MULTI-OMICS INTEGRATION

Rossella Alfano

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MDAW workshop: multi-domain data integration

21st April 2021

Outline

- **The multi-omics era**
- Methods
- Example 1
- Example 2
- The microbiome and the multi-omics

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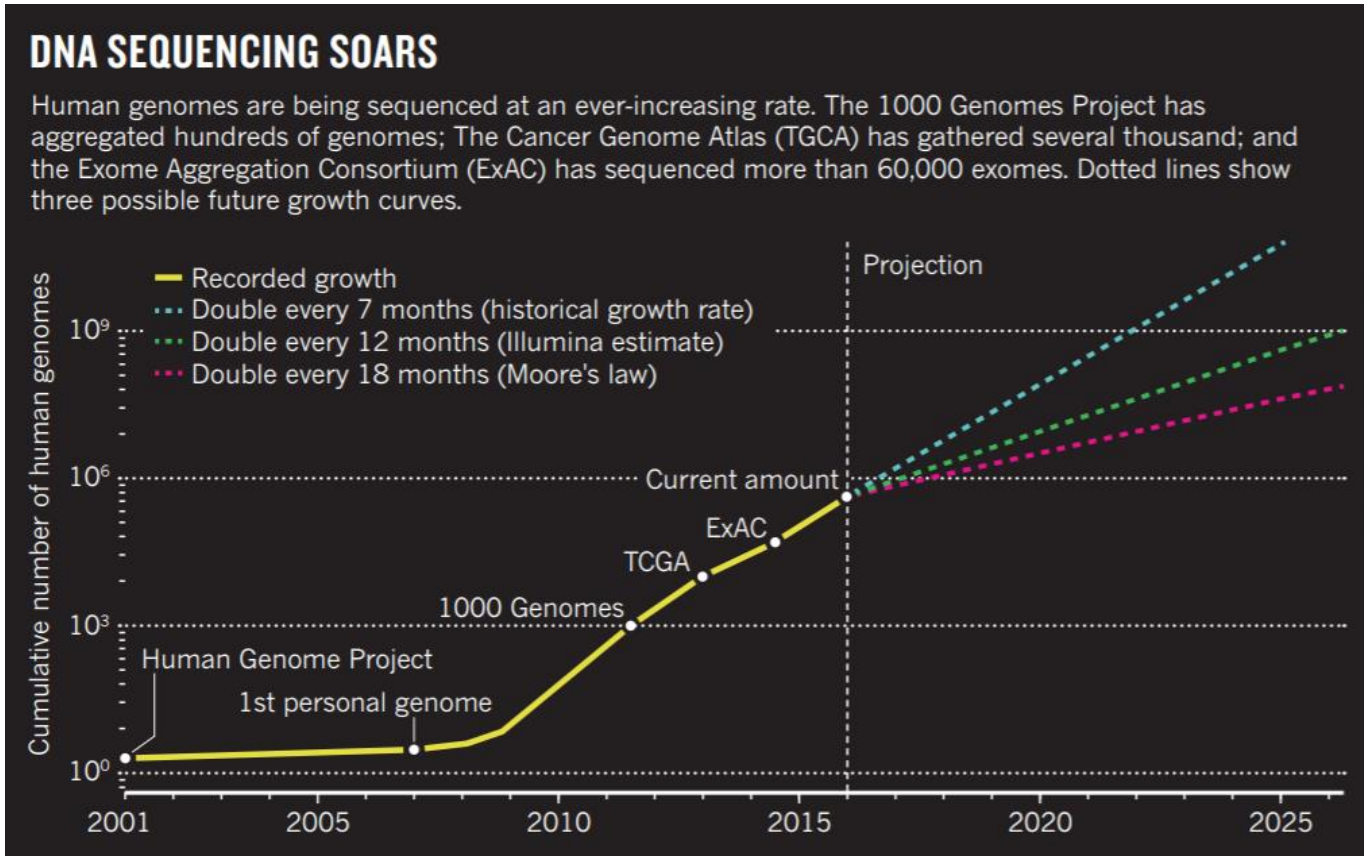
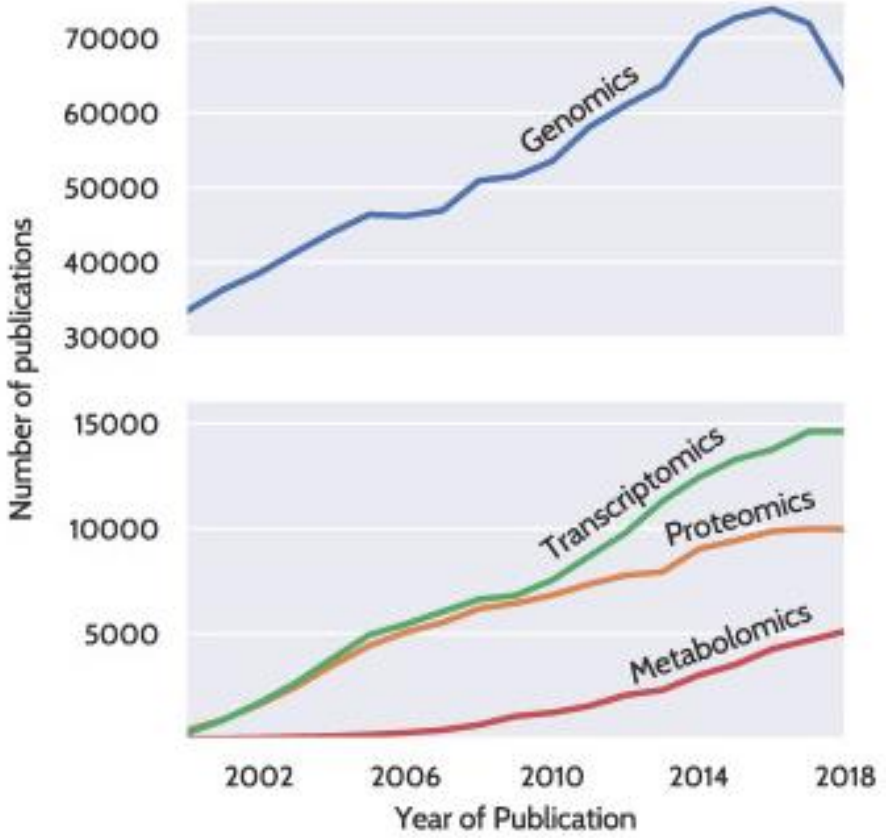
Big data





Eisenstein, Nature 2015; Noor et al, Curr Opinion Syst Biol 2019

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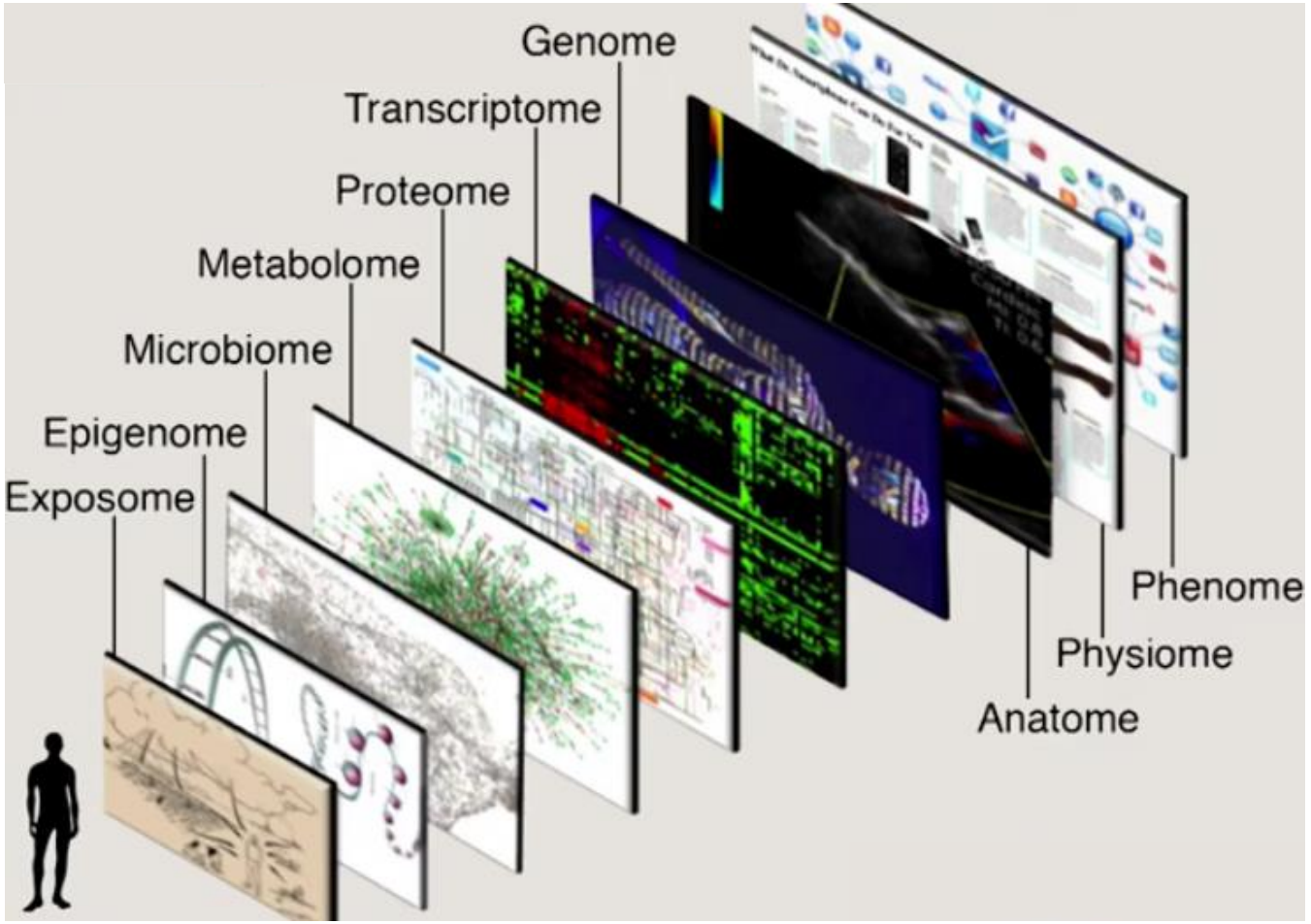
The human GIS



Topol, Cell 2014

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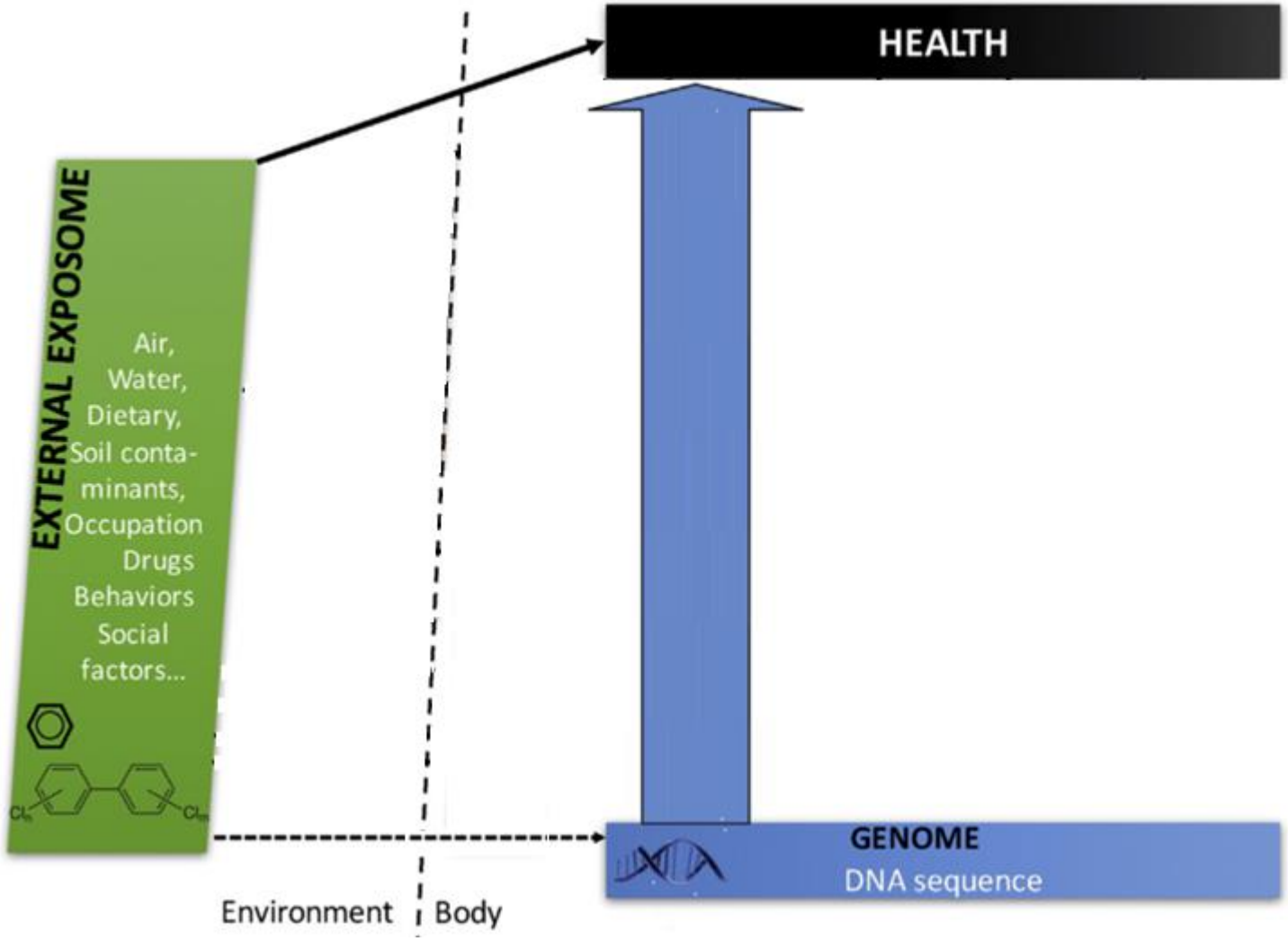
Omics



Siroux et al, Eur Respir Rev 2016

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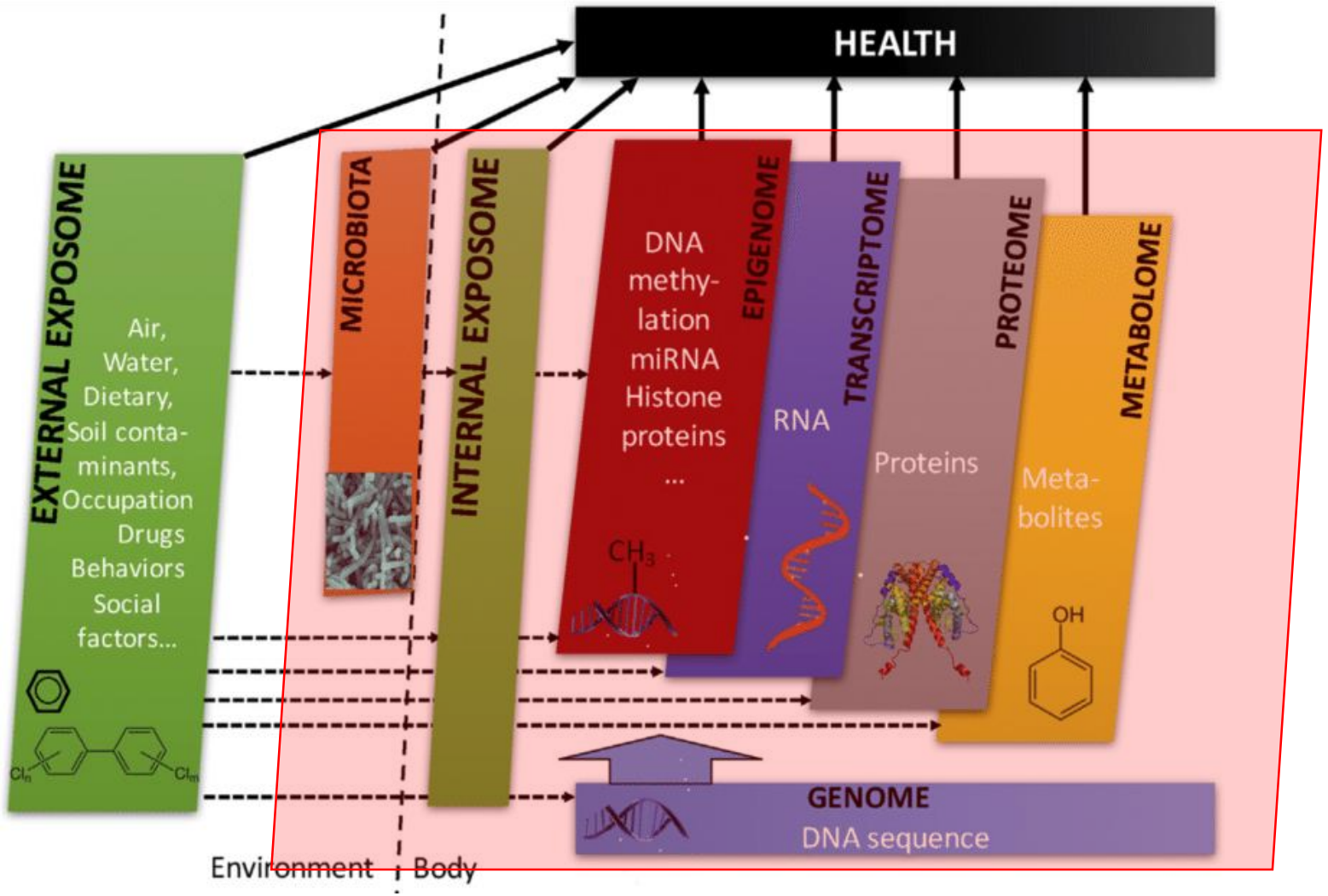
Omics



Siroux et al, Eur Respir Rev 2016

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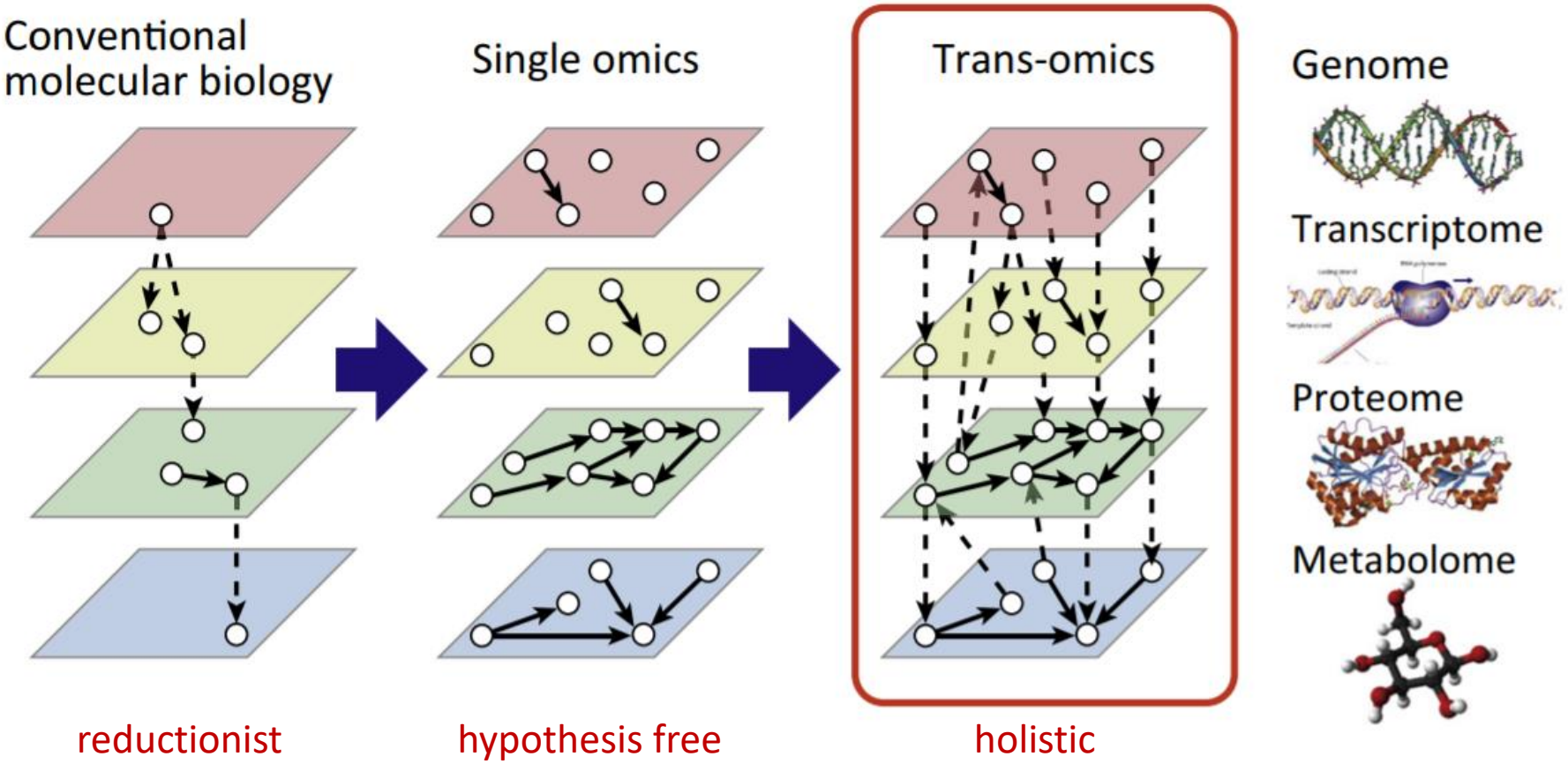
Conventional biology vs multi-omics



Yugi et al, Trends Biotechnol 2016

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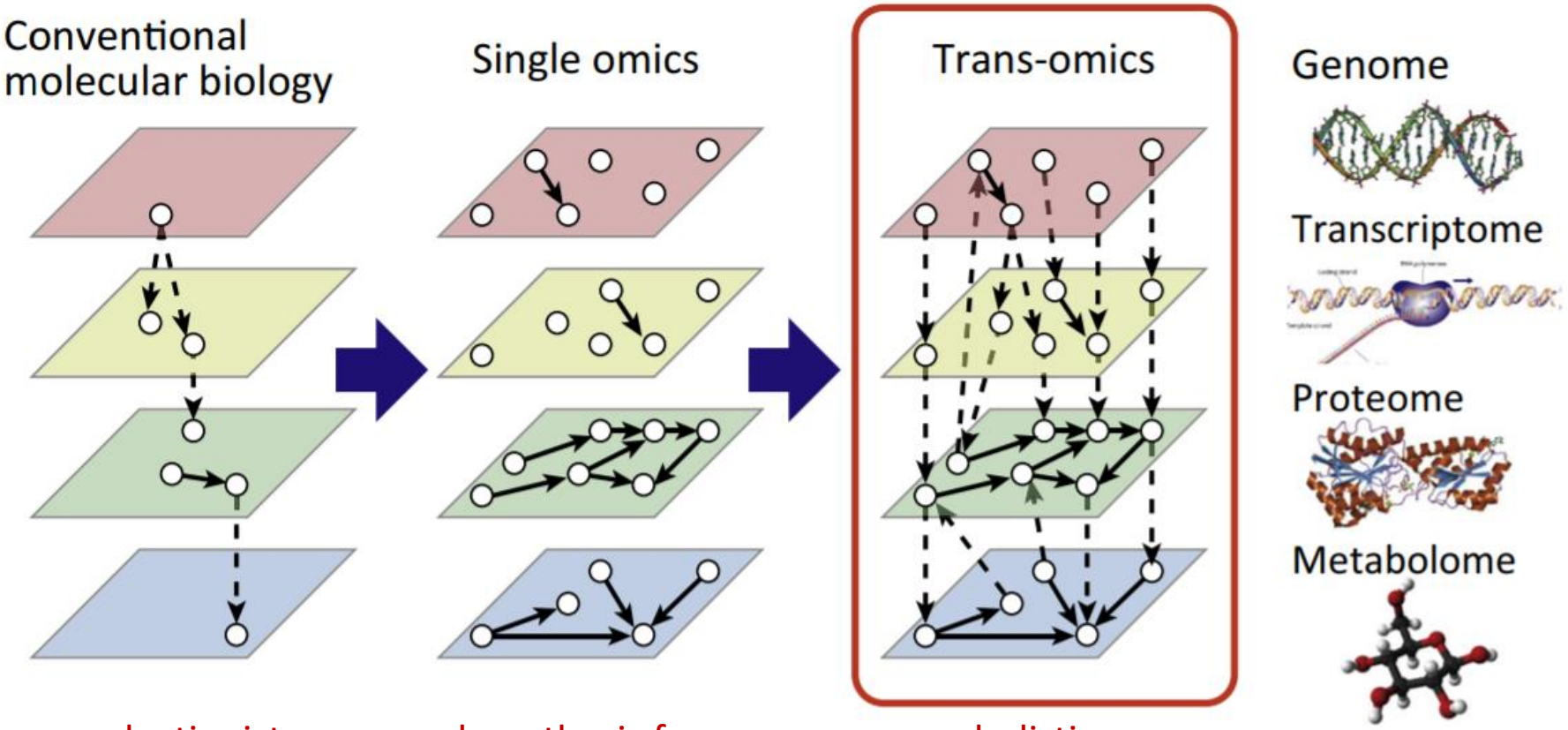
Conventional biology vs multi-omics



Yugi et al, Trends Biotechnol 2016

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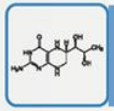
Omics integration challenges

- Data collected from different sources and **techniques**
- **Biological** heterogeneity
- High data **dimensionality**:
  - Small sample size (N<p)
  - Data dimensionality different by omic type
- **Missing values**
- **Methods** for integrative analyses

	Supporting Structure	Platforms (log_{10} order of magnitude)	Features
	DNA	Microarrays (6) Sequencing (9)	Categorical data Distance-driven correlation Extremely stable over time
	DNA methylation Histone modifications Non-coding RNA	Microarrays (5) Bisulfite sequencing (1)	Continuous data Affected by time and exposures (with reduced plasticity)
	mRNA	Microarrays (5) RNA sequencing (9)	Continuous data Affected by time and exposures Strong measurement noise
	Proteins	Microarrays (5) Mass spectrometry (5)	Continuous data Affected by time and exposures
	Small molecules	Mass spectrometry (5) NMR spectroscopy (4)	Continuous data Structured correlation Strongly affected by exposures

Chadeau-Hyam et al, in Dagnino et al, Unraveling the Exposome, 2018

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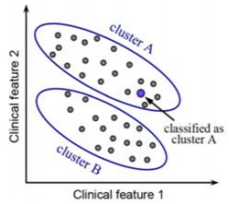
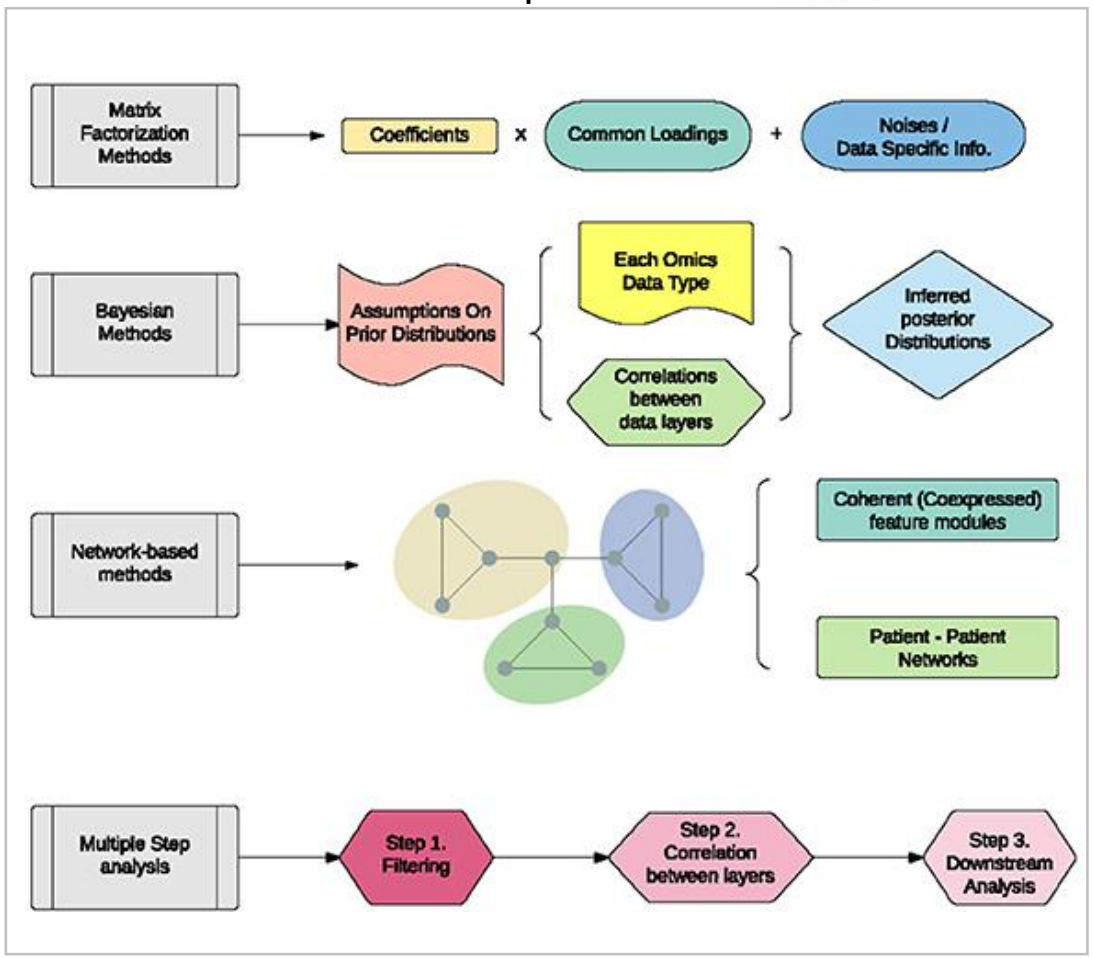
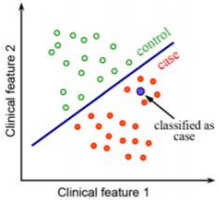
Methods

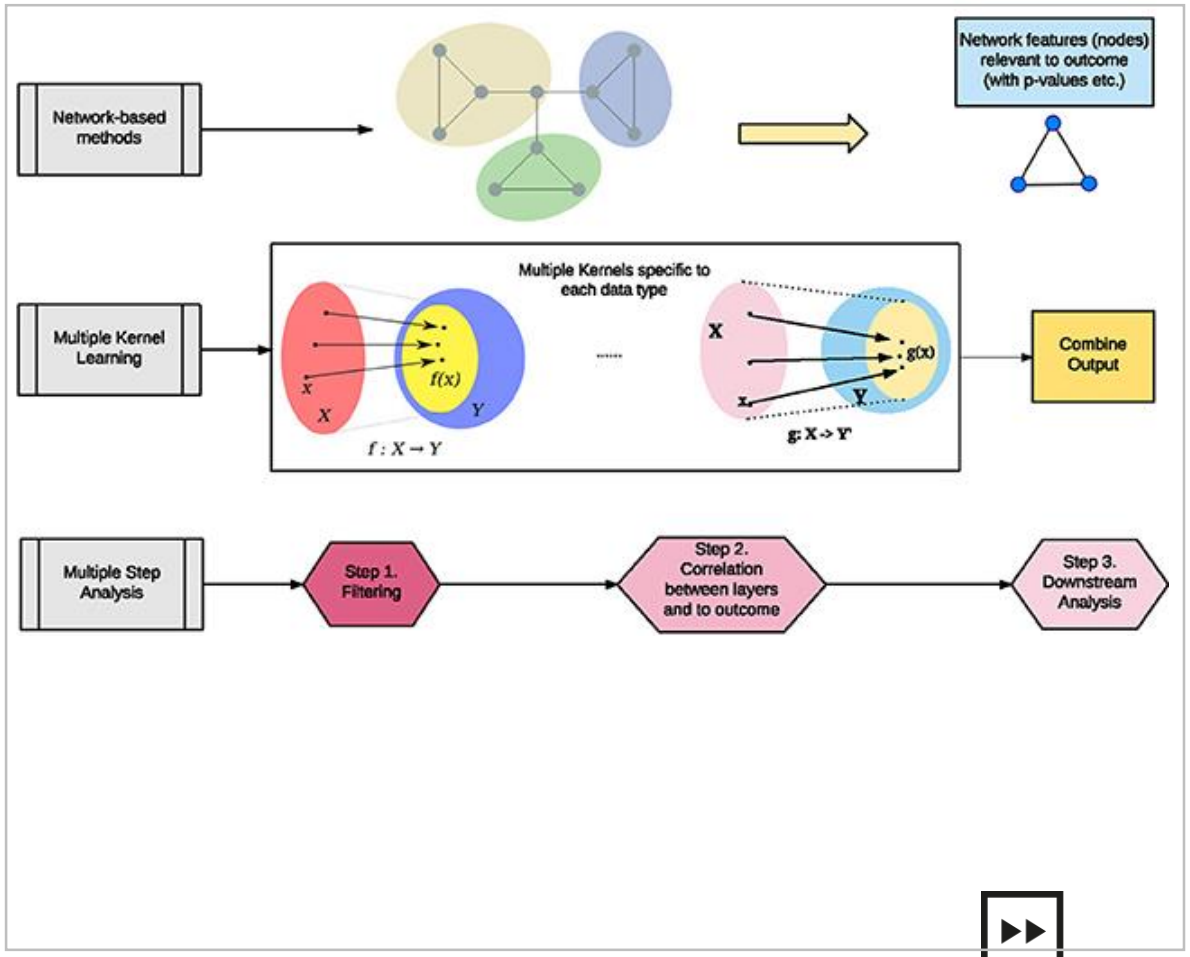
Unsupervised





Supervised





Huang et al, Front Genet 2017

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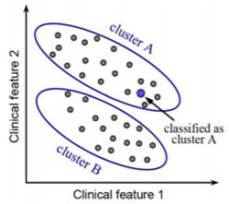
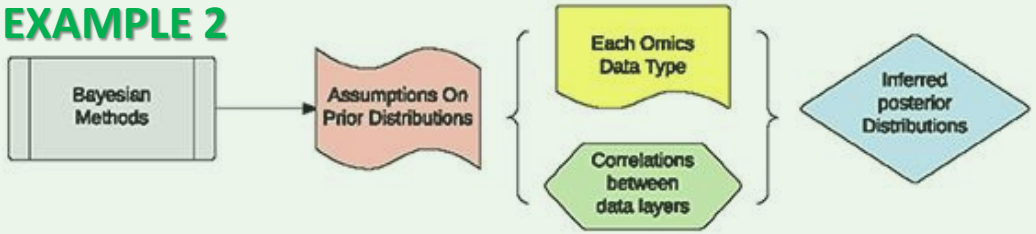
Methods

Unsupervised



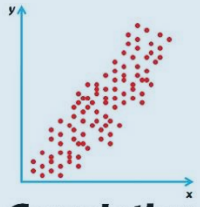
EXAMPLE 2



MOFA

Multi-Omics Factor Analysis V2 (MOFA+)

EXAMPLE 1



Huang et al, Front Genet 2017

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stop

Science and Technology in childhood Obesity Policy

MULTI-OMICS ANALYSIS OF BIRTHWEIGHT

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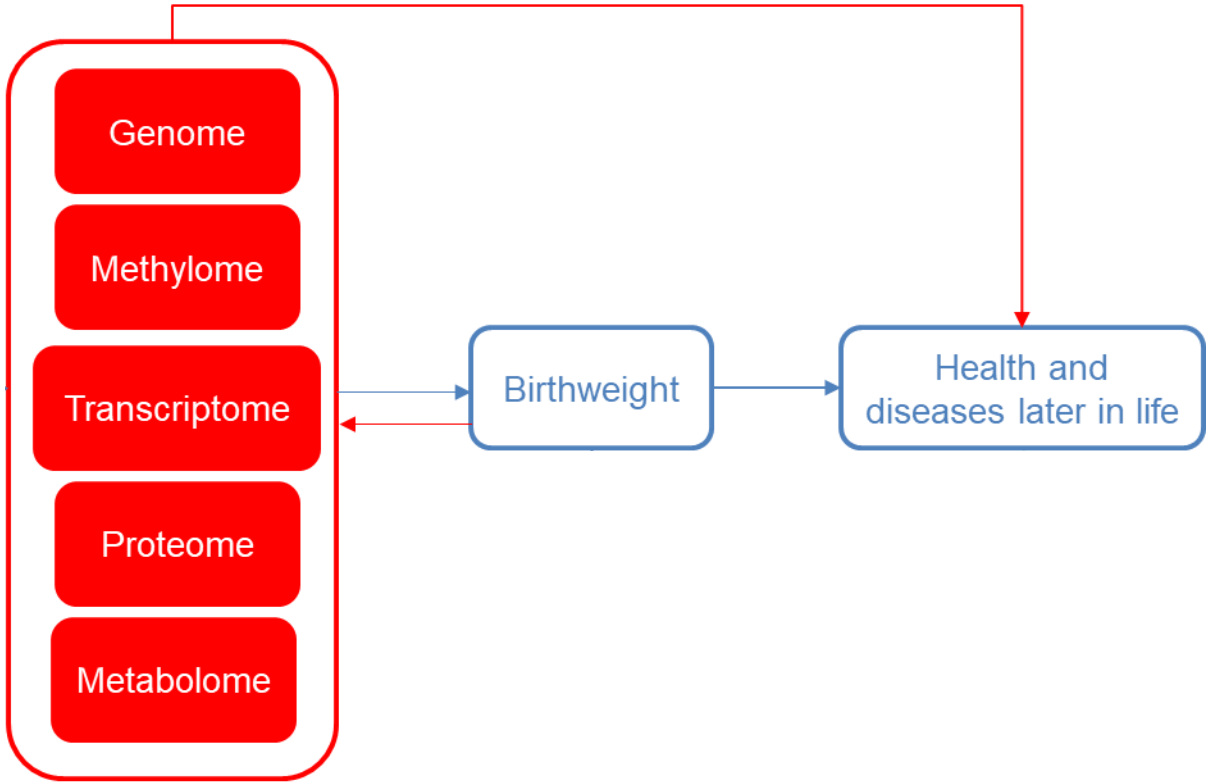
Birthweight



Alfano et al, Metabolism 2020

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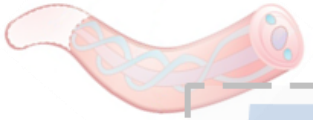
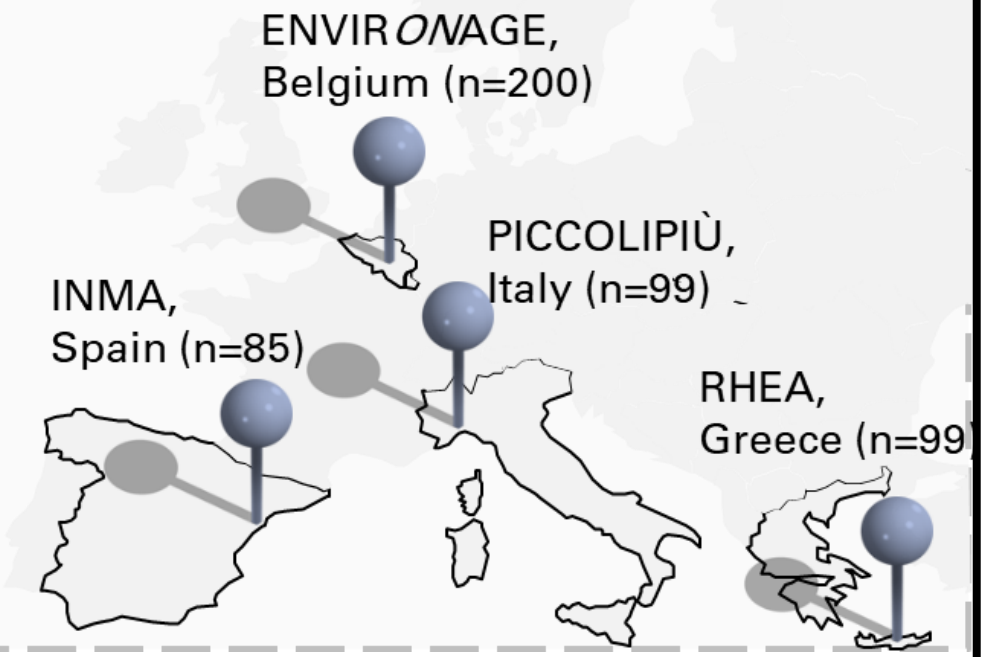
Population and samples



Cord blood

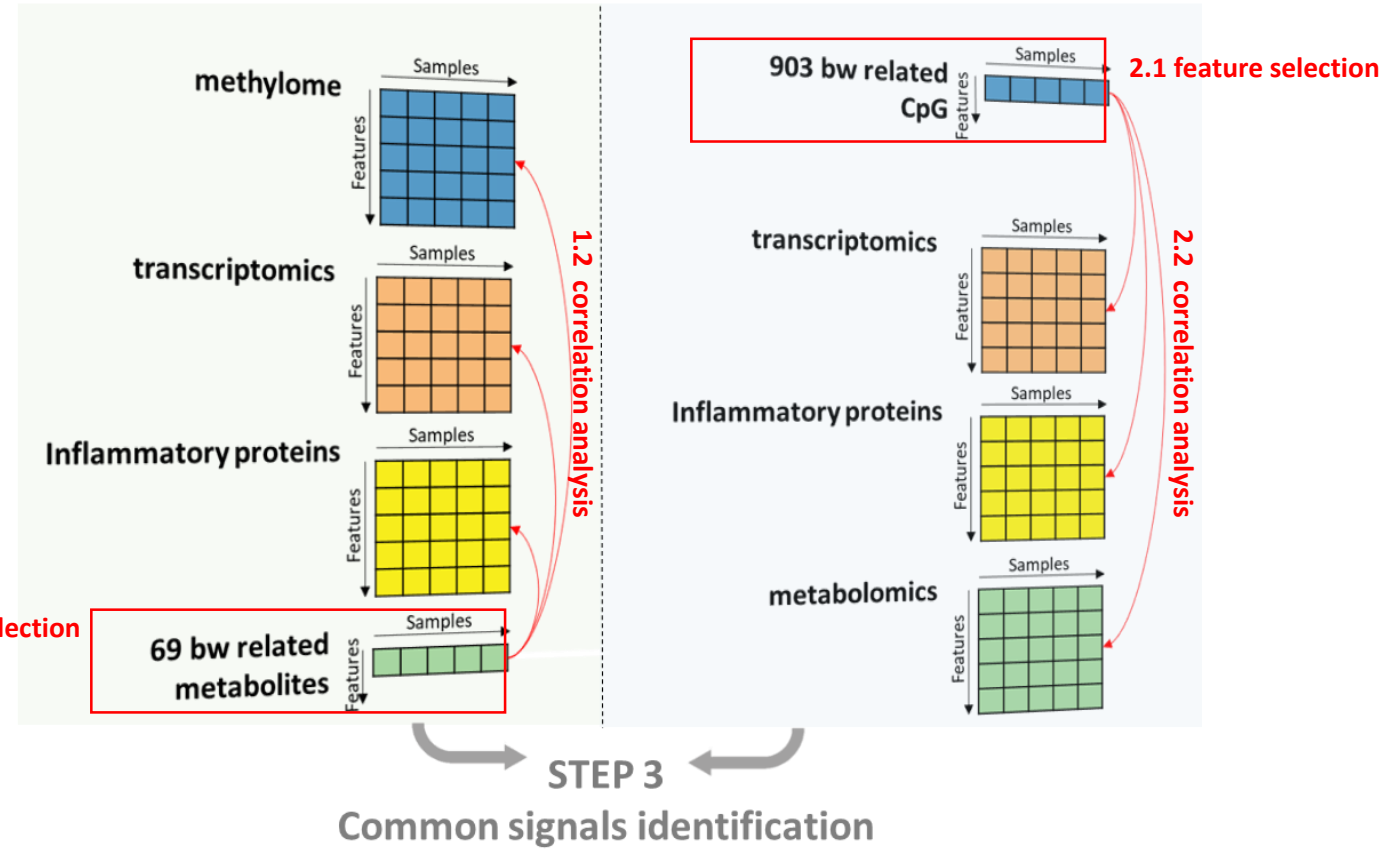
Methylome	485,577 CpGs
Transcriptome	29,164 Transcripts (ENVIR*ON*AGE only)
Inflammatory proteins	16 Inflammatory proteins
Metabolome	4,712 Metabolites

4 EXPOsOMICS birth cohorts (n=483)



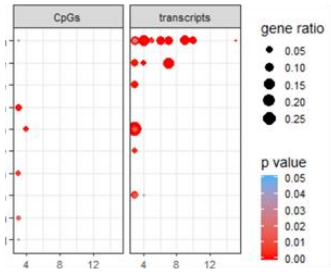
Multi-step method

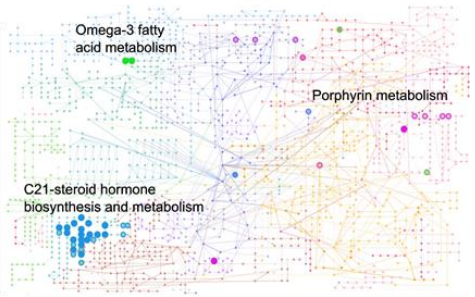
Model overview



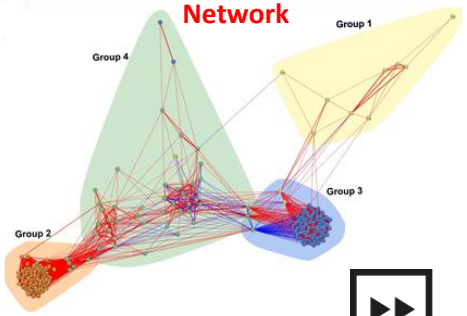
Downstream analyses

Pathways





Network



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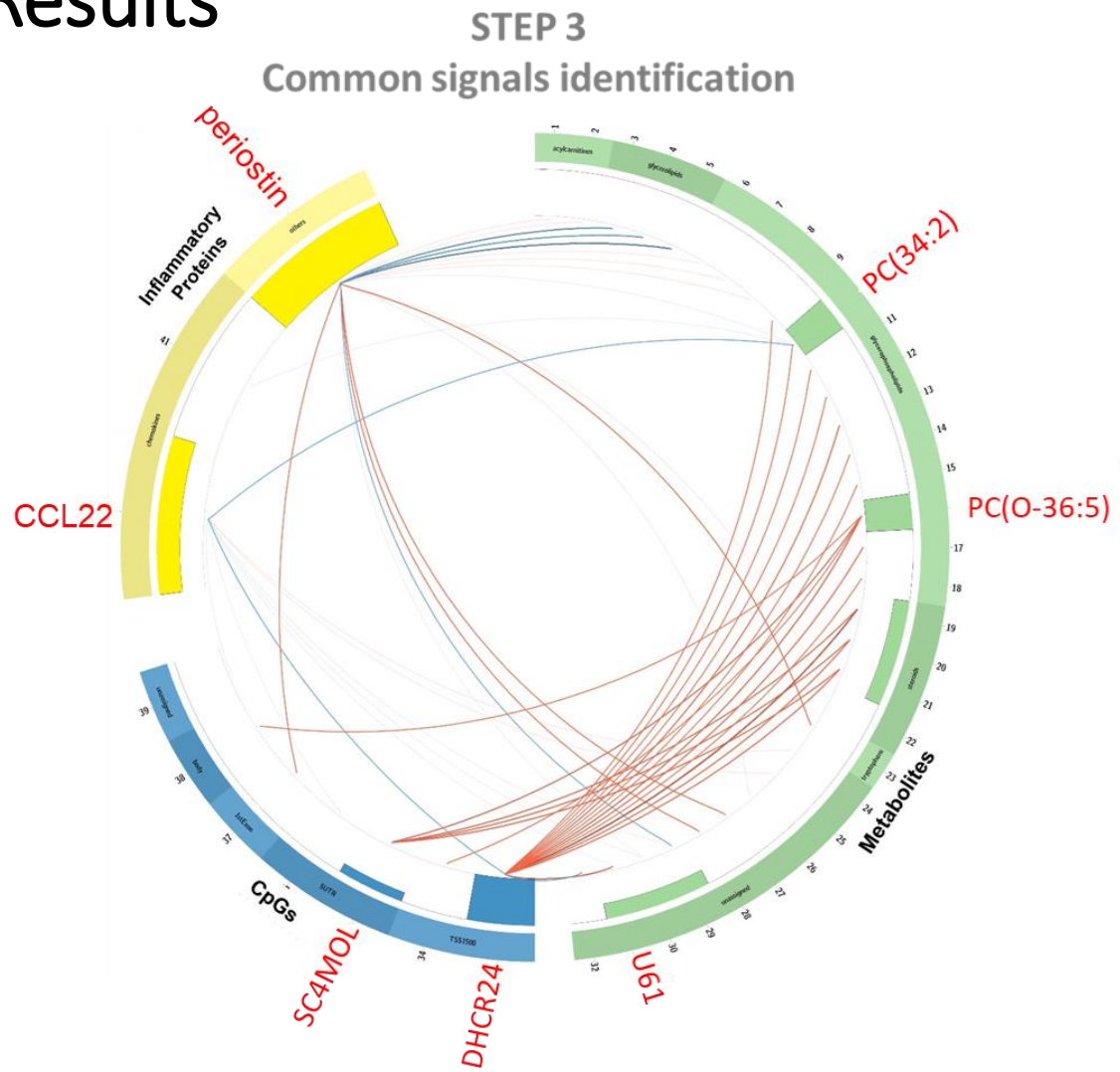
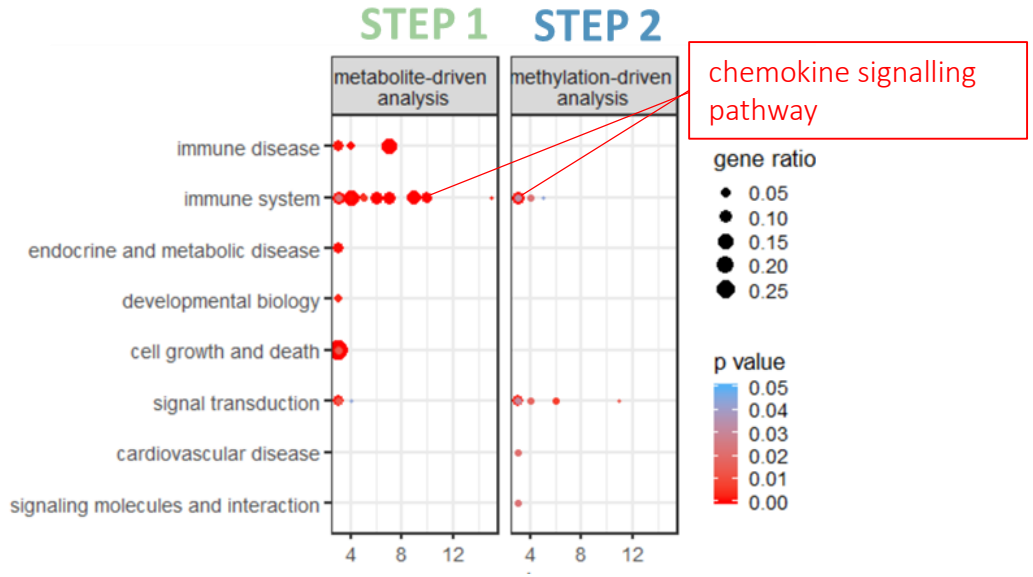
Results





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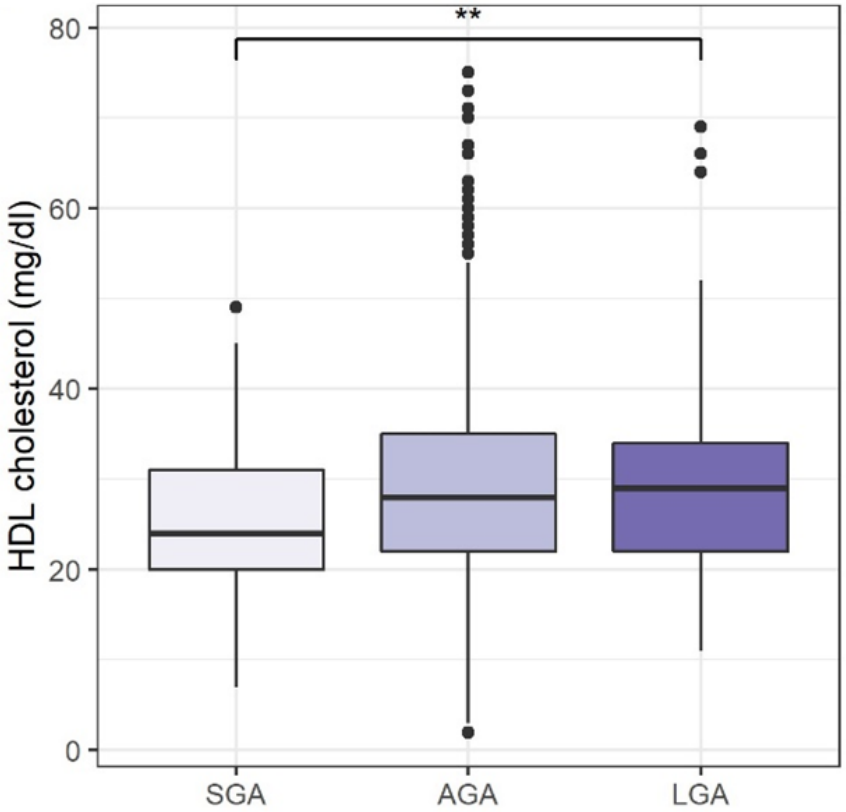

N=1097 newborns

LIMBURGS ENVIRONAGE GEBOORTECOHORT
Wij volgen je stap na stap!

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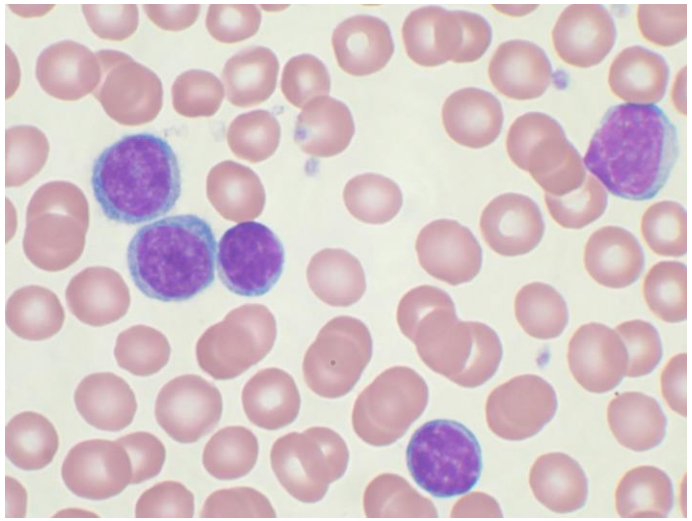

Multi-Omics Factor Analysis (MOFA) of chronic lymphocytic leukemia

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Chronic lymphocytic leukemia study

Study of chronic lymphocytic leukaemia (CLL), which combined:

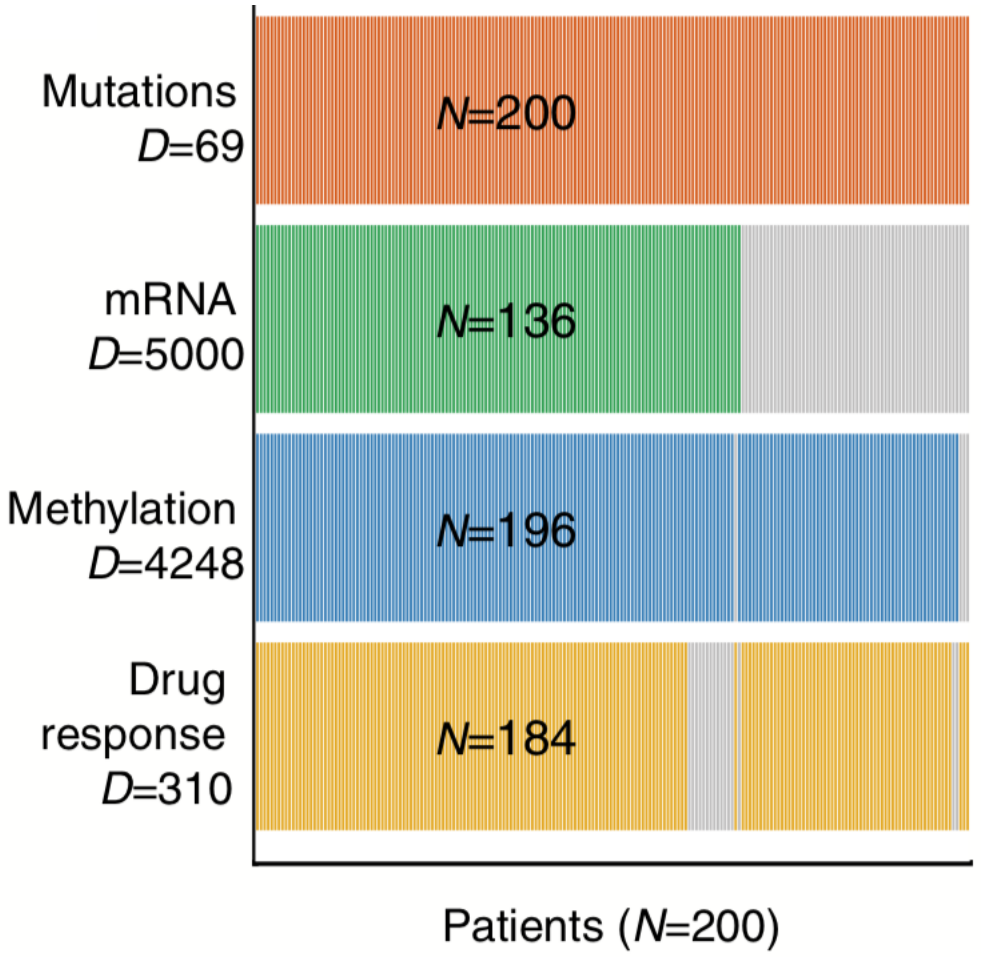
-somatic mutation status

-transcriptome profiling

-DNA methylation assays

-*ex vivo* drug response measurements

Nearly 40% of the 200 samples were profiled with some but not all omics types



Argelaguet et al, Mol Syst Biol 2018

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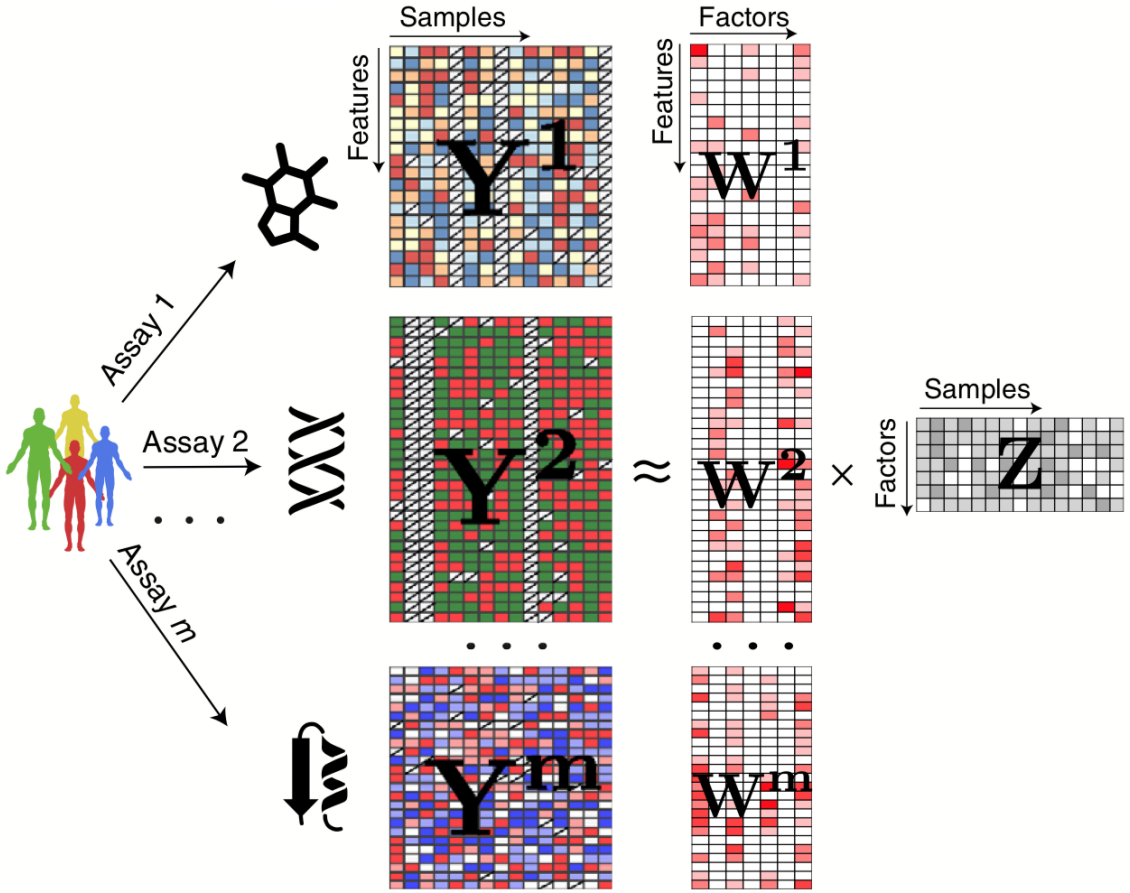
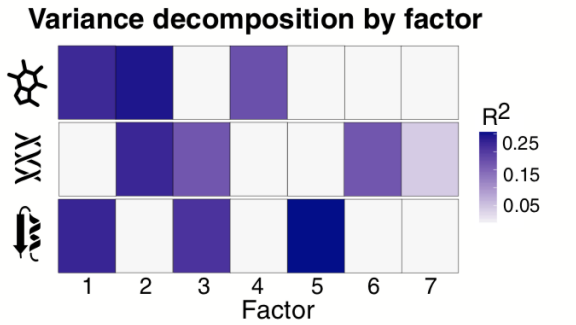
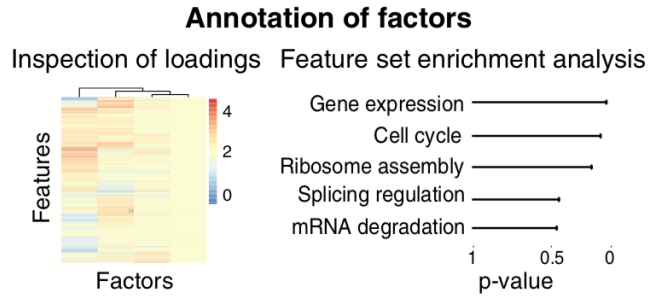
MOFA method

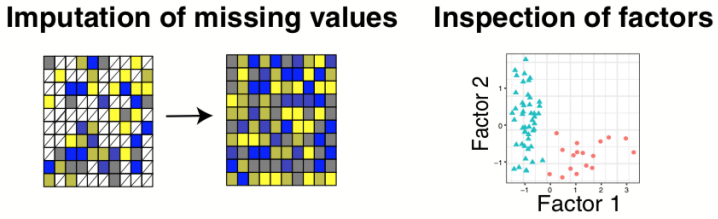
Model overview



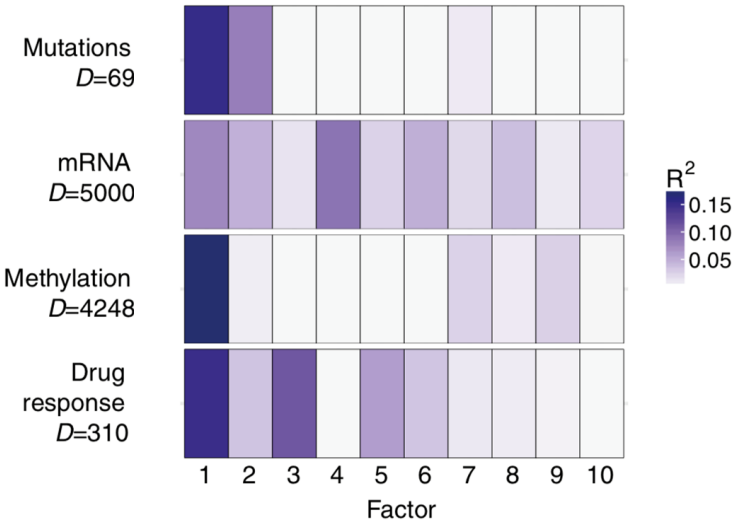
Downstream analyses

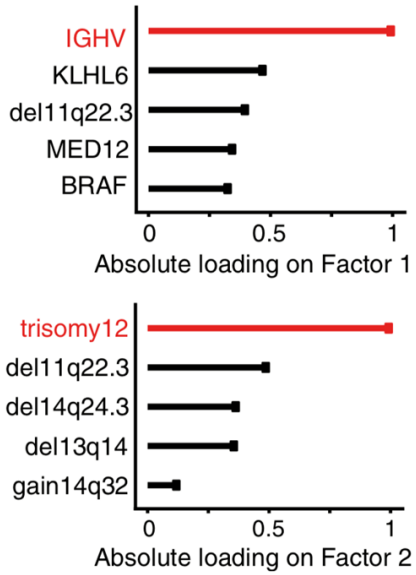


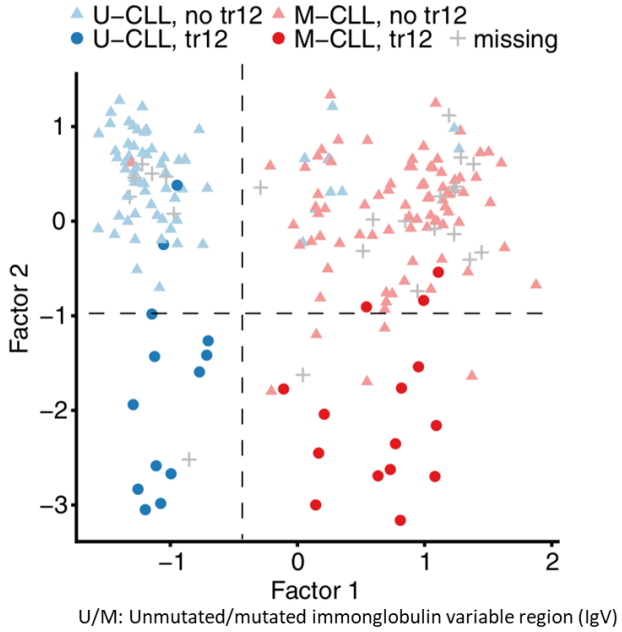




Results







U/M: Unmutated/mutated immonglobulin variable region (IgV)

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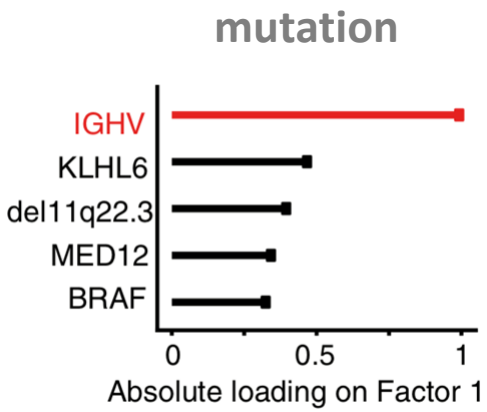
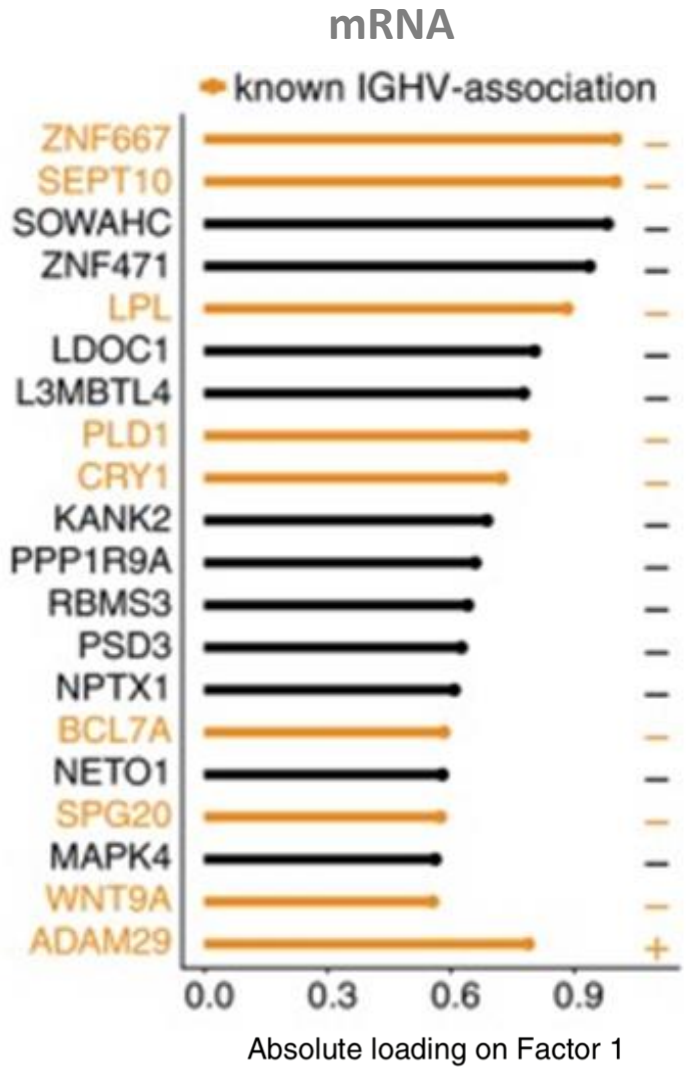
Results


mutation
IGHV
KLHL6
del11q22.3
MED12
BRAF
0
0.5
1
Absolute loading on Factor 1


mRNA
known IGHV-association
ZNF667
SEPT10
SOWAHC
ZNF471
LPL
LDOC1
L3MBTL4
PLD1
CRY1
KANK2
PPP1R9A
RBMS3
PSD3
NPTX1
BCL7A
NETO1
SPG20
MAPK4
WNT9A
ADAM29
0.0
0.3
0.6
0.9
Absolute loading on Factor 1

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- Examples
- **The microbiome and the multi-omics**

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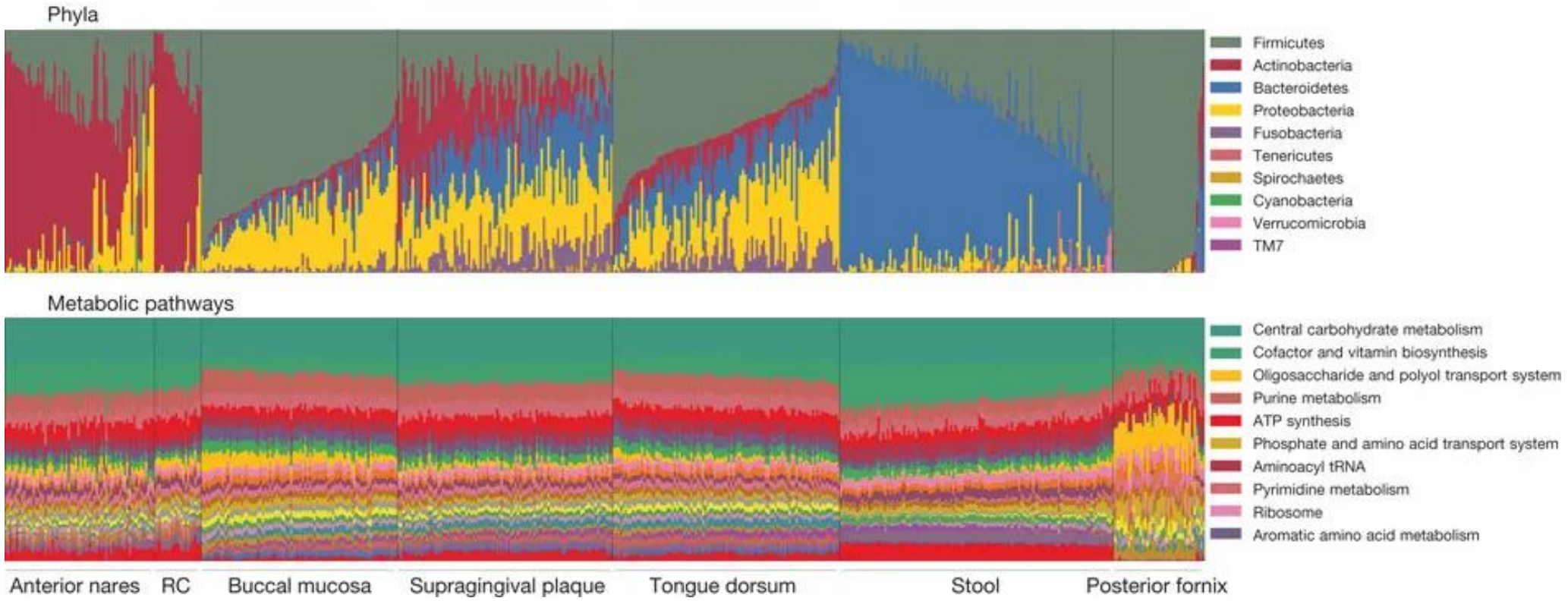
Why 16s rRNA is not enough?



Carriage of microbial taxa varies while metabolic pathways remain stable within a healthy population

Huttenhower et al, Nature 2012

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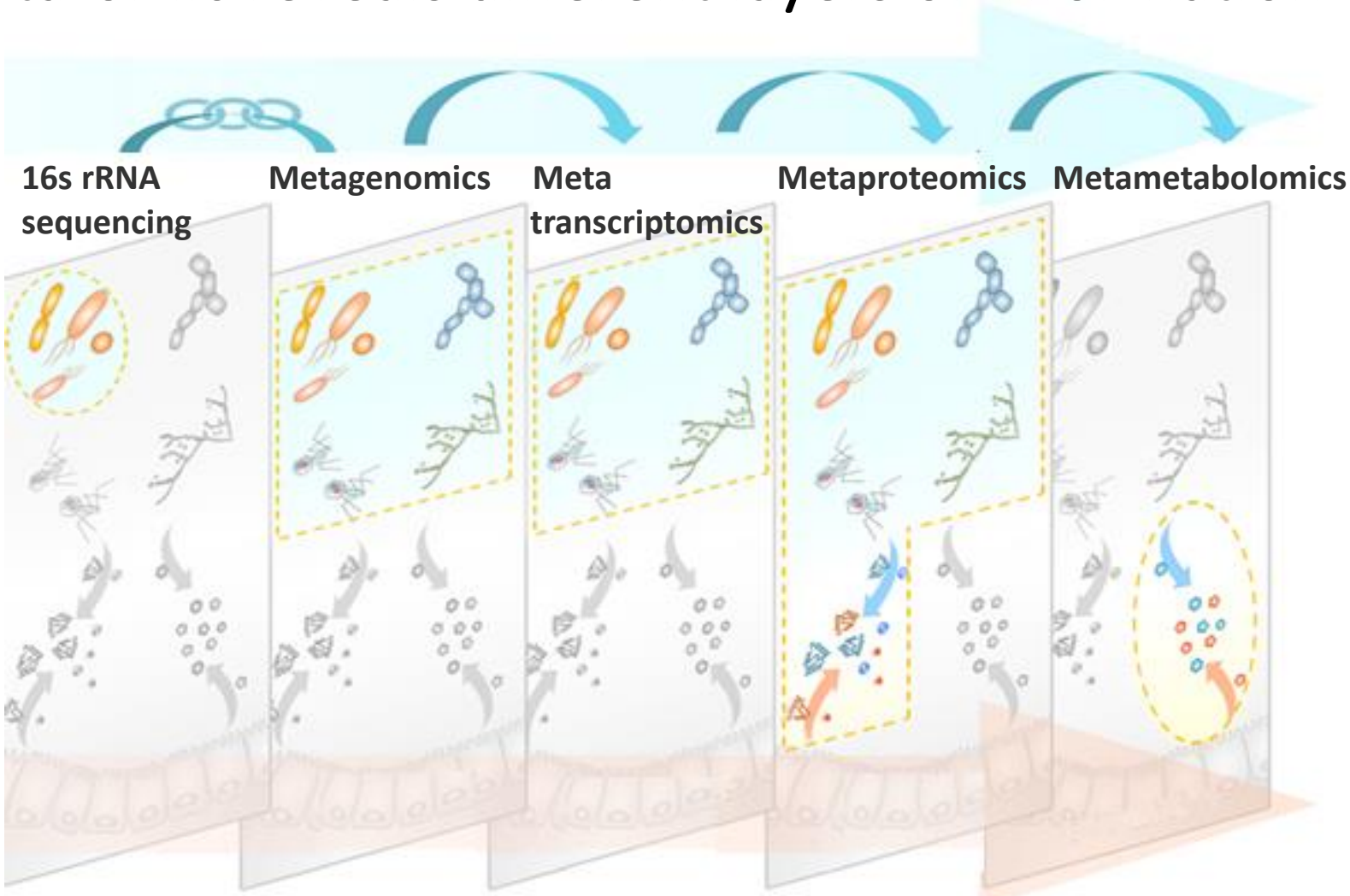
Each meta-omic reveals different layers of information



Zhang et al, Microbiome 2019

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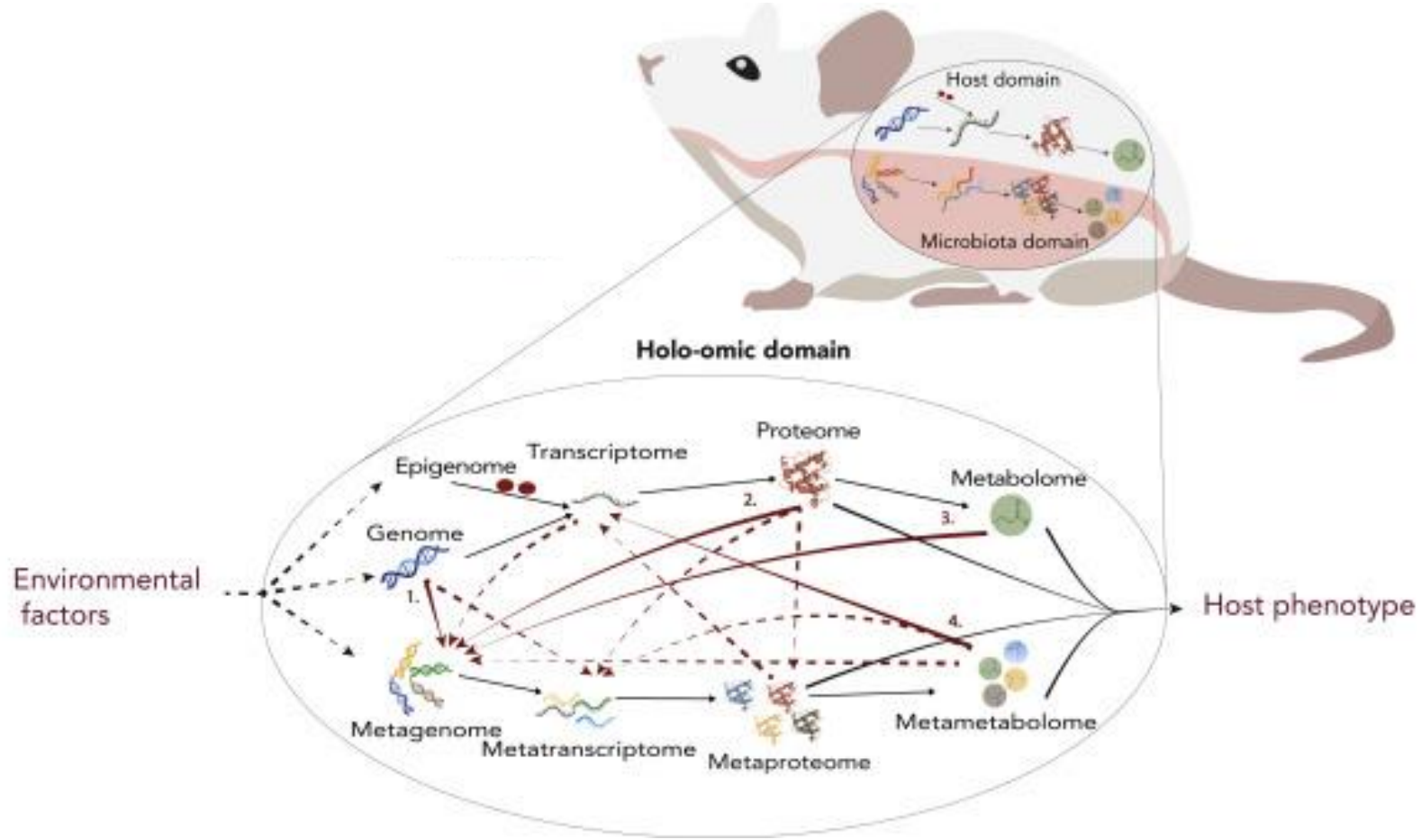
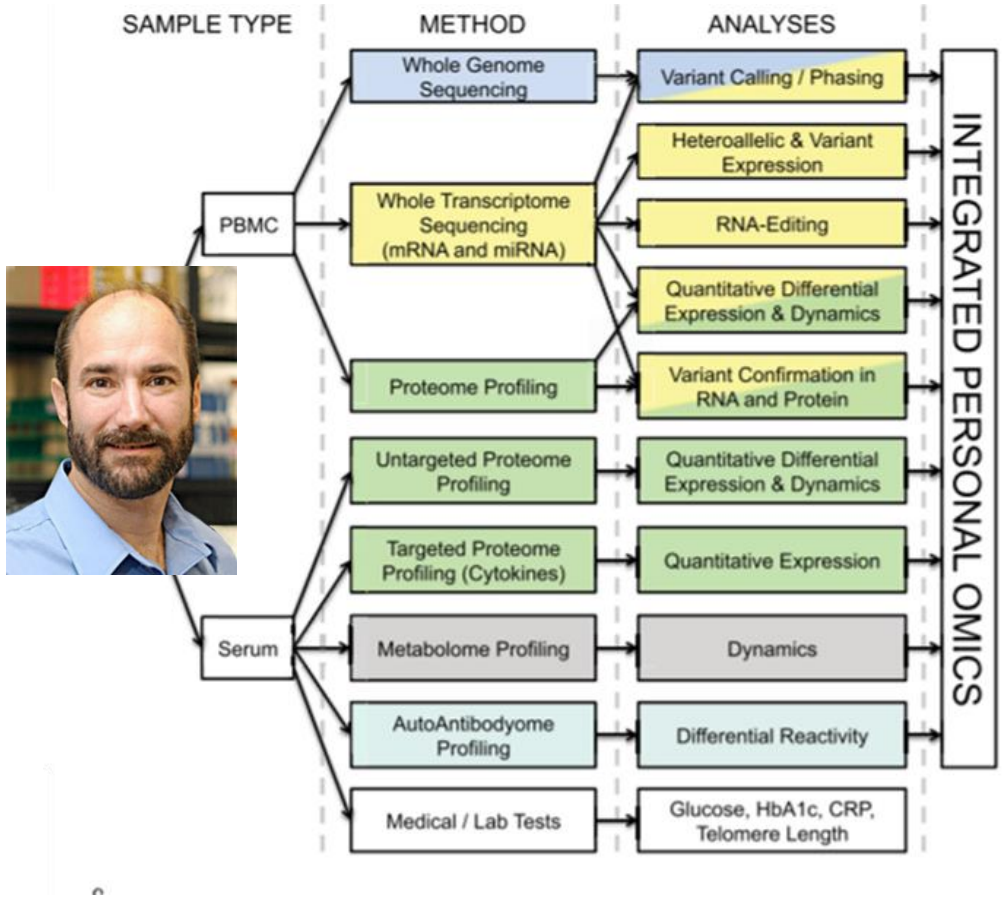
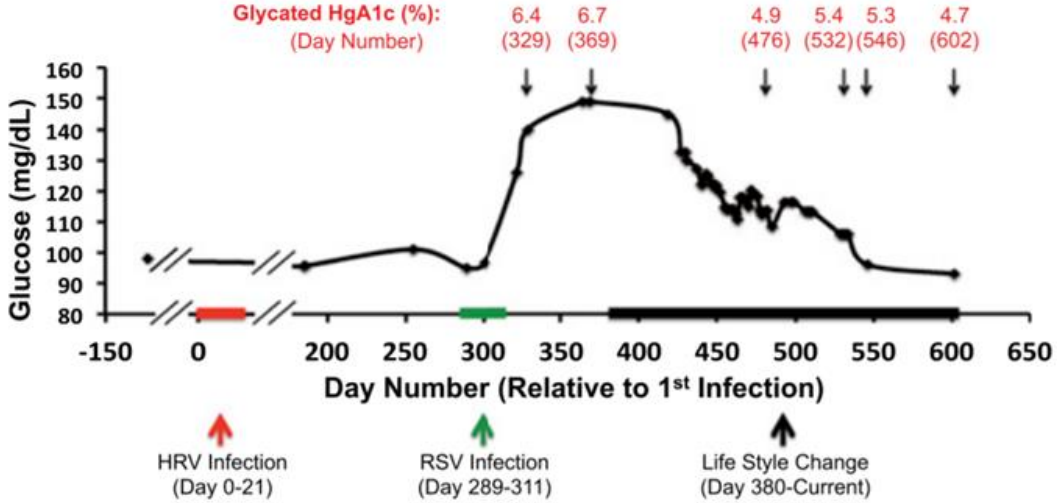
Holo-omic domain



Nyholm et al, iScience 2020

Integrated Personal Omics Profiling (iPOP)





Chen et al, Cell 2012

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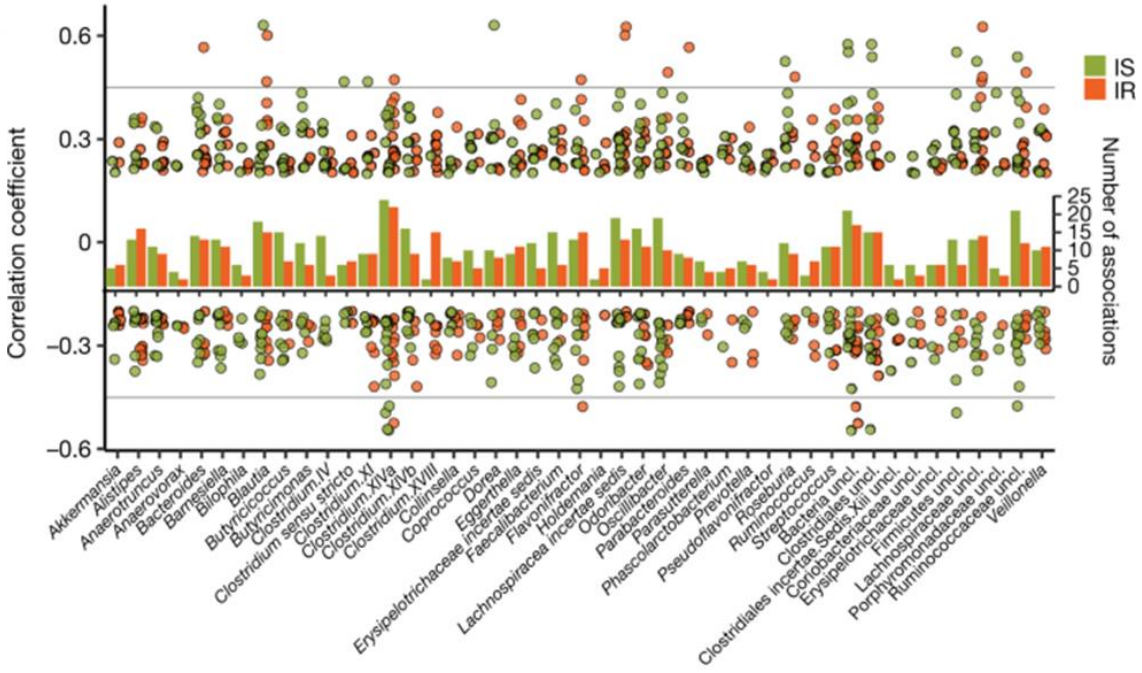
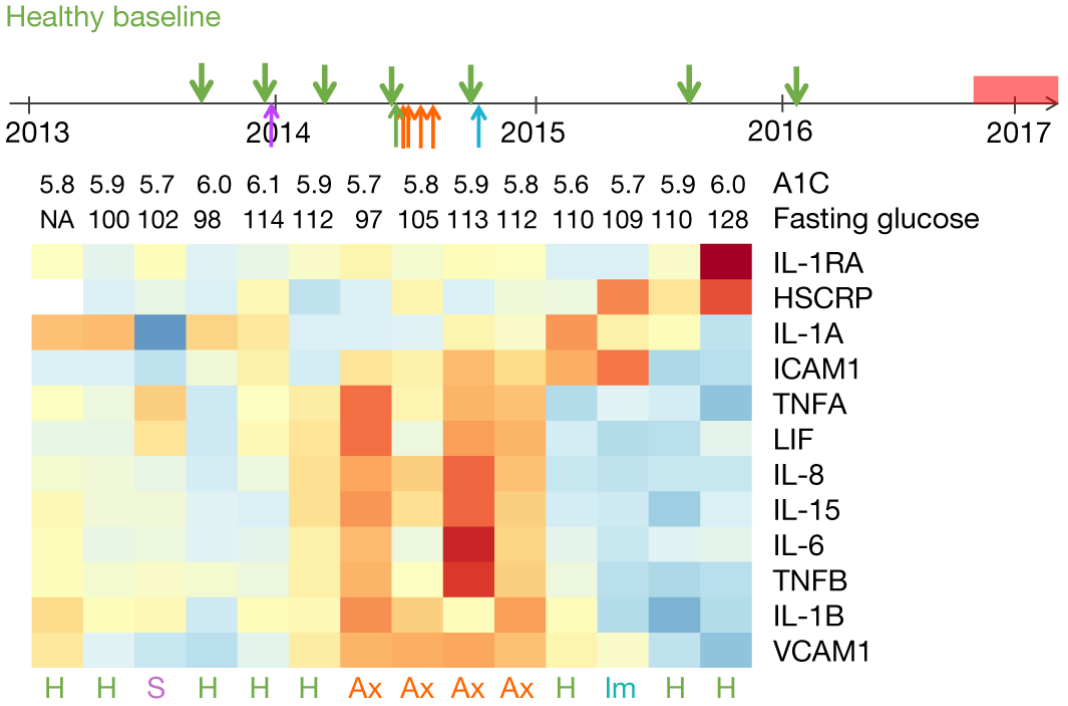
Host–microbe multi-omics dynamics in prediabetes





Zhou et al, Nature 2019

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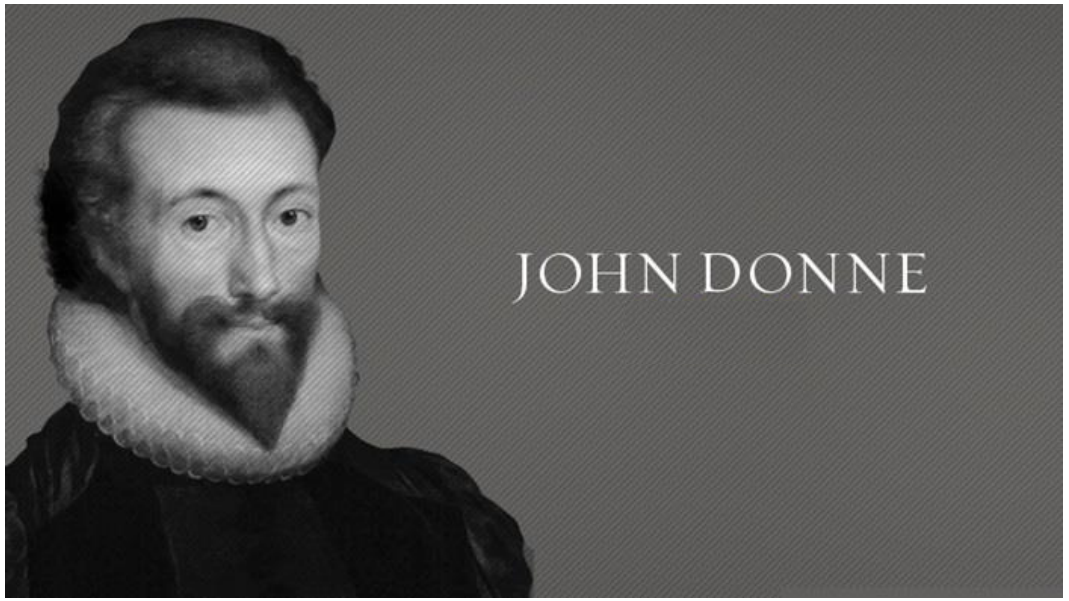

NO MICROBIOME IS AN ISLAND ENTIRE OF ITSELF

Adapted from Zhang et al, Mol Cell Proteomics 2019

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Prof. Michelle Plusquin

Prof. Tim Nawrot

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Prof. Marc Chadeau

Prof. Paolo Vineis

Dr Oliver Robinson

Imperial College London

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Hands-on session 4

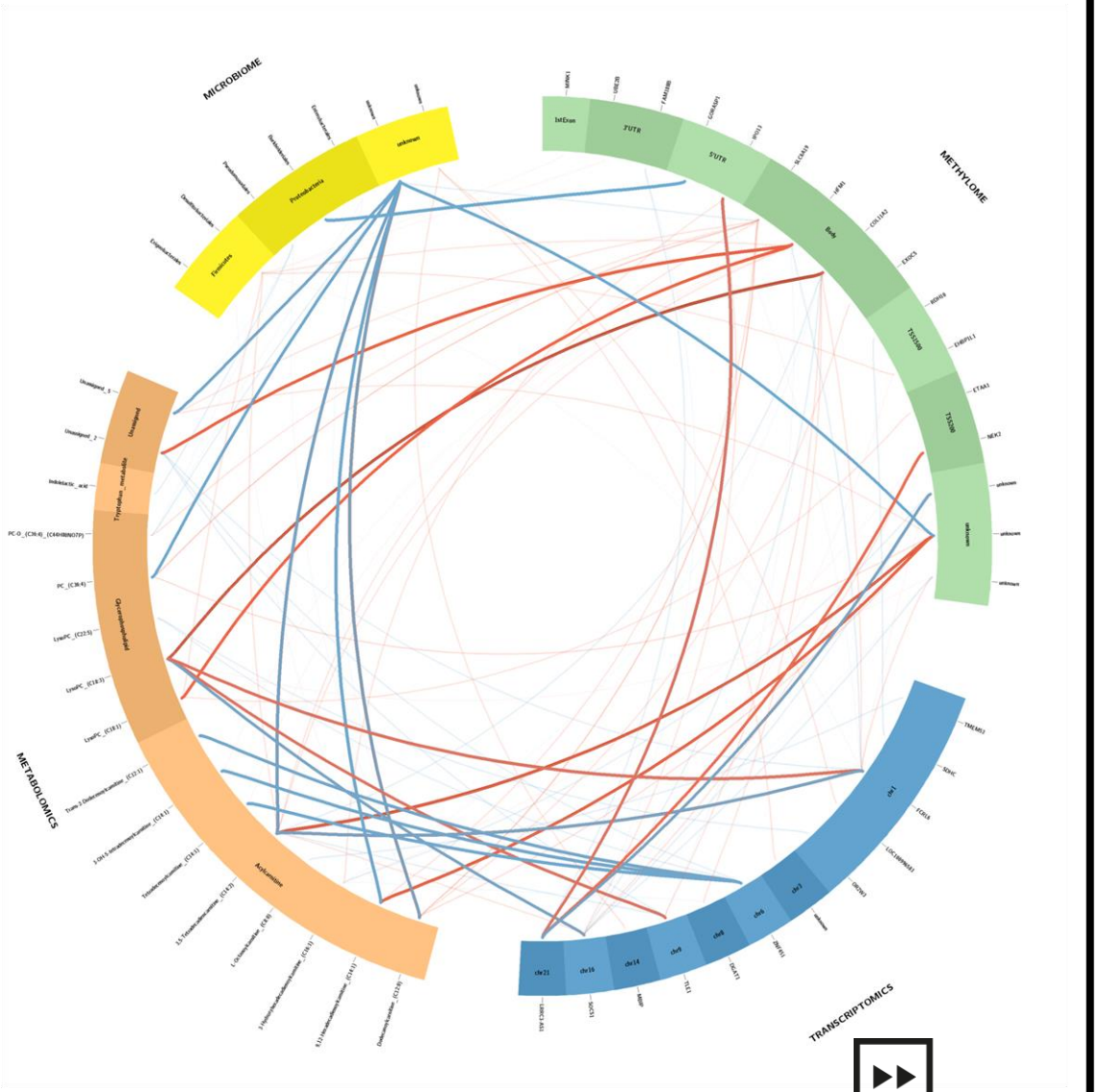
03:30 PM - 05:00 PM | Workshop room

Hands-on session # 4: Visualisation of multi-omics data

- Leo Lahti
- Rosella Alfano

Brigitte Reimann

Congrong Wang



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KNOWLEDGE IN ACTION