FNS - Cloud
Food Nutrition Security

Making Diet & Microbiome data FAIR –

The FNS-Cloud Diet & Microbiome DEMONSTRATOR

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Quadram Institute
Science Health Food Innovation

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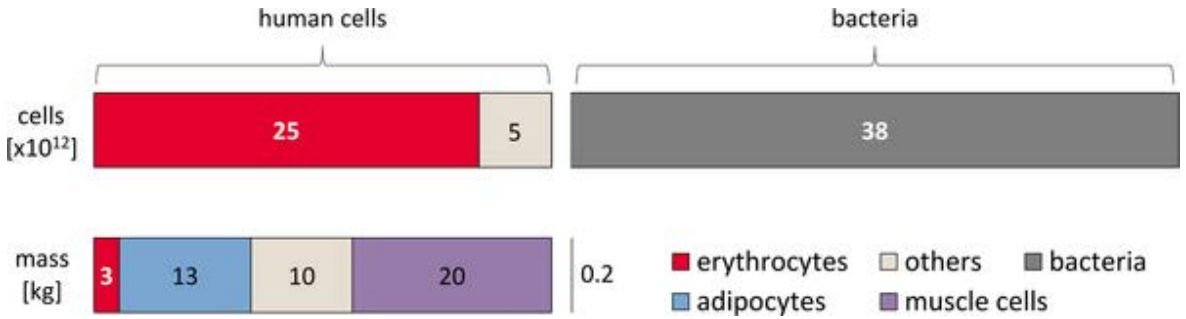
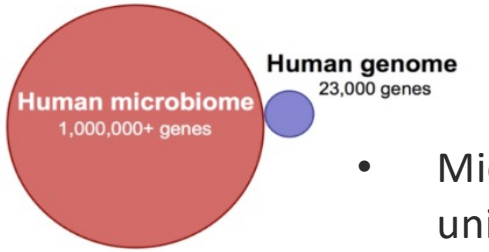
Food Nutrition Security Cloud (FNS-Cloud) has received funding from the European Union's Horizon 2020 Research and Innovation programme (H2020-EU.3.2.2.3. – A sustainable and competitive agri-food industry) under Grant Agreement No. 863059 – www.fns-cloud.eu

The human microbiota: we are home to highly diverse and dynamic microbial communities

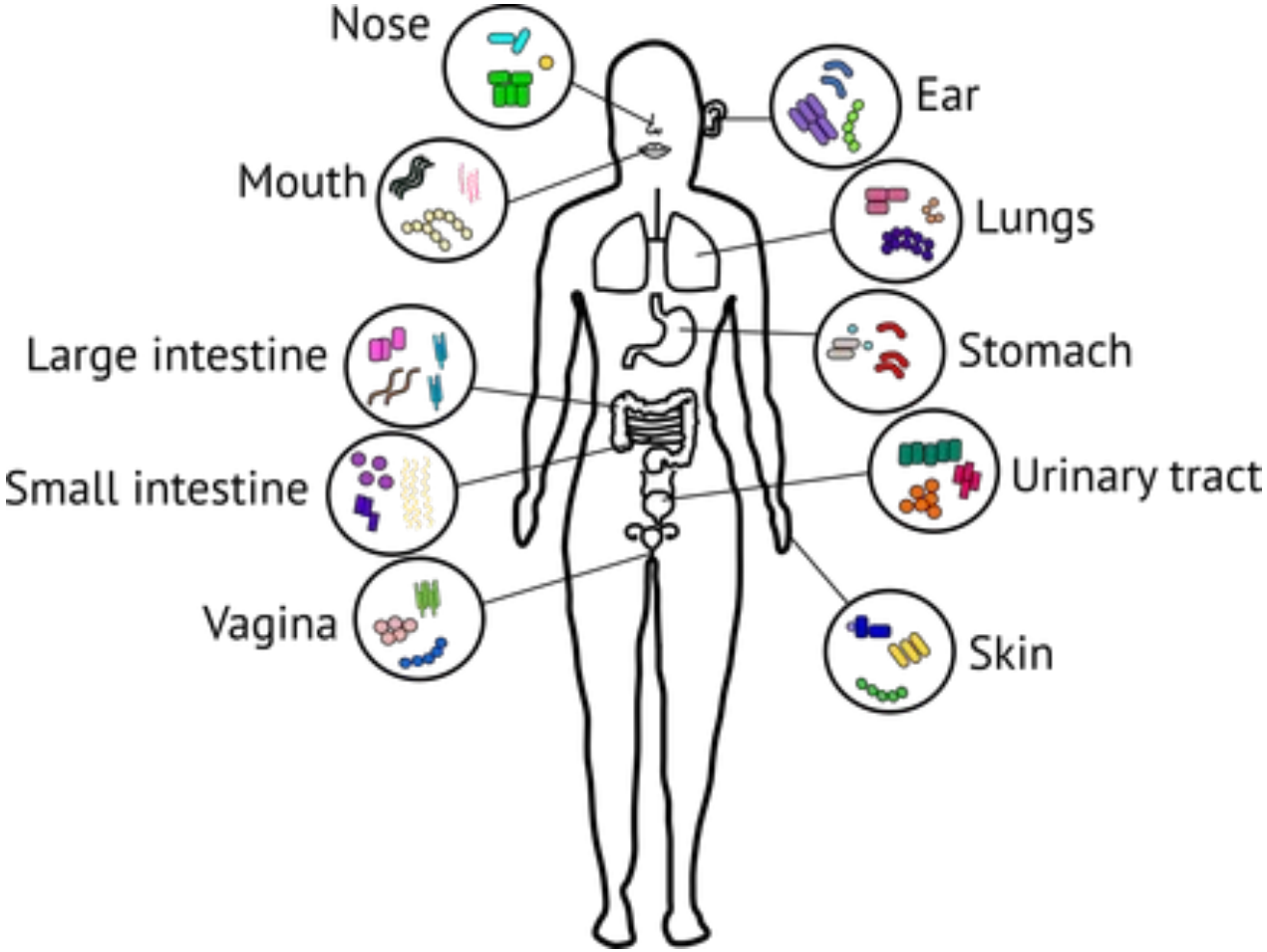
- **Are we more human or microbial?**
  - **1:1 ratio**
  - **10:1 ratio (nucleated cells)**



Sender et al, 2016. PLOS Biology 14(8): e1002533.



- Microbiome contains **150X** more unique genes than human genome



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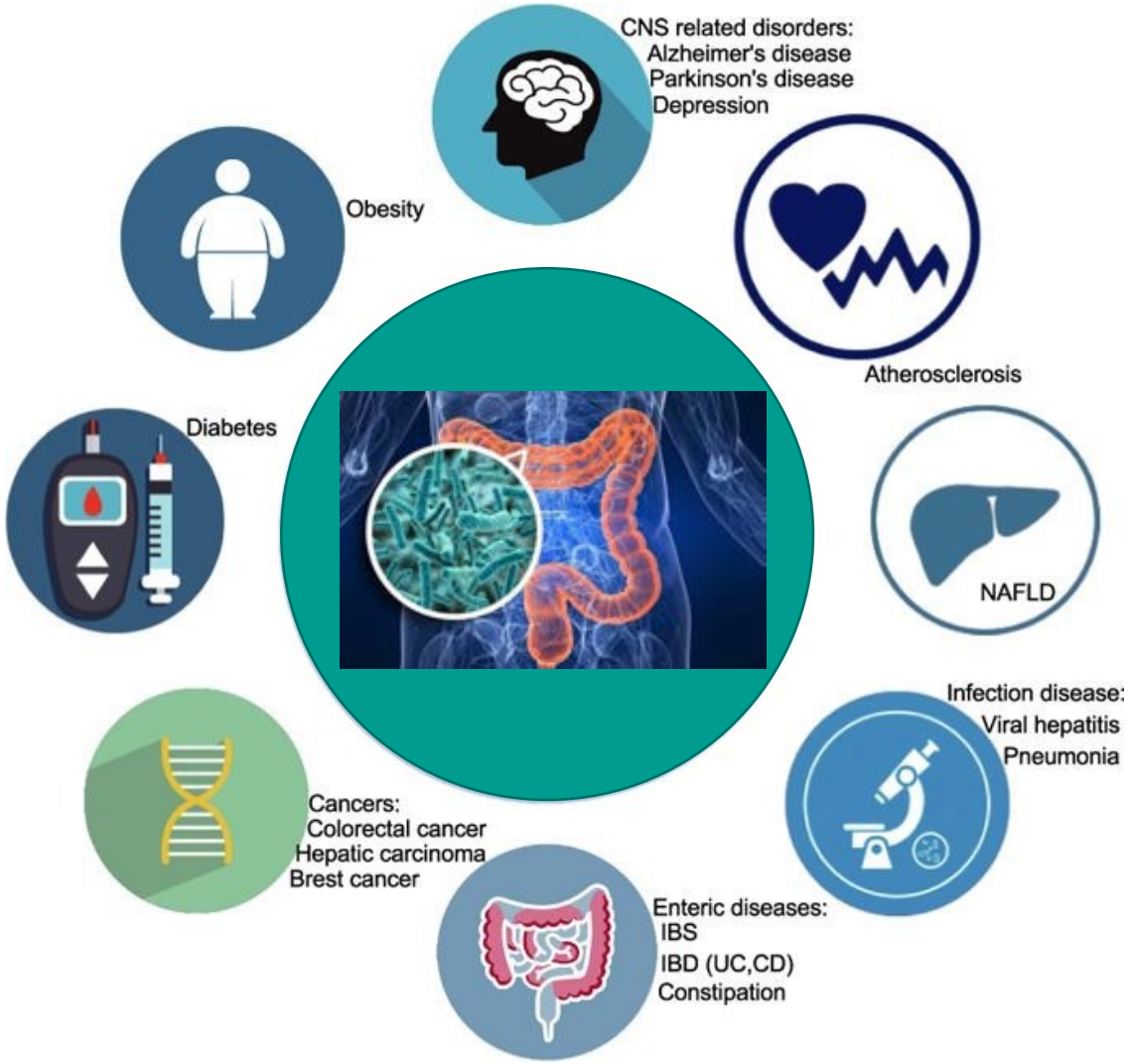
Gut Microbiota and Health



Cheng *et al.* (2020). J. Func. Foods, 74:104197

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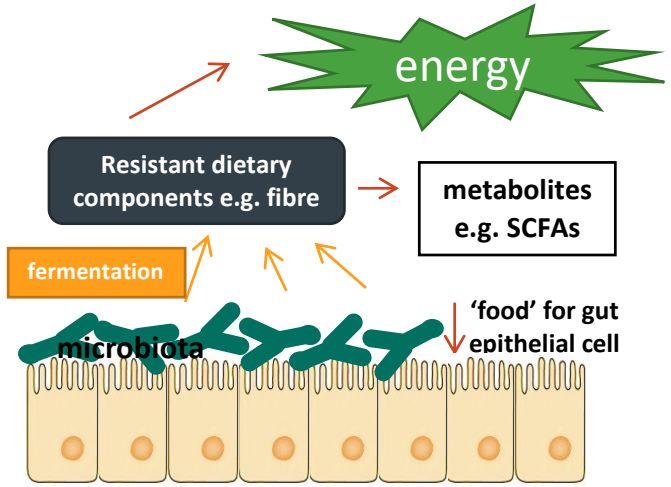
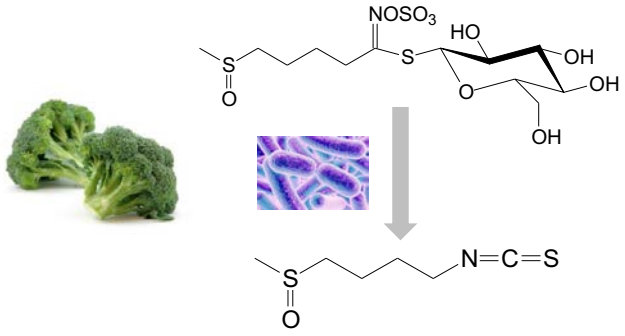
What do gut microbiota do?

Fibre Fermentation for **Energy Harvest**



Non-nutrient metabolism: **Food Bioactives**

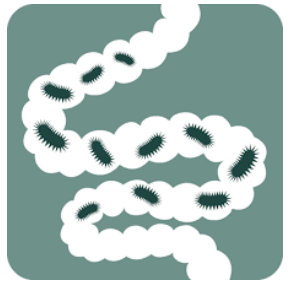


4-methylsylphinylbutyl isothiocyanate – **Sulforaphane**

Immune system development

Vitamin & Nutrient metabolism

Protection from **pathogens**



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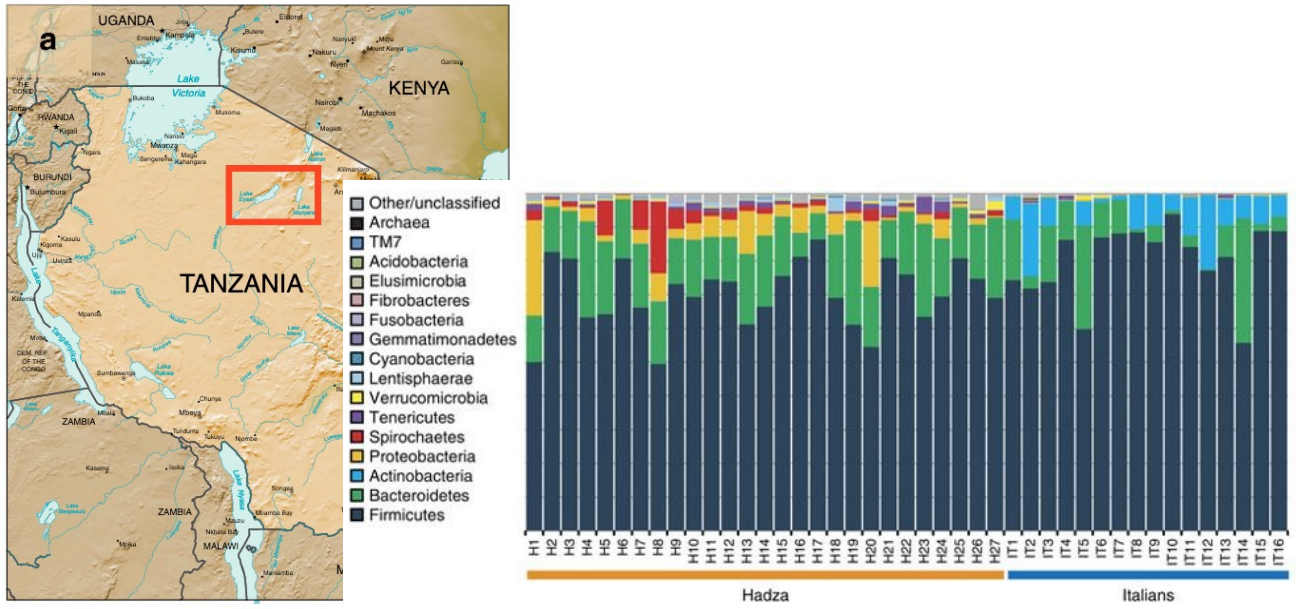
Diet modifies gut microbiota

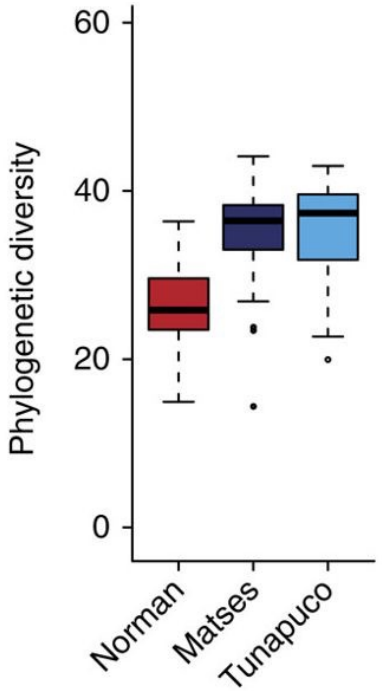
Hadza community of hunter-gatherers

- wild foods (meat, honey, baobab, berries and tubers)
- High fibre



Schnorr *et al.* (2014). Nat Communications, 5:3654

- **Matses |** remote hunter-gatherer population from the Peruvian Amazon **| tubers, plantain, fish, limited game**
- **Tunapuco |** traditional agricultural community from the Andean highlands **| stem tubers (potatoes, oka, mashua), fruit, meat**
- **Norman, Oklahoma, US |** typical US urban-industrialized lifestyle **| processed foods, bread and prepackaged meals**



Matses and Tunapuco are enriched in genus *Treponema*, an efficient carbohydrate metaboliser

Obregon-Tito *et al.* (2015). Nat Communications, 6:6505

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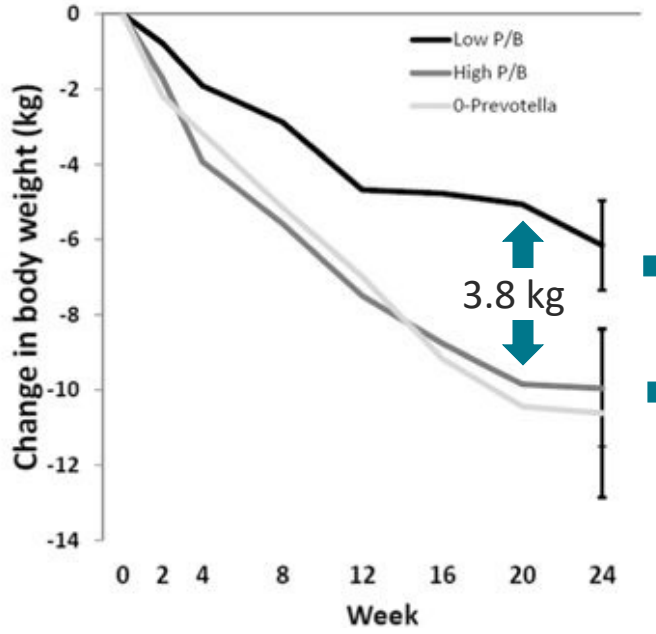
Evidence from human studies (RCTs) – Taxonomic information

Obese individuals stratified by **Prevotella–to–Bacteroides (P/B)** ratio (n=52) on low calorie diets (500 kcal/d) for 24w



High fibre >30g

3.2 kg more

8.3 kg more

- **Prevotella |** high CHO and fibre diets
- **Bacteroides |** high protein and animal fat

Hjorth *et al.* (2019). Int. J. Obesity, 43:149-157

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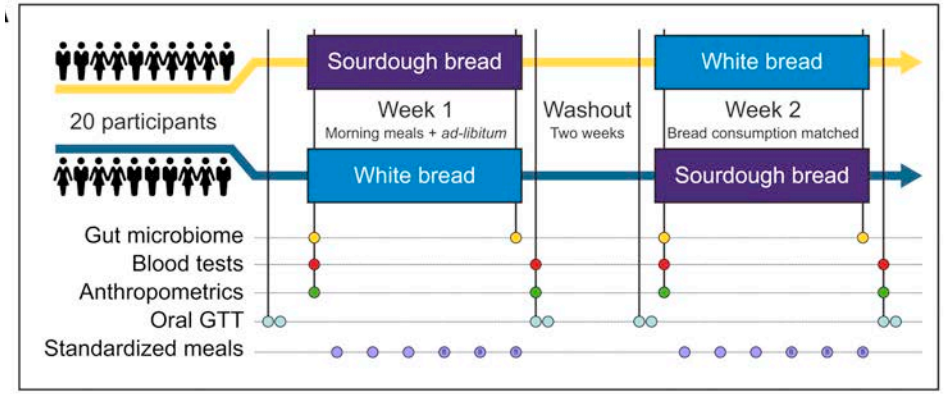
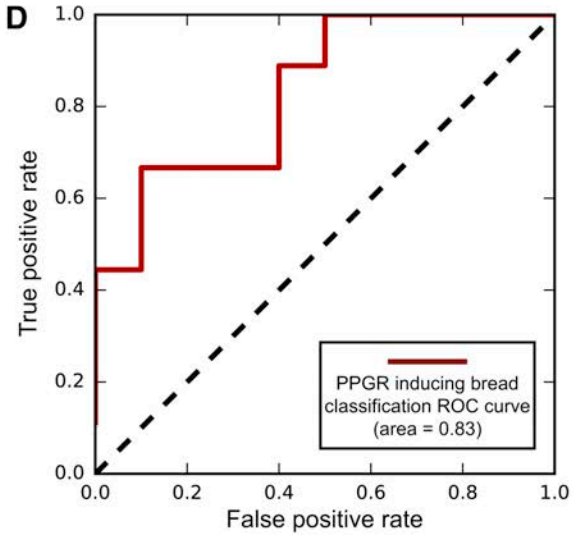
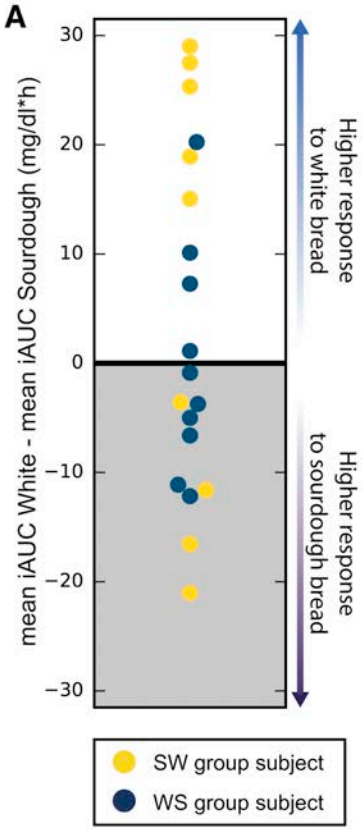
Using taxonomic AND functional information
Not just what is present but what they are doing

In healthy (n=20) **no difference** in metabolic or clinical parameters



When only gut microbiota were used in a classification algorithm they could predict the bread that induced lower glycemic response





Korem *et al.* (2017). Cell Metabolism, 25: 1243-1253

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Dietary Intervention human studies (RCTs)

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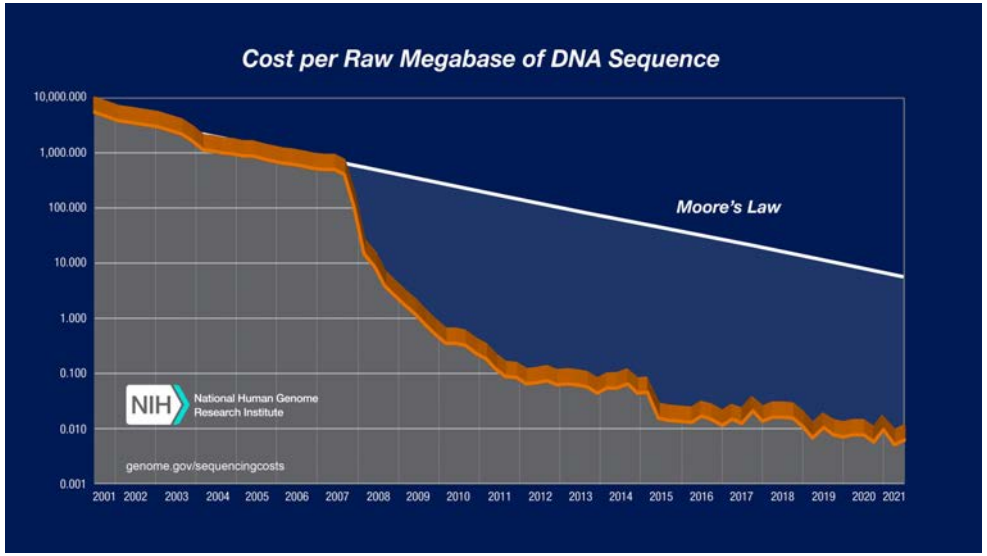
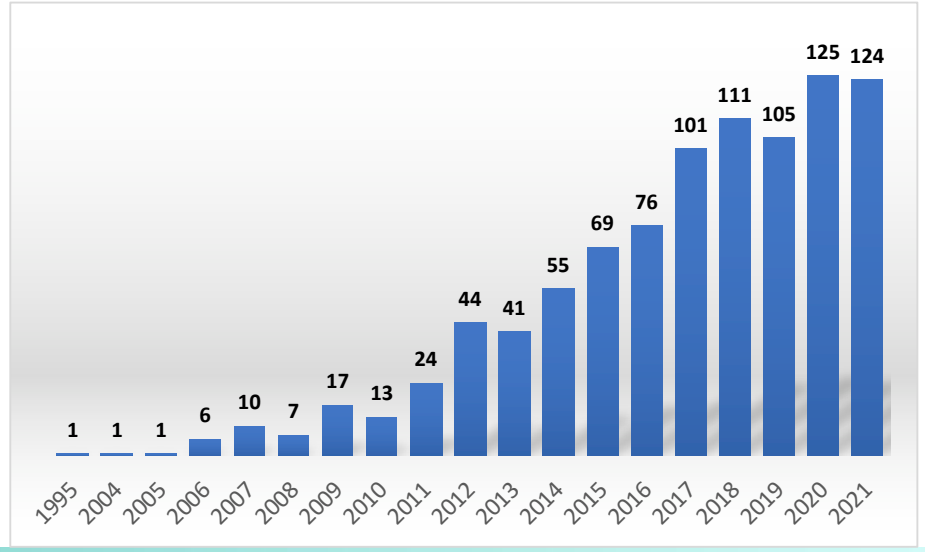
Diet and Microbiome

- As cost of sequencing goes down, more projects will incorporate microbiome analysis



- If we search 'diet AND microbiome' in clinical trials on PubMed.gov, we see an upward trend



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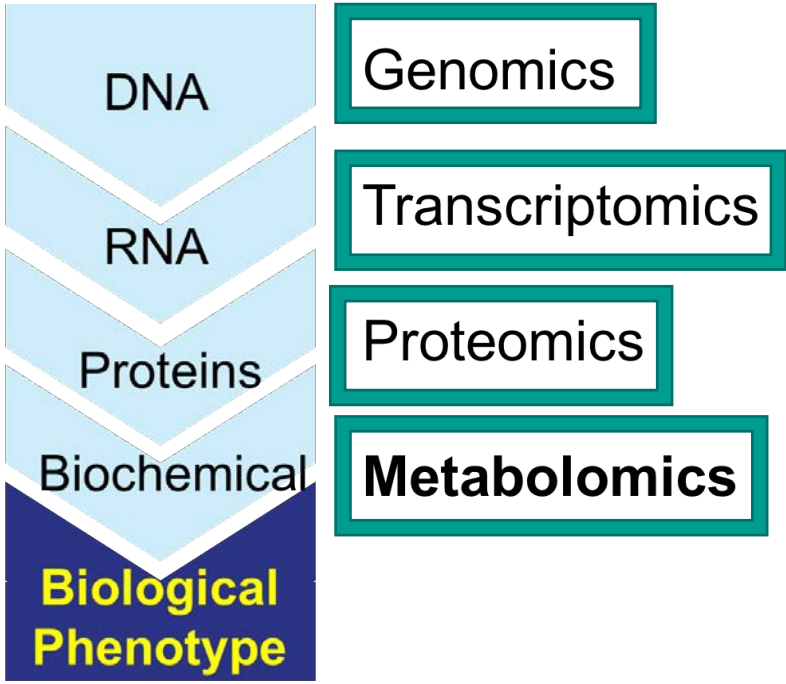
Data generation

Data can be broken down into raw and processed data

- Dietary data
  - Food diaries/Surveys (raw) – Records of what people ate
  - Nutrition composition (processed) – How much protein is there?
- Microbiome data (raw files are large)
  - Metagenomics – What bacteria/genes are there?
  - Metatranscriptomics – What genes are being expressed?
  - Metaproteomics – What proteins are present?
  - Metabolomics – What small molecules are present?
- Health & Lifestyle data
  - Clinical data – Blood biomarkers
  - Wearable – Continuous blood glucose monitor, Sleep monitor



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Data storage/Repositories

- EMBL-EBI
  - European Nucleotide Archive – Raw sequencing read
  - MGnify – Processed Metagenomics
  - MetaboLights – Raw & Processed Metabolomics
  - PRIDE Archive – Proteomics
  - BioSamples – Metadata
- Nutritional Phenotype Database (dbNP)
  - Study and sample metadata – Study design
  - Metabolomic markers – Blood tests etc
- Dietary data
  - Food consumption
  - Nutrient intake data

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Current issues

There is no requirement for depositing data in a public repository

(except sequencing data)

Let's take an example

Personalized Nutrition by Prediction of Glycemic Responses

David Zeevi,[1,2,8] Tal Korem,[1,2,8] Niv Zmora,[3,4,5,8] David Israeli,[6,8] Daphna Rothschild,[1,2] Adina Weinberger,[1,2] Orly Ben-Yacov,[1,2] Dar Lador,[1,2] Tali Avnit-Sagi,[1,2] Maya Lotan-Pompan,[1,2] Jotham Suez,[3] Jemal Ali Mahdi,[3] Elad Matot,[1,2] Gal Malka,[1,2] Noa Kosower,[1,2] Michal Rein,[1,2] Gili Zilberman-Schapira,[3] Lenka Dohnalová,[3] Meirav Pevsner-Fischer,[3] Rony Bikovsky,[1,2] Zamir Halpern,[5,7] Eran Elinav,[3,9,*] and Eran Segal[1,2,9,*]

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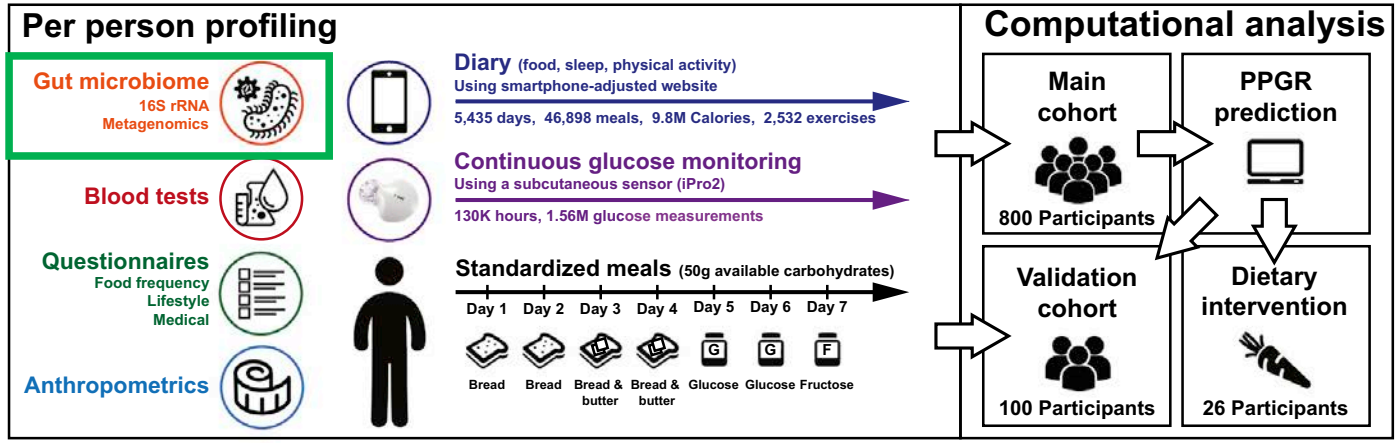
[6]Day Care Unit and the Laboratory of Imaging and Brain Stimulation, Kfar Shaul Hospital, Jerusalem Center for Mental Health, Jerusalem 9106000, Israel
[7]Digestive Center, Tel Aviv Sourasky Medical Center, Tel Aviv 6423906, Israel
[8]Co-first author
[9]Co-senior author
*Correspondence: eran.elinav@weizmann.ac.il (E.E.), eran.segal@weizmann.ac.il (E.S.)
http://dx.doi.org/10.1016/j.cell.2015.11.001



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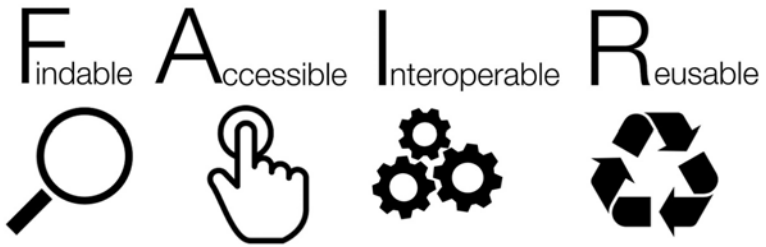
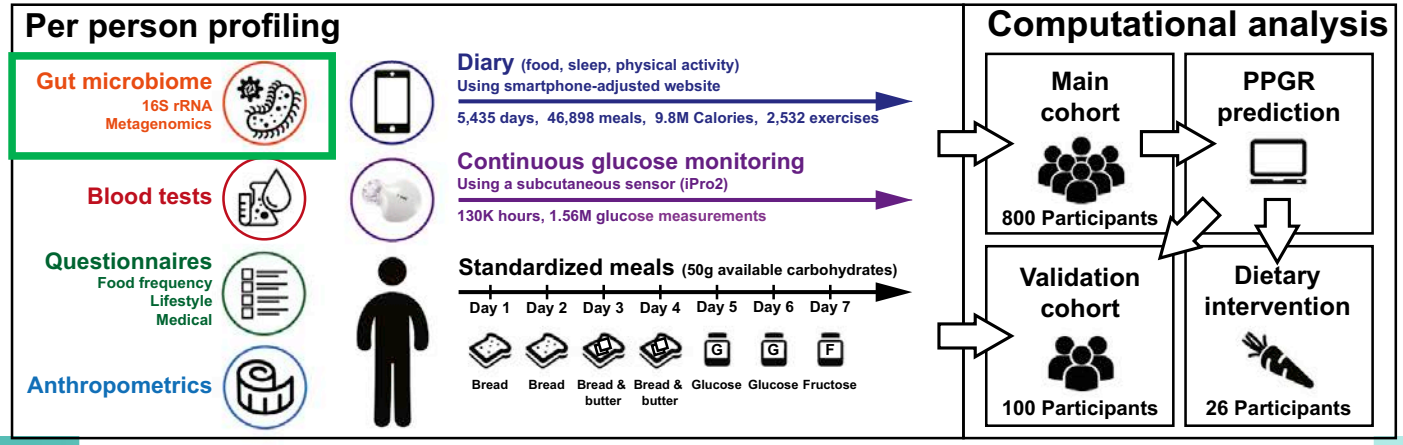
How FAIR is it?



- **Findable**
  - We can find the metagenomic reads
  - No mention of other datasets
- **Accessible**
  - We can retrieve metagenomics reads
- **Interoperable**
  - Only interoperable after getting feature tables
- **Reusable**
  - No metadata provided
  - Can only analyse metagenomic profiles



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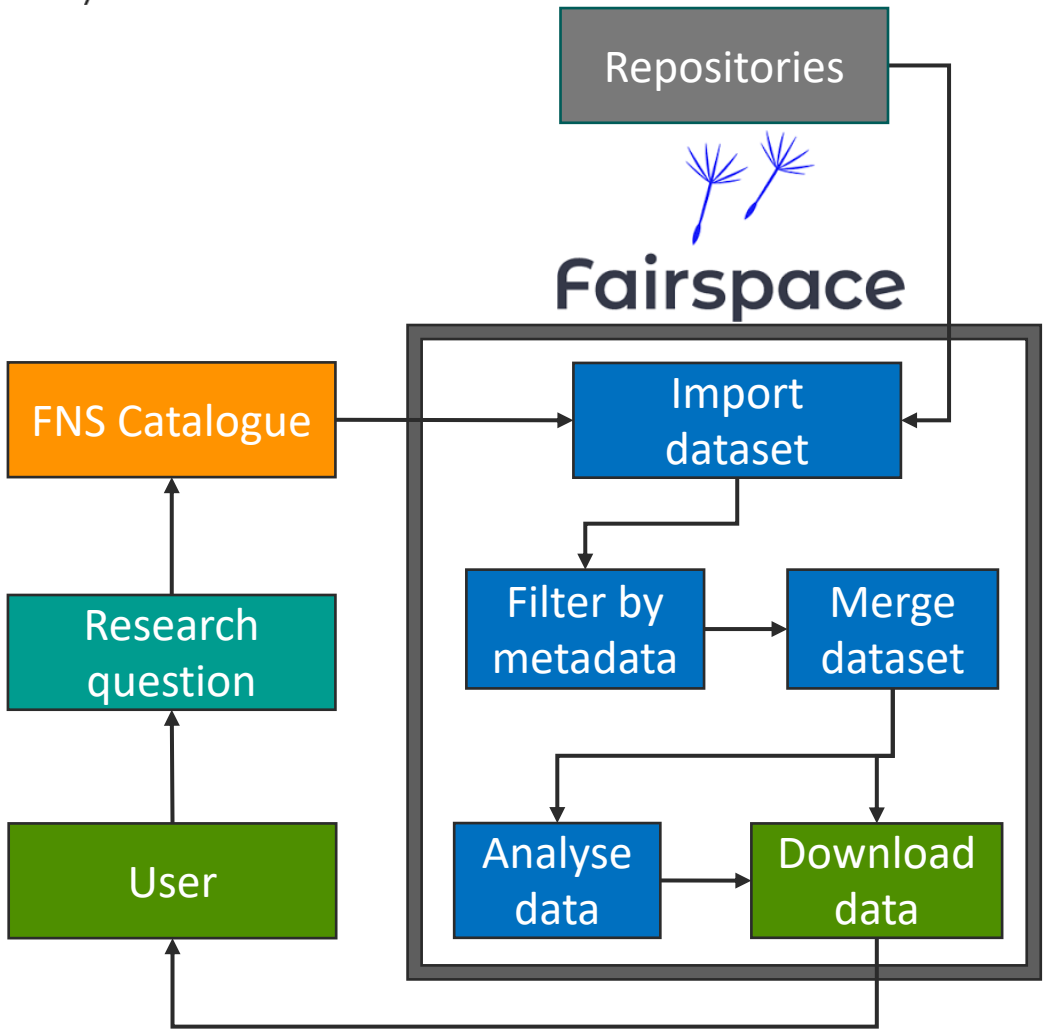
FNS - Cloud
Food Nutrition Security

- FNS-Cloud aims to make the food & nutrition data FAIR
- How we envision it
  1. User has research question
  2. User finds relevant studies in FNS Catalogue
  3. Studies of interest are transferred into FAIRSPACE
  4. FAIRSPACE will pull data from repositories and link different datasets on a sample level
  5. FAIRSPACE will allow for filtering based on available metadata
  6. User can choose to analyse the data prior to downloading it for further analysis



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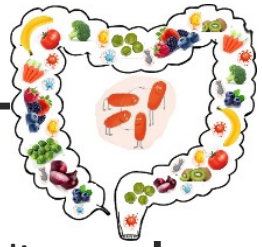
DIME Study: *D*ietary B*I*oactives and *M*icrobiome Div*E*rsity

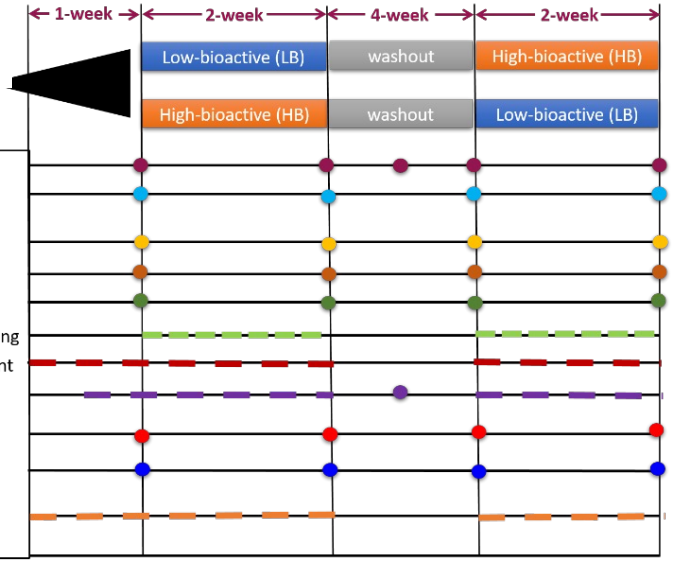
FNS-Cloud
Food Nutrition Security



Objectives:

- ❖ Does a diverse diet rich in plant bioactive compounds lead to a diverse gut microbiome?
- ❖ Does our microbiome influence our metabolic response to food?

N=20



Outcome measures

- Gut microbiota profiling
- Urine metabolomics
- Anthropometric tests (blood pressure, BMI, etc)
- Blood tests (lipids etc)
- Oral GTT and insulin
- Continuous glucose monitoring
- App-based dietary assessment
- Recording of stool form and frequency
- Assessment of GI transit
- Assessment of stress and mood
- Assessment of activity levels and sleep

DATA

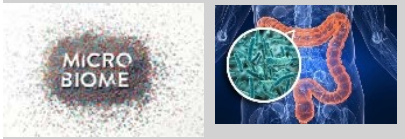
Food & Nutrition

Diet app tool development –wearables integration (sleep, CGM)

Biomarker & Anthropometric

Weight, age, inflammation, HbA1c, TGs, hip/waist), etc.

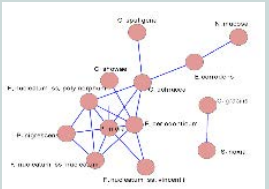
Microbiome

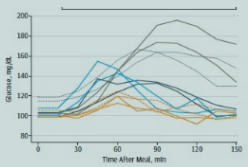


Whole genome sequencing bacterial community composition and function

TOOLS

Bioinformatics tools on **metagenomics** and **metabolomics** integration

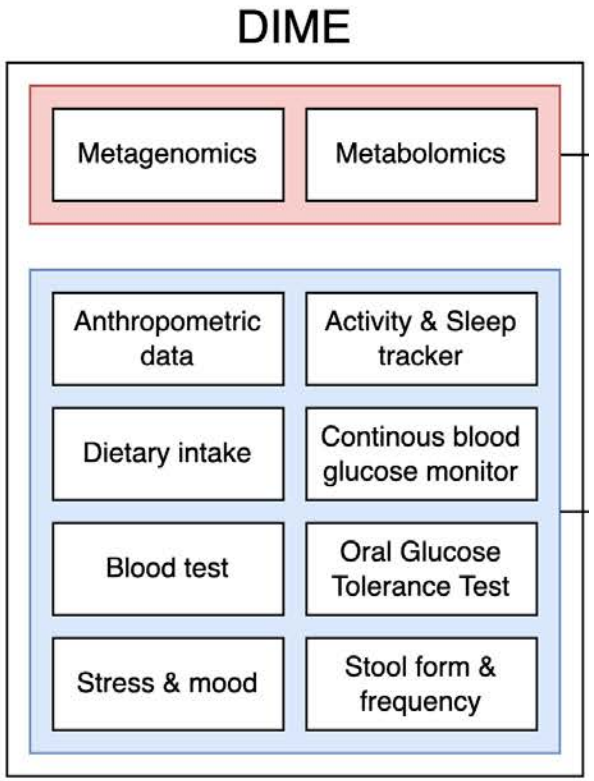




Machine learning dynamic algorithms for metabolic response to foods using microbiome

How will DIME help?

Link samples by BioSamples (generated by ENA)



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Demonstrator Use Cases

RESEARCH QUESTION 1: Does a diet rich in plant bioactives affect our gut microbiome, and how?

- demonstrate user pathway
- the metagenomics and metabolomics datasets and bioinformatic analytical pipelines (handling emerging metagenomics datasets for higher resolution microbial analysis e.g. long-read sequencing)

RESEARCH QUESTION 2: Does our baseline gut microbiome define how species composition shifts upon dietary interventions? Does dietary intervention lead to a similar reduction in strain persistence in independent cohorts?

- Finding, accessing and merging datasets from different diet & microbiome studies

RESEARCH QUESTION 3: Does our gut microbiome contribute to our metabolic response to foods? Can we predict metabolic responses to foods using microbiome data?

- How a user can access community-generated tools through FAIRSPACE (e.g. machine-learning classification tool for microbiome datasets)

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In summary…

- A lot of Diet & Microbiome studies are not FAIR
- FNS-Cloud attempts to solve this issue
- FNS catalogue will show well curated food & nutrition studies
- FAIRSPACE will fetch the data, filter, merge, and analyse the data
- DIME study will test the FNS-Cloud infrastructure through the microbiome demonstrator

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Acknowledgements

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- Duygu Dede Sener

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