

METAGENOMICS

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INTRODUCTION

LET'S START WITH A TRUE STORY

Megan Newman was dealing with **bacterial infection** that impacts the gastrointestinal system, named **Clostridium difficile**.

- diarrhea
- weight loss
- dehydration
- loss of blood platelets

LET'S START WITH A TRUE STORY

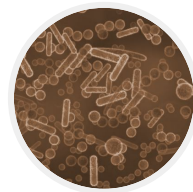
Megan Newman was dealing with **bacterial infection** that impacts the gastrointestinal system, named **Clostridium difficile**.

→ diarrhea

→ weight loss

→ dehydration

→ loss of blood
platelets

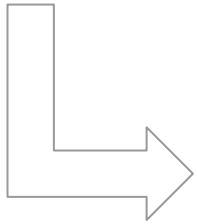


fecal
transplant

*and after 2 weeks,
some symptoms disappeared...*



New Insights Into the Cancer– Microbiome–Immune Axis: Decrypting a **Decade of Discoveries**



HEALTH

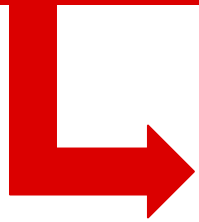
relationship



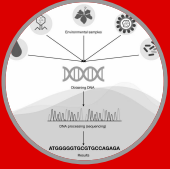
MICROORGANISM DIVERSITY
HEALTHY MICROORGANISM

How to assess the microorganism **diversity**
and find **new** healthy microorganism ?

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and find **new** healthy microorganism ?



METAGENOMICS



METAGENOMICS OVERVIEW



MAIN TECHNIQUES



DATA ANALYSIS

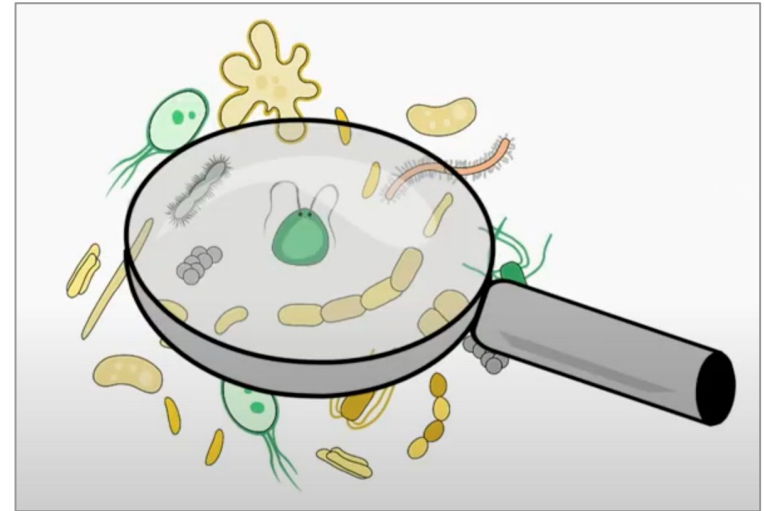


PERSPECTIVES

WHAT IS METAGENOMICS ?

- **genomic analysis of DNA**
from organisms in a sample,
ex. microbial organisms

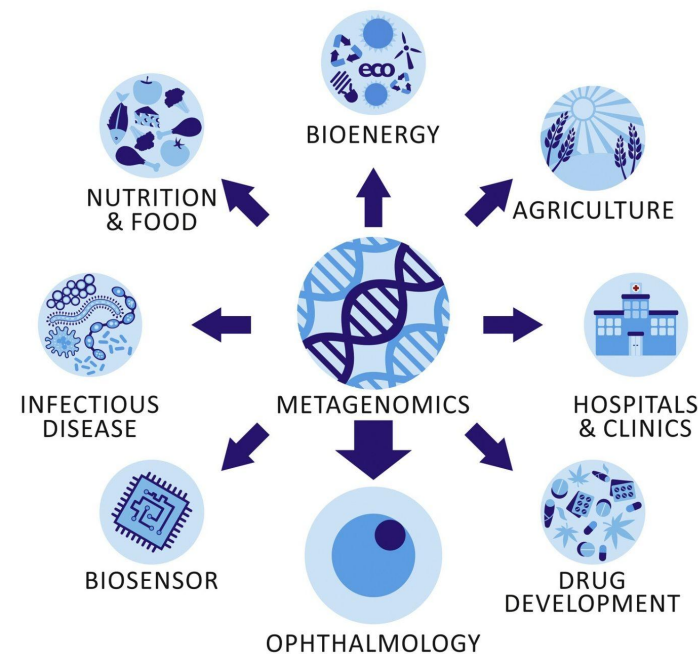
- studying the **whole community at once**
ex. human skin, gut, soil or water



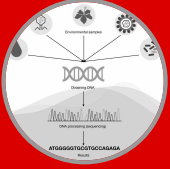
The virtual European Molecular Biology Laboratory practical course: Microbial Metagenomics: A 360° Approach.

WHY USE METAGENOMICS ?

- analysis of **un-culturable** or **unknown** microorganisms
- **directly in their natural environment**
- study of the **structure** and **function** of entire nucleotide sequences



Paola Gallon, Mohit Parekh, Stefano Ferrari, Adriano Fasolo, Diego Ponzin, Davide Borroni, Metagenomics in ophthalmology: Hypothesis or real prospective?, Biotechnology Reports, Volume 23, 2019, e00355, <https://doi.org/10.1016/j.btre.2019.e00355>.



METAGENOMICS OVERVIEW



MAIN TECHNIQUES

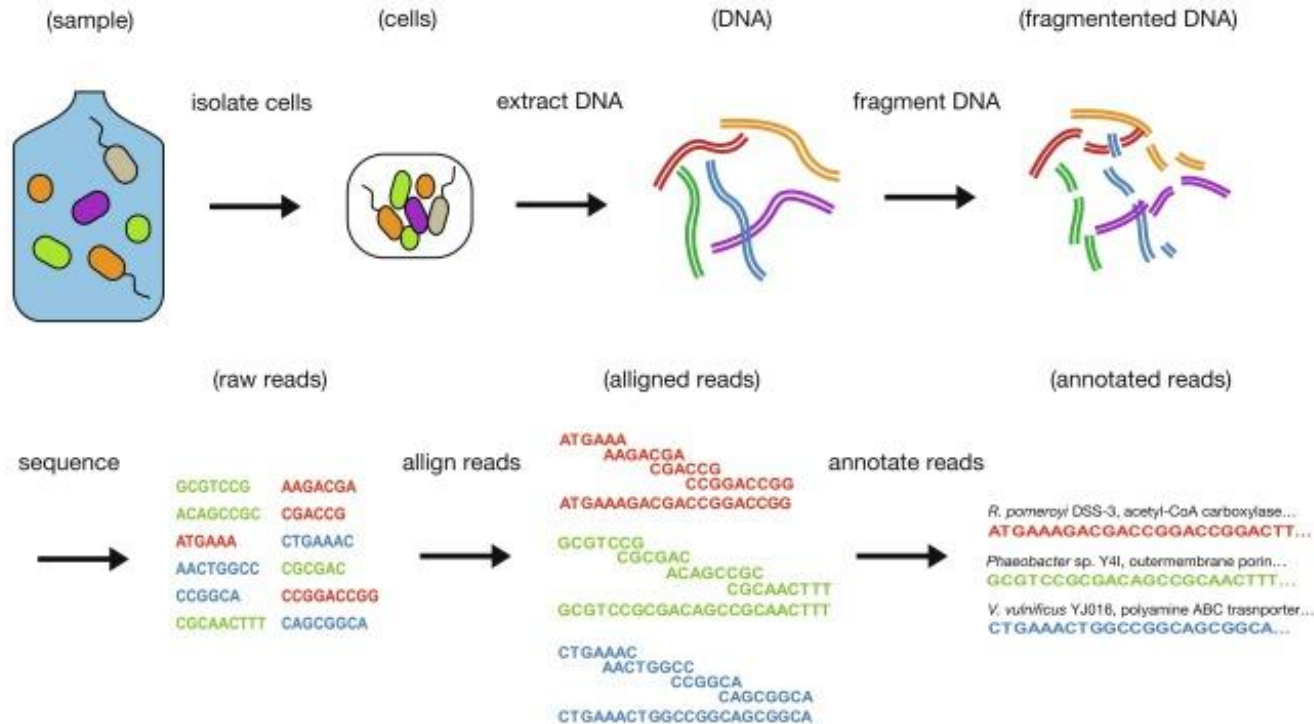


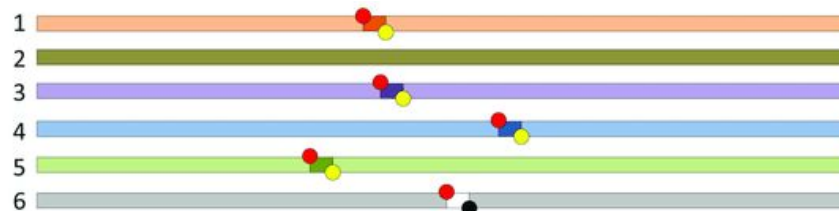
DATA ANALYSIS



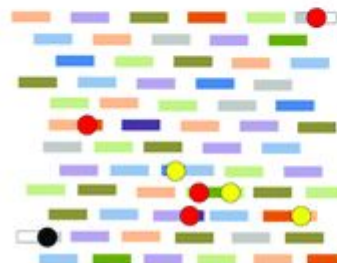
PERSPECTIVES

HOW DOES IT WORK ?





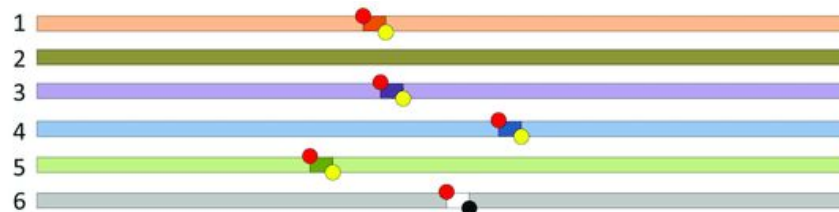
Shotgun sequencing



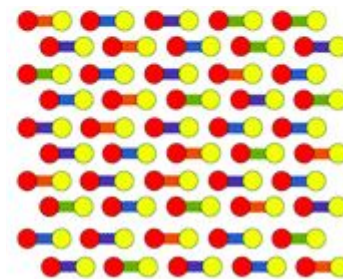
Whole approach

- community biodiversity
- function

- + Surveys all microbes present in the sample
- + Reveals functional pathway enrichment and novel chemistry
- Expensive and computational intensive

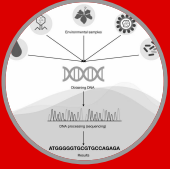


Amplicon sequencing



- 16S rRNA gene**
- identification
 - classification
 - quantitation

- + Cheap and doesn't need much DNA
- Limited in resolution and doesn't reveal functional pathways



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DATA ANALYSIS



PERSPECTIVES

ALPHA DIVERSITY

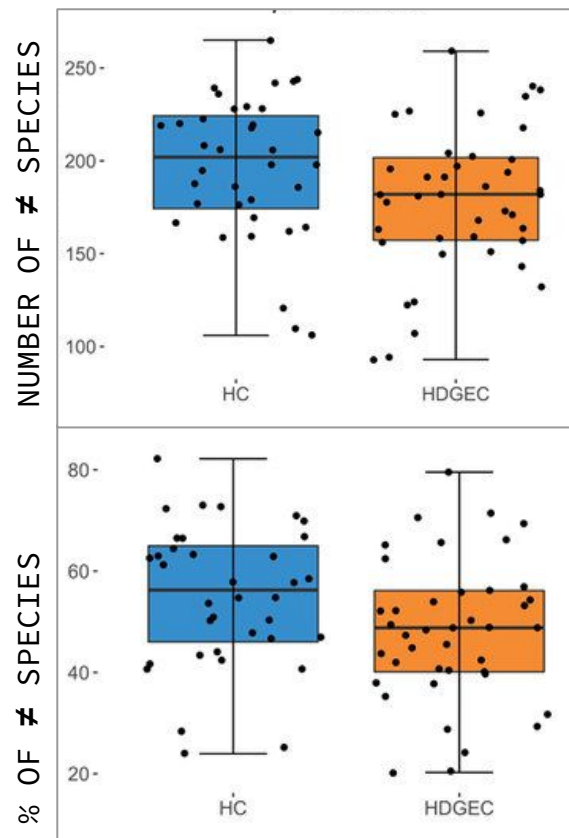
within sample diversity



RICHNESS



EVENNESS



Example

Gut dysbiosis in Huntington's disease [...]

Wasser et. al, 2020

HDGEC

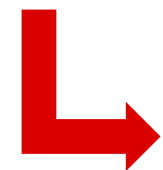
Huntington's
Disease
Gene
Expansion
Carriers

HC

Healthy
Controls

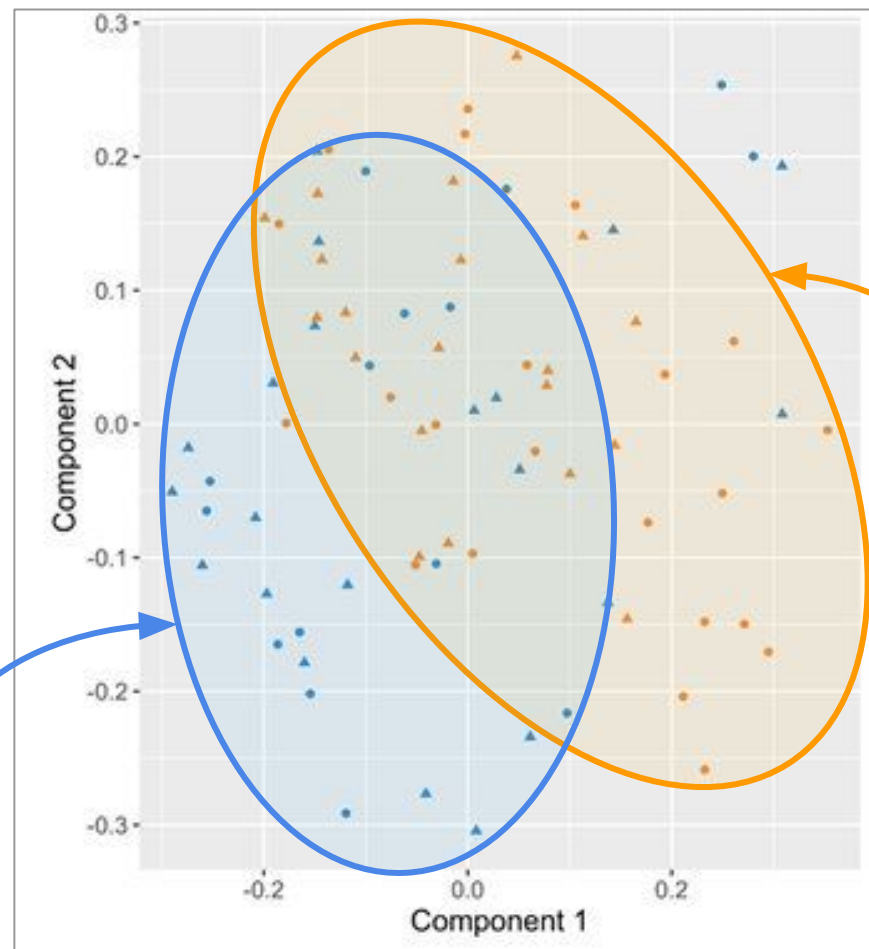
BETA DIVERSITY

between samples diversity



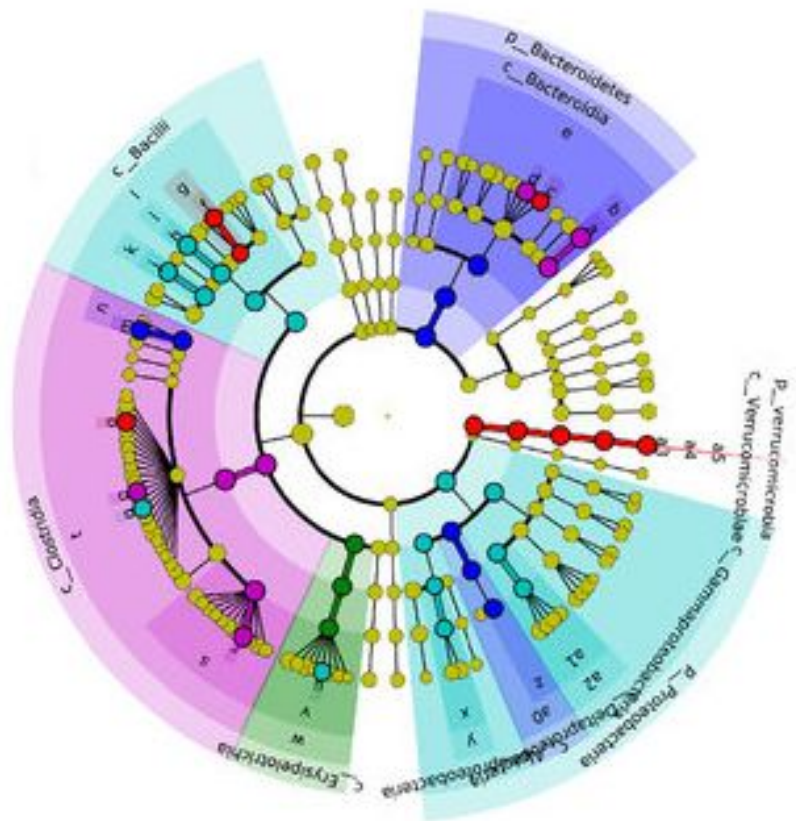
SIMILARITY

HC
Healthy
Controls



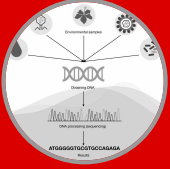
HDGEC
Huntington's
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TAXONOMIC CLASSIFICATION



classifying
biological organisms
based on shared
characteristics





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PERSPECTIVES

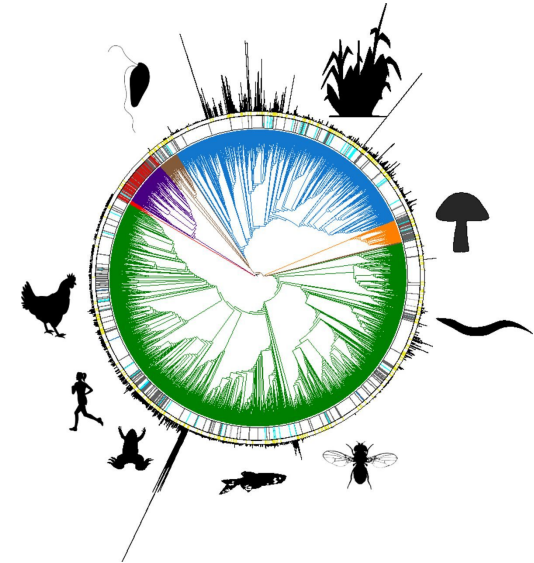
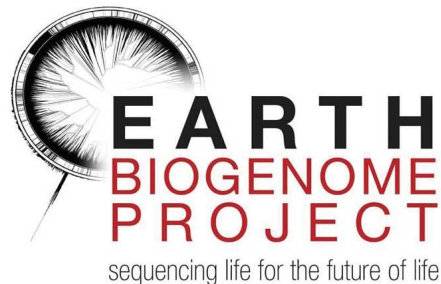
METAGENOMICS & BIODIVERSITY : WHY IS IT IMPORTANT ?

- Understanding the **distribution** and **abundance** of microorganisms
- Understanding the role of **microorganisms** in **ecosystem functioning**
- Identifying the impact on **environmental changes**



METAGENOMICS & BIODIVERSITY : EARTH BIOGENOME PROJECT

→ aims to **sequence**, **catalog**, and **characterize** the genomes of all of Earth's eukaryotic biodiversity over a period of **10 years**.



A.Lewin, Earth BioGenome Project: Sequencing life for the future of life, PNAS, 2018, www.pnas.org/cgi/doi/10.1073/pnas.1720115115
<https://www.earthbiogenome.org/>

METAGENOMICS & BIODIVERSITY : EARTH BIOGENOME PROJECT

Why Sequence Life?



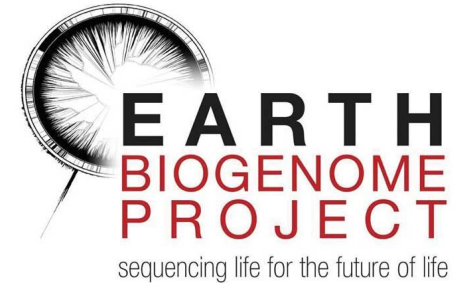
REVOLUTIONIZE OUR
UNDERSTANDING OF BIOLOGY
AND EVOLUTION



CONSERVE,
PROTECT, AND RESTORE
BIODIVERSITY

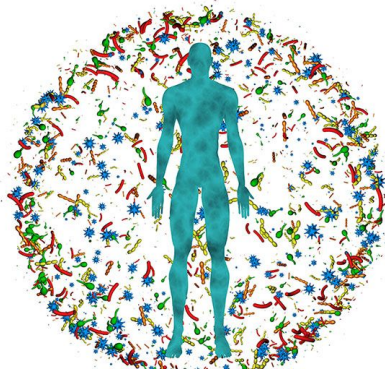


CREATE NEW
BENEFITS FOR SOCIETY
AND HUMAN WELFARE



→ Fundamental knowledge of Earth's biodiversity may also lead to new **food sources**, revolutionary **bio-inspired materials**, and innovations to treat human, animal, and plants diseases.

NIH HUMAN MICROBIOME PROJECT




→ Understand the role of the **human microbiome** and its relationship **to human health**.

MetaHIT



→ Aims to understand the role of the **gut microbiome** in **health and disease**



The Relationship Between the Gut Microbiome and Neurodegenerative Diseases

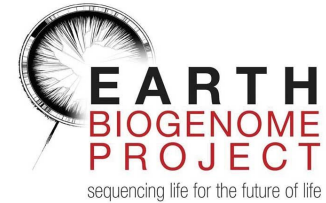
[Xueling Zhu](#),^{#1,2} [Bo Li](#),^{#1,2} [Pengcheng Lou](#),^{1,2} [Tingting Dai](#),^{1,2} [Yang Chen](#),³ [Aoxiang Zhuge](#),^{1,2} [Yin Yuan](#),^{1,2} and [Lanjuan Li](#)^{✉1,2}

CONCLUSION

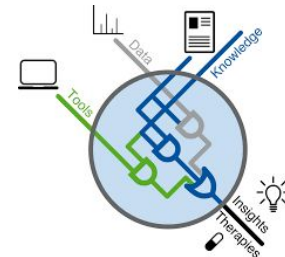
→ **Metagenomics** assesses microorganism diversity



→ **Promising projects** based on metagenomics leading to **innovations**



→ **Relies** on computational tools, software to ensure high accuracy



QUESTIONS

QUESTION 1

**What are the main sequencing techniques used
in metagenomics ?**

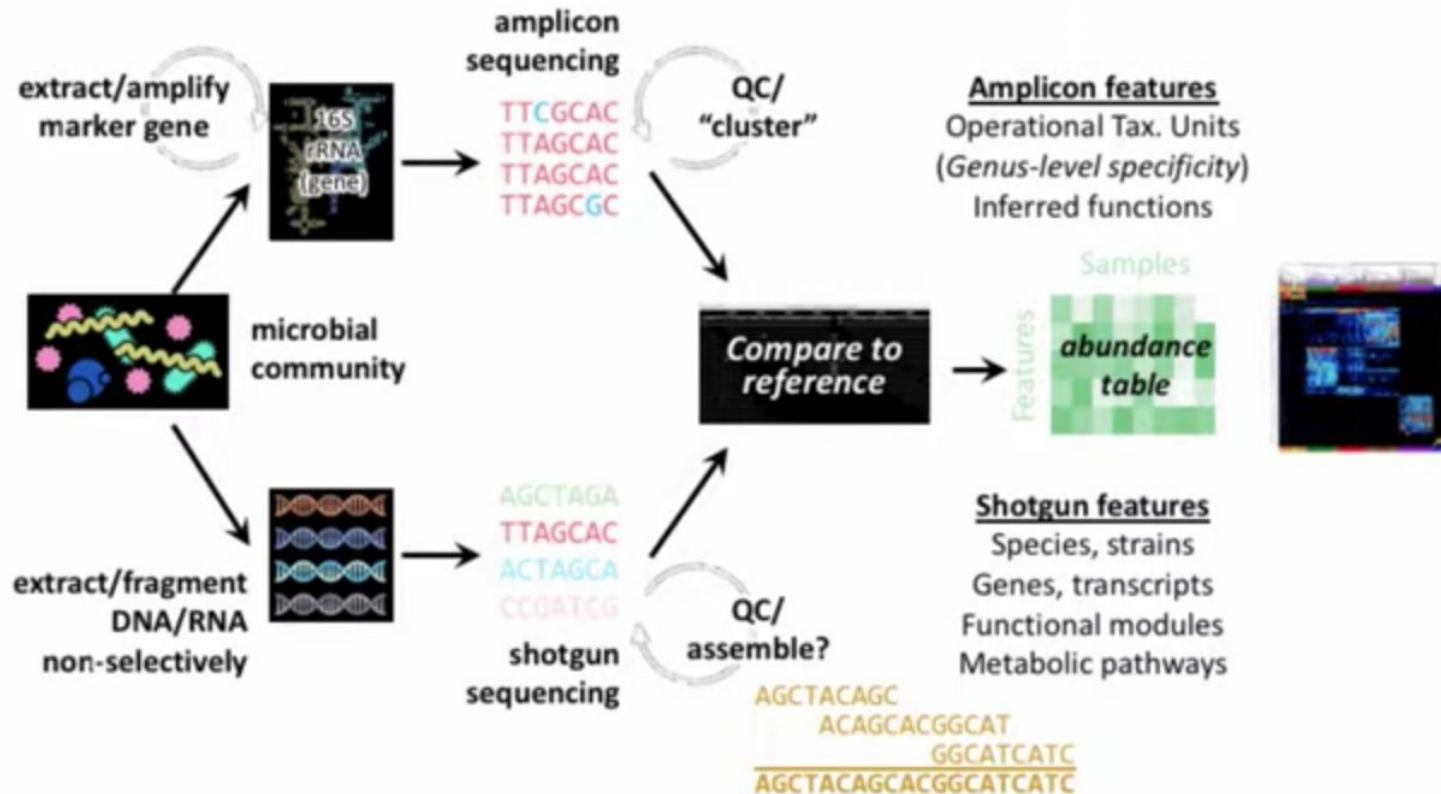
Amplicon sequencing & Shotgun sequencing

What are some of the potential future applications of metagenomics ?

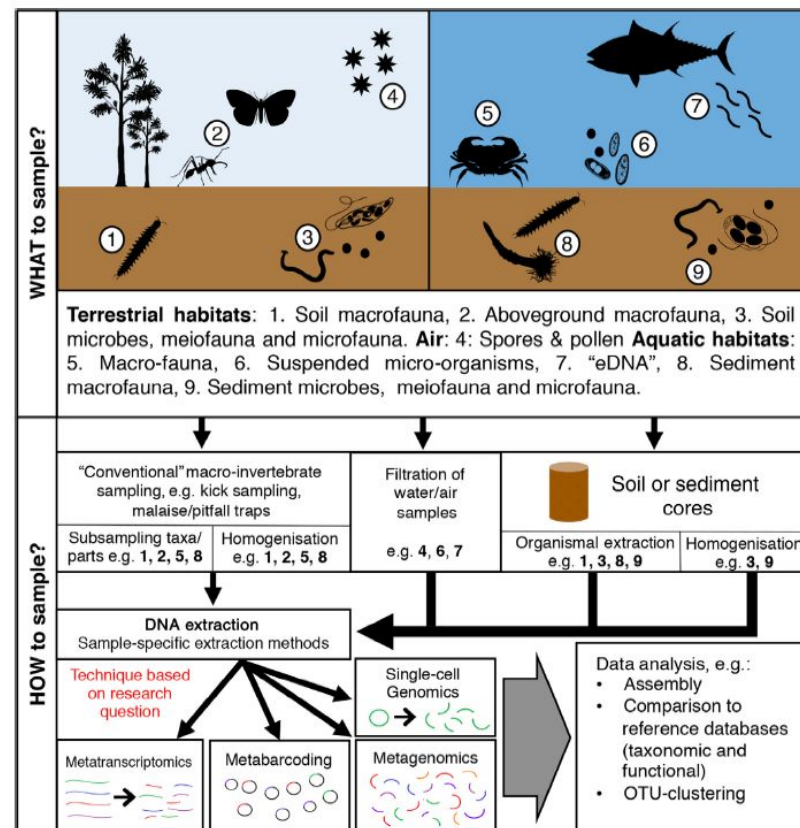
- Development of **new biotechnology products**.
- Development of **new diagnostic tools** for identifying pathogenic microorganisms.
- Study of the impact of **anthropogenic activities** on the environment and the **biodiversity** of microbial communities.

THANK YOU !

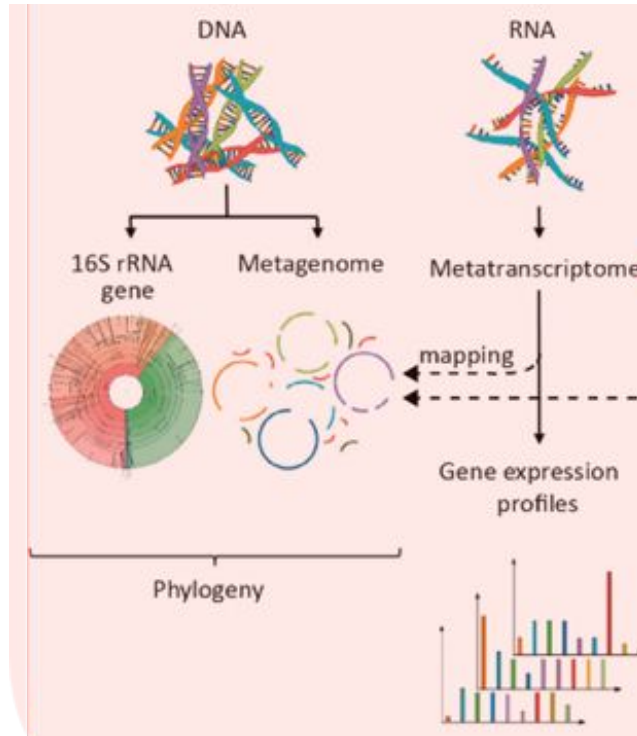
APPENDIX



From Metagenomics to Meta-omic

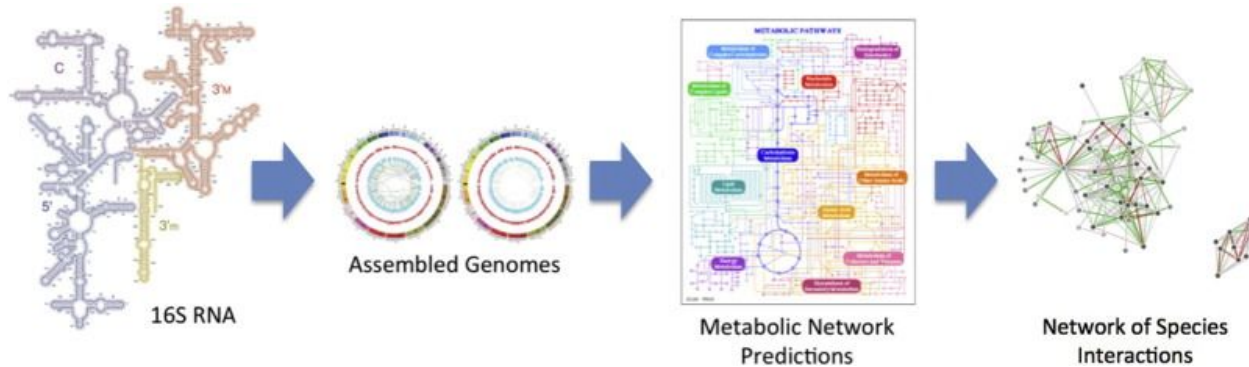


Metatranscriptomics



- **Metagenomics** study of all genetic material (DNA)
- **Metatranscriptomics** focuses on the analysis of the RNA; identification of which genes are expressed.

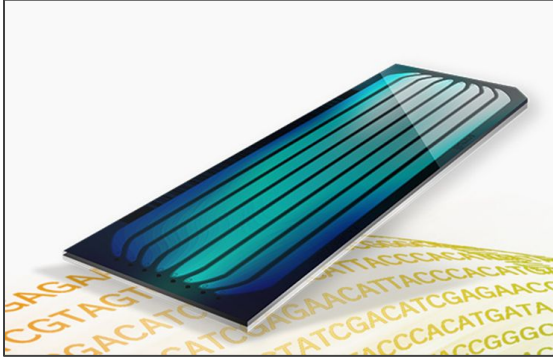
Community metabolism



Metabolic modeling with Big Data and the gut microbiome, J.Sung, February 2016, Applied and Translational Genomics, DOI : 10.1016/..atg.2016.02.001

- **Metagenome sequencing** tells us the biological functions each microbial species can potentially perform.
- Understand the biochemical mechanisms of each microbe and **its metabolic activity**.

Sequencing speed



- **Illumina sequencing** speed ranges from **10 to 30 million** bases per hour (depending on the specific platform)

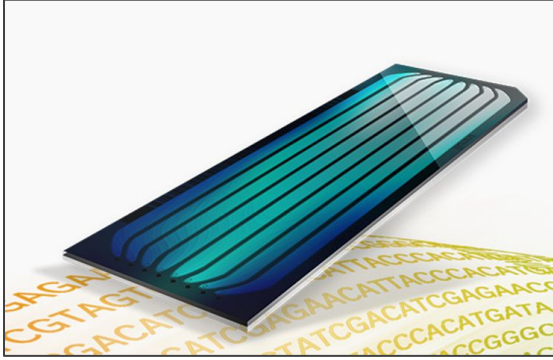
PacBio

- **PacBio sequencing** speed ranges from **0.5 to 2 million** bases per hour. Reconstruction of complex genomes and identification of structural variations.

<https://www.illumina.com/systems/sequencing-platforms.html>

<https://www.cd-genomics.com/pacbio-smrt-system-single-molecule-real-time-sequencing.html>

Sequencing cost



- **Illumina sequencing** have a cost per base around **0.05 to 0.10** cents per base.

PacBio

- **PacBio sequencing** have a cost per base around **0.10 to 0.15** cents per base. (long reads and real-time analysis)