

### The 1st Microbiome CRO

Comprehensive microbiome research services

Atlas Biomed Group R&D department

## **Atlas Biomed Group**

### **Atlas Biomed**

Global provider of DTC genetic and microbiome tests in 15+ countries (UK, EU, Japan, Asia, Russia/CIS)

Aimed to develop a cloud system for multisource data co-interpretation to diseases prevention

The head company of the group

#### Atlas rnd

Contract Research
Organisation specialised in
microbiome-focused clinical
trials and research projects.

Knomics Biota – a proprietary microbiome data analysis SaaS

100+ publications

60+ completed projects

50+ partners

#### **Oncoatlas**

The leader of laboratory services providing and diagnostic kits development in the oncology field in Russia

The sole NGS-based diagnostic kit for tumors profiling registered in Russia

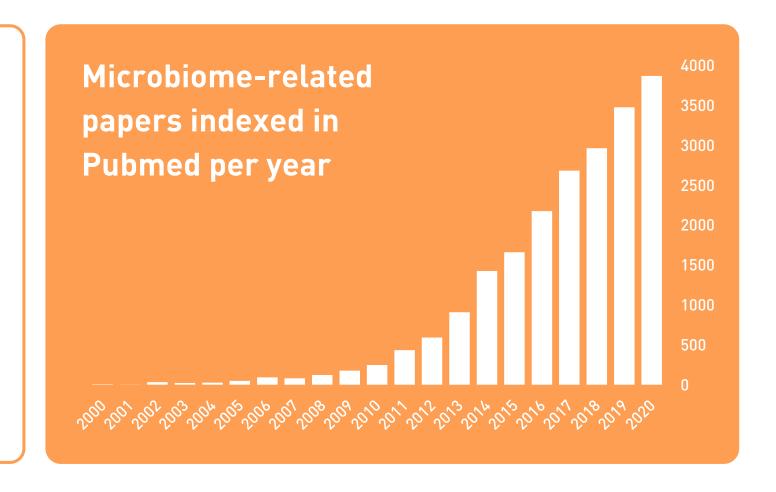
1000+ cases processed

# Microbiomics: a rapidly accelerating global research trend

The microbiome is a complex community of microbes inhabiting many niches. Numerous links between the microbiome and a wide variety of health conditions have been elucidated.

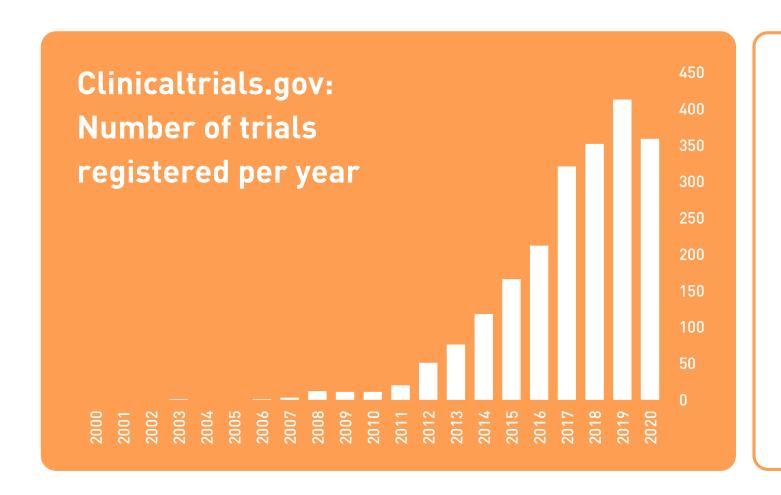
### **Top 5 topics**

- 1. Gastrointestinal disorders
- 2. Oncological microbiomics
- 3. Autoimmune conditions
- 4. CNS + gut-brain axis
- 5. Metabolic disease



### Microbiome clinical trials market

Developments in microbiome-targeted therapies are a major driving force in market evolution. Efficacy of each such product has to be confirmed via in vitro experiments and well designed clinical trials.



### Key market foci

- 1. Live biotherapeutic products
- 2. Specialised nutrition
- 3. Functional foods
- 4. Research projects
- 5. Pharmaceuticals

## Atlas R&D: from idea to publication

### What are we offering?

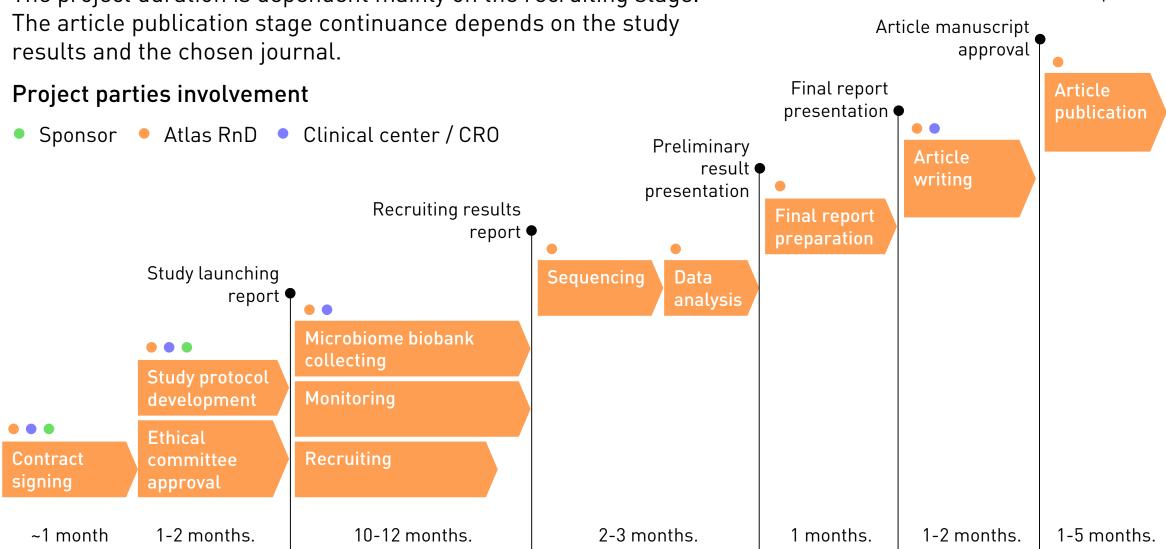
- 1. Microbiome services
- 2. Data analysis platform (SaaS)
- 3. Full-cycle CRO services

### **Project types**

- 1. Research projects
- 2. Observational studies
- 3. Interventional clinical trials
- 4. Pharmacomicrobiomics

# Standard project's roadmap

The project duration is dependent mainly on the recruiting stage.



Project

completion

# Project example

### **Description**

#### Cohort

Healthy volunteers 18-40 years old without immune system diseases signs

#### Groups

- Experimental group (n = 60)
- 2. Placebo group (n = 60)

### Research participant's path

#### Operational part

Inform consent signing Microbiome collection kits giving out

#### Clinical data collection

Inclusion / exclusion criteria compliance assessment

Clinical examination

Questionnaire

Incidence rate

Adverse events monitoring

### Samples collection

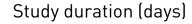
Blood

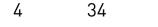
Saliva

Feces

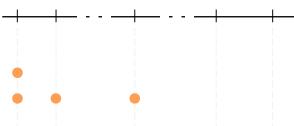
#### Intervention

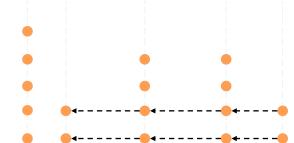
Product intake
Placebo intake







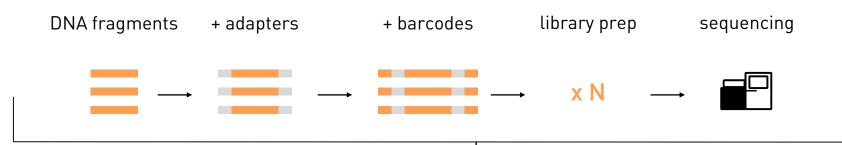






# Microbiome analysis: Sample processing

16S rRNA sequencing for key taxa searching in large-scale clinical trials



Sample collection and stabilisation

DNA isolation

High-throutput sequencing

Data analysis

Stabilization is an essential stage for bias avoiding

Specific kits for different tissues

Mechanical cell lysis stage – the second key point for relative abundance retention (Bead Beating) Any type of microbiome NGS

Any sequencing platform

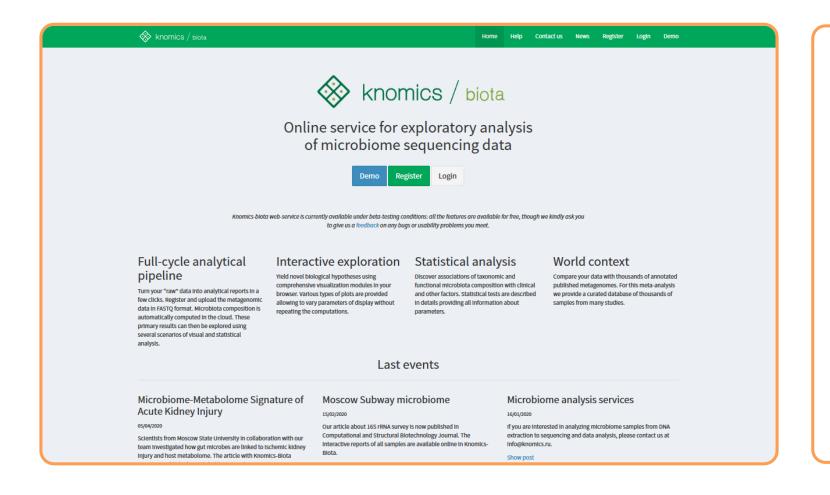
Any covering rate

The most significant stage, not proposed by lab services providers

## Microbiome data analysis

For microbiome data analysis and presentation, we propose our cloud platform Knomics-Biota. Push the logo at the right to explore the demo.





### **Options**

- 1. Fully automatic analysis
- 2. Interactive visualisation
- 3. Collaborative mode
- 4. Large-scale data sets supported

# Data analysis roadmap

1 Preprocessing

2 Taxa composition analysis

Functional potential analysis

4 Factor analysis

After receiving the sequencing data from the laboratory, the first step is to check the data quality and filter the low-quality reads.

# Data analysis: quality control

#### **Purpose**

Trimming of low-quality read ends, removing shot reads and denoising

### **Description**

All reads on the right of the red dotted line are pass quality control examination. Samples not passed through QC are not reliable for further analysis



## Data analysis roadmap

Preprocessing

**2** Taxa composition analysis

Functional potential analysis

4 Factor analysis

The next step is identification of taxonomic composition. Reads are aligned against reference sequences databases. Based on the comparison results, we obtain a list of detected bacterial taxa along with their reads counts. It allows to assess community diversity and relative abundance of the identified taxa.

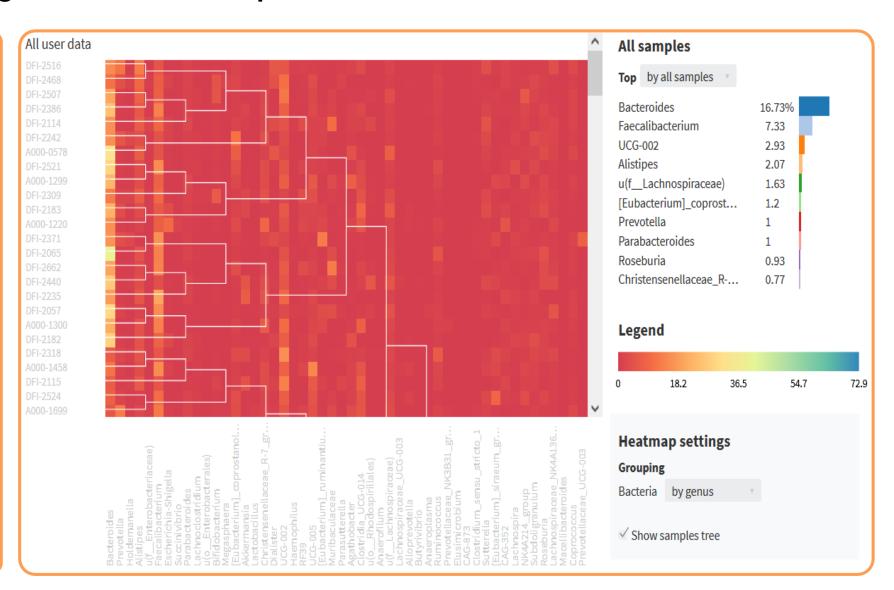
## Taxonomy investigation: heat map

#### Purpose

Samples and whole cohort taxonomy visualisation

### **Description**

Samples placed horisontally, bacterial taxa vertically. Samples clustered based on microbial composition



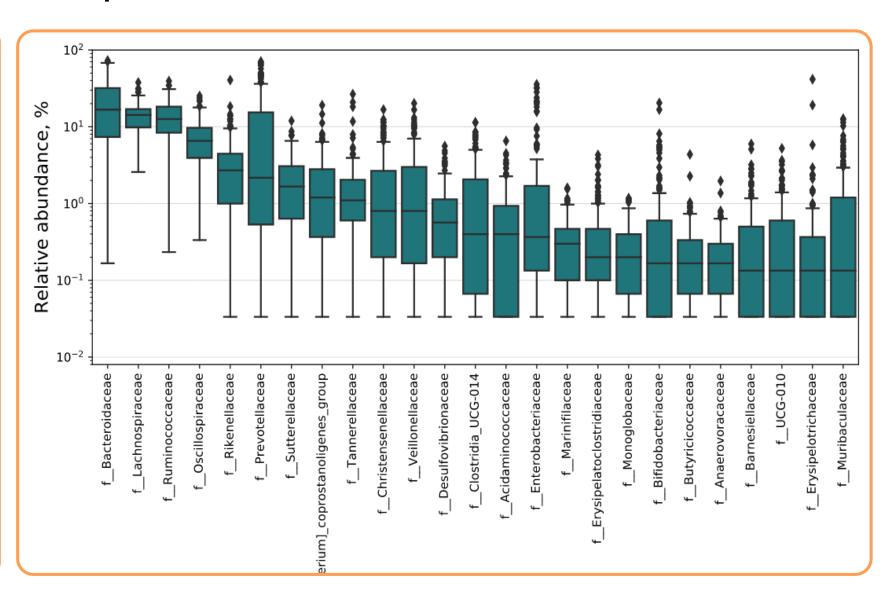
## Cohort taxonomy description

#### **Purpose**

Description of taxa abundance in whole cohort

### **Description**

Relative abundance of microbes on configurable taxonomy level.



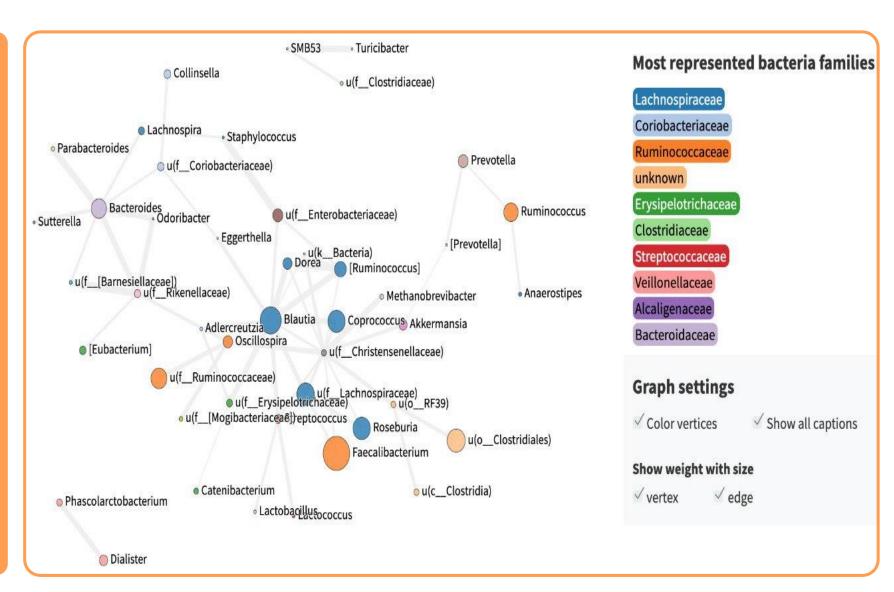
### Microbial cooperatives visualisation

### **Purpose**

Associated taxa identification

#### **Description**

Clusters of cooccurring taxa which
can be used for the
analysis of microbial
cooperation. Clusters
can be also transmitted
to statistical analysis.



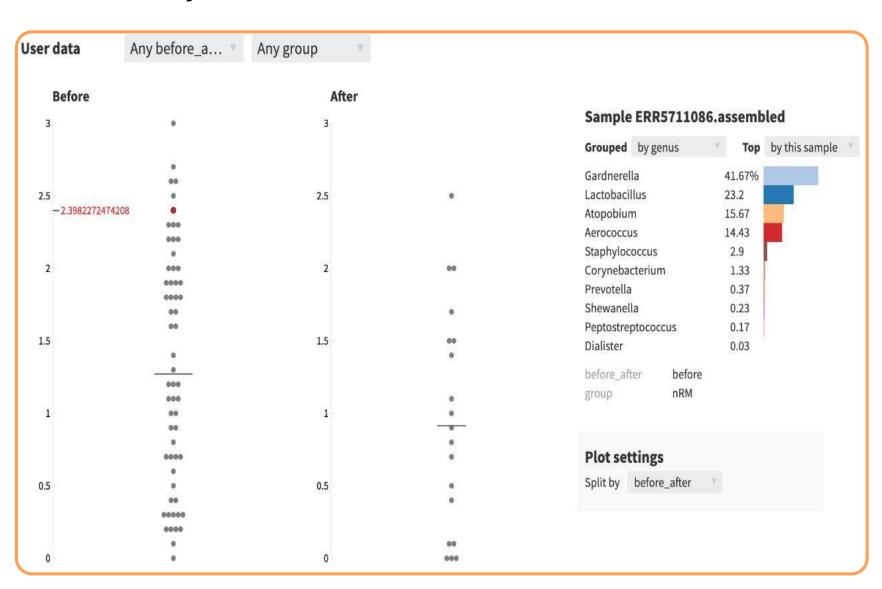
## Integral index: Alpha diversity

### **Purpose**

Microbiome richness visualisation

### **Description**

Automatically calculating with two scores using (Chao and Shannon indexes).



# Data analysis roadmap

Preprocessing

2 Taxa composition analysis

3 Functional potential analysis

4 Factor analysis

By knowing the taxonomic composition, it becomes possible to predict the microbiome metabolic potential. For this purpose, both publicly available and in-house metabolic pathway databases are used.

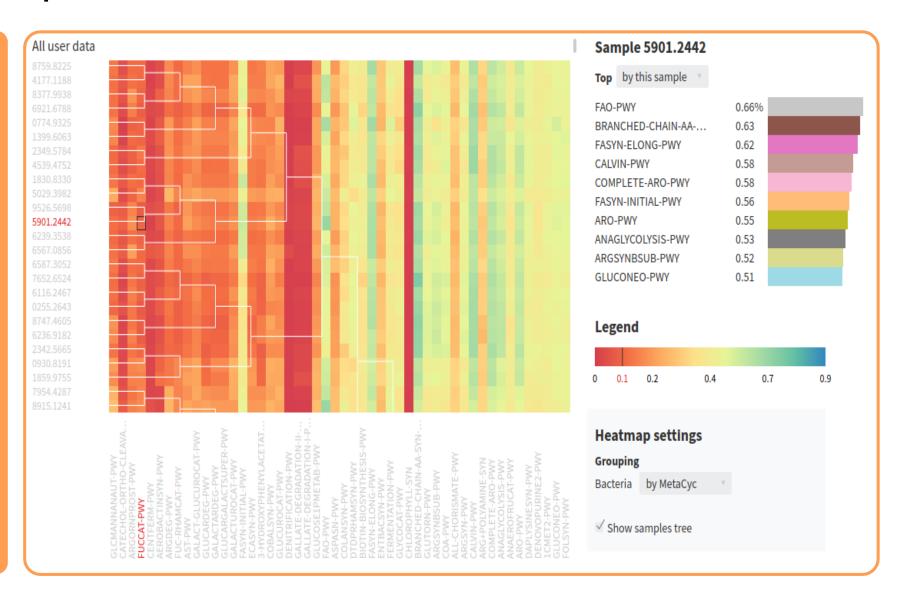
## Metabolic potential prediction

#### **Purpose**

Visualisation of whole microbiome metabolic potential

### **Description**

Samples placed horisontally, pathways vertically. Metabolic pathways relative abundance presented on the right



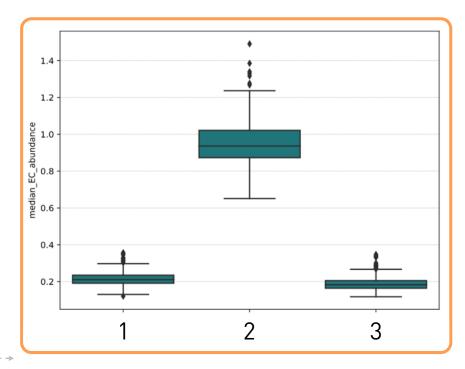
## Metabolic potential: specific pathways

#### **Purpose**

Manually curated metabolic pathways for the most clinically-relevant pathways in human gut microbiome differentiation

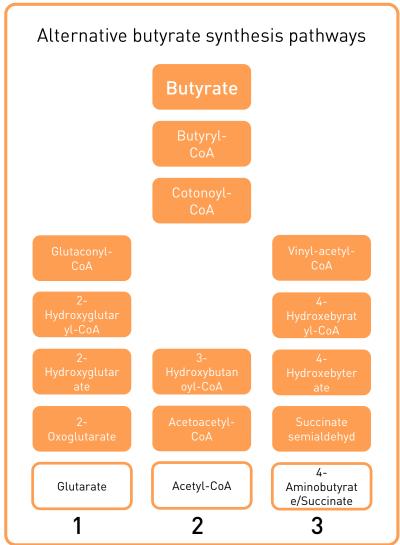
#### **Description**

Pathways relative abundances are shown as boxplots and can be downloaded



### Pathways curated

Right now curated pathways for SCFA and vitamins synthesis



# Data analysis roadmap

Preprocessing

2 laxa composition analysis

Functional potential analysis

4 Factor analysis

For the clinical trials, the crucial part is to identify the specific taxa and metabolic functions associated with clinical data. For this purpose, multiple modules of processing clinical data were integrated into our platform.

## Beta diversity: Categorical factors

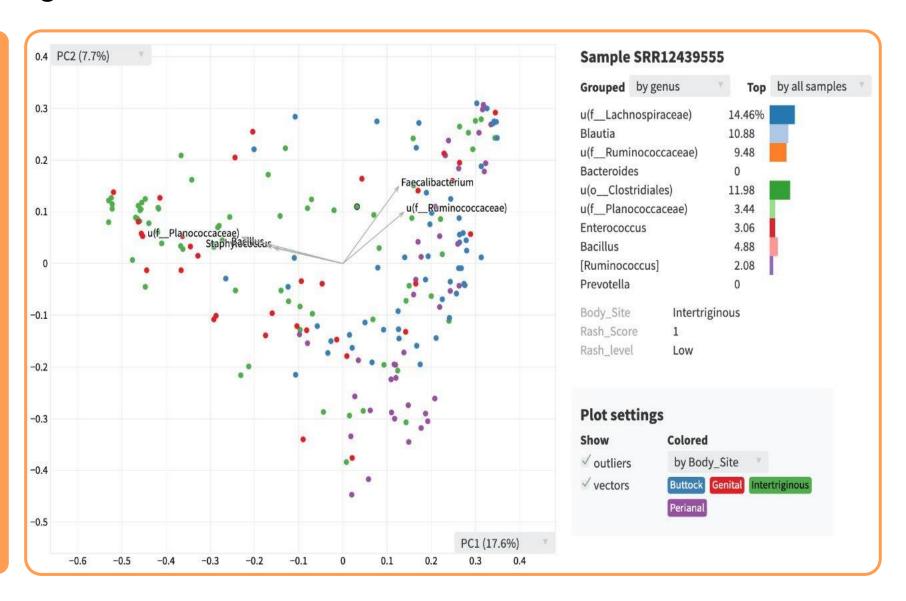
#### **Purpose**

Observational clinical trials, single time-points comparison

#### **Description**

Samples are shown in the space of microbes using relevant dimensionality reduction methods.

Two options of visualisation available: color and form



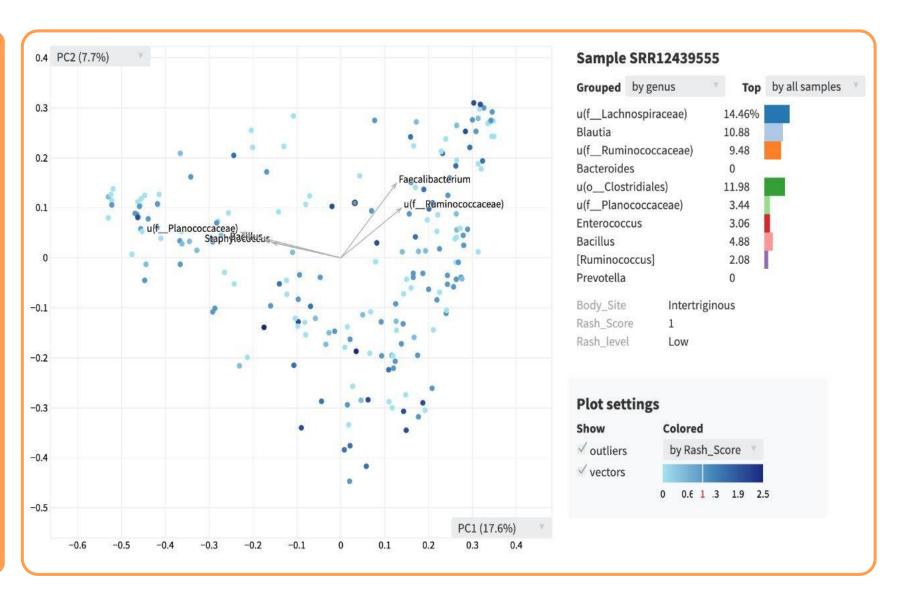
## Beta diversity: Continuous factors

#### **Purpose**

Observational clinical trials, single time-points comparison

#### **Description**

Every point on the plot is a single sample.
The numerical factor visualized as a brightness of points.



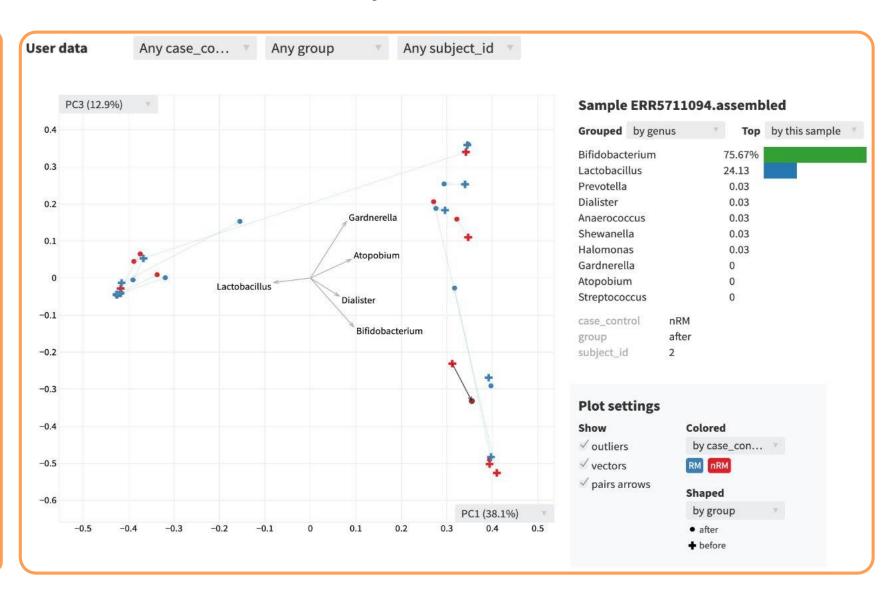
# Beta diversity: Paired case-control study

### **Purpose**

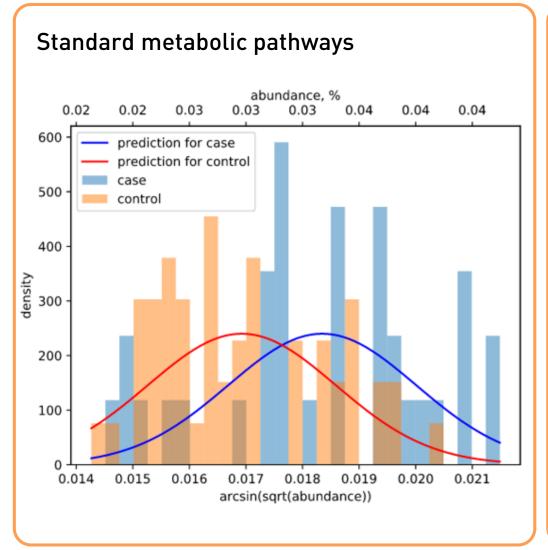
Classical interventional placebo - controlled clinical trial design

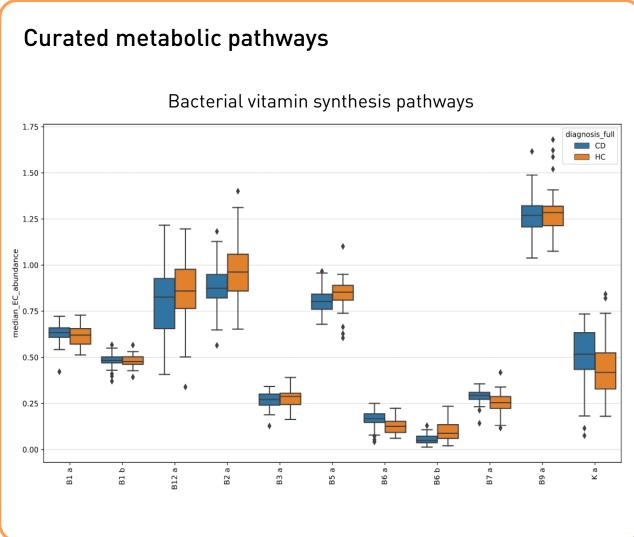
#### **Description**

Paired samples are connected by lines.
Before/after and placebo/control visulisation can be configured by user



# Metabolic potential comparison

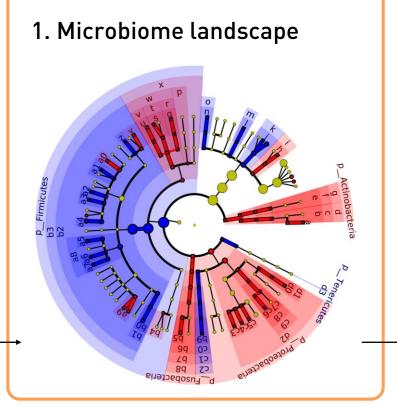


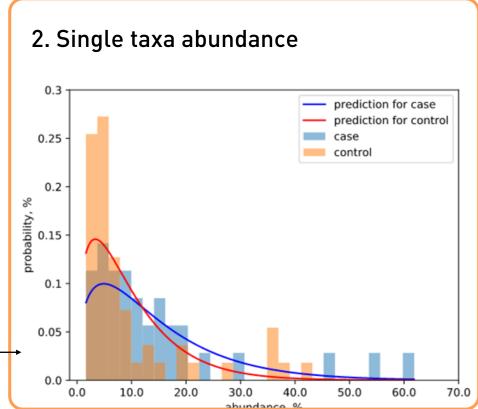


# Key taxa discovering

The main goal is to define statistically significant links between factors and microbes on the different taxonomic levels

increased in case increased in control





taxon	taxa level	case mean, %	case sd, %	control mean, %	control sd, %	p-value	adjusted p-value	lda score	sample size
pFusobacteria	phylum	4.338	9.277	0.937	1.393	0.000	0.000	4.664	87
pActinobacteria	phylum	1.139	1.449	0.536	0.575	0.001	0.003	4.381	87
pProteobacteria	phylum	14.532	13.983	9.937	10.362	0.034	0.040	4.122	87

### **Publications**

The platform is being applied in many microbiome studies conducted in house as well as by our customers. Some of results are presented on the slide

To see the list of publications with Knomics Biota in Google scholar (Click here)



#### Journal of Functional Foods

Volume 83, August 2021, 104572



Yogurt fortified with vitamins and probiotics impacts the frequency of upper respiratory tract infections but not gut microbiome: A multicenter double-blind placebo controlled randomized study



Food Microbiology Volume 94, April 2021, 103658



Characteristics of bacterial and yeast microbiomes in spontaneous and mixed-fermentation beer and cider



Acta Tropica
Volume 217, May 2021, 105835



The impact of *Opisthorchis felineus* infection and praziquantel treatment on the intestinal microbiota in children



Computational and Structural Biotechnology Journal



Volume 18, 2020, Pages 314-322

Co-occurrence patterns of bacteria within microbiome of Moscow subway



#### Critical Care

Serum and fecal profiles of aromatic microbial metabolites reflect gut microbiota disruption in critically ill patients: a prospective observational pilot study



#### **Orphanet Journal of Rare Diseases**

Gut microbiome signature of Viliuisk encephalomyelitis in Yakuts includes an increase in microbes linked to lean body mass and eating behaviour



Microbiome Responses to an Uncontrolled Short-Term Diet Intervention in the Frame of the Citizen Science Project



Human Gut Microbiome Response Induced by Fermented Dairy Product Intake in Healthy Volunteers



Subfractional Spectrum of Serum Lipoproteins and Gut Microbiota Composition in Healthy Individuals

#### Open Access Article

Host-Microbiome Interactions Mediated by Phenolic Metabolites in Chronically Critically III Patients



Microbiome-Metabolome Signature of Acute Kidney Injury



Microbiological Activity during Co-Composting of Food and Agricultural Waste for Soil Amendment



nutrients



nutrients



microorganisms



metabolites



metabolites



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