Clinical metabolomics for AI in drug development

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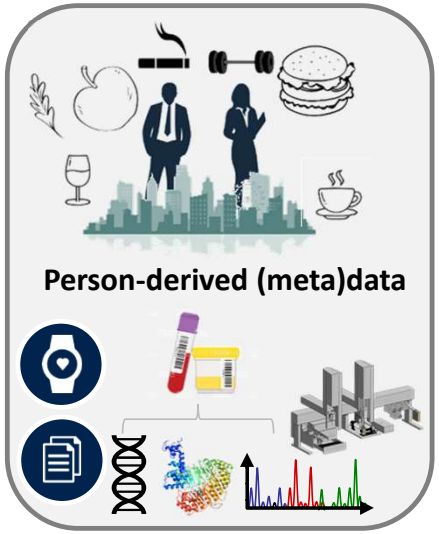
Metabolomics and big data in clinical drug development opportunities: informative data are key for AI

- Drug discovery & preclinical testing for target identification
- Improved clinical trial design & patient stratification
- Real world data for predicting drug response
- Development of companion diagnostics
- Repurposing drugs and rescuing drug candidates

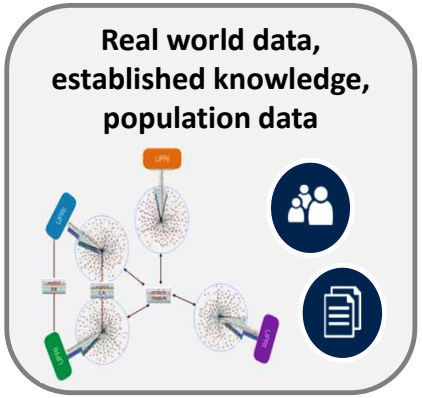
Translational metabolomics & data analytics for personalized medicine using real-world data



Person-derived (meta)data

Digital twin

Genome-scale models
C13 flux-based models
Dynamic, ODE models
PK/PD models
AI & ML

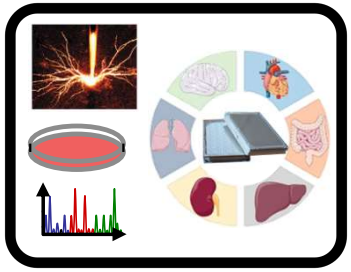


Real world data, established knowledge, population data

Hypothesis, data acquisition, testing

FAIR data analytics, integration, modelling, interpretation

HT metabolomics
Single-cell omics
Organ-on-a-chip
In-vitro models
Genetic variants

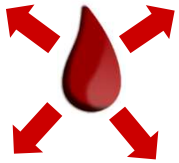


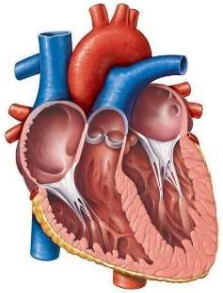
Experimental twin

Examples of metabolic biomarkers of early disease pathways (pathways we have to modulate)

Early prediction of dementia

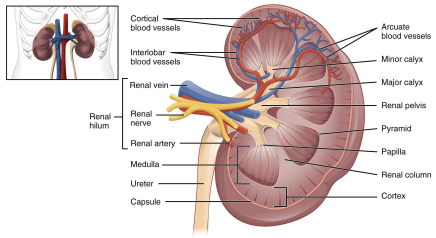
Van der Lee et al (2018)
Alzheimers Dement. 14: 707 ff





Prediction of sudden cardiac death

Zhang YY et al, PLoS One (2016) 11:e0157035



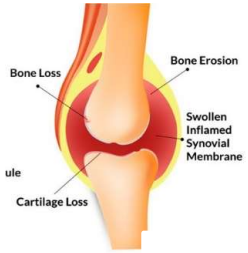
Prediction of kidney failure

Van der Kloet F et al (2012)
Metabolomics 8: 109ff

Prediction of healthy aging

Gonzalez-Covarrubias et al, Aging Cell, 2013

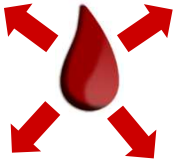
Metabolic biomarkers of prediction of treatment outcome (do drugs or nutrition modulate the right pathways?)



Prediction of response to rheumatoid arthritis drugs

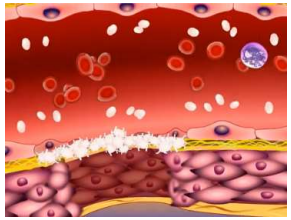
Teitsma XM et al, Arthritis Res Ther (2018) 20: 230

Prediction of responders/non-responders to breast cancer treatment



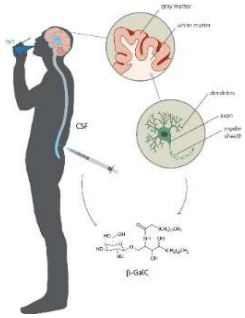
Prediction of weight loss by diet intervention (Diogenes Study)

Vogelzangs N, Int. J. Obesity, in press



Prediction of anti-platelet effect

Yerges-Armstrong LM et al, CPT (2018) 94: 952

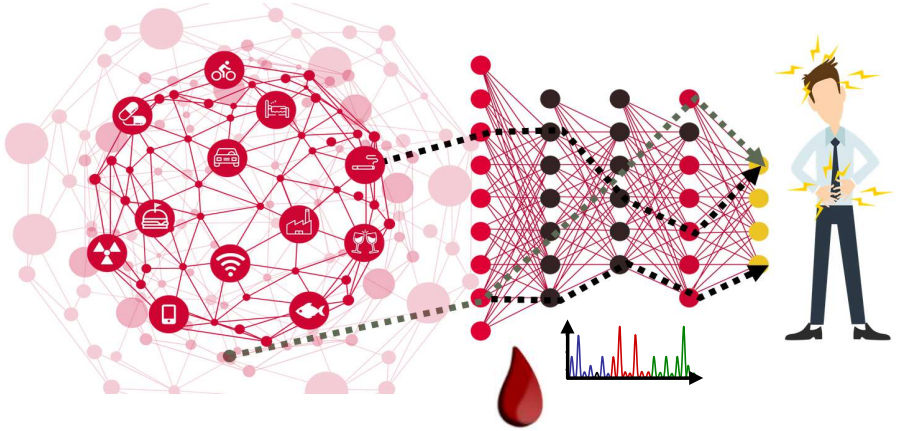


Determine myelin turnover for multiple sclerosis drugs

Kanhai KMS et al. 2016. Clinical and Translational Sciences. 9: 321ff

Exposome-Scans to identify environmental drivers of health and disease

Molecular data (metabolome/exposome) to provide dynamic comprehensive view on our health, as influenced by chemicals, our diet, lifestyle, genome, gut microbiome and socioeconomic status



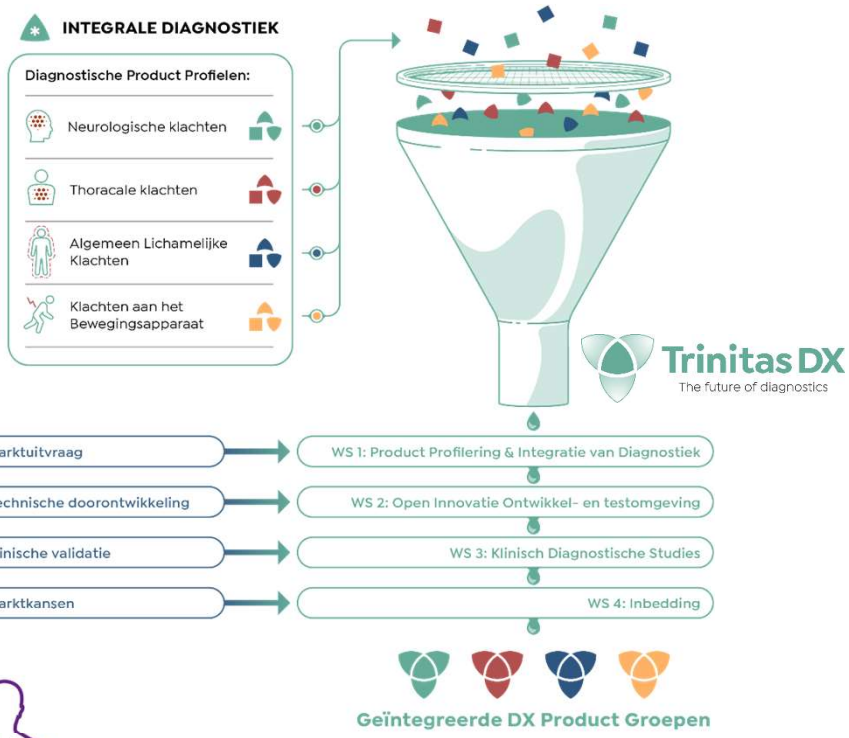
Measuring health real-time

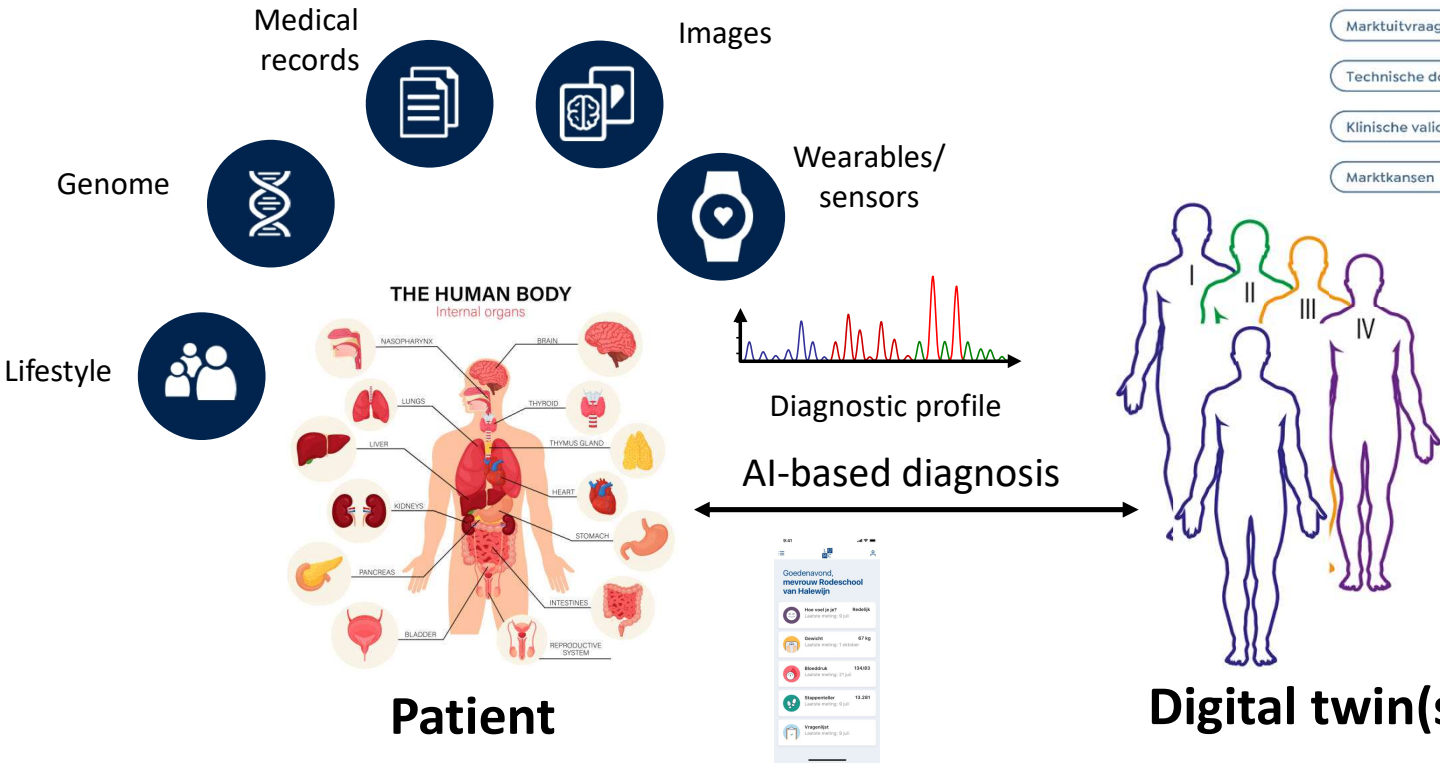
=> Systematic understanding of diseases to develop strategies for more years in good health

=> Delivering leads for development of interventions to cure, or prevent

Innovative diagnostics

- Right diagnosis at the start
- Right referral of patients
- Reduction of workload in clinics





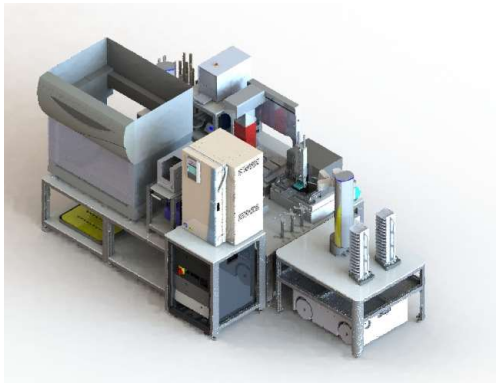
Exposome-Scan facility

Combining **powerful technologies** with **proven methodologies** and **innovative analytics** to deliver quantitative measurements of the metabolome and exposome using targeted and global platforms

Research metabolomics lab

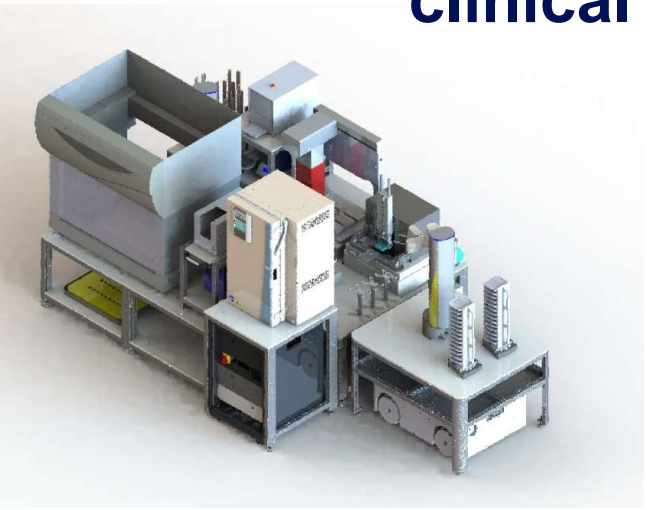
Establishing automated metabolomics platform:

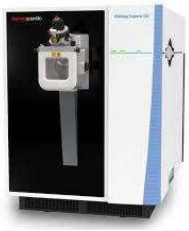
- ✓ **Robust**
- ✓ **Scalable**
- ✓ **Quantitative**
- ✓ **Quality controlled**
- ✓ **More than 2500 metabolites**
- ✓ **Including exposome (food, drugs, pollutants)**
- ✓ **FAIR data output enabling omics integration & open science**

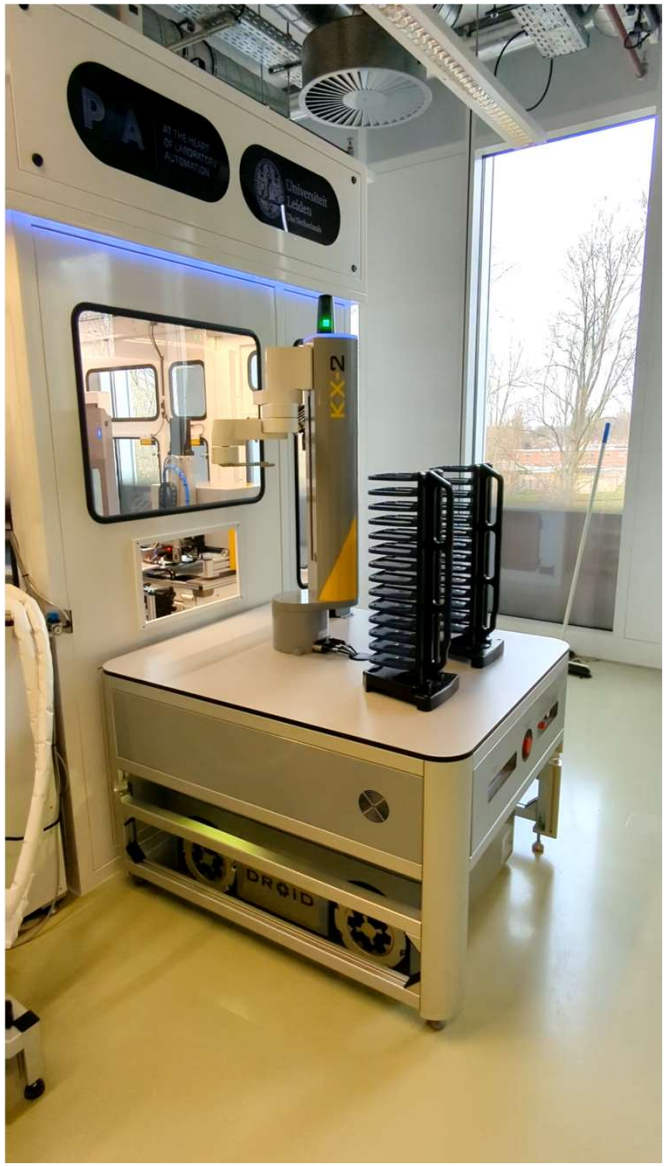


Automated metabolomics analysis

Exposome-Scan facility: clinical diagnostic lab of the future

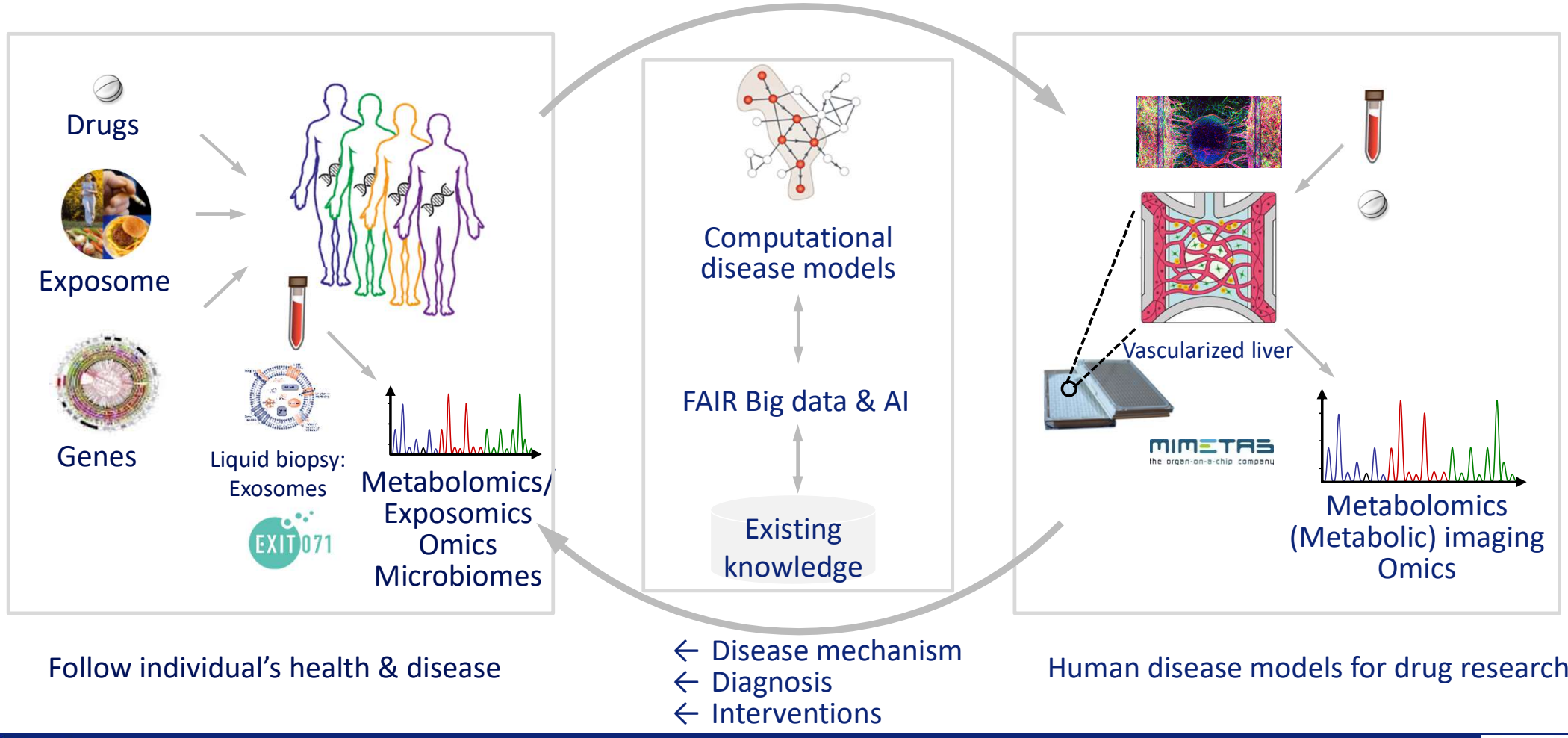






- Controlled environment to protect samples (Exposome-ready!) and technicians (infectious samples from rapid COVID MS test!)
- High throughput metabolomics and MS-based diagnostics!

Drug research:
Translational biomarkers & AI for drug development and clinical trials



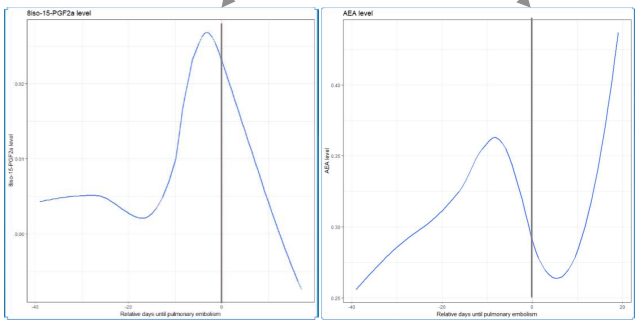
Follow individual's health & disease

← Disease mechanism
← Diagnosis
← Interventions

Human disease models for drug research

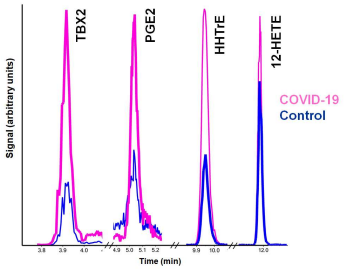
Inflammatory/other factors in COVID-19 leading to severe symptoms: Identifying treatment options

Pulmonary embolism

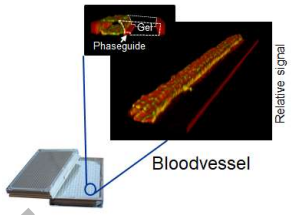


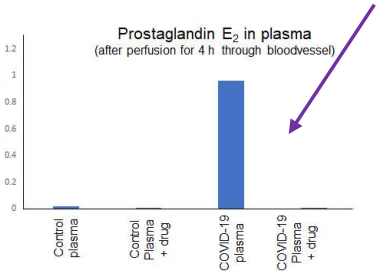
Computational disease models

Real-world COVID data & existing knowledge



mPGES-1 inhibitor

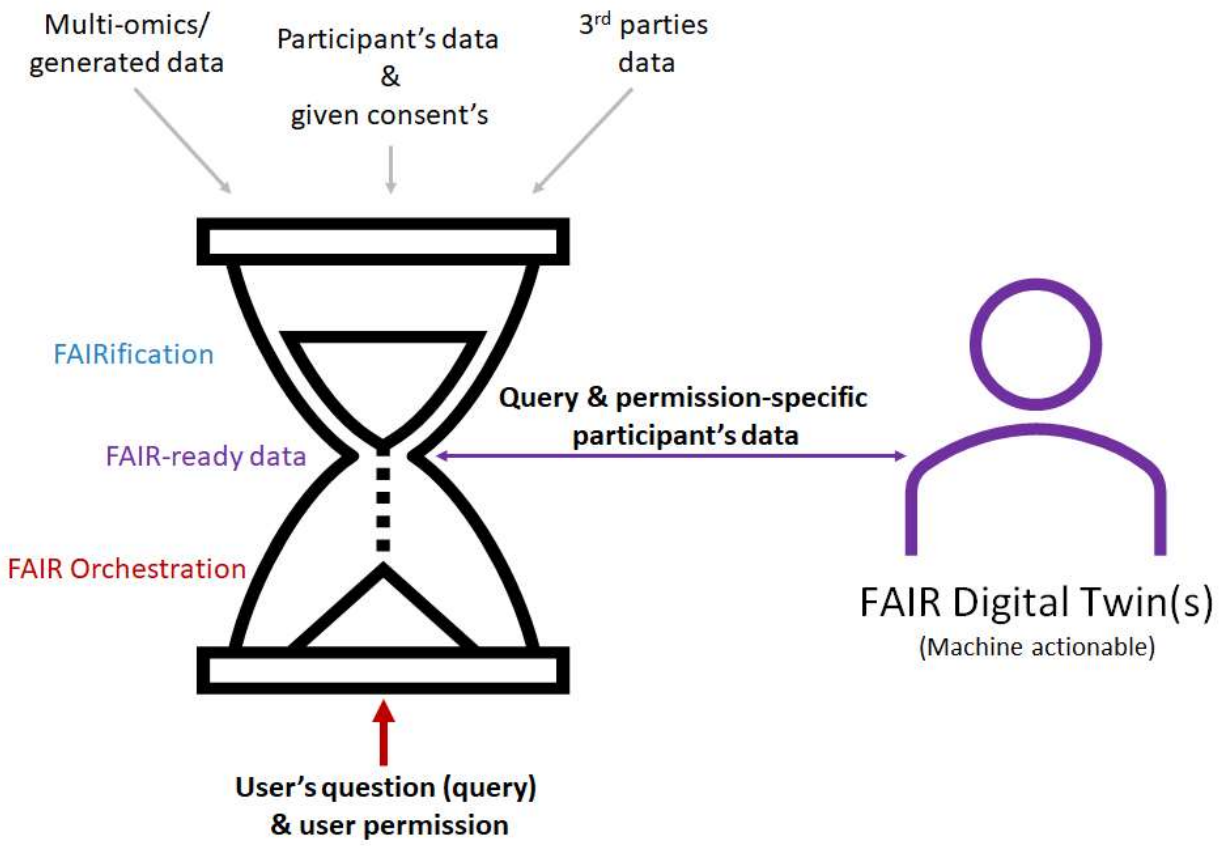




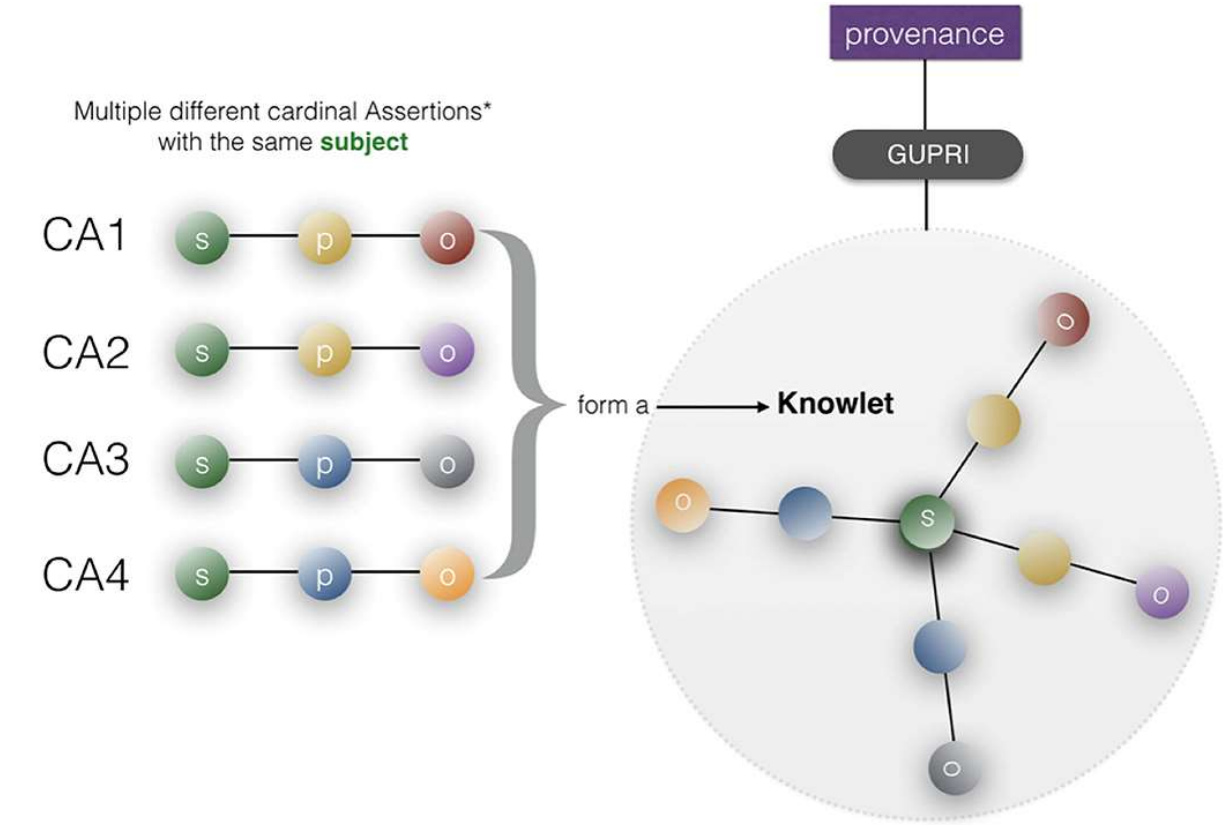
Follow COVID-19 patient disease course

Patient-derived microfluidic COVID-19 disease model

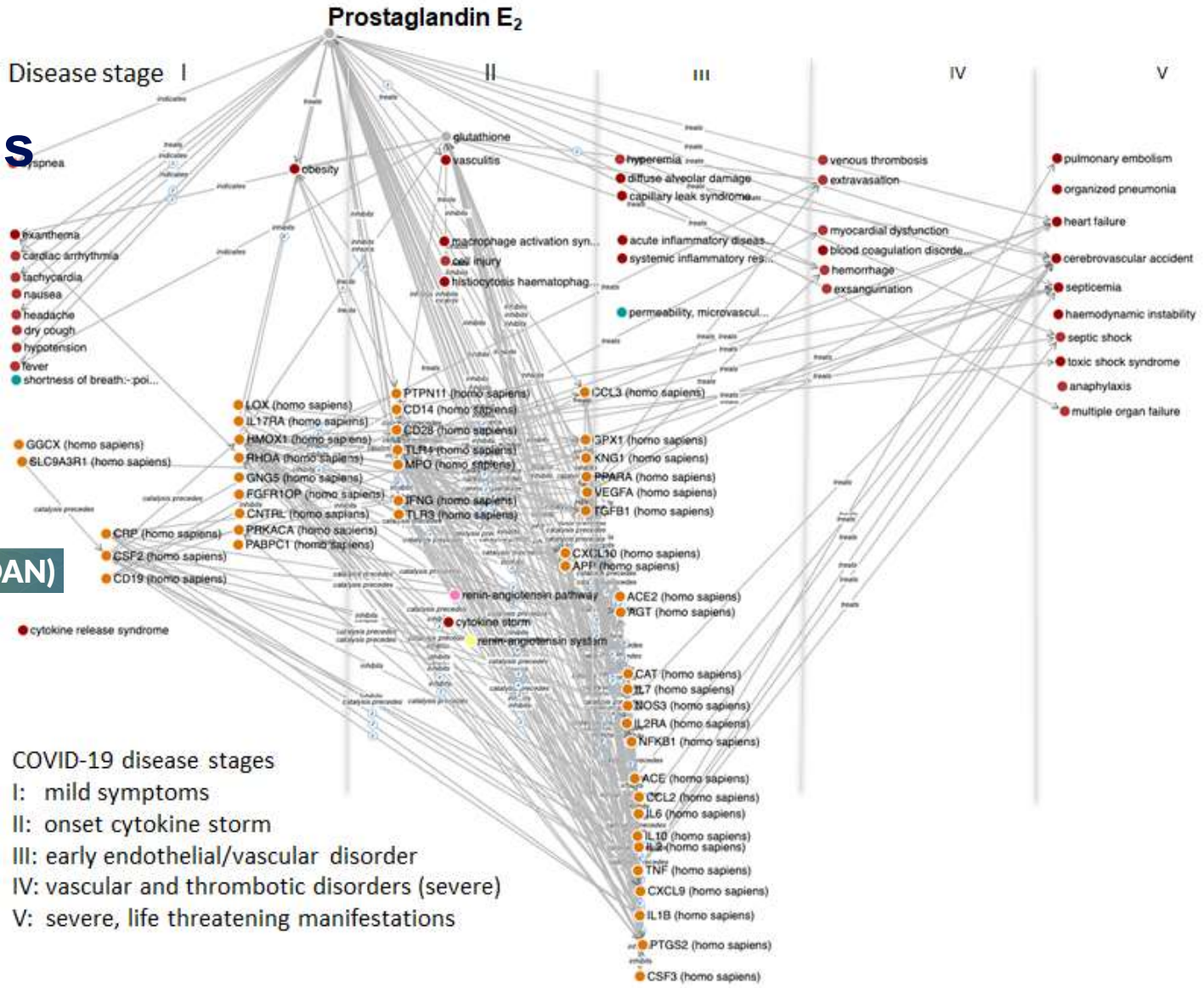
FAIR digital twinning for data-intensive research



FAIR digital twinning for data-intensive research



COVID-19: Rationalizing biochemical findings



COVID-19 disease stages
I: mild symptoms
II: onset cytokine storm
III: early endothelial/vascular disorder
IV: vascular and thrombotic disorders (severe)
V: severe, life threatening manifestations

Virus Outbreak Data Network (VODAN)

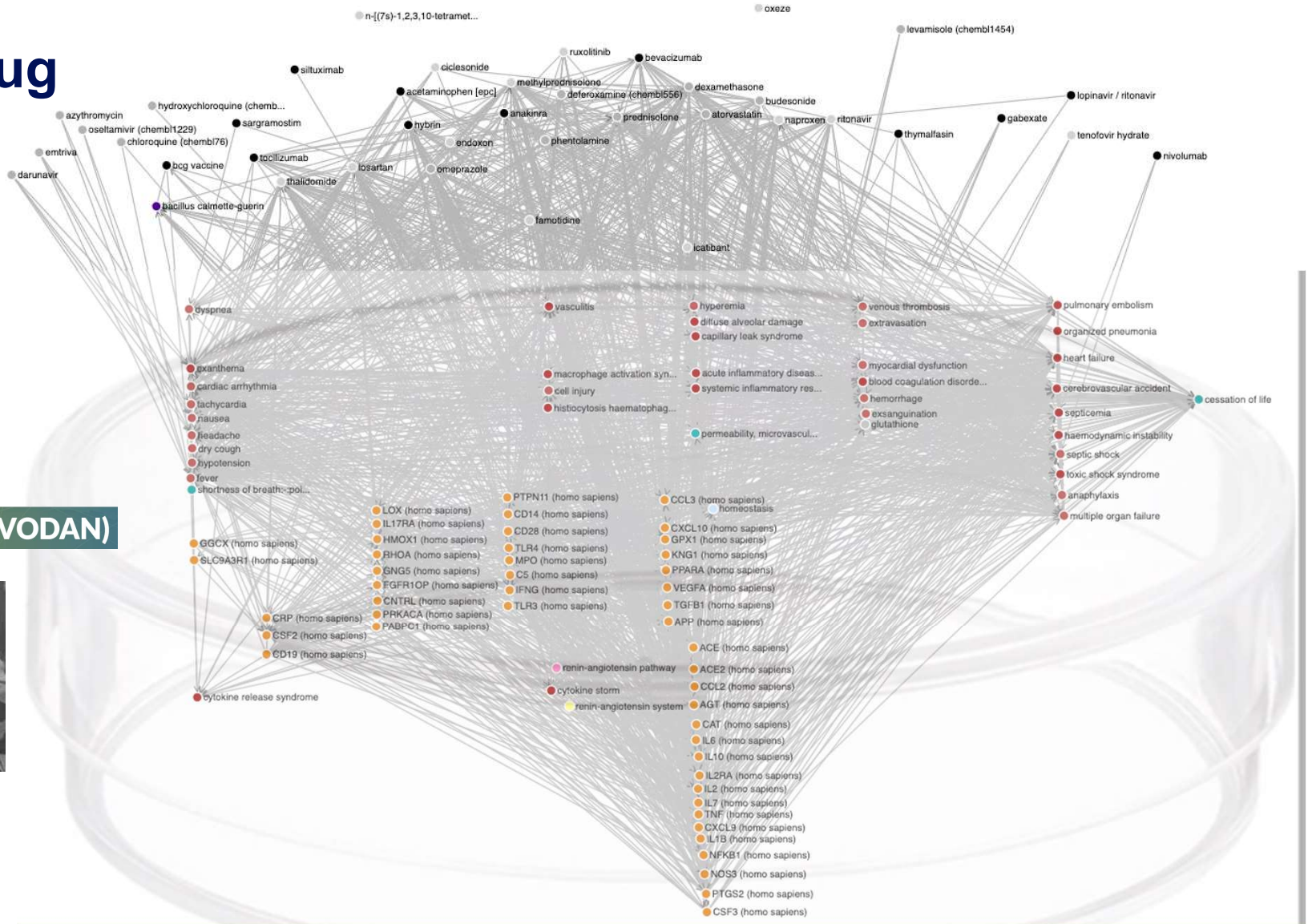
Barend Mons

Arie Baak

GO FAIR foundation

EURETOS

COVID-19: Rationalizing drug repurposing



Virus Outbreak Data Network (VODAN)

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Arie Baak

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FAIR digital twinning for data-intensive research: making MAC FAIR

Metabolomics & Analytics Center

MAC FAIR Governance Group

Erik Schultes

Elham Memarian

Max van den Boom

Data
Metadata

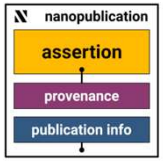
FAIR
Enabling
Resources

MAC
FAIR Data
Orchestration
Platforms

MAC FAIR Data Point

Data Station

Data Lake



Nanopub-based FDOs

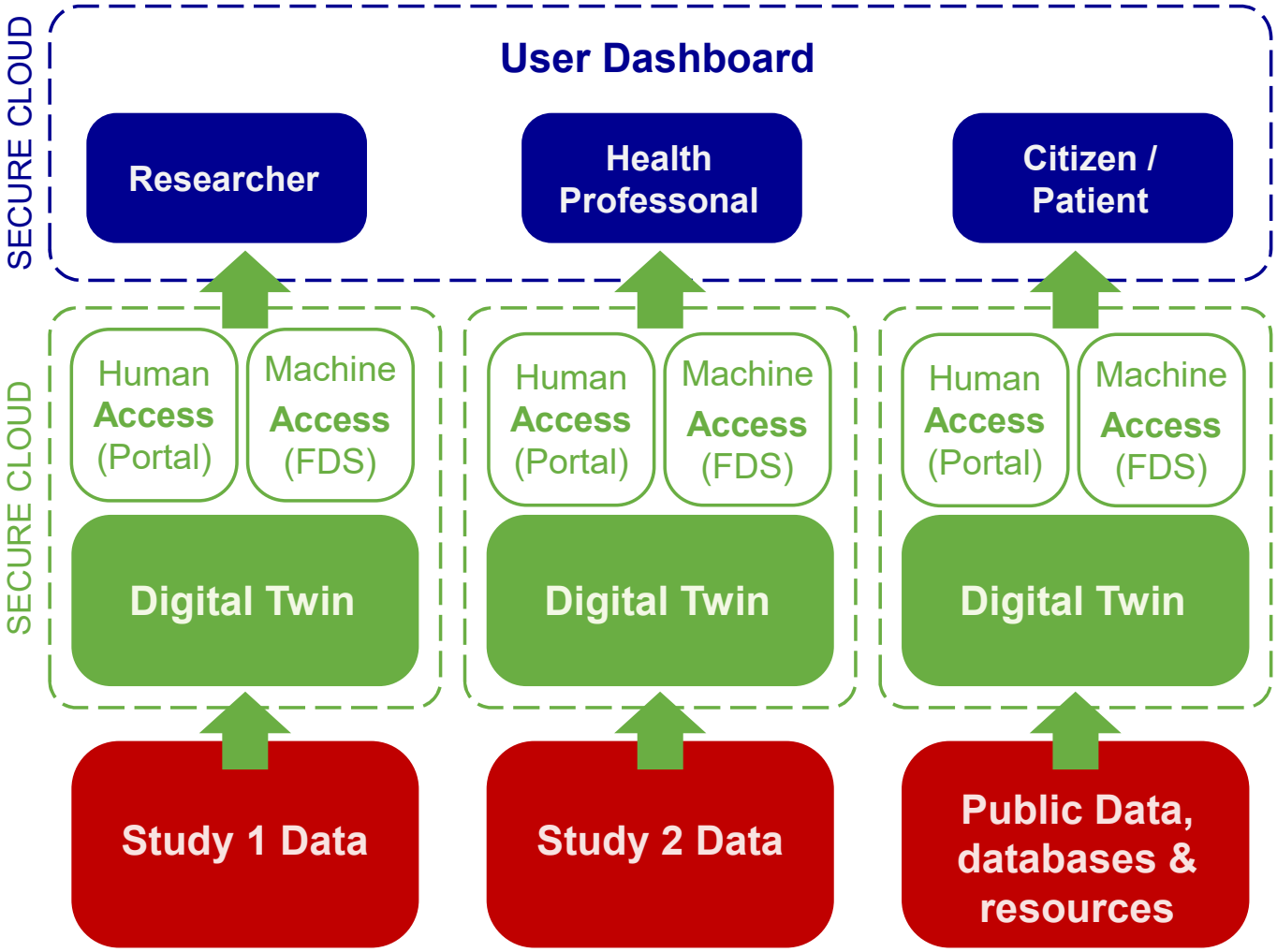
Published findings in conventional (not FAIR) research articles & data repositories

Exemplars for…

LIFES

Human Immunome Project

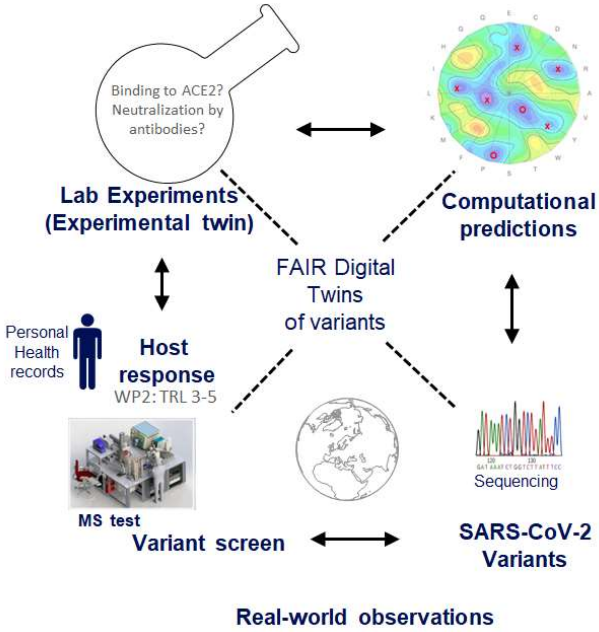
FAIR digital twinning for data-intensive research & healthcare

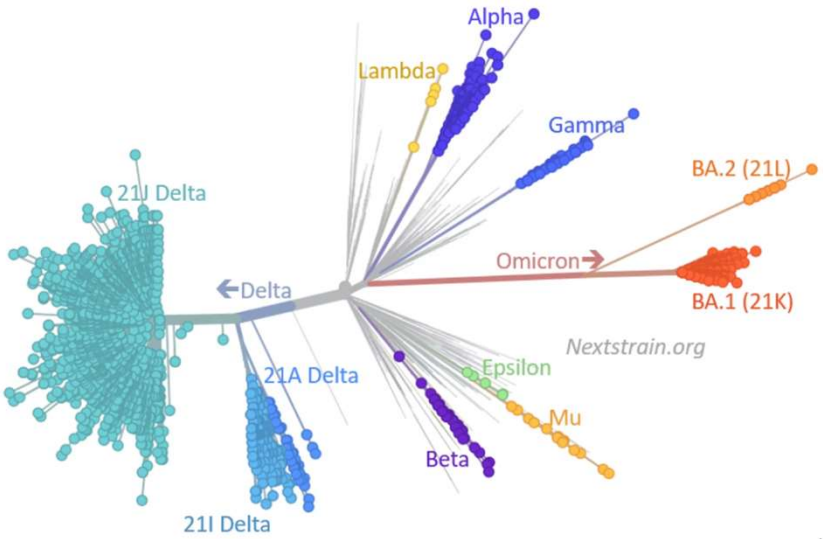


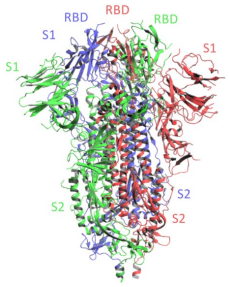
EURETOS

LIFES

Staying ahead of the virus







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Sanquin
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Human Immunome Project
NL Health~Holland

Take home message

- Metabolomics for clinical trials and drug development
- Large scale FAIR data integration key for AI automated analysis
- Understanding and targeting inflammation & metabolism for novel interventions of various diseases
- Building public-private partnerships for using large scale FAIR molecular data and real world data, patient-derived in-vitro models, existing knowledge & AI data analytics to innovate diagnostics & drug research

Interest in collaboration or metabolomics analysis?

Contact: hankemeier@lacdr.leidenuniv.nl