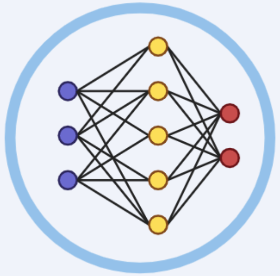
TNO's translational muscle pipeline

TNO innovation for life

In silico / in vitro | **Pre-clinical** | **Human**



In silico target prediction

Target discovery from complex datasets

1

- Pathway and Receptor modulation
- Knock-out simulation
- Mechanistic modeling
- Ingredient identification

In vitro models

Cell models delivering rapid, mechanistic readouts

2

- Myoblasts/myotubes
- Fusion index
- Myotube size
- Mitochondria
- Electrical pulse stimulation

Translational models

Use mouse models with confidence on translational relevance

3

Extensive profiling of muscle atrophy and underlying mechanisms by:

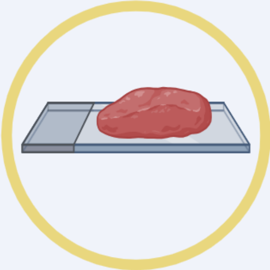
- Caloric restriction
- Immobilization
- Natural aging
- Obesity

Compound testing

Efficacy testing for confident go/no-go calls

4

- Muscle mass
- Muscle strength
- Physical activity
- Blood samples
- Myofibers (histology)
- Muscle transcriptome
- Tracer technology
- Body composition
- Muscle triglycerides

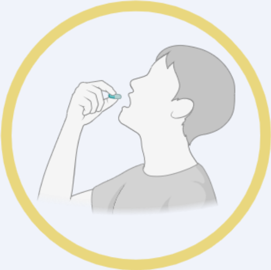


Cohorts / Human sample

Access to human tissues and cohort data to confirm real-world relevance

5

- Large omics datasets
- Aging vs. frailty effects
- Expertise in the role of sex
- Translational biomarkers and mechanisms



Human trials

Extensive functional and physiological read-out parameters

6

- Muscle mass
- Muscle strength
- Physical function
- Blood samples
- Muscle biopsies
- Nutrition, fibers, supplements, disuse, physical activity, drug repurposing

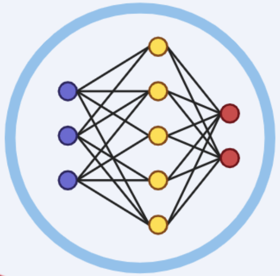
Biomarkers/ Diagnostics

Develop and refine muscle health biomarkers and tools

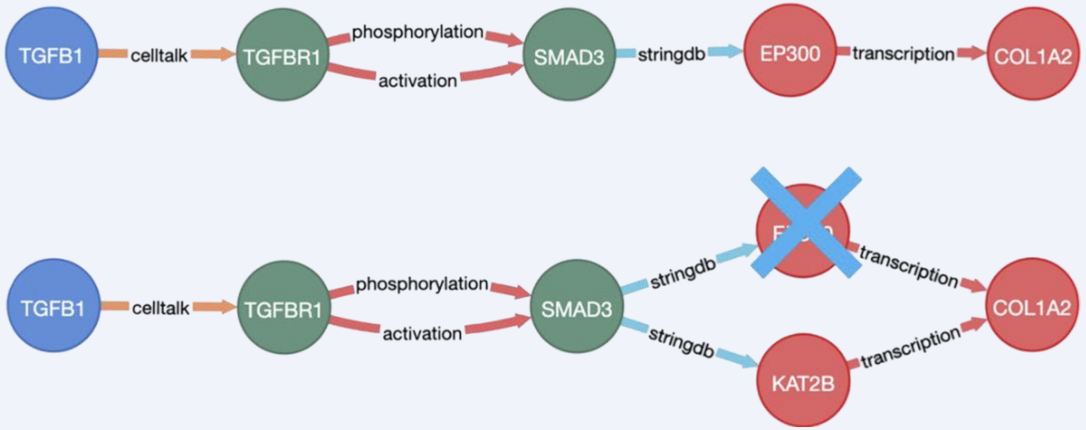
7

- Innovative diagnostics
- Omics technologies
- Assay development
- Algorithms
- High-resolution accelerometry
- Remote data collection platform

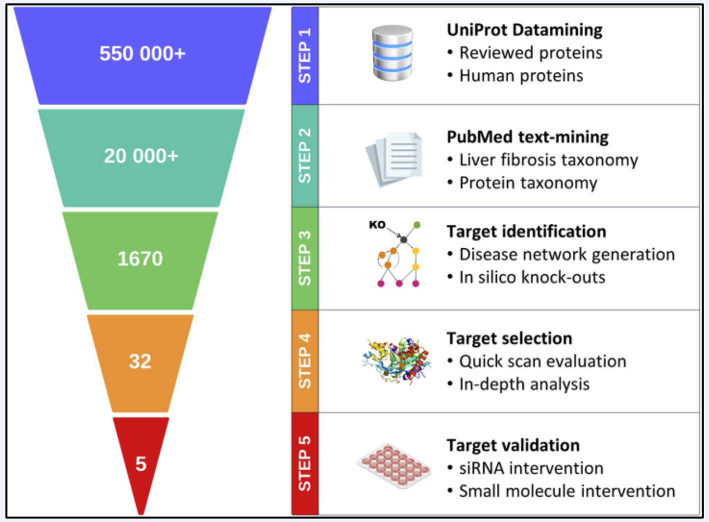
① In silico target prediction



We offer a network-based in silico target prediction service that integrates literature, omics datasets and systems biology to identify disease-driving pathways and druggable targets.
The output is a mechanistically grounded, **ranked shortlist of targets and candidate compounds** that can be directly taken forward into preclinical or translational validation.



Example of in-silico knock-out disease network (Venhorst et al., 2024)



‘Using directional, weighted interaction networks and in silico knock-out simulations, we prioritise key molecular nodes and link them to existing **compounds, ingredients or nutraceuticals** for **drug repurposing** or **mechanism-based intervention strategies**.’

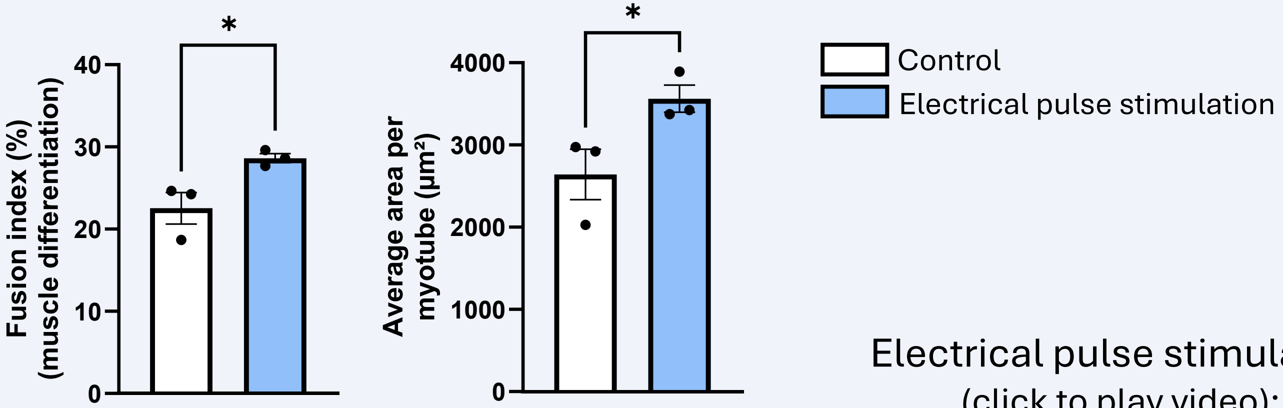
Dr. McCormack-Venhorst
Scientific lead
Target prediction

References:
Venhorst, 2024 (target identification for MASH-induced liver fibrosis)
González Hernández, 2024 (stratification of patient subgroups and therapies)

② In vitro muscle model

We offer a robust in-vitro screening platform using differentiated C2C12 skeletal muscle cells to evaluate the **efficacy** and **mechanism of action of compounds, nutrients or nutraceuticals.**
The service delivers quantitative efficacy data and mechanistic insight to **support compound prioritization** and translation to in-vivo or human studies.

Example of immunohistochemistry staining for measuring muscle cell differentiation



‘Interventions can be tested under basal conditions or in a **physiologically relevant** electrical pulse stimulation (EPS) setting that mimics muscle contraction and exercise.’

Dr. de Jong Scientific lead
Muscle in-vitro platform

Electrical pulse stimulation
(click to play video):

Reference:
Van de Meene, 2025 (literature review for identification of EPS protocols)

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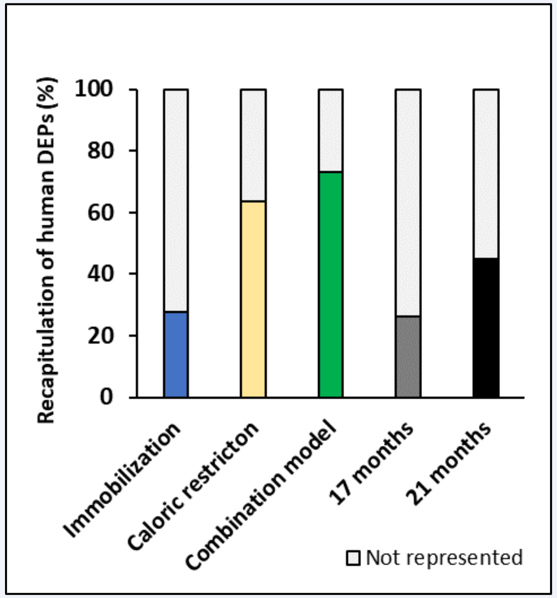
③ Translational models

We have systematically assessed the **translatability** of mouse models for human muscle-aging by integrating **functional, histological and transcriptomic analyses** in both mice and humans. Using large-scale RNA-seq comparisons, aging-related pathways in mouse quadriceps muscle were benchmarked against aged human vastus lateralis biopsies.

Aged mouse

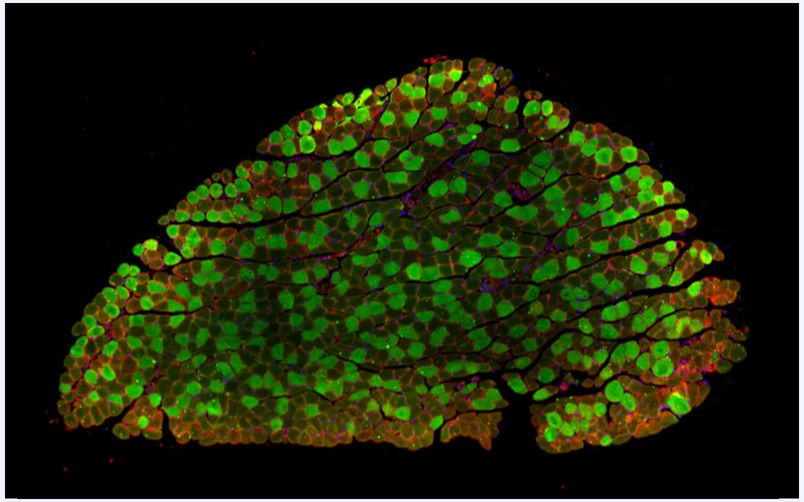
Immobilized and/or CR mouse

Obese mouse



Translatability of mouse models for muscle-aging based on RNA-seq

MYH7 (slow myofibers)/Laminin (sarcolemma)



Example of myofiber type specific staining

‘Translation is not assumed here, **it’s measured**. Our combined model captures 73% of human muscle-aging pathways, **outperforming** the commonly used naturally aged mice (45%).’

Dr. van den Hoek Scientific lead pre-clinical models

References:

de Jong, 2024 (translatability and the role of sex in naturally aged mice)
de Jong, 2023 (assessment of translatability of multiple mouse models)

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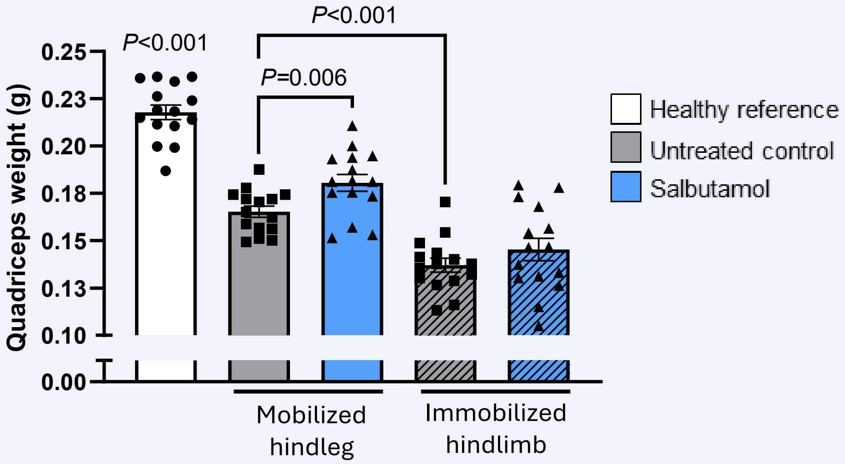
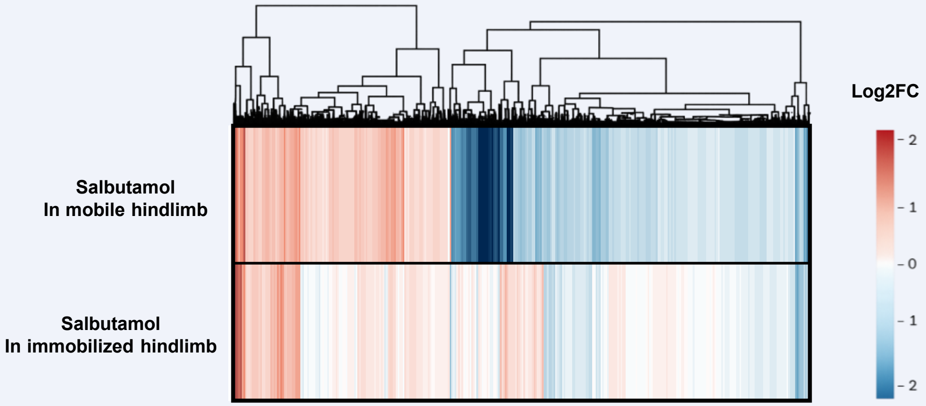
④ Compound testing

We provide **in-vivo efficacy** and **mechanistic screening** of nutritional and pharmacological interventions using well-characterized mouse models of muscle atrophy, which together **reproduce key functional and molecular features** of human sarcopenia and disuse atrophy. Interventions can be evaluated in a prevention or recovery design.





Differentially expressed genes reflecting differences between mobile and immobile hindlimb

Read-outs include:

- Body composition
- Grip strength
- Voluntary movement
- Muscle weights
- Histology
- Muscle triglycerides
- Muscle protein synthesis
- Transcriptomic pathway analysis
- Blood analyses

Validation experiments with:

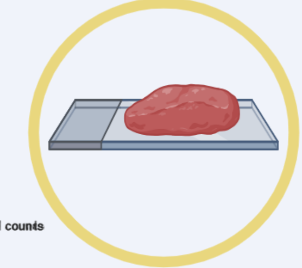
- Activin modulator
- Ghrelin
- Salbutamol
- Apelin
- Oral nutrition supplements
- Fiber supplement
- GLP1RA (obese sarcopenia model)

‘We don’t test compounds in mice to see *if* they work, but to **understand** when, why, and under which **physiological conditions** they work, or fail.’

Dr. van den Hoek Scientific lead pre-clinical models

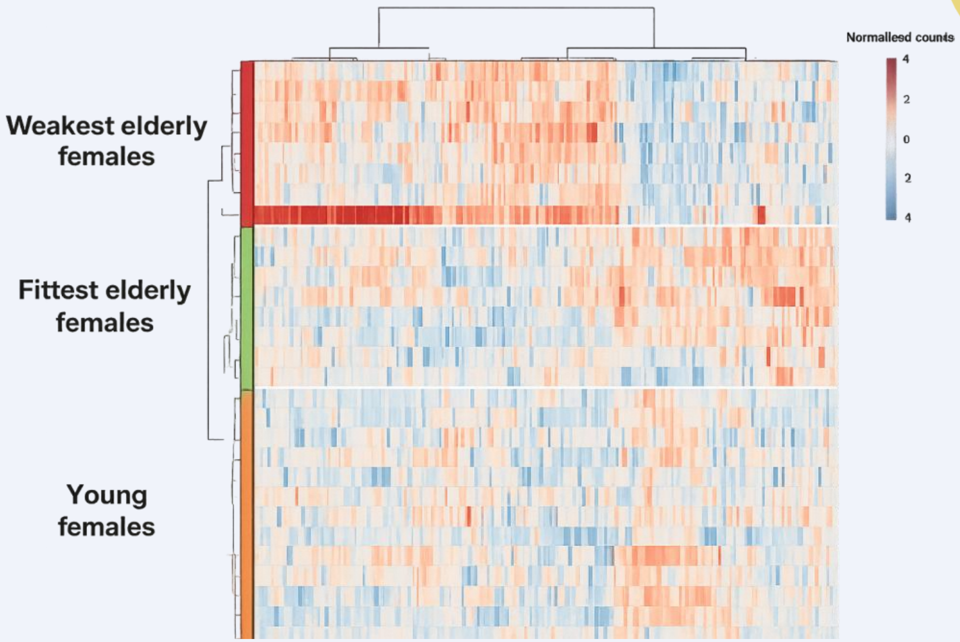
References:
van den Hoek, 2019 (testing of nutritional supplement)
de Jong, 2025 (testing of salbutamol)

⑤ Cohorts/human sample



We have access to well-phenotyped human cohorts spanning **muscle-aging, frailty and menopause**, with deep molecular and functional data that can be directly leveraged for translational research and product development. These datasets allow **human anchoring of targets, biomarkers and interventions**: candidate compounds or nutrients can be linked to human-relevant pathways, stratified by sex and life stage, and benchmarked against real muscle function outcomes, substantially reducing translational risk before moving into costly clinical trials.

<u>Aging vs. frailty effects:</u>



Example of muscle transcriptome reflecting differential effects of muscle-aging vs. weakness

'From healthy aging to frailty, and from pre- to post-menopause, we can test whether a mechanism is real in the people you ultimately care about.'

Dr. Verschuren Scientific lead Data Science

Examples of available types of datasets:

- Muscle transcriptomics
- Blood proteomics & metabolomics
- Muscle fiber characteristics
- Physical function

References:
de Jong, 2023a (sex & muscle-aging)
de Jong, 2023b (sex & physical weakness)

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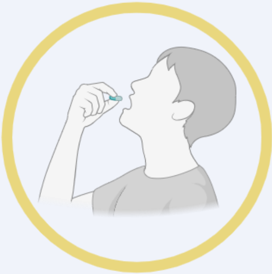
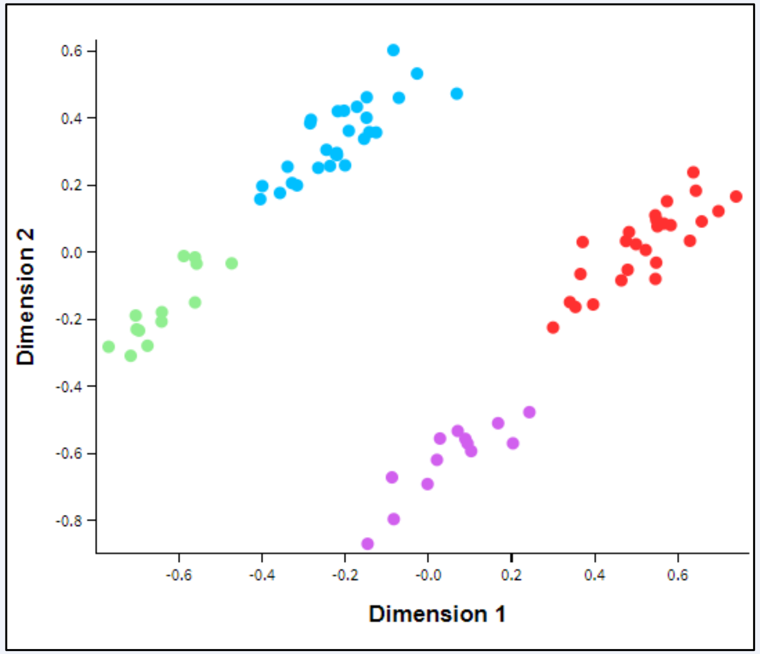
⑥ Human trials



We can contribute to **the organization and analysis** of human intervention studies conducted together with an academic partner (e.g., Wageningen University). This may include input on study set-up, alignment of interventions and endpoints with underlying biological questions, and support in the **analysis and interpretation of complex datasets** such as muscle biopsies, blood markers and functional outcomes.

Transcriptome profiles of muscle biopsies (*vastus lateralis*)



Transcriptome profiles reflecting sex and aging differences

'We help turn human trials into insights by connecting molecular signals to functional outcomes without over-engineering the study.'

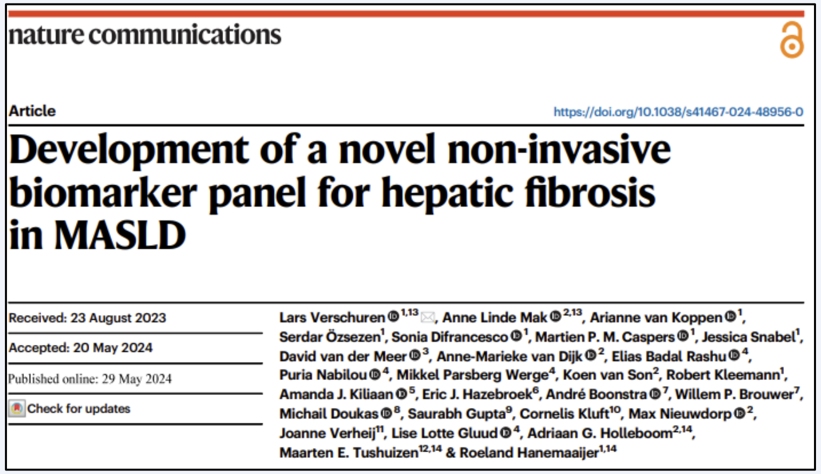
Dr. van den Hoek Scientific lead muscle research

References:
de Jong, 2025 (salbutamol in human immobilization model)
van der Hoek, 2020 (role of carnitine in muscle-aging)

7 Clinical biomarker identification

We work on the identification, development and validation of blood-based and digital biomarkers linked to muscle health, aging and frailty. This includes **integrating molecular data** (e.g. circulating proteins, omics-derived candidates) **with functional outcomes**, as well as developing digital biomarkers from wearable and sensor data to capture physical function, activity patterns and early functional decline over time. Across both domains, the focus is on mechanistic relevance, sex-specific effects and clinical interpretability, so biomarkers are not only statistically associated, but also meaningful for decision-making in research and development.

Example of previously established biomarkers for hepatic fibrosis



nature communications

Article https://doi.org/10.1038/s41467-024-48956-0

Development of a novel non-invasive biomarker panel for hepatic fibrosis in MASLD

Received: 23 August 2023

Accepted: 20 May 2024

Published online: 29 May 2024

Check for updates

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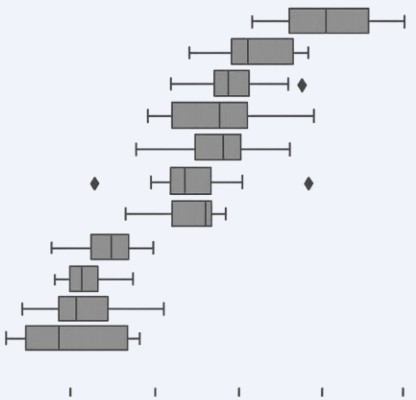
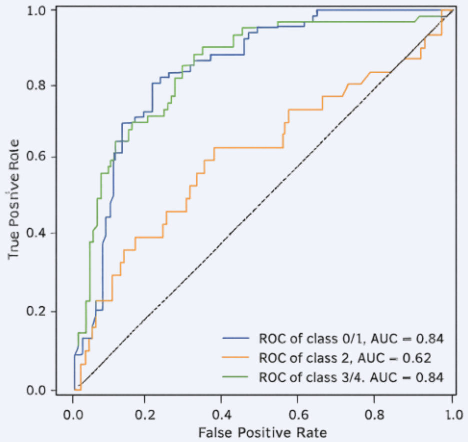
Translational biomarker identification:





'Biomarkers help identify when decline starts, not just when it's obvious.'

Dr. Verschuren Scientific lead
Data Science

References:
Verschuren, 2024 (biomarkers for hepatic fibrosis)
de Jong, 2024 (biomarkers for early frailty)

Contact

Let us know in which part(s) of the pipeline you are interested and talk directly with the most relevant expert.

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Digital biomarkers