September 2014

Newsletter Issue I

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

IN THIS ISSUE

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imi innovative medicines initiative

AETIONOMY

EDITORIAL

Novel Classification of Alzheimer's and Parkinson's Disease

Today 6 million people in the USA are suffering from **Alzheimer's (AD) and Parkinson's disease (PD)**, the two most common neurodegenerative conditions. As the population ages this number will increase to 12 million in the next 30 years. Despite billions of Euros being spent on drug discovery and drug development for these diseases, there are no disease modifying treatments yet available. One of the key reasons for this is the fact that we still classify these diseases using similar criteria to when they were first described by Dr. Aloysius Alzheimer and Dr. James Parkinson respectively.

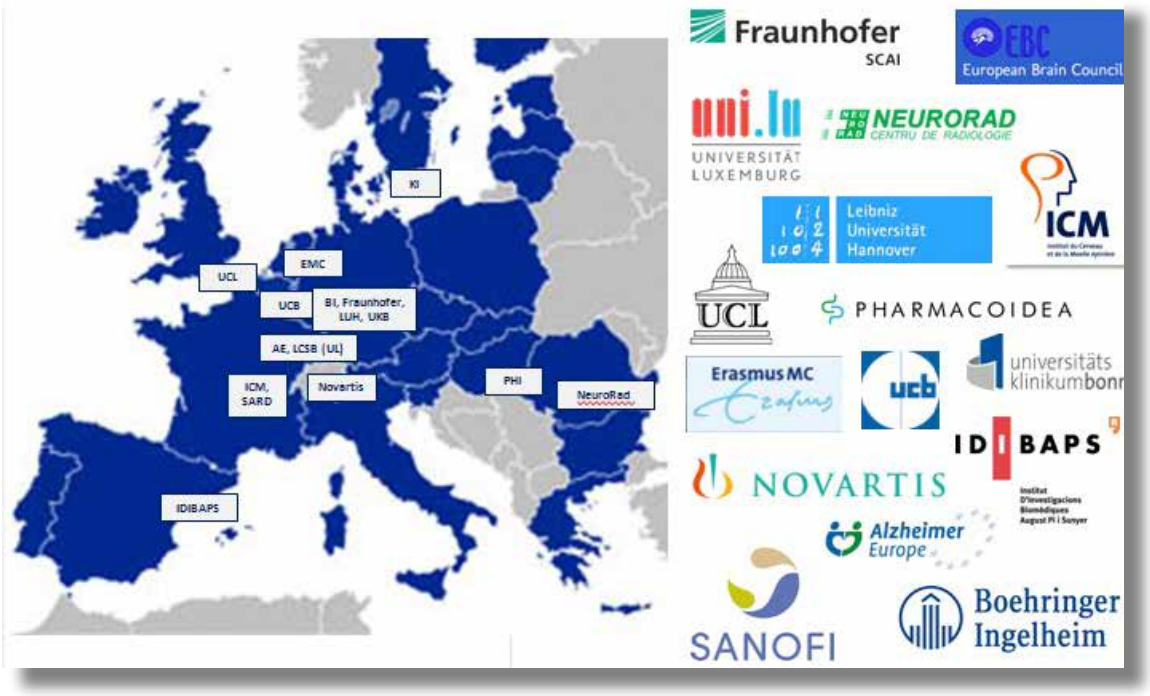
Developing drugs is a high risk business. The chance of a compound going into human testing and becoming an actual drug is less than 1 in 20. This means we fail 19 times for every successful drug we find. Part of this failure rate is the fact that we classify diseases according to the effects of the disease rather than their causes. This is because the current classification system has changed little in 100 years and until recently it has been far easier for physicians to measure and record the effects of the disease than determine the cause. If we are to be successful in developing new treatments which will prevent neurodegeneration, then we have to address this problem.

AETIONOMY is a consortium brought together under the European Innovative Medicines Initiative (IMI) to tackle this problem of the classification of neurodegenerative diseases. Revising the taxonomy (classification) of neurodegenerative diseases will take many years to complete and to be accepted by the biomedical community. AETIONOMY is the first step on this journey. The Consortium is jointly led by Professor Martin Hofmann-Apitius from the Fraunhofer Institute SCAI in Germany and Professor Duncan McHale from the biopharmaceutical company UCB.

„Reclassification is important as it will lead to new drug targets that focus on the disease process and identify which patients should get which drug."

Prof. Duncan McHale, UCB,
AETIONOMY EFPIA Coordinator

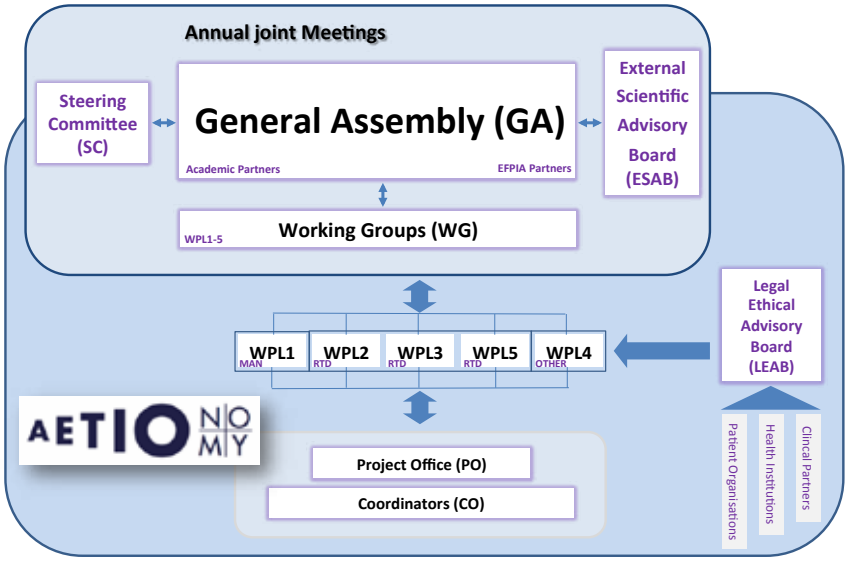
Within the **consortium** there are 8 academic partners; Fraunhofer Institute SCAI, University of Luxembourg, University College of London, Leibnitz University of Hannover, Institute du Cerveau et de la Moelle Epiniere, Karolinska Institute, University of Bonn, Institute D'Investigacions Biomediques August Pi i Sunyer and Erasmus University, 2 patient organisations; Alzheimer Europe and European Brain Council. There are 4 large pharmaceutical companies, UCB, Novartis, Sanofi and Boehringer Ingelheim and 2 SMEs; Pharmacoidea and NeuroRad. We will introduce each of the partner organisations in future editions of the newsletter.



The AETIONOMY partnership combining European expertises in patient advocacy, computing and bioinformatics, clinical research and imaging, neurology, and drug development

AETIONOMY is novel in terms of both, its scientific approach and its scale. There is a lot of published literature on the potential causes of Alzheimer's and Parkinson's disease and a significant number of major collaborations already funded and working well. The majority of these are looking at individual hypotheses or approaches to the problem e.g. genetic association studies, imaging studies, non-motor Parkinson's disease or familial Alzheimer's disease. Rather than start another similar approach, AETIONOMY will identify all of the available data either from published literature, publically available datasets or datasets from our collaborators. A common framework will be developed which will allow the integration of data relevant for modelling and mining. Once this data has been curated (re-annotated and quality controlled) and put into the common framework, novel data mining and visualisation approaches will be used to identify the pathophysiological changes occurring in the disease process at a molecular level. The knowledge extracted from the datasets will be used to cluster individual patients into separate mechanism based sub-groups leading to a new taxonomy of Alzheimer's disease and Parkinson's disease. The final part of the project AETIONOMY is an observational clinical study which will be used to collect biomarkers and prospectively validate 1 or more of the proposed new sub-groups.

AETIONOMY is divided into 5 work packages. Each work package will be described in much more detail in future editions of the newsletter. In the following graphic, we present the structure of the consortium and how it communicates:



Project structure and communications

AETIONOMY is now 9 months into our 5 year program. We have taken the first steps into developing a whole new way of looking at neurodegenerative diseases. If we are successful, then we will pave the way for better diagnosis, more accurate prognosis and an environment where new drugs to treat neurodegenerative disease can discovered, developed and used.

„We have set up core elements of the project in a way that they will go beyond the end of the funded period. For example the AETIONOMY knowledge base will be maintained for further 5 years."

Prof. Martin Hofmann-Apitius, Fraunhofer SCAI, AETIONOMY Academic Coordinator

We hope you like the first newsletter and get new insights in this European approach to treat Alzheimer's and Parkinson's diseases. If you would like to send us a comment, please send an email to: *contact@aetionomy.eu*

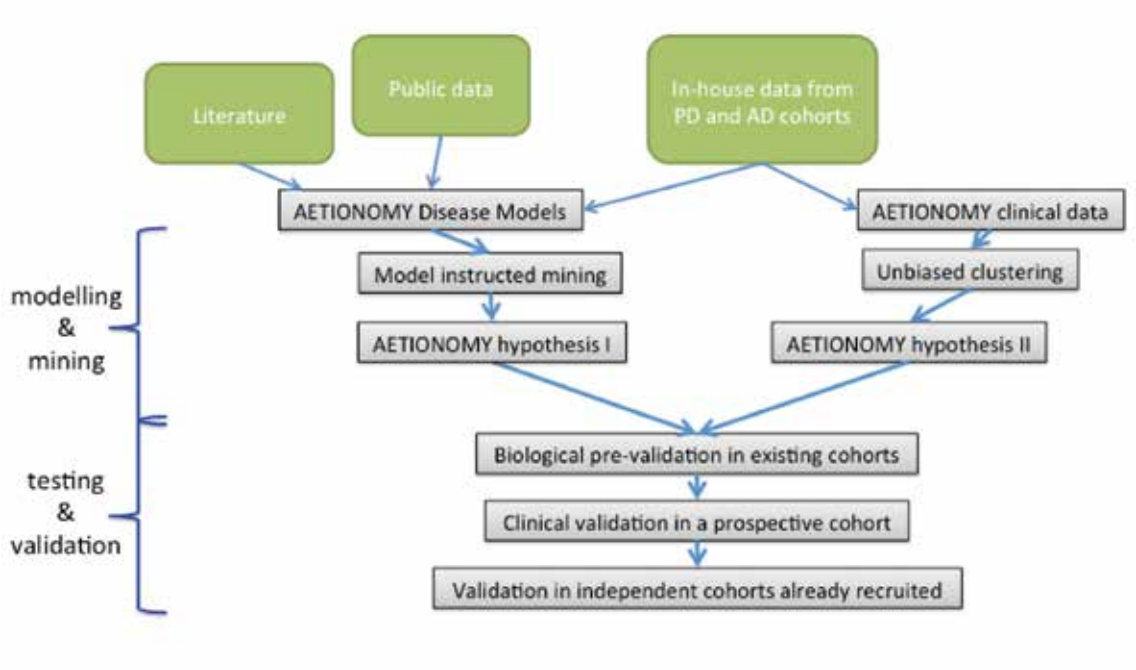
Yours sincerely,

Duncan McHale
Martin Hofmann-Apitius

OBJECTIVES

Generating Taxonomies on Disease causing Mechanisms

Currently, the established **disease classification systems** such as ICD (International Classification of Disease) makes use of phenotypes measured clinically or using standard laboratory and imaging techniques to establish major types and subtypes of disease. In contrast to the established disease classification systems, a "mechanism-based taxonomy" is based upon the knowledge about the biological pathways involved in the aetiology of a disease in the classification of disease classes and subclasses.



The AETIONOMY modeling, mining and validation strategies

A specific challenge we face in the course of the AETIONOMY project lies in the fact that for most neurodegenerative diseases the **dysfunctional biological pathways** underlying the disease are not known. AETIONOMY will therefore have to first define new routes towards the **identification of the underlying disease mechanisms** before organising these and proposing a rational disease taxonomy for Alzheimer's and Parkinson's disease. Thus main outcomes of the AETIONOMY project are reclassifications of the Alzheimer's and Parkinson's diseases based on causing mechanisms, moving away from phenotypic descriptions.

Moreover, we will validate the mechanism-based taxonomy at least partially in the course of a prospective clinical study.

ACCOMPLISHED MILESTONES

Project Activities

In this section we would like to inform you about the project milestones that have been accomplished.

Work Package 1

WP1 focuses on the project governance and project management. First milestones reached were: *Project manual available, Communication and Dissemination Strategy Plan, and External Scientific Advisory Board members* nominated.

Work Package 2

WP2 are acquiring, curating and building the data cube infrastructure which will integrate the available data. Milestones reached up to now are: *Data model provided, and Mapping file developed. The adaption of the eTRIKS curation workflow* will follow very soon.

Work Package 3

WP3 performs the data mining, visualisation and taxonomy building. As a first milestone a joint workshop with the sister Taxonomy Consortium, PRECISESADS, was organized, which serves as a basis for the collaboration on the *NDD Pathophysiology Knowledge Base*.

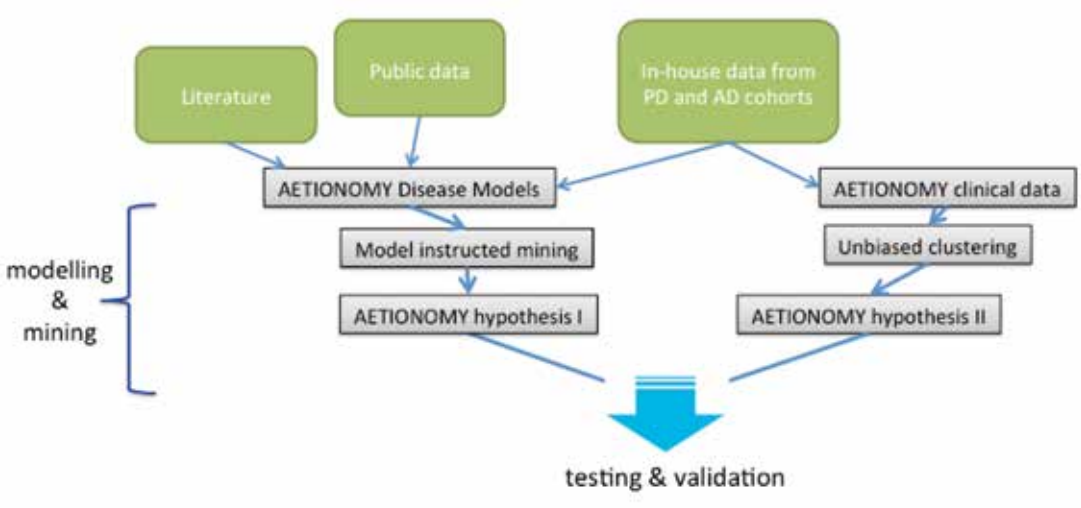
Work Package 4

WP4 oversees the ethical and legal aspects of the program. The first milestone, establishing the *Legal and Ethical Advisory Board* was achieved.

Work Package 5

WP5 is focussing on the validation of the new classification including the running of the observational clinical study. The first two milestones were reached: *Joint meeting to be done between EFPIA and Academic partners in WP 3 & WP 5 to decide which biomarkers should go into the final protocol, as well as the Identification of success criteria and initial design of study.*

Summarizing the status of the project (see graphic of the 'AETIONOMY strategies') we are still in the first phase 'modeling and mining', which Includes the generation of the knowledge base, and the definition of the disease models and hypotheses.



Partner Profiles

Joint Expertise for Research

The structure and size of the project consortium and the proposed project activities have been formulated to ensure a cost effective approach while realising the project objectives.

We would like to introduce in this issue the coordinator partners: UCB and the Fraunhofer Institute for Algorithms and Scientific Computing SCAI.

UCB

UCB is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system.

We combine biology and chemistry to make major breakthroughs. By integrating our expertise in large, antibody-based molecules and small, chemically-derived molecules, we can offer families with severe diseases and their specialist physicians the advantages of both large and small molecules to produce extraordinary breakthroughs.

We partner with the leaders in the pharmaceutical-industry. The complexities of severe diseases are beyond the expertise and resources of a single organisation. That is why we have teamed up with partners - we play to our strengths and tap into the organisations with greater or complementary strengths.

UCB has already participated in several research projects under the initiative and our CEO, Roch Doliveux, is Chair of the IMI governing board. This helps keep UCB at the heart of medicines research in Europe and ensures that our view of patient-centered innovation is shared with other stakeholders.

UCB is a significant contributor to the IMI and is involved in 21 consortia, including projects which support patient education and research on disease taxonomy. Our company leads three IMI projects with academic partners. The initiative has become a role model for open innovation and knowledge sharing with the capacity to drive innovation, growth and patient well-being in the decades ahead.

More information at www.ucb.com

Inspired by **patient**
Driven by **science.**

Fraunhofer Institute for Algorithms and Scientific Computing SCAI, Department for Bioinformatics

The **Fraunhofer Institute SCAI** conducts research in the field of computer simulations for product and process development, and is a prominent corporate partner in the industrial and science sectors. SCAI designs and optimizes industrial applications, implements custom solutions for production and logistics, and offers calculations on high-performance computers. Our services are based on industrial engineering, combined with state-of-the-art methods from applied mathematics and information technology.

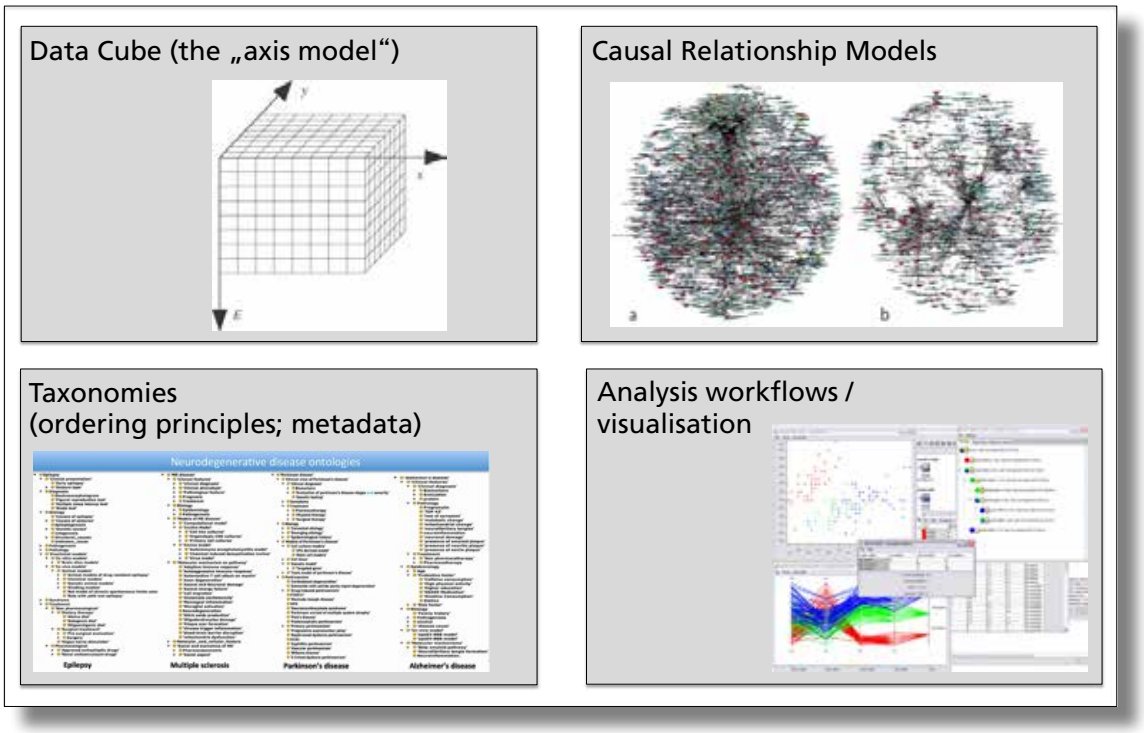
SCAI especially excels in coupled simulation of different physical disciplines, and develops software for visualization of calculation results. In bioinformatics, SCAI offers work-flow-oriented and integrated IT infrastructures for information extraction. SCAI has accumulated specialized expertise in both structured storing and administration of data and research results, and in the organization of projects.

The Fraunhofer SCAI Bioinformatics team

The Department of Bioinformatics at the Fraunhofer Institute for Algorithms and Scientific Computing SCAI is doing applied research and development in the field of:

- Disease modeling and data mining
- Information Extraction / Semantic Text Analysis
- Applied Chemoinformatics

Fraunhofer SCAI will contribute in AETIONOMY its experience in **information extraction (text mining), named entity recognition and relationship mining** automated methods for the **identification of causal and correlative statements** in scientific text, scalable software architectures for unstructured information mining (e.g. UIMA), and the **generation of dedicated knowledge bases**. The following graphic shows the components of the AETIONOMY knowledge base.



The AETIONOMY Knowledge base –
A high level view of the modular structure

In compliance with the general mission of a Fraunhofer Institute, the Department of Bioinformatics is working closely with industrial partners – including small and medium size enterprises – to enhance their competitiveness through **mediating knowledge and technology transfer** from academic research to industrial application. Collaborative research and development projects of the Department of Bioinformatics deliver solutions to the pharmaceutical industry, the biotech industry and to the life science software industry. Positioned at the boundary between pure commercial and pure academic research we maintain strong links to both communities. As an organisation dedicated to applied research we take part in the education of students of the Life Science Informatics curriculum of the Bonn-Aachen International Centre for Information Technology (B-IT) and we particpate actively in various national and European research initiatives.

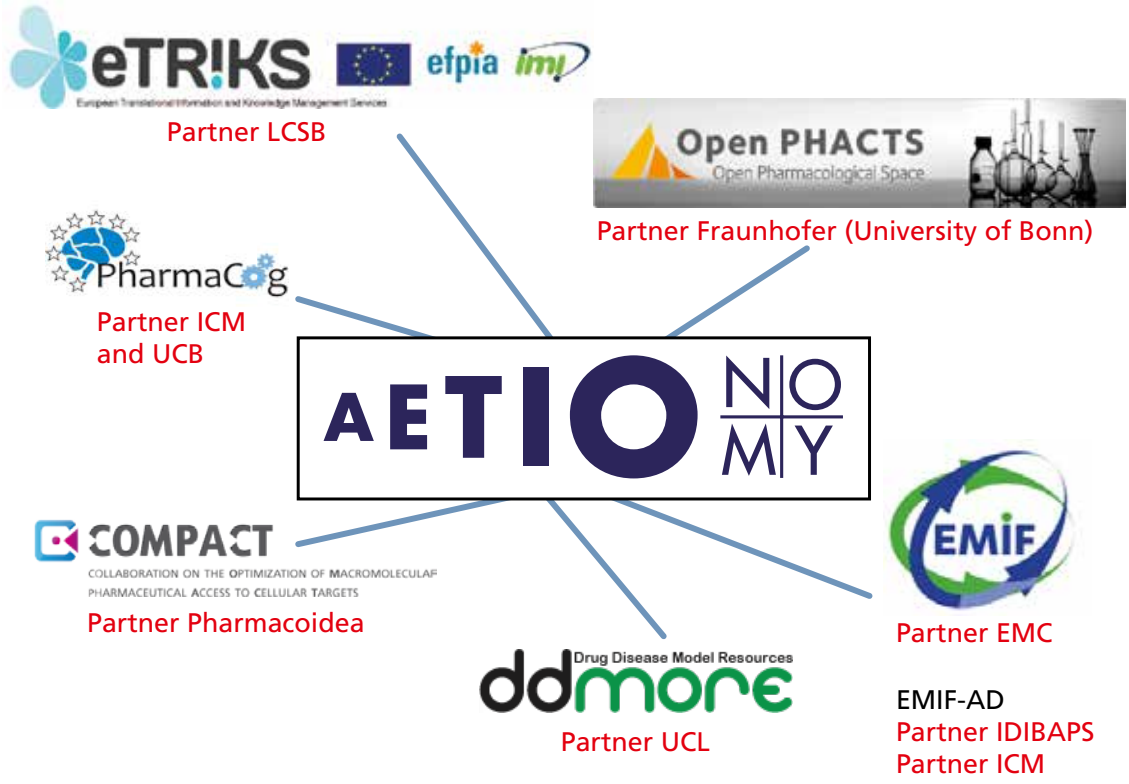
More information at www.scai.fraunhofer.de

Fraunhofer
SCAI

RELATED INITIATIVES

Exchange of Data, Knowledge and Experience

The majority of the EFPIA and academic partners in AETIONOMY are involved in other IMI projects and thus are able to mediate uptake of essential developments made in other IMI projects or feedback results of AETIONOMY to other IMI projects. Of utmost importance for AETIONOMY are the involvement of University of Luxembourg with **eTRIKS**; the involvement of Fraunhofer with **OpenPHACTS**, the coordination of EMIF through partner EMC and the involvement of partners ICM in **PharmaCog**, UCL in **DDMoRe** and Pharmacoidea in **COMPACT**. Moreover, two partners in AETIONOMY (IDIBAPS and ICM) are involved in **EMIF-AD**, the Alzheimer pillar of the EMIF project. Besides these, AETIONOMY partners are active in more than 40 IMI projects.



AETIONOMY and related research initiatives on Alzheimer's and Parkinson's diseases

In the following we would like to briefly introduce initiatives, which are collaborating intensively with AETIONOMY.

PRECISESADS

Molecular reclassification to find clinically useful biomarkers for systemic autoimmune diseases

Inflammatory autoimmune diseases such as rheumatoid arthritis and lupus affect 1-3% of the population, and while treatments exist, these have a number of serious side effects and are costly. There is growing evidence that many of these conditions may be incorrectly classified. The PRECISESADS project will study patients with various autoimmune diseases, gathering data on the molecular causes of their disease as well as their clinical symptoms. Using this information, they will pave the way for a new classification of these diseases, something that will allow doctors to offer patients more personalised treatments at an earlier stage of their disease. Chronic inflammatory autoimmune disorders like systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are found in 1-3% of the general population. They are particularly prevalent in women, with SLE affecting nine times more women than men. Symptoms of these diseases can be severe, and patients need regular check-ups. In fact, the pharmaceutical companies face major problems in trying to identify tests to determine the usefulness of drugs in clinical trials.

A new classification of inflammatory diseases

By establishing a Europe-wide, large-scale team, PRECISESADS will provide new data to offer a more appropriate classification of these patients. The project will analyse in great detail blood and urine samples of 2 500 people with a range of systemic autoimmune diseases, as well as patients with suspected autoimmune disease who don't have a diagnosis because they do not fulfil current clinical criteria for any of the systemic autoimmune diseases. By evaluating the molecular and clinical data using the latest technology, the project will deliver new biomarkers for use in more targeted clinical trials. Clinicians can then tailor therapies according to the specific molecular pathways found in individual cases. In short, treatments will become more personalised.

Towards targeted treatments

A personalised approach to the treatment of autoimmune diseases would allow patients to receive an earlier and more accurate diagnosis. Since the new data will reveal the molecular mechanisms specific different groups of diseases, a tailored approach to clinical therapy can be identified and the precise molecular pathway can then be targeted. What's more, earlier detection and more effective treatments will mean that the damaging effects of a late diagnosis can be avoided, and the patient's disease progression can be better controlled.

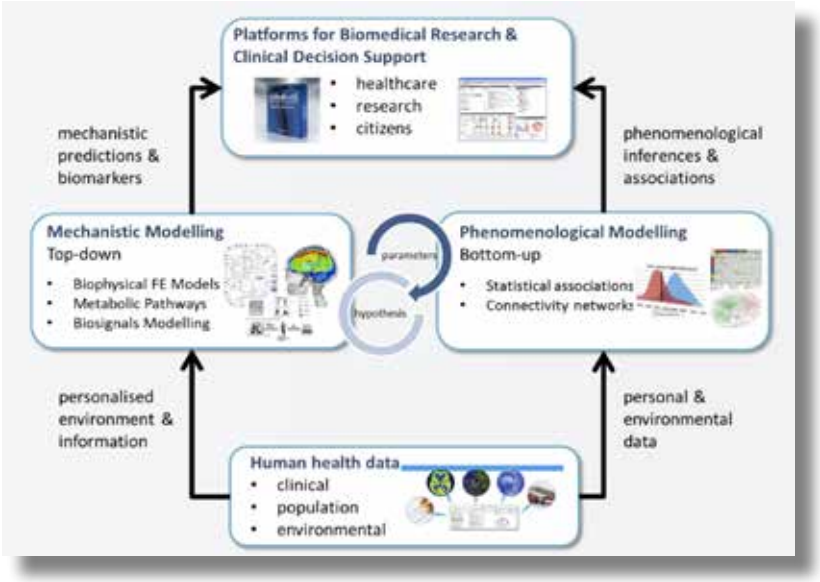
More information at www.precisesads.eu

PRECISESADS

VPH-DARE

Virtual Physiological Human: DementiA Research Enabled by IT

The DementiA Research Enabled by IT (VPH-DARE@IT) project responds to the European Parliament's 2011 resolution for a European Initiative on Alzheimer's disease and other dementias, and the EU Year of the Brain 2014 Initiative. The number of individuals suffering from dementia today is roughly 36 million and, due to ageing societies, will increase to 115 million by 2050. The annual costs are estimated to be €55B in Europe and €450B worldwide (1% of the World Gross Domestic Product). In 2012, the WHO declared dementia a global health priority, highlighting the urgent need for improvements in this area.



Multiscale multifactorial multiparadigm modeling

VPH-DARE@IT will deliver the first **patient-specific predictive models for early differential diagnosis of dementias** and their evolution through the following objectives:

- Deliver a systematic, multi-factorial and multi-scale modeling approach to understanding dementia
- Explore the lifestyle and environmental factors that predispose individuals to the development of dementia
- Deliver more objective and accurate differential diagnoses than those currently available in Europe
- Shorten the current average time-lapse between the onset of cognitive and memory deficits and its specific clinical diagnosis

More Information at www.vph-dare.eu

EVENTS

Coming Workshops and Conferences

An essential activity in AETIONOMY is the dissemination of the results and the experience gained in the project to maximize its impact. AETIONOMY has been designed to provide a generalized approach towards the generation of mechanism-based taxonomies for Alzheimer's and Parkinson's disease; we therefore aim explicitly at a wider deployment and transferability of our results. Besides this general dissemination, we will organize conferences and workshops to exchange information between partners and related projects:

Global Dementia Legacy Event: Harnessing the Power of Discoveries – Maximizing Academia-Industiry Synergies.

11-12 September 2014, Ottawa, Canada
Aiming to bring together global leaders from industry and academia to identify new and innovative ways to foster investigative approaches and partnership models to address the pressing challenge of dementia.
More: http://news.gc.ca/web/article-en.do?nid=868569

AETIONOMY General Assembly, External Scientifc Adivsory Board, and Steering Committee Meetings.

17-19 September 2014, Biberach, Germany
Strategic Project Board meetings to monitor the project status and future steps.

World Alzheimer's Day

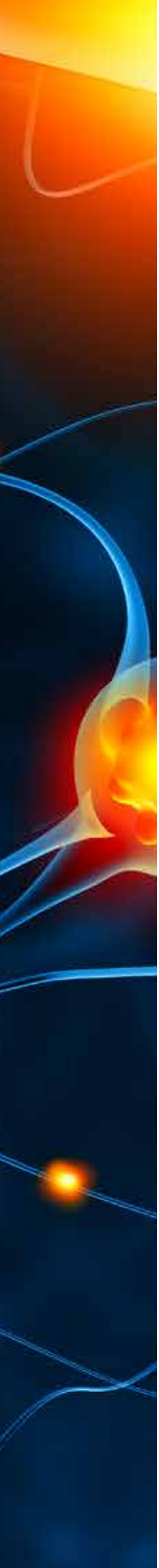
21 September 2014, Worldwide
World Alzheimer's Day, September 21st of each year, is a day on which Alzheimer's organizations around the world concentrate their efforts on raising awareness about Alzheimer's and dementia.
More: www.alzinfo.org/08/alzheimers/world-alzheimers-day

IMI 2 Open Info Day.

30 September 2014, Brussels (B)
Information on IMI 2's funding and intellectual property (IP) rules, tips on applying for funding under IMI 2, and workshops/presentations of the IMI 2 Call 1 topics by the project coordinator.
More: www.imi.europa.eu/events/2014/06/16/imi-2-open-info-day-2014

2nd Joint Work Packages 3 & 5 Taxonomy construction and validation Workshop.

December 2014, Basel , Switzerland
The work packages responsible for 'taxonomy construction, knowledge modeling, data-/ graph-mining and hypotheses generation' (WP3) and 'clinical studies for the validation of the mechanism-based taxonomy' (WP5) plan their interactions.



2th International Conference on Alzheimer's and Parkinson's Diseases and related neurological disorders (AD/PD™ 2015)

18-22 March 2015, Nice , FranceUnraveling the mechanisms and improving the treatment of Alzheimer's, Parkinson's and other related neurodegenerative diseases.
More: www2.kenes.com/adpd

The 9th World Conress on Controversies in Neurology (CONy)

26-28 March 2015, Budapest, HungaryRaising the most dynamic and controversial topics facing clinicians in the fields of neurology.
More: http://www.comtecmed.com/cony/2015/

World Parkinson's Day

11 April 2015, Worldwide
Supported by the European Parkinson's Disease Association, aims to raise awareness of Parkinson's disease, promoting a greater understanding of this condition and how it can affect a person.
More: www.whathealth.com/awareness/event/worldparkinsonsday.html

1st Congress of the European Academy of Neurology (EAN)

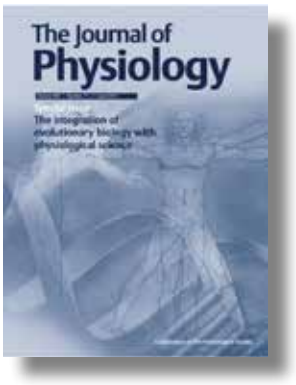
20-23 June 2015, Berlin, Germany
EAN is the joint subsequent organisation of the EFNS (European Federation of Neurological Societies) and ENS (European Neurological Society), and thereby the first united voice of European Neurology continuing education in all fields of neurology.
More: http://www.eaneurology.org/Neurope-comes-to-Berlin-in-2015.1860.0.html

REFERENCES

Publications and Articles

We do emphasize the role and importance of joint publications, reflecting the close collaboration between industrial and academic partners in AETIONOMY, which will soon be intensified.

P.J. Hunter, B. de Bono:
Biophysical constraints on the evolution of tissue structure and function.
In: The Journal of Physiology,
Vol. 592, Issue 11, June 2014.
More: http://onlinelibrary.wiley.com/doi/10.1113/jphysiol.2014.273235/abstract



D. McHale, M. Hofmann-Apitius:
AETIONOMY: Reclassifying Alzheimer's disease to find new drug targets.
In: Dementia in Europe, Issue 17, June 2014.
More: http://www.alzheimer-europe.org/Publications/Dementia-in-Europe-Magazines

Imprint

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