The AETIONOMY Knowledge Base

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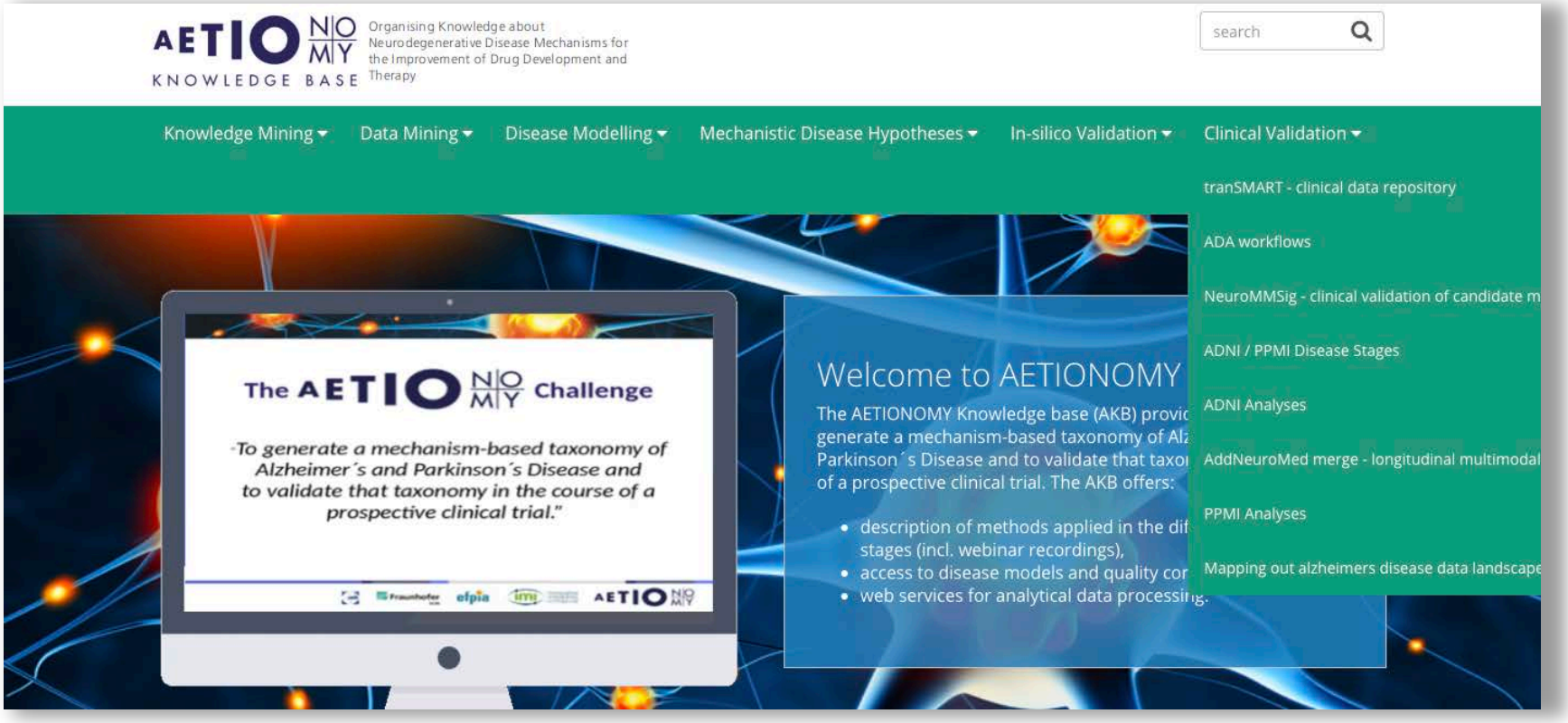
AETIONOMY Final Symposium and IMI Neurodegenerative Initiatives 29th November 2018

Mission

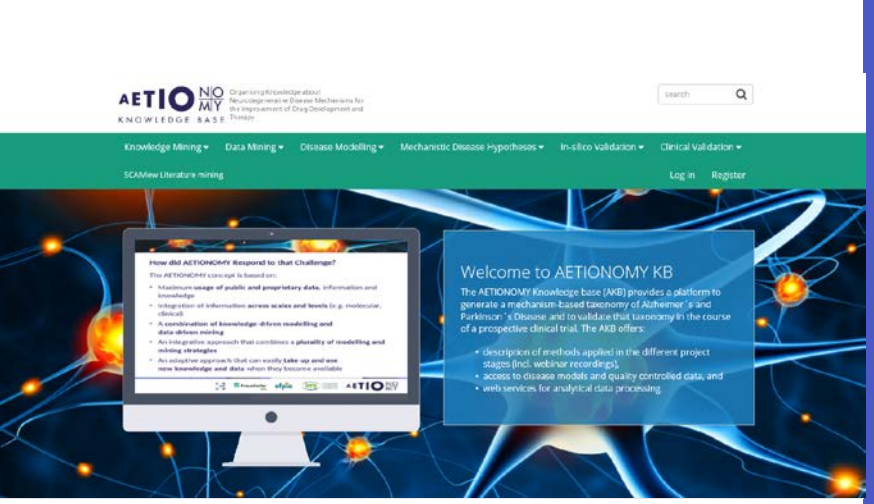
To increase knowledge of the causes of Alzheimer´s and Parkinson´s Disease by generating a mechanism-based taxonomy; to validate the taxonomy in a prospective clinical study that demonstrates its suitability for identifying patient subgroups (based on discrete disease mechanisms); to support future drug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

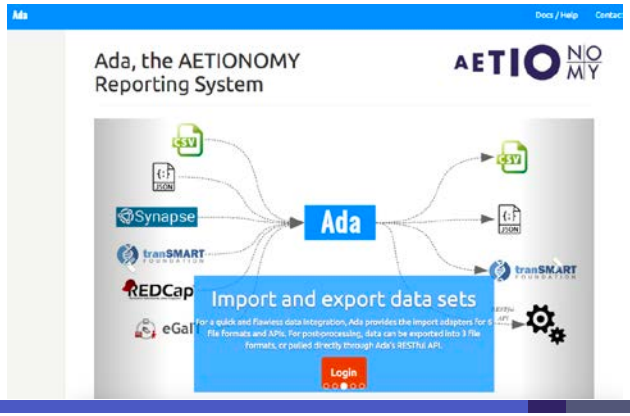
AETIONOMY Knowledge Base (AKB)



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

AETIONOMY Knowledge base





- 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

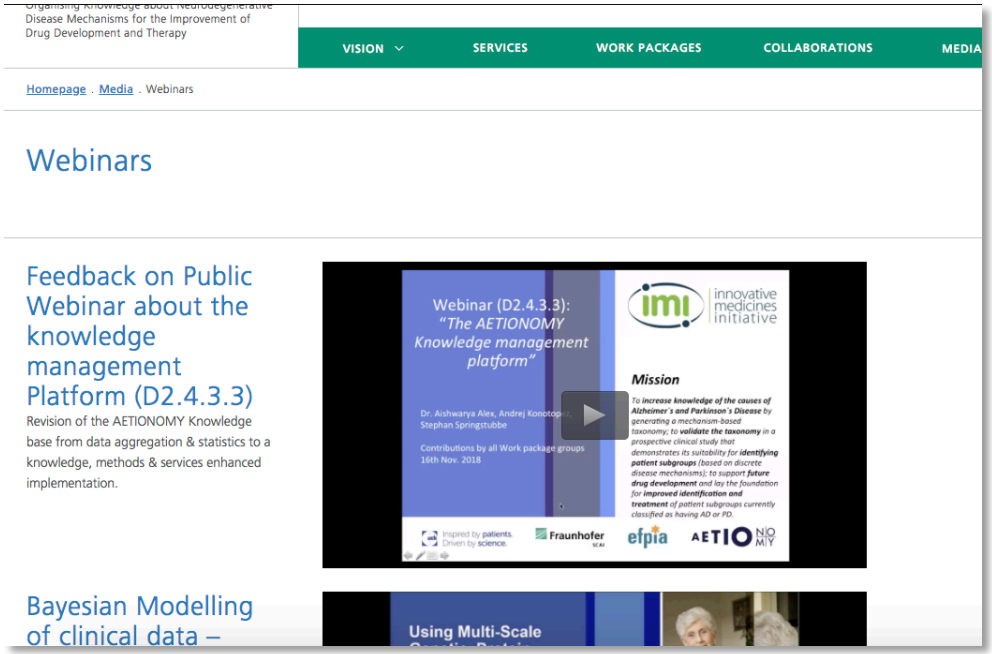
AETIONOMY Knowledge Base: who can benefit?

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



Links to services, tutorials and webinars:

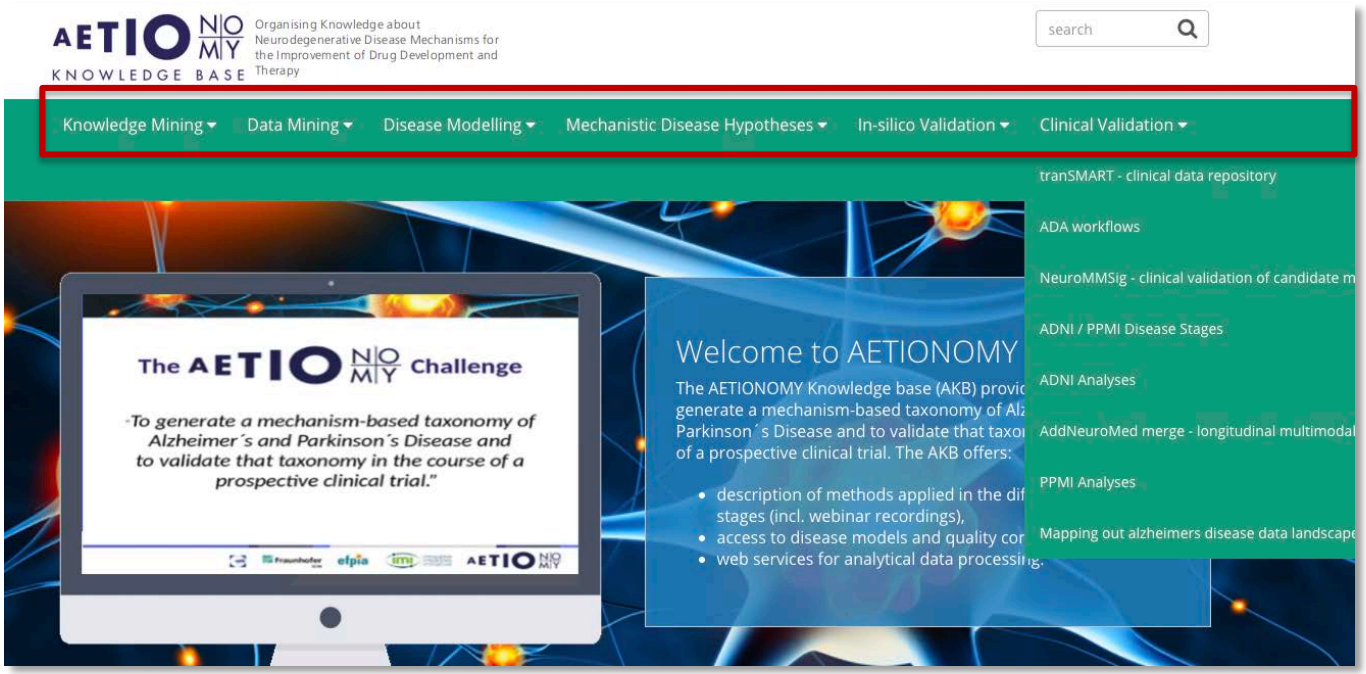
6. How to get access to services?

- **Information retrieval (literature mining):** SCAIView Neuro
- **BEL disease model viewer (collected knowledge):** BEL-Commons
- **Mechanistic candidates repository (graph mining):** NeuroMMSig
- **Data features:** Bayesian Network Viewer
- **Trajectories:** EPAD longitudinal viewer
- **Clinical data management:** tranSMART
- **Statistical and analysis workflows:** ADA

Images - Google Drive

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

AETIONOMY Knowledge Base: Linked to project phases



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

AETIONOMY KNOWLEDGE BASE

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

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

- Mitochondrial-Dysfunction
- SNCA Methylation
- Neuroinflammation
- Astrogliainflammation
- Insulin pathway
- Stress-induced comorbidity
- Syndecans uptake

Home / Mechanistic disease hypotheses

Mechanistic disease hypothese

The proposal of new taxonomies for the neurodegenerative diseas…kir… mechanisms. Addressing these challenges the following activities a…

- Construction of a knowledge database with AD and PD da…ge… (mechanisms),

Further information

Mitochondrial-Dysfunction

Neuroinflammation

Insulin pathway

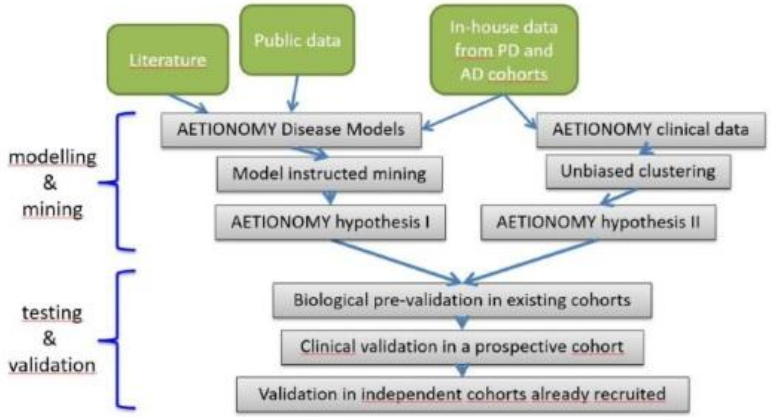
SNCA Methylation

Syndecans uptake

Astrogliainflammation

Stress-induced comorbidity

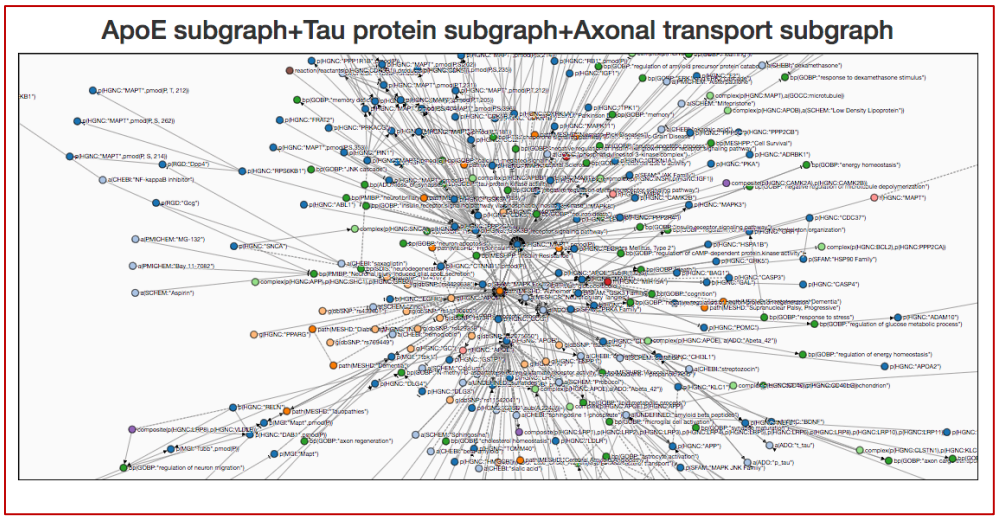
The Mining & Validation Strategies



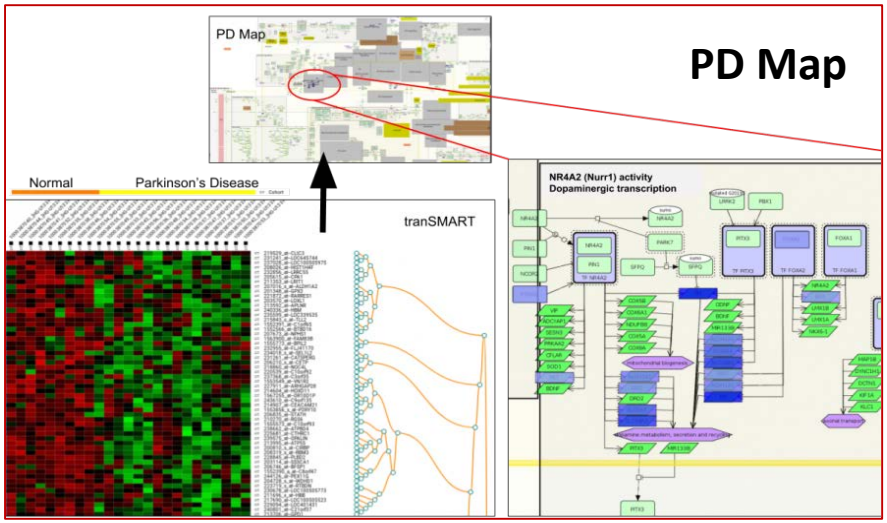
https://data.aetionomy.scai.fraunhofer.de/mechanistic-disease-hypotheses

AETIONOMY Knowledge Base: Disease Models

PD and AD Disease maps and models



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



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

AETIONOMY Knowledge Base: BEL Disease Models

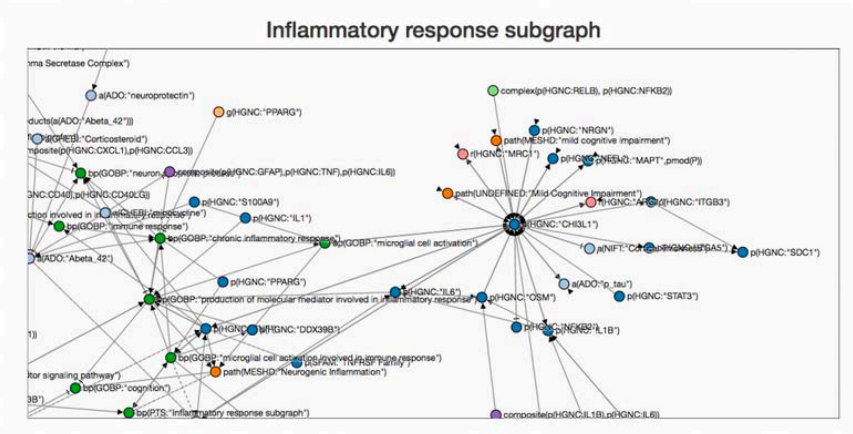
Disease maps as support to hypothesis generation

Home / Mechanistic Disease Hypotheses / Astrogliainflammation

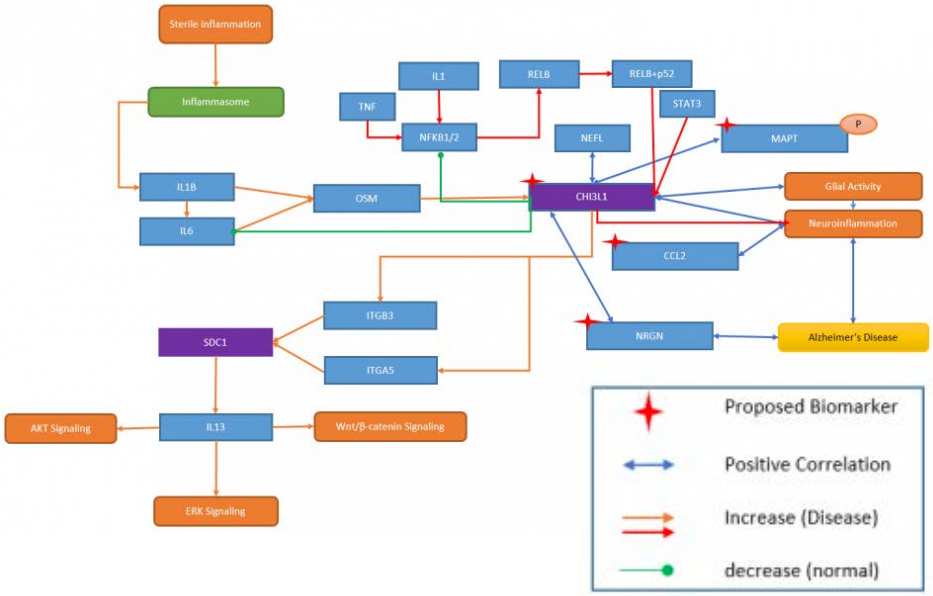
Astrogliainflammation

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

NeuroMMSig inflammatory response subgraph:



NeuroMMSig inflammatory response subgraph (AD BEL model)

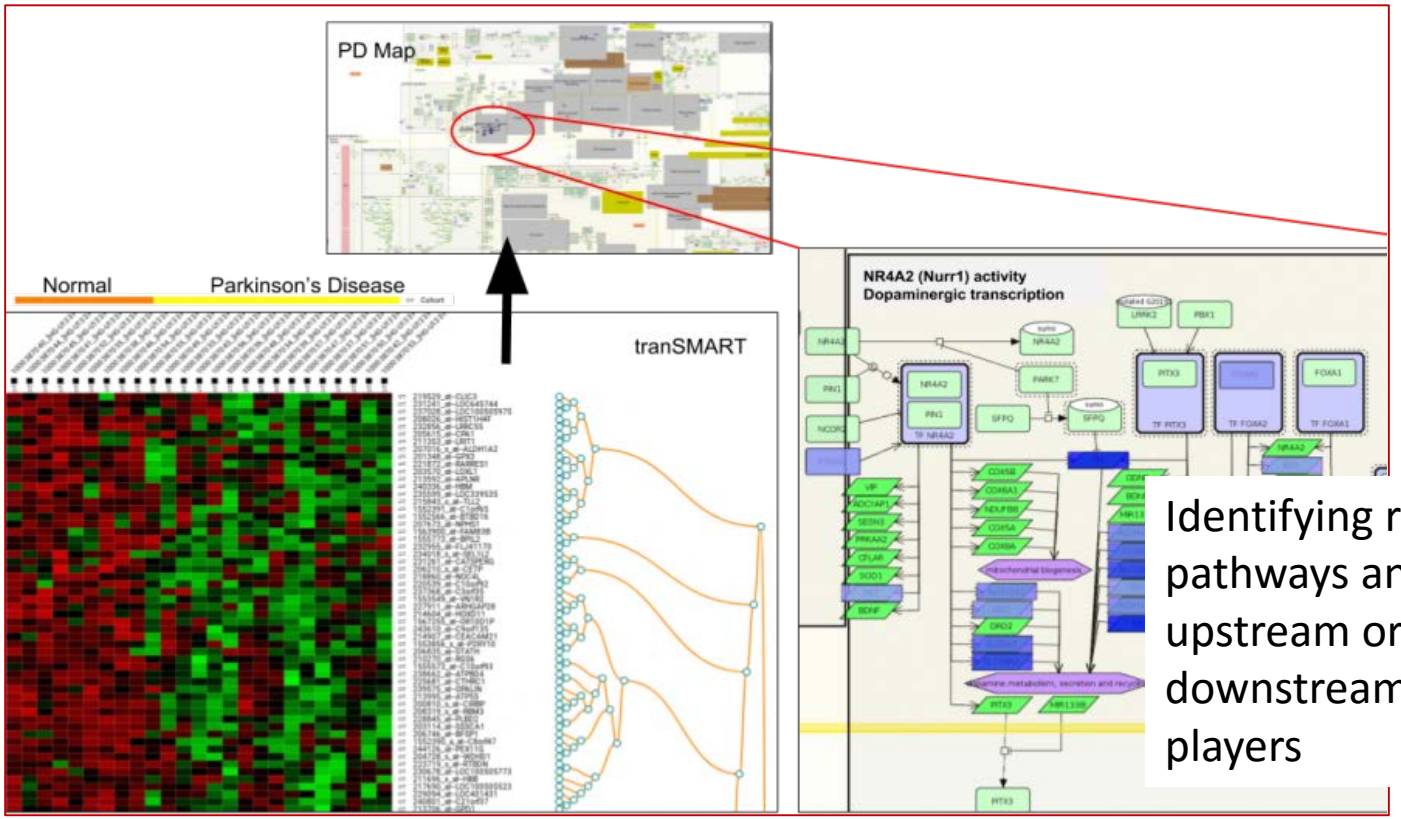


Cartoon of the candidate mechanism

AETIONOMY Knowledge Base: SBML Disease Maps

Disease maps as support to hypothesis generation

Overlayed on disease maps (PD Map)



Differentially expressed genes from analysis (tranSMART)

Identifying relevant pathways and upstream or downstream players

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**

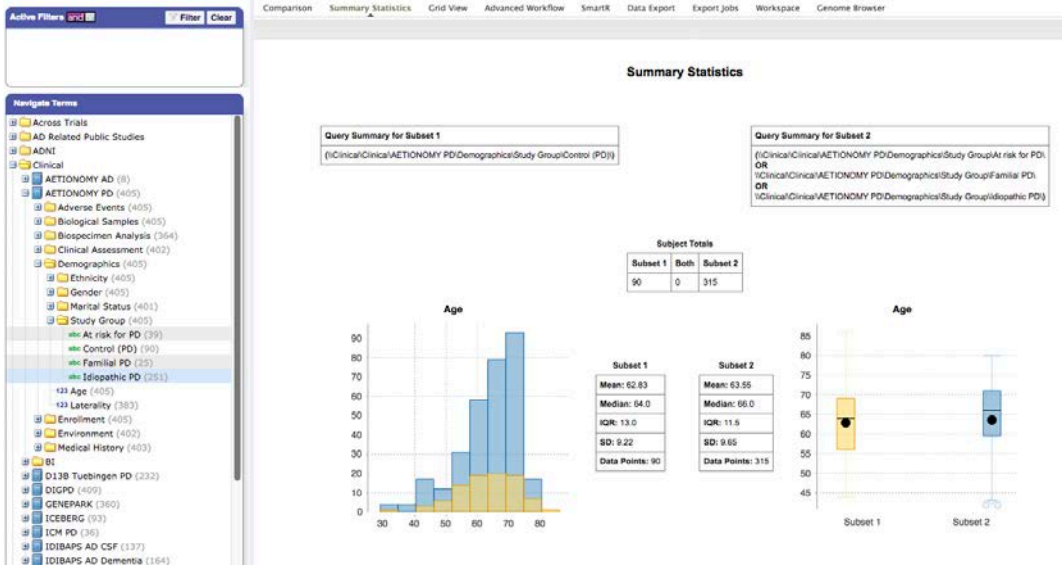
- AD Related Public Studies
- ADNI
- Clinical
  - AETIONOMY AD (8)
  - AETIONOMY PD (405)
  - BI
  - D13B Tuebingen PD (232)
  - DIGPD (409)
  - GENEPARK (360)
  - ICEBERG (93)
  - ICM PD (36)
  - IDIBAPS AD CSF (137)
  - IDIBAPS AD Dementia (164)
  - IDIBAPS AD Screening (17)
  - IDIBAPS AD Validation (35)
  - INSIGHT (23)
  - Kings College London PD (98)
  - NGC (5011)
  - UKB AD Cytokine (95)
  - UKB AD Inflammation 2 (220)
  - UKB AD Inflammation (399)
  - UKB PD Methylation (1057)
- Imaging Data
- PD Related GEO Studies
- PPMI

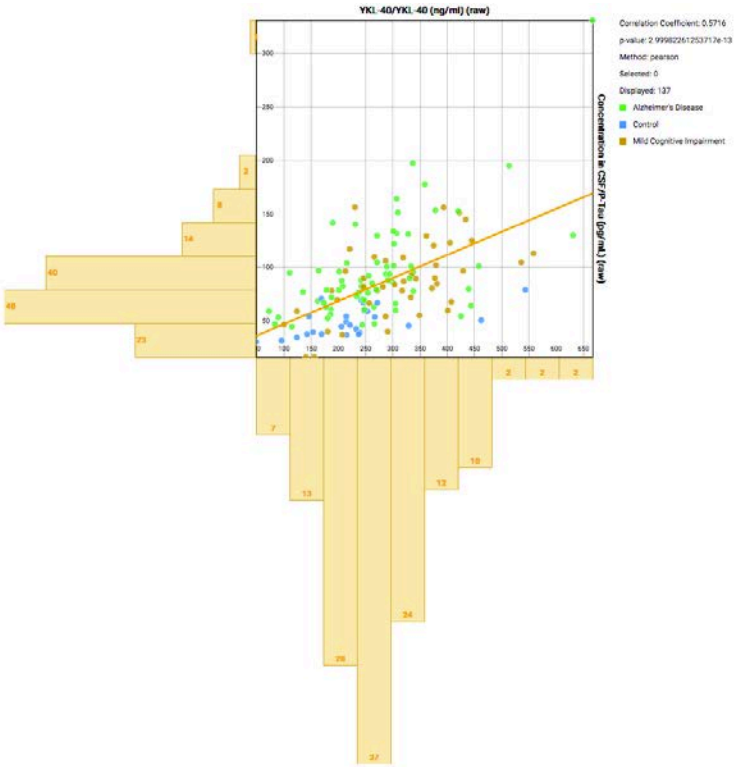
- AETIONOMY PD (405)
  - Adverse Events (405)
    - Adverse Event 1 (30)
    - Adverse Event 2 (25)
    - Adverse Event 3 (2)
    - Clinical Center (29)
    - Did an Adverse Event Occur (405)
    - Serious Adverse Event (5)
  - Biological Samples (405)
    - Blood Sampling (405)
    - Cells sorting (405)
    - 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



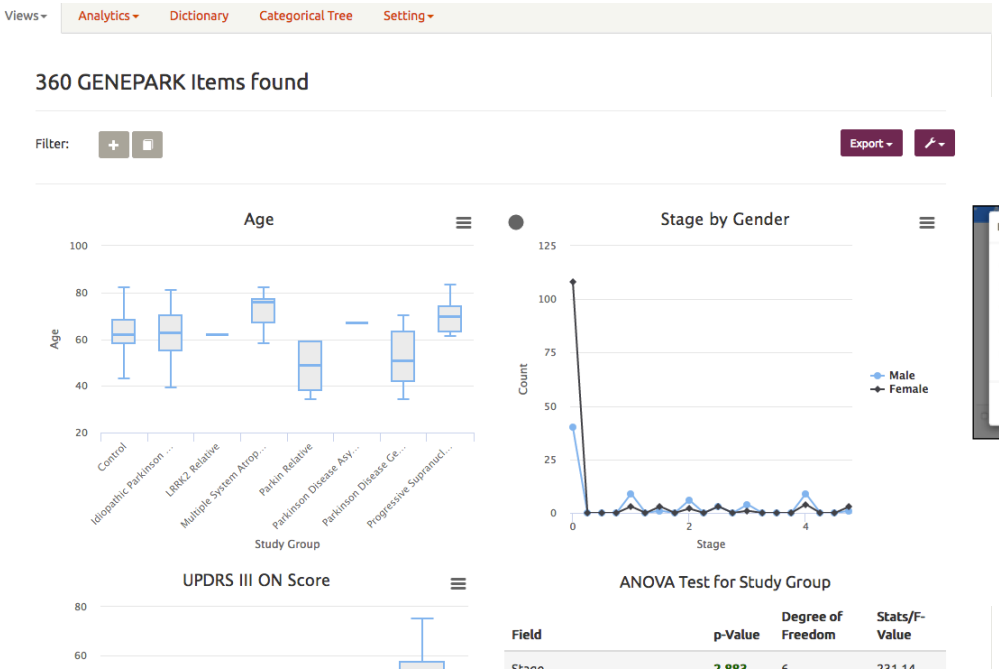


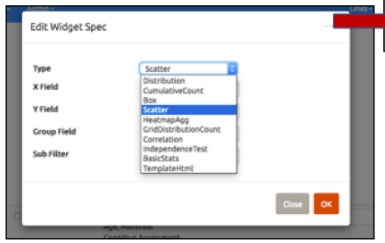
AKB Component: Ada - *advanced statistical and analysis workflows*

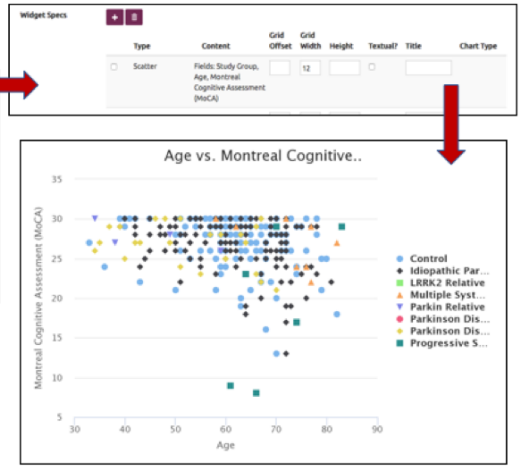
https://aetionomy-ada.lcsb.uni.lu/

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

Customised user views and dynamic and interactive analytics







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AETIONOMY KB
data.aetionomy.scai.fraunhofer.de

AETIONOMY KNOWLEDGE BASE

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

Log In Register

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

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Questions ?