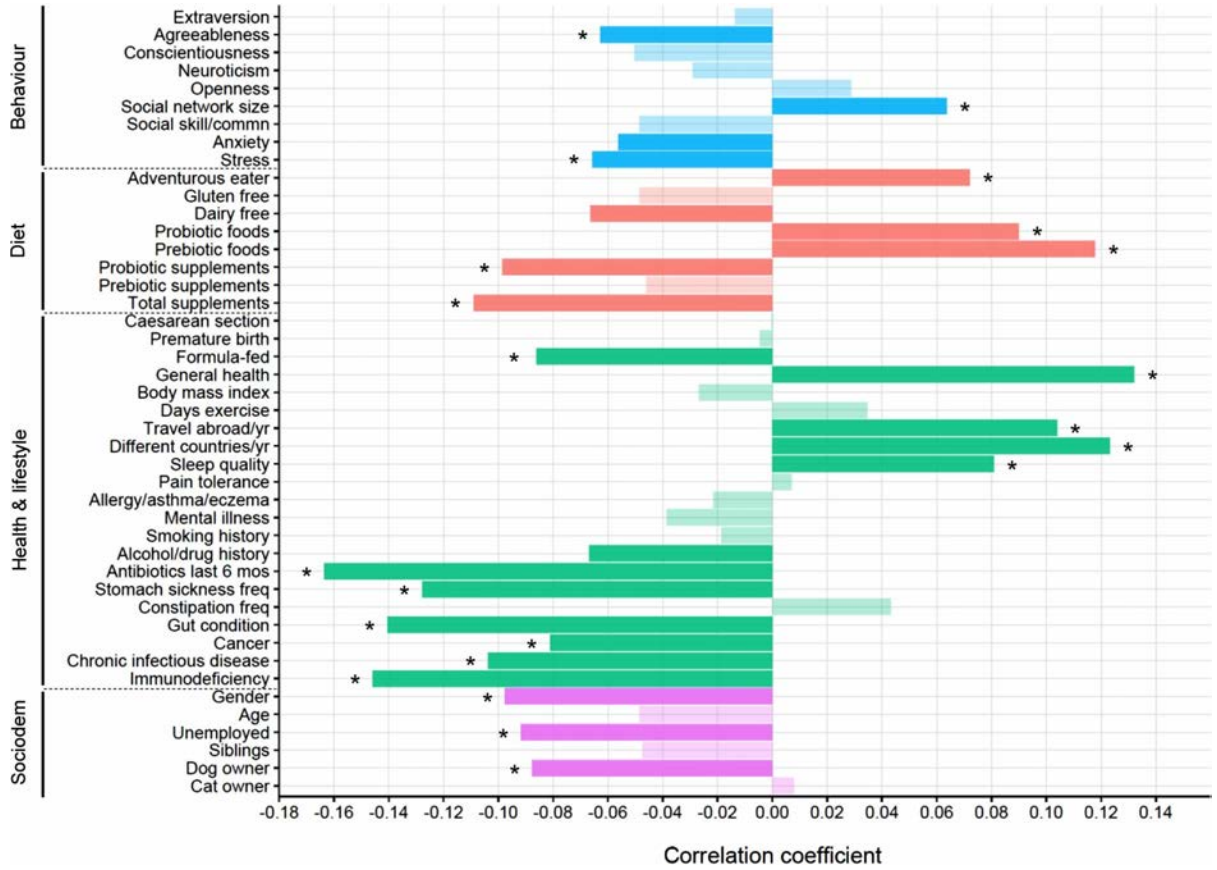
- Association of lower diversity and Western lifestyles

Moeller AH et al. PNAS 2014

Impact of lifestyle on bacterial diversity



Johnson KVA, Human Microbiome Journal 2020



Continuous changes of the gut microbiome in humans.
By 2050, 2/3 of the world population will live in cities

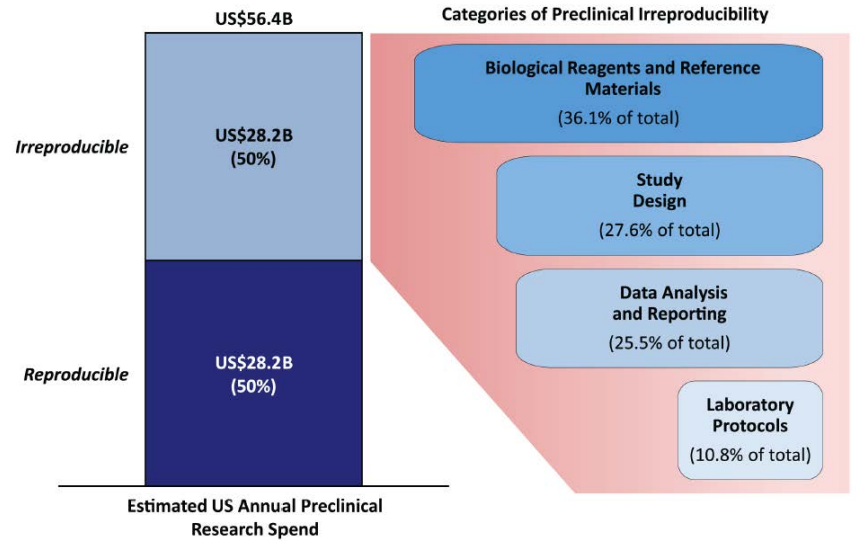
But diversity is also important in other fields

- **Environment**
  - Global warming has a tremendous impact on biodiversity!
  - Warming reduces diversity of soil bacteria, fungi, protists by altering environmental selections and biotic interactions, potentially disrupting the functional processes of the soil ecosystem.[1]
- **Fermented food**
  - Traditional food production changes
  - Industralization and massproduction e.g. cheese[2], wine[4,5], bread[6]
  - Cultural diversity changes [3]

1 Wu L, Zhang Y, et al. Nature Microbiology 2022; 2 Morandi S Battelli G et al. LWT 2019; 3 Dunn RR et al. Current Anthropology 2021; 4 Liu D, Zhang P et al. Front Microbiol 2019; 5 Rivas GA, Guillade AC et al. Front Microbiol 2021; 6 Landis EA, Oliverio AM, et al. eLife 2021

Scientific reproducibility is critical and has a crisis

- High quality increases the reproducibility of research results[1,2]
- Low or no reproducibility is a major issue: 28 billion $ per year[3]



- Increasing the quality of biobanks e.g., standardization, process management, etc.

[1] Caixeiro NJ, et al. J Clin Patho 2016; 69(3):260-5; [2] Mobley A et al. Plos One 2013; 8(5):e63221; [3] Freedman LP et al. Plos Biology 2015; 13(6): e 1002165;

Infrastructure is needed!
But what is a biobank?

- Simple question, not such an easy answer
- Biobanks[1,2]
  - add actively to the progress of biomedical research and development (RnD)
- Shared characteristics[3]
  - Collection of biological material in standardized form
  - Linkage with additional other (meta)data e.g., antibiotic resistance of single strains
  - Future usage of the stored material (infinite for single strains, limited for microbiota)
- Examples
  - Population based e.g., cross-sectional study from nasopharyngeal swab for microbiota
  - Disease based e.g., *Streptococcus pneumoniae* causing invasive infection

[1] Kinkorova J, EPMA journal 2015; 7: 4; [2] Vaugh J et Lockhart N Clin Chim Acta 2012; [3] Shaw DM, et al. Clinical genetics 2014; 85 (3): 223-227

Well curated metadata is key

- What and why? e.g., set of single strains, microbiota, tissue, extracted DNA, …
- Subsequent usage?

→ Contextual information (metadata) increases the value of the biobank[1]

  - Storage e.g., location, time of collection, freezing conditions
  - Associated information e.g., phenotypes, metagenomic sequencing data
  - Quality e.g., sample handling such as time to freeze, DNA extraction kit
  - Quantity e.g., availability of your sample such as DNA ug/uL
  - Consent e.g., study specific or general consent (governance/legal/ethics)

[1] Ryan MJ, Schloter M, et al. Trends in Microbiology, 29, 2, 2021

The Nagoya protocol

- The *Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity* is an international agreement. Protocol adapted in 2010 in Nagoya, Japan.
- Aims: Sharing benefits arising from the utilization of genetic resources in a fair and equitable way.
- Users who seek access to a genetic resource in another country are obliged to: (i) comply with the relevant national access regulations in the country providing the resource in question; (ii) ensure that the provider of the resource enjoys a fair and equitable share of the benefits.

Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity

What is the purpose of a microbiota biobank?

- For what later purpose do we store a sample? e.g., research

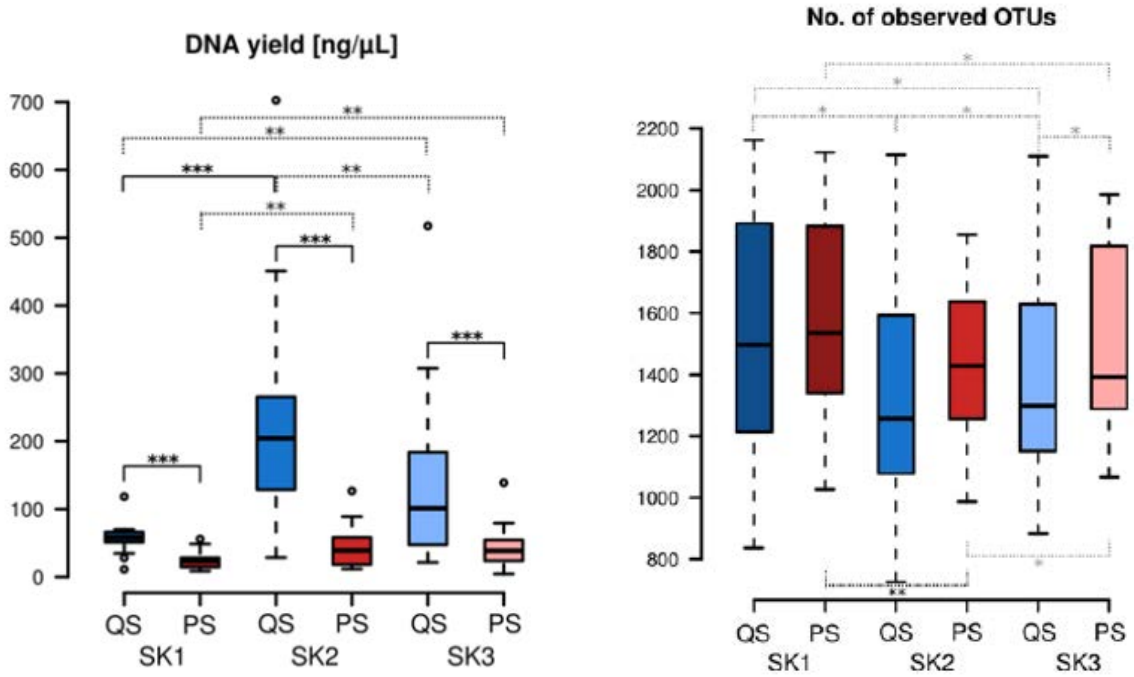
→ Require benchmarking of quality for this specific use-case

→ Viable bacteria for re-culture or therapies (fecal transplantation)

- Benchmarking e.g., time to freeze or biomarkers for quality such as metabolites[5]
- Standard operating procedures e.g., processing of samples, freezing of samples
  - Massive variability in protocols how samples are being processed.

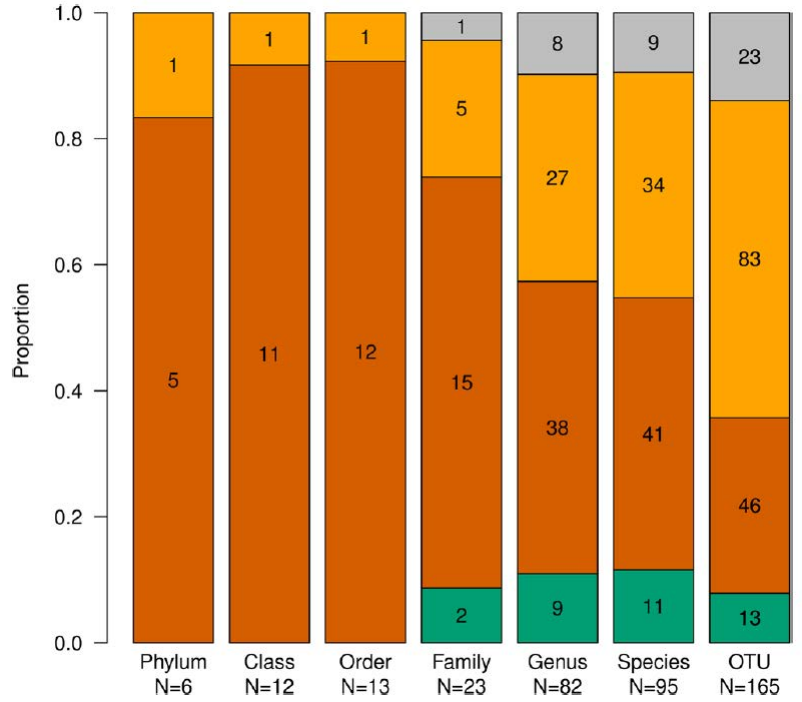
[5] Anton G et al. Plos One 2015; 10(3): e0121495

Impact of sampling and DNA extraction method: stool[1-7]



SK1 stool container; SK2 flocked swab; SK3 cotton swab

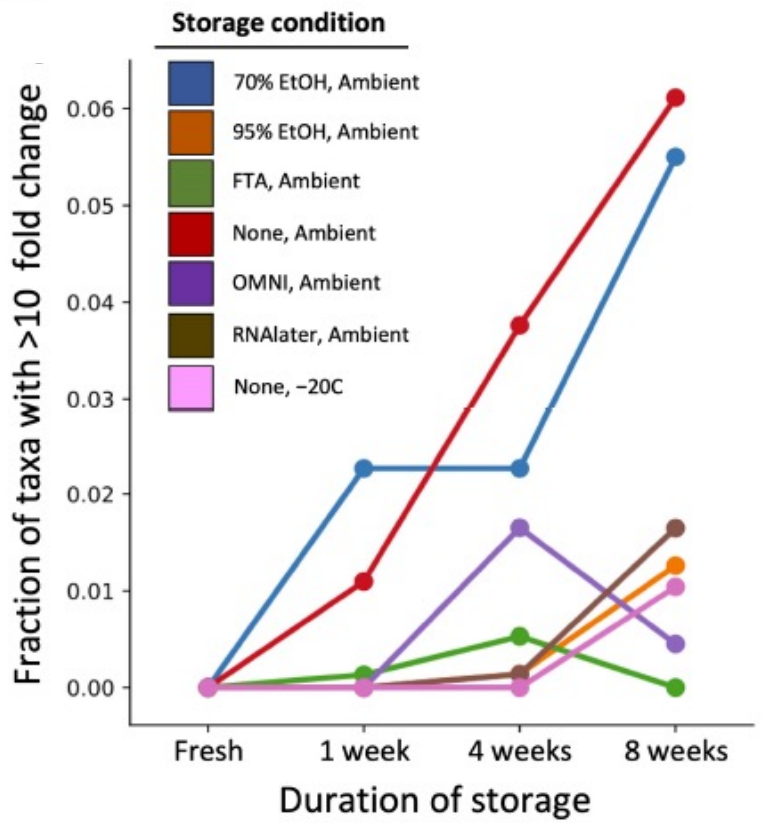
QS QiampDNA Stool Mini Kit; PS Power Lyzer Power Soil DNA Isolation Kit

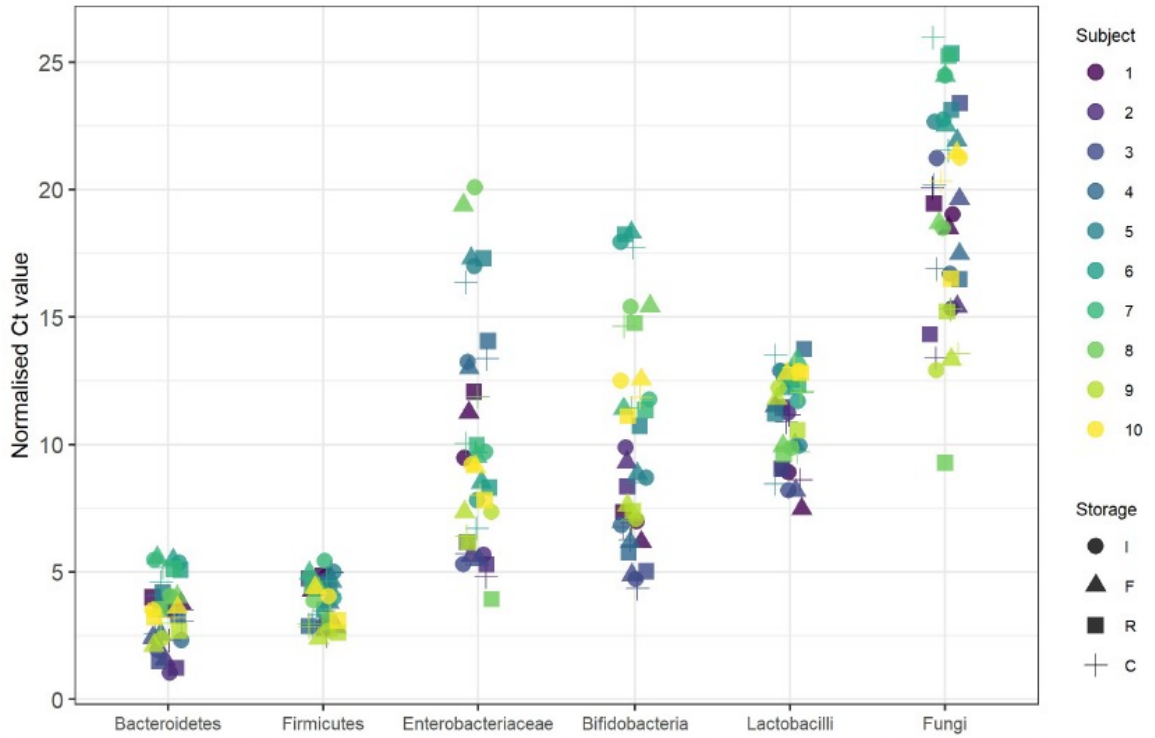


Green Sampling kit only; yellow Isolation kit only; brown both

[1] Videnska P, Smerkova K, et al. Scientific Reports 2019; [2] Van Zyl KN, Whitelaw AC, Newton-Foot M, Plos one 2020; [3] Wu WK, Chen CC, et al. J Form Med Ass 2019; [4] Hsieh YH, Peterson CM, et al. Front Micro 2016; [5] Hickl O, Heintz-Buschart A, et al. Microorganisms 2019; [6] Byrd DA, Chen J et al. Plos one 2019; [7] Marotz C, Cabagnero KJ et al. mSystems 2021

Impact of storage on microbial populations is individual



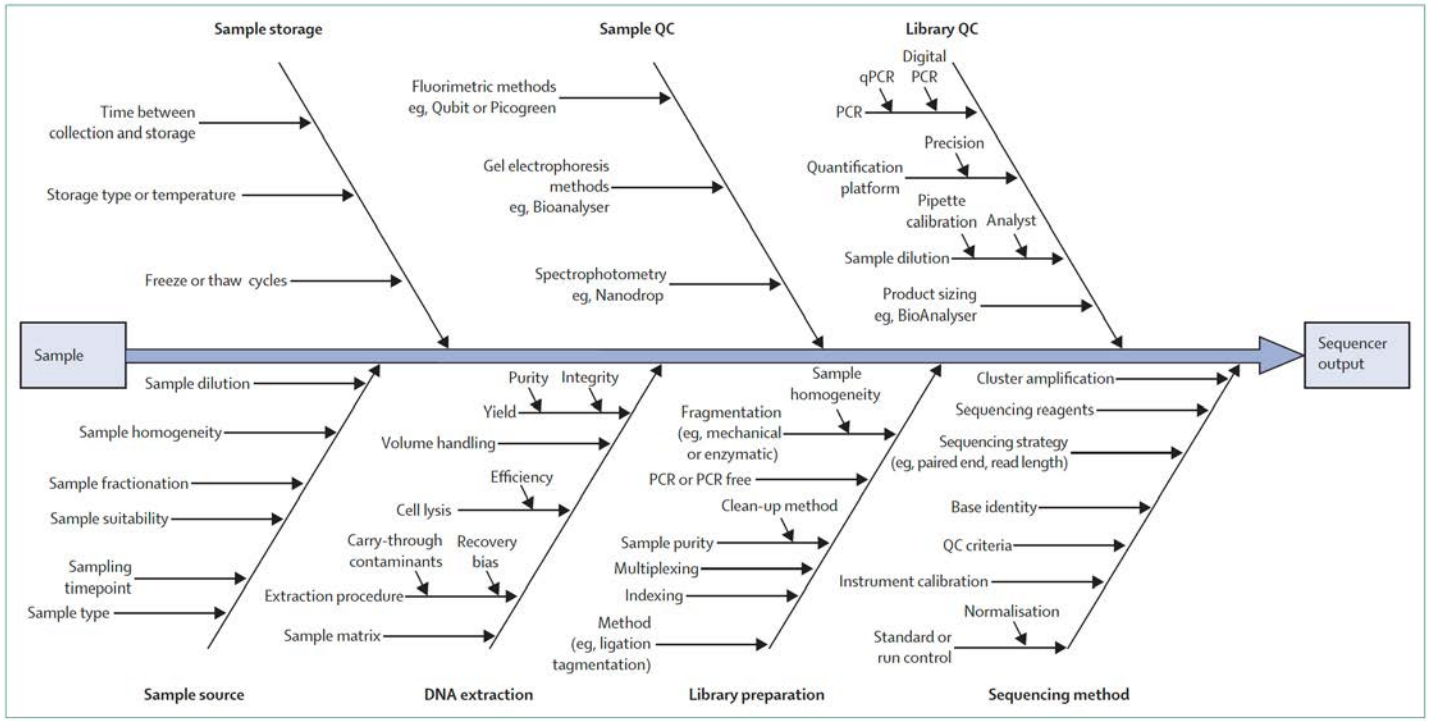


	Bacteroidetes	Firmicutes	Enterobacteriaceae	Bifidobacteria	Lactobacilli	Fungi
Storage	0.9925	0.3662	0.8773	0.9649	0.9958	0.9736
Subject	< 0.0001	< 0.0001	< 0.0001	< 0.0001	< 0.0001	0.0001

[1] Van Zyl KN, Whitelaw AC, Newton-Foot M, Plos one 2020; [2] Marotz C, Cabagnero KJ et al. mSystems 2021

A looooooong way to standardization…

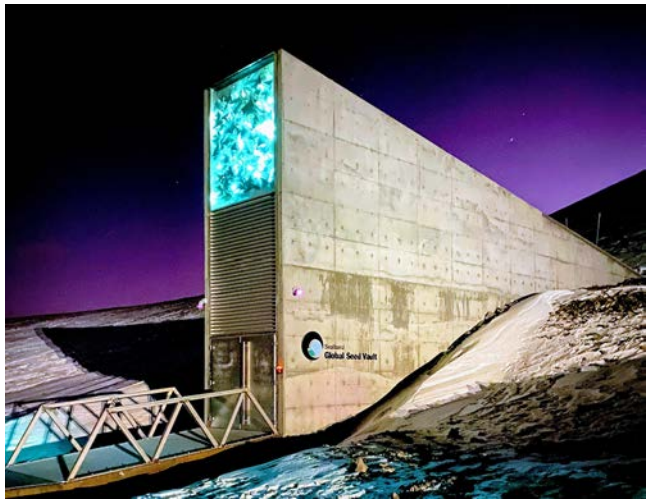
- International attempts to standardize e.g. International Human Microbiome Standards (http://www.human-microbiome.org/)



Bharucha T, Oeser C et al. Lancet Infect Dis 2020

Are there examples of global biobanks? The Svalbard Global Seed Vault!

- The **Svalbard Global Seed Vault** (Norwegian: *Svalbard globale frøhvelv*) is a secure backup facility for the world's crop diversity on the Norwegian island of Spitsbergen in the remote Arctic Svalbard archipelago.
- The Seed Vault provides long-term storage of duplicates of seeds conserved in genebanks around the world. → Security of the world's food supply against the loss of seeds in genebanks due to mismanagement, accident, equipment failures, funding cuts, war, sabotage, disease, and natural disasters.
- Conserves 1,081,026 distinct crop samples
- Storage at -18°C



What is the Microbiota Vault?

- The Microbiota Vault is a global non-profit initative to converve long-term health for humanity.

- **Collect.** Close interaction with local collections and research efforts.
- **Preserve.** Acting on behalf of the local working collections, providing safe backup storage and a framework for data services and collaboration.
- **Enable.** Empowering research of local working collections, help setting protocols and standards, preserving biodiversity, and allowing future restoration of health.

Time line of the Microbiota Vault

www.microbiotavault.org

The Microbiota Vault concept

- The feasibility study found that the Microbiota Vault initiative has great significance and potential.

- The Microbiota Vault initiative has decided **to initiate the operational phase** of the project in Switzerland and has designed a program for a **two-year launch phase.**

Who is behind the Microbiota Vault?


Maria Gloria Dominguez-Bello
Rudgers University


Rob Knight
UC San Diego


Jack Gilbert
UC San Diego


Manuel Fankhauser
Seerave Foundation


Claire Fraser
University of Maryland


Martin Blaser
Rutgers University


Thomas Bosch
University of Kiel


Dominique Caugant
Norwegian Institute of PH


Deborah Delgado-Pugley
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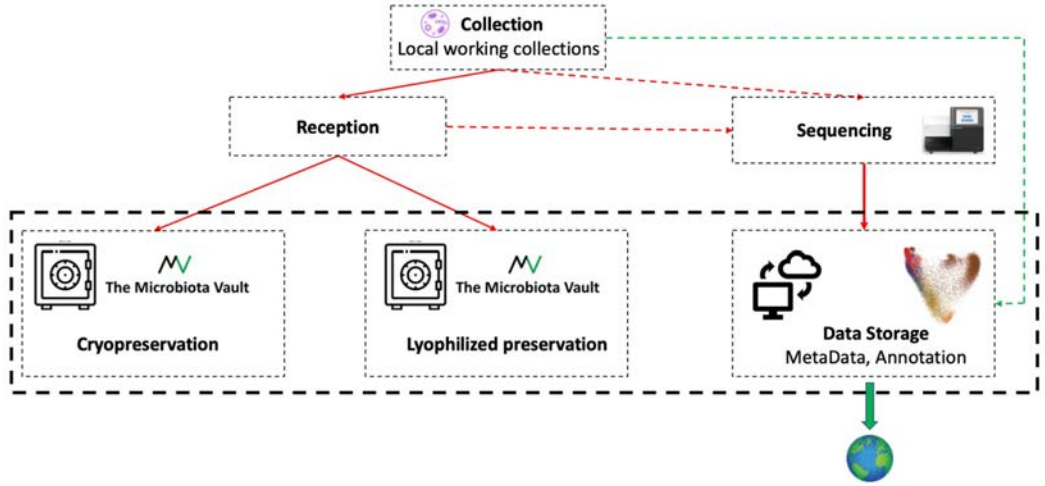
Seerave Foundation

Goals of the launch phase

- **1. Proof-of-principle during the launch phase, including**
  a. installation of the biobanking infrastructure in Switzerland.
  b. initiating collaboration projects for sample collection with local working collections.
  c. shipping of such samples from the local working collections to the biobanking infrastructure.
  d. collecting metadata associated with the samples in an interoperable fashion.
  e. developing databases and platforms for specimen's metadata.
  f. performing annotation and metagenomic characterization and data analysis of authorized samples.
  g. concretizing the Microbiota Vault concept in such a fashion will be instrumental in addressing the political level and scaling.
- **2. Establishment of the management capabilities** to build the organization and international network, to develop the required legal frameworks, and to drive the development at the political level.

Working plan for the pilot period

- **WP1:** Governance structure and associated legal framework to store the samples on behalf of the local collections.
- **WP2:** Validate standard operating procedures for collection and storage of fecal samples.
- **WP3/4:** Relationships with Local Working Collections (LWCs) and validate a pipeline for collection and shipping of samples.
- **WP5:** Secure storage of cryopreserved and lyophilized samples (Vault biobank).
- **WP6:** Data management and metadata standards.
- **WP7:** Metagenomic analysis of specimens and provide a platform to collect and share Vault related data including metadata and metagenomic data.



Progress on the pilot project

- Team Vonaesch: Experiments on nine storage media over 1 year, three storage conditions (N2, -80°, lyophilization), and seven subculture plates. Access to working collections in low- and middle income countries.
- Team Egli: Sequencing based on 16S amplicon based metagenomics. Storage.
- Team Bokulich: Development of analytical platform
- All: Regulatory work e.g. MTA, Consortium agreement

- Funding sources

Take home message

- **Storage of microbiota is important**
  - Loss of biodiversity due to multiple and complex reasons
  - Reproduction crisis of science

- **Standardization of protocols are key**
  - Pre- to post-analytics
  - Collection, storage, sequencing, and analysis -> all may introduce bias

- **The Microbiota Vault**
  - Pilot phase ongoing
  - Optimize and push standardization -> capacity forming
  - Safe harbour for low- and middle income countries
  - Sequencing of samples

THANK YOU for your attention! Questions?

- Contact:

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www.microbiotavault.org

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