

# The AETIONOMY Knowledge Base



innovative  
medicines  
initiative

## AETIONOMY Final Symposium and IMI Neurodegenerative Initiatives 29<sup>th</sup> November 2018

### *Mission*

*To increase knowledge of the causes of Alzheimer's and Parkinson's Disease by generating a mechanism-based taxonomy; to validate the taxonomy in a prospective clinical study that demonstrates its suitability for identifying patient subgroups (based on discrete disease mechanisms); to support future drug development and lay the foundation for improved identification and treatment of patient subgroups currently classified as having AD or PD.*

Prof. Dr. Reinhard Schneider





# AETIONOMY Knowledge Base (AKB)

The screenshot shows the AETIONOMY Knowledge Base (AKB) website. At the top left is the logo: **AETIO** **NIO** **MIY** **KNOWLEDGE BASE**, with the tagline "Organising Knowledge about Neurodegenerative Disease Mechanisms for the Improvement of Drug Development and Therapy". A search bar is located at the top right. Below the header is a green navigation bar with menu items: Knowledge Mining, Data Mining, Disease Modelling, Mechanistic Disease Hypotheses, In-silico Validation, and Clinical Validation. The main content area features a large blue and orange graphic with a computer monitor displaying "The AETIO NIO MIY Challenge" and a text box with the text: "Welcome to AETIONOMY. The AETIONOMY Knowledge base (AKB) provides a mechanism-based taxonomy of Alzheimer's and Parkinson's Disease and to validate that taxonomy in the course of a prospective clinical trial. The AKB offers: description of methods applied in the different stages (incl. webinar recordings), access to disease models and quality control, and web services for analytical data processing." On the right side, there is a vertical list of links: tranSMART - clinical data repository, ADA workflows, NeuroMMSig - clinical validation of candidate molecules, ADNI / PPMI Disease Stages, ADNI Analyses, AddNeuroMed merge - longitudinal multimodal data, PPMI Analyses, and Mapping out alzheimer's disease data landscape.

<https://data.aetionomy.scai.fraunhofer.de/>



# AETIONOMY Knowledge base

Original Knowledge about Neurodegenerative Disease Mechanisms for the development of Drug Development and Therapy

Knowledge Mining | Data Mining | Disease Modelling | Mechanistic Disease Hypotheses | In-silico Validation | Clinical Validation

SCANew Literature mining | Log in | Register

**How did AETIONOMY respond to that Challenge?**  
The AETIONOMY concept is based on:

- Integration of public and proprietary data, information and knowledge
- Integration of information across scales and levels (e.g. molecular, clinical)
- A combination of knowledge-driven modelling and data-driven mining
- An integrative approach that combines a plurality of modelling and mining strategies
- An adaptive approach that can easily take up and use new knowledge and data when they become available

**Welcome to AETIONOMY KB**  
The AETIONOMY Knowledge base (AKB) provides a platform to generate a mechanism-based taxonomy of Alzheimer's and Parkinson's Disease and to validate that taxonomy in the course of a prospective clinical trial. The AKB offers:

- Descriptions of methods applied in the different project stages (incl. webinar recordings),
- access to disease models and quality controlled data, and
- web services for analytical data processing.

**Integrated Storage:** Bring **heterogeneous data** together



Ada, the AETIONOMY Reporting System

**Import and export data sets**

For a quick and flawless data integration, Ada provides the import adapters for 5 file formats and APIs. For postprocessing, data can be exported into 3 file formats, or pulled directly through Ada's RESTful API.

Login

- One point stop for AETIONOMY knowledge and services
- platform to generate a mechanism-based taxonomy of Alzheimer's and Parkinson's disease
- description of methods applied (incl. webinar recordings, publications and use cases)
- access to disease models and quality controlled data
- web services for analytical data processing



## AETIONOMY Knowledge Base: who can benefit?



### Users who can benefit

AETIONOMY intends to disseminate the approaches and methodologies and how they can be adapted to benefit differently from these information:

- **General public and Patient Organizations** with new information for both the diseases.
- **Policy makers** with insights into new disease models,
- **Bioinformaticians and students** evaluating new data mining approaches,
- **Medical experts** validating new mechanistic disease hypotheses, and

### Addresses targeted Usergroups with linked information:

1. General public and Patient Organizations
2. Policy makers
3. Bioinformaticians and students
4. Medical experts



# AETIONOMY Knowledge Base: Awareness and training

Offers training on bioinformatic methods and services

Organising knowledge about neurodegenerative Disease Mechanisms for the Improvement of Drug Development and Therapy

VISION SERVICES WORK PACKAGES COLLABORATIONS MEDIA

Homepage - Media - Webinars

## Webinars

**Feedback on Public Webinar about the knowledge management Platform (D2.4.3.3)**

Revision of the AETIONOMY Knowledge base from data aggregation & statistics to a knowledge, methods & services enhanced implementation.

Webinar (D2.4.3.3): "The AETIONOMY Knowledge management platform"

Dr. Ashwarya Alex, Andrey Kononov, Stephan Springstube

Contributions by all Work package groups  
16th Nov. 2018

**Mission**  
To increase knowledge of the causes of Alzheimer's and Parkinson's Disease by generating a mechanism-based taxonomy, to validate the taxonomy in a prospective clinical study that demonstrates its suitability for identifying patient subgroups (based on discrete disease mechanisms), to support future drug development and lay the foundation for improved identification and treatment of patient subgroups currently classified as having AD or PD.

inspired by patients. Driven by science. Fraunhofer SCAI efpia AETIO N/O M/Y

Bayesian Modelling of clinical data –

Using Multi-Scale

## Links to services, tutorials and webinars:

### 6. How to get access to services?

- Information retrieval (literature mining):  
[SCAView Neuro](#)
- BEL disease model viewer (collected knowledge):  
[BEL-Commons](#)
- Mechanistic candidates repository (graph mining):  
[NeuroMMSig](#)
- Data features:  
[Bayesian Network Viewer](#)
- Trajectories:  
[EPAD longitudinal viewer](#) [Images - Google Drive](#)
- Clinical data management:  
[transSMART](#)
- Statistical and analysis workflows:  
[ADA](#)

<https://data.aetionomy.scai.fraunhofer.de/>  
<https://www.aetionomy.eu/en/media/webinars.html>





# AETIONOMY Knowledge Base: Linked to project phases

**AETIONOMY** KNOWLEDGE BASE Organising Knowledge about Neurodegenerative Disease Mechanisms for the Improvement of Drug Development and Therapy

search

Knowledge Mining ▾ Data Mining ▾ Disease Modelling ▾ Mechanistic Disease Hypotheses ▾ In-silico Validation ▾ Clinical Validation ▾

transSMART - clinical data repository

ADA workflows

NeuroMMSig - clinical validation of candidate molecules

ADNI / PPMI Disease Stages

ADNI Analyses

AddNeuroMed merge - longitudinal multimodal data

PPMI Analyses

Mapping out alzheimers disease data landscape

**The AETIONOMY Challenge**

*"To generate a mechanism-based taxonomy of Alzheimer's and Parkinson's Disease and to validate that taxonomy in the course of a prospective clinical trial."*

**Welcome to AETIONOMY**

The AETIONOMY Knowledge base (AKB) provides a platform to generate a mechanism-based taxonomy of Alzheimer's and Parkinson's Disease and to validate that taxonomy in the course of a prospective clinical trial. The AKB offers:

- description of methods applied in the different stages (incl. webinar recordings),
- access to disease models and quality controlled data,
- web services for analytical data processing.

## Project phases and applied approaches & methods:

1. Knowledge mining
2. Data Mining
3. Disease modelling
4. Mechanistic disease hypotheses
5. In-silico validation
6. Clinical validation



# AETIONOMY Knowledge Base: Linked to Mechanistic Disease Hypothesis

Organising Knowledge about  
Neurodegenerative Disease Mechanisms for  
the Improvement of Drug Development and  
Therapy

KNOWLEDGE BASE

Knowledge Mining ▾
Data Mining ▾
Disease Modelling ▾
Mechanistic Disease Hypoth

Home / Mechanistic disease hypotheses

## Mechanistic disease hypotheses

The proposal of new taxonomies for the neurodegenerative disease mechanisms. Addressing these challenges the following activities are performed:

- Construction of a knowledge database with AD and PD data (mechanisms),

Further information

Mitochondrial-Dysfunction

Neuroinflammation

Insulin pathway

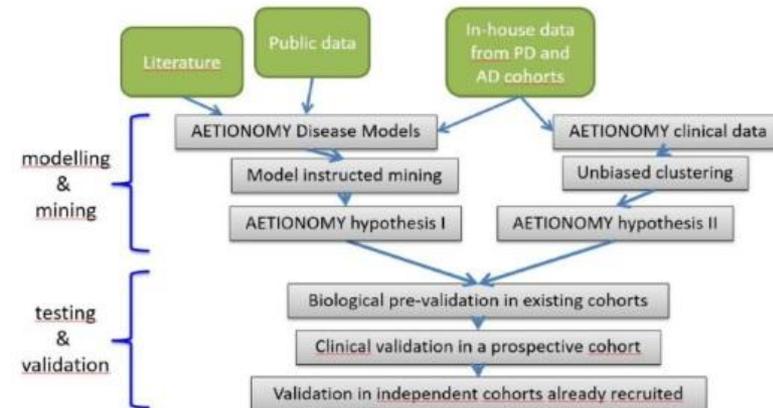
SNCA Methylation

Syndecans uptake

Astroglialinflammation

Stress-induced comorbidity

## The Mining & Validation Strategies



<https://data.aetionomy.scai.fraunhofer.de/mechanistic-disease-hypotheses>

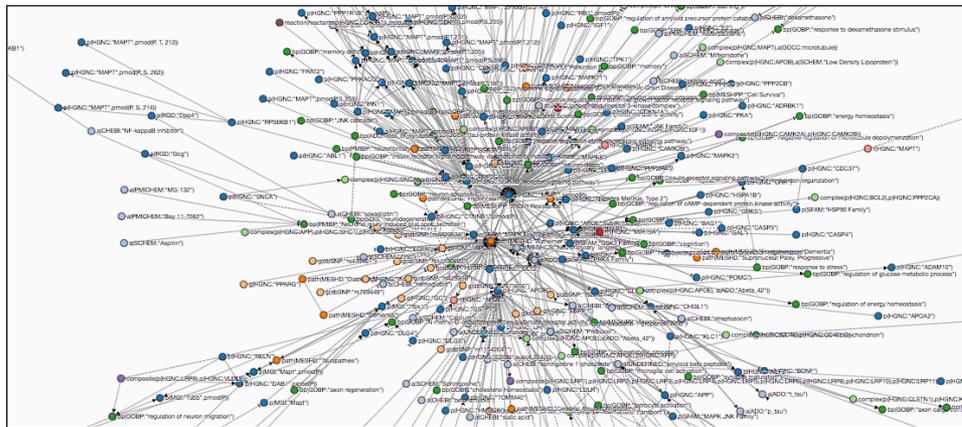




# AETIONOMY Knowledge Base: Disease Models

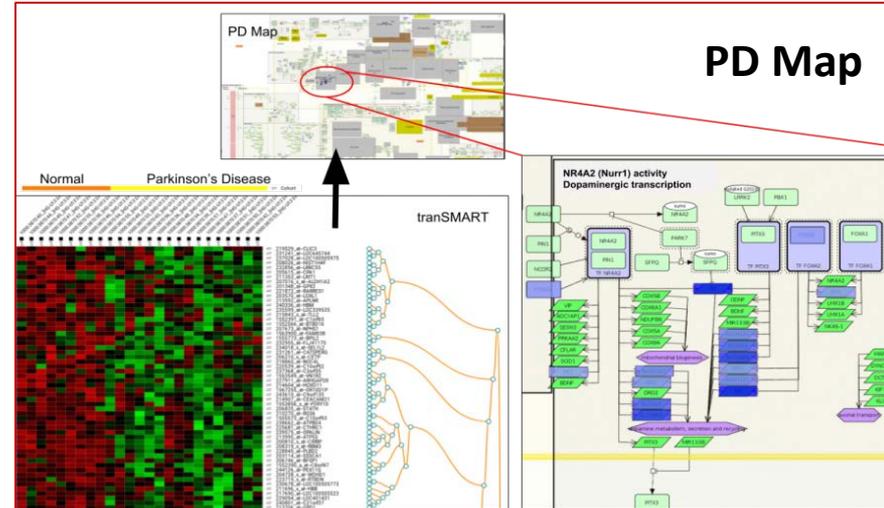
## PD and AD Disease maps and models

ApoE subgraph+Tau protein subgraph+Axonal transport subgraph



AD BEL model visualized via the NeuroMMSIG  
<https://neurommsig.scai.fraunhofer.de/>  
 Hosted and updated by Fraunhofer

PD Map



PD Map visualized via the MINERVA platform  
<https://pdmap.uni.lu/minerva/>  
 Hosted and updated by UL



# AETIONOMY Knowledge Base: BEL Disease Models

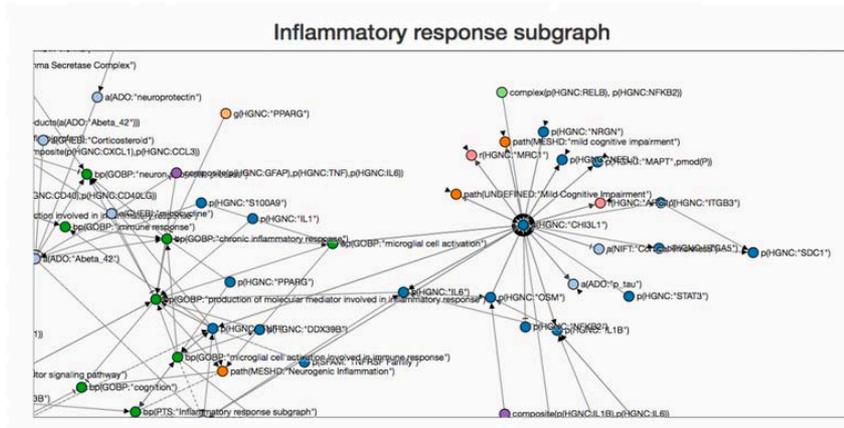
## Disease maps as support to hypothesis generation

Home / Mechanistic Disease Hypotheses / Astroglialinflammation

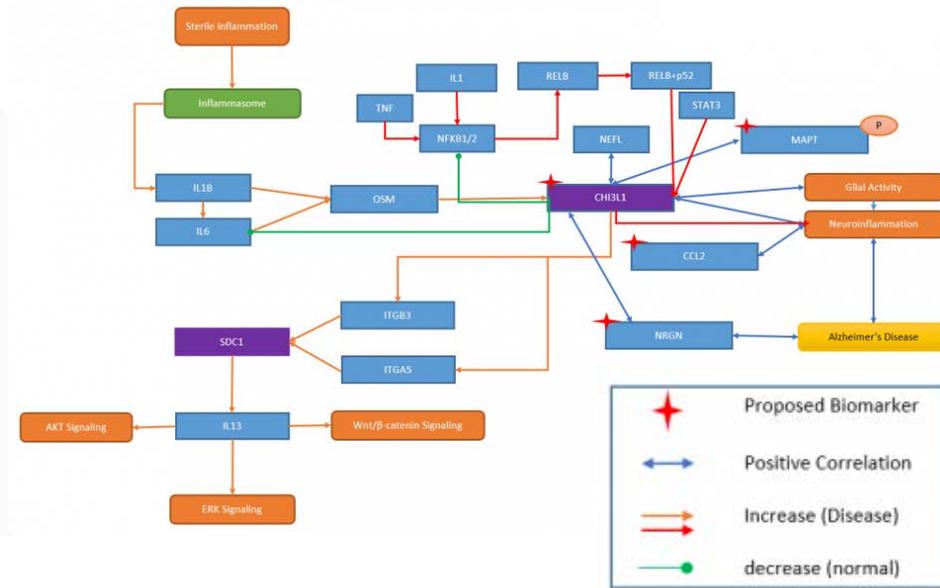
### Astroglialinflammation

Astroglialinflammation (in AD, IDIBAPS/BBRC)  
=> YKL-40 (CHI3L1)

NeuroMMSig inflammatory response subgraph:



NeuroMMSig inflammatory response subgraph (AD BEL model)



Cartoon of the candidate mechanism





# AETIONOMY Knowledge Base: Data harmonisation and curation

Systematic Inclusion of clinical, EFPIA and public datasets in the **tranSMART clinical repository**





# AETIONOMY Knowledge Base: Datasets available through tranSMART

Systematic Inclusion of clinical, EFPIA and public datasets in the tranSMART clinical repository

The screenshot displays the tranSMART interface with a hierarchical tree of datasets. The left pane shows a list of folders, with 'AETIONOMY PD (405)' highlighted in red. A red arrow points from this folder to its expanded view in the right pane. The right pane shows the following sub-folders and their counts:

- AETIONOMY PD (405)
  - Adverse Events (405)
    - Adverse Event 1 (30)
    - Adverse Event 2 (25)
    - Adverse Event 3 (2)
    - Clinical Center (29)
    - Did an Adverse Event Occur (405)
    - Serious Adverse Event (5)
  - Biological Samples (405)
    - Blood Sampling (405)
    - Cells sorting (405)
    - CSF Collection (405)
    - Skin Biopsy (405)
  - Biospecimen Analysis (364)
    - Blood Sampling (364)
    - CSF (75)
  - Clinical Assessment (402)
    - Epworth Sleepiness Scale (ESS) (394)
    - Hoehn and Yahr Scale (391)
    - Hospital Anxiety and Depression Scale (HADS) (395)
    - International Physical Activity Questionnaire (IPAQ) (401)
    - MDS UPDRS (397)
    - Neuropsychological Assessment (395)

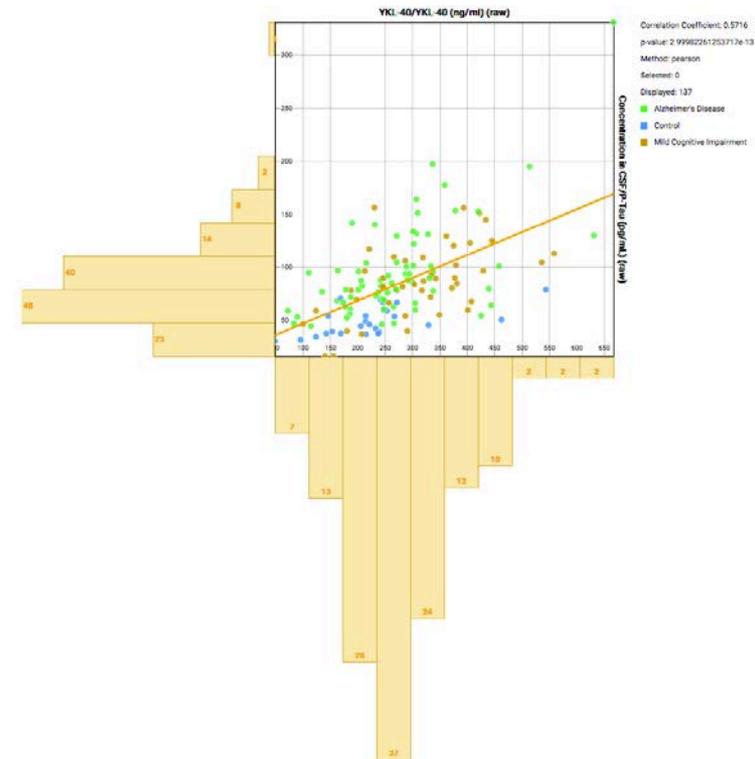
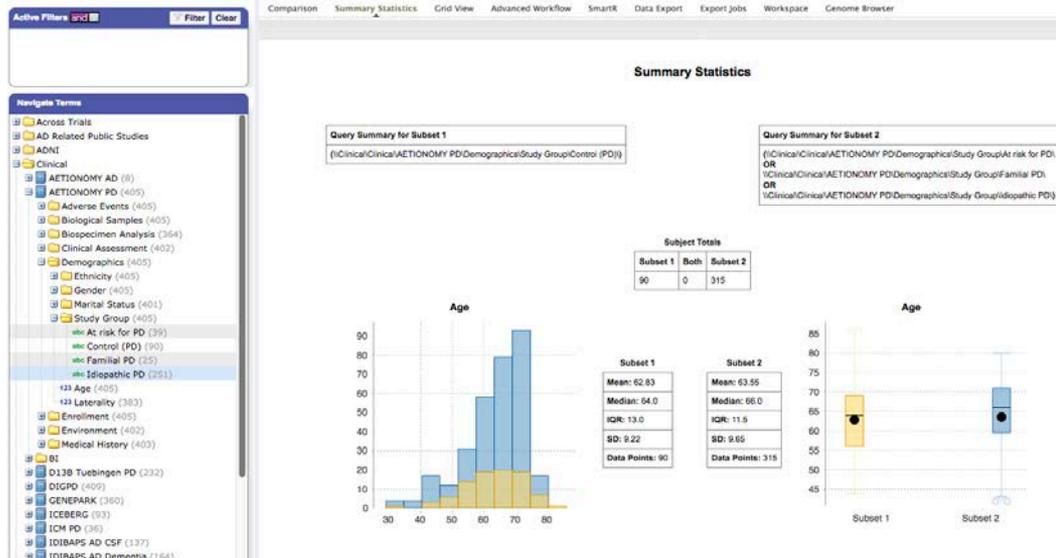
<https://aetionomy.uni.lu/tranSMART/login/auth>





# AETIONOMY Knowledge Base: Datasets available through tranSMART

Advanced analytics through smartR analytics in tranSMART





# AKB Component: Ada - *advanced statistical and analysis workflows*



<https://aetionomy-ada.lcsb.uni.lu/>





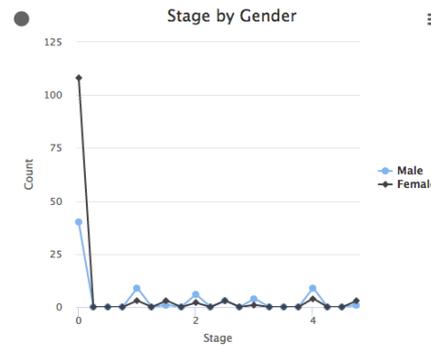
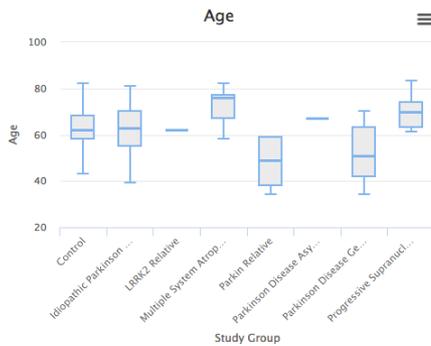
# AKB Component: Ada - advanced statistical and analysis workflows

Customised user views and dynamic and interactive analytics

Views ▾ Analytics ▾ Dictionary Categorical Tree Setting ▾

360 GENEPARK Items found

Filter: + ▣ Export ▾ ↶



ANOVA Test for Study Group

Field	p-Value	Degree of Freedom	Stats/F-Value
Stage	0.003	6	23.14

**Edit Widget Spec**

- Type: Scatter
- X Field: Fields, Study Group, Age, Montreal Cognitive Assessment (MoCA)
- Y Field: Scatter
- Group Field: Heatmap, Agg
- Sub Filter: Grid, ContributionCount, Correlation, IndependenceTest, BasicStats, Templatanent

Buttons: Close, OK

**Widget Specs**

Type	Content	Grid Offset	Grid Width	Grid Height	Textual?	Title	Chart Type
<input type="checkbox"/> Scatter	Fields, Study Group, Age, Montreal Cognitive Assessment (MoCA)		12		<input type="checkbox"/>		

**Age vs. Montreal Cognitive..**

Legend:

- Control
- Idiopathic Par...
- LRRK2 Relative
- Multiple Syst...
- Parkin Relative
- Parkinson Dis...
- Parkinson Dis...
- Progressive S...



**Welcome to AETIONOMY KB**

The AETIONOMY Knowledge Base (AKB) provides a platform to generate a mechanism-based taxonomy of Alzheimer's and Parkinson's Disease and to validate that taxonomy in the course of a prospective clinical trial. The AKB offers:

- description of methods applied in the different project stages (incl. webinar recordings);
- access to disease models and quality controlled data; and
- web services for analytical data processing.

### Users who can benefit

AETIONOMY intends to disseminate the approaches and methodologies and how they can be adapted to other projects and research areas. User groups can benefit differently from these information:

- **General public and Patient Organizations** with new information for both the diseases;
- **Policy makers** with insights into new disease models;
- **Bioinformaticians and students** evaluating new data mining approaches;
- **Medical experts** validating new mechanistic disease hypotheses; and

### Further information



## After AETIONOMY ...

- The AETIONOMY Knowledge Base will continue to be maintained for another 5 years
- All clinical and public datasets will be available for access through a Data Access Committee
- The disease models and services will continue to be developed and updated regularly



## Acknowledgements

### **Fraunhofer SCAI**

Prof Dr. Martin Hofmann-Apitius  
Stephan Springstubbe  
Christian Ebeling  
Andrej Konotopez

### **Erasmus Medical College**

Henri Vrooman

### **Université d'Aix Marseille (AMU)**

Dr. Viktor Jirsa  
Irene Yujnovsky  
Marcel Carrere

### **Boeringer Ingelheim**

Dr. Nathan Lawless  
Prof. Dr. Bastian Hengerer

### **Univeristy of Luxembourg**

Dr. Aishwarya Alex  
Dr. Adriano Barbosa da Silva  
Kavita Rege  
Dr. Wei Gu

### **Leibniz Universität Hannover (LUH)**

Prof. Dr. Nikolaus Forgo  
Dr. Marc Stauch

We would also like to thank all our data providers and collaborators at : ICM, UKB, KI, IDIBAPS, BI, Sanofi and UCB





Questions ?