The Innovative Medicines Initiative dementia projects

Dementia already affects over 47 million people globally, and as populations age, this figure is set to rise to over 131 million by 2050. The disease places a huge and growing burden on health and social care systems and on the families and carers of those affected. Yet despite decades of research, there is still neither treatment nor cure for the disease. The challenge of developing new, effective treatments for dementia is simply too great for any organisation to tackle alone, and so IMI has launched a number of projects that bring together leading experts from the pharmaceutical industry, universities, small biotechs, and patient organisations from across Europe and beyond.

The IMI Alzheimer's Disease Research Platform

The IMI Alzheimer's disease projects AETIONOMY, EMIF and EPAD have a combined budget of €138 million and jointly address many key challenges for medicines research and development. In March 2015 they decided to form the IMI Alzheimer's Disease Research Platform. The goal of the platform is to facilitate collaboration between the three projects, helping them to deliver results faster. The platform has a global reach through a Memorandum of Understanding between IMI and the Global Alzheimer's Platform (GAP)

AETIONOMY – getting to the underlying causes of Alzheimer's disease

Today, diseases are defined largely on the basis of their symptoms, yet while two patients may share the same diagnosis, the underlying causes of their symptoms may be very different. This means that a treatment that works in one patient may prove ineffective in another. There is now broad recognition that a new approach to disease classification is needed, and that is where the AETIONOMY project comes in. It aims to identify subgroups of dementia and Parkinson's disease - based on the underlying genetic or molecular causes of the variants - in order to allow tailored therapies. The project involves the collection of clinical data, imaging and genetic data and will create a new way to combine all of these together to look for patterns which could identify sub-groups of patients with similar causes of their disease.

- Project website: **www.aetionomy.eu**

Key achievements

- AETIONOMY knowledge base: all currently available data has been integrated in a secure data warehouse. This includes over 200 samples and images from existing datasets from ADNI, EMIF-AD, GAP and EFPIA clinical trial data.
- Cross-queries: the project has implemented cross-querying capabilities among three different tools connected to the knowledge base, making it easier to carry out data mining to identify disease mechanisms.
- User Guidelines: the first version of the User Guidelines has been released, and users are invited to suggest the inclusion of additional studies.
- Protocol approval: the AETIONOMY protocol has been finalised and approved in France, Germany and Sweden and the first participants were recruited in September 2015.
- Legal & ethical issues: a data protection framework has been approved and is currently being installed, while a strategy to confront legal and ethical risks associated with patient stratification is in development.

EMIF – creating a European medical information framework

Recent years have seen an explosion in the number of databases containing medical and research data, yet because this data is scattered across diverse platforms, it cannot be fully exploited. The EMIF project aims to create an environment that allows for efficient re-use of existing health data (EMIF-Platform). To ensure immediate applicability, the EMIF project includes two specific research topics that will help guide the development of the Information Framework: the identification and validation of protective and precipitating factors for conversion to Alzheimer's disease (EMIF-AD), and predictors of metabolic complications of obesity (EMIF-Metabolic).

- Project website: **www.emif.eu** | Twitter: **@IMI_EMIF**

Key achievements

- Data availability: information has already been received from 40+ Alzheimer's disease cohorts and more than 10 new cohorts are expected in 2016.
- Biomarker discovery: a core sample set of biomarkers has been identified to allow combination of multiple omics in a unified sample. The samples were selected based on the quality of existing clinical and biomarker data.
- Extreme phenotypes: initial definitions of extreme phenotypes have been established, based on biomarkers, cognitive markers or clinical presentations and diagnostic criteria for mild cognitive impairment (MCI) and Alzheimer's disease.
- EMIF Catalogue: an online, searchable data catalogue containing information on 45 Alzheimer or ageing cohorts with a total of around 60 000 subjects. The catalogue is being used by IMI projects EMIF, AETIONOMY and EPAD.

EPAD – a new approach to Alzheimer's clinical trials

One important way of tackling dementia could lie in treating people while they are in the very earliest stages of the disease, when they may have little or nothing in the way of symptoms. The EPAD project is creating a pan-European platform to identify and follow up patients identified as being at risk of developing dementia symptoms. EPAD will then draw on the platform to test a number of novel treatments designed to prevent the onset of Alzheimer's dementia. By using a pioneering 'adaptive' clinical trial model, the project will be able to test multiple treatments at the same time, and analyse the results continuously. The adaptive trial model also allows a more rapid assessment of treatments and the identification of groups of patients that respond best to them.

- Project website: **www.ep-ad.org** | Twitter: **@IMI_EPAD**

Key achievements

- EPAD register: after identifying potential parent cohorts in Europe, a 'fingerprinting' process leveraging the EMIF catalogue for collecting meta-data from these cohorts is now in place.
- PREPAD: a research participant discovery tool was developed to identify research participants from parent cohorts, ensuring that all scientific, legal and ethical requirements are met.
- Clinical trial sites: 6 (of a potential 30) centres have already been certified in France, the Netherlands, Switzerland, Spain, Sweden and the UK.
- Regulatory consultation: EPAD has received positive feedback from the European Medicines Agency after completing a scientific consultation for its longitudinal cohort study (LCS) protocol.
- EPAD LCS: The first research participant was enrolled on 3 May at the University of Edinburgh trial delivery centre.

IMI's wider dementia project portfolio

IMI has two other projects on Alzheimer's disease – Pharma-Cog and PRISM, as well as a number of projects in the pipeline.

Pharma-Cog – improving the development of Alzheimer's treatments

Pharma-Cog was IMI's first project on Alzheimer's disease. Here, the focus was on improving our ability to identify the most promising new medicines of the future. The project team carried out research into tools and methods designed to improve our ability to identify successful new medicines as early as possible in the drug development process, while halting work on those destined to fail.

- Project website: **www.alzheimer-europe.org/EN/Research/PharmaCog**

PRISM – uncovering the causes of social withdrawal

Social withdrawal is a common early symptom of many neurological disorders, including schizophrenia, Alzheimer's disease, and major depressive disorder. However, the underlying, biological causes of this symptom are still poorly understood and may differ from one disease to another. Launched in 2016, the PRISM project will carry out a range of tests, including blood tests, brain scans, and measures of behaviour, on patients with these all too common diseases in a bid to determine which biological parameters correlate with specific clinical symptoms, like social withdrawal. The hope is that the project's findings will shed new light on the causes of mental illness and their symptoms and facilitate the development of much-needed new treatments.

Projects in the pipeline

Inflammation and Alzheimer's disease: This project aims to identify new drug targets for Alzheimer's disease focusing on two proteins (called TREM2 and CD33) that are linked to inflammation and are thought to affect people's risk of developing Alzheimer's disease.

Amyloid imaging biomarkers: Many people with Alzheimer's disease have clumps of protein called amyloid plaques in their brains. This project will seek to review the usefulness of knowing a patient's amyloid brain status for diagnosis and treatment, and determine the value of amyloid imaging in drug development.

Alzheimer's disease and patient engagement: Dementia researchers are increasingly focusing their efforts on finding ways to prevent the onset of Alzheimer's symptoms in the first place. The goal of this project is to identify the most effective ways of identifying and engaging with people who are in the very earliest stages of the disease. This will add to our understanding of the early stages of the disease, help patients access support from early on in their disease, and facilitate recruitment for clinical trials.

Apolipoprotein E (ApoE) biology: People who have the ApoE4 gene are at greater risk of developing Alzheimer's disease. This project will explore precisely how ApoE4 influences the development of Alzheimer's disease and pave the way for new treatment strategies for Alzheimer's and better identification of individuals at greatest risk for developing the disease.

Big data and Alzheimer's disease: IMI's Big Data for Better Outcomes programme aims to facilitate the use of diverse data sources to deliver results that reflect health outcomes of treatments that are meaningful for patients, clinicians, regulators, researchers, healthcare decision-makers, and others. The first project in the programme focuses on Alzheimer's disease. Here the goal is to evaluate existing and develop new outcome measures, identify sources of outcomes data, and pave the way for a framework to gather new data so that it can be ultimately used to improve Alzheimer's care and prevention.

Tangled proteins in Alzheimer's and Parkinson's diseases: The focus of this project is on how protein tangles, which are hallmarks of both diseases, spread throughout the brain. The project results will therefore increase our chance of identifying new targets for drugs.

About the Innovative Medicines Initiative

The Innovative Medicines Initiative (IMI) is working to **improve health by speeding up the development of, and patient access to, the next generation of medicines**, particularly in areas where there is an **unmet medical or social need**. It does this by facilitating **collaboration** between the key players involved in healthcare research, including universities, pharmaceutical companies, other companies active in healthcare research, small and medium-sized enterprises (SMEs), patient organisations, and medicines regulators. This approach has proven **highly successful**, and IMI projects are delivering **exciting results** that are helping to advance the development of urgently-needed new treatments in diverse areas.

IMI was launched in 2008 as a **public-private partnership** (PPP) between the **European Union**, represented by the European Commission, and the **European pharmaceutical industry**, represented by the European Federation of Pharmaceutical Industries and Associations (EFPIA). The partnership was renewed in 2014 with the creation of the IMI 2 programme.

IMI currently has **around 70 ongoing projects**, with more in the pipeline. Some focus on **specific health issues** such as neurological conditions (Alzheimer's disease, schizophrenia, depression, chronic pain, and autism), infectious diseases (including antimicrobial resistance and Ebola), diabetes, lung disease, oncology, inflammation & infection, tuberculosis, and obesity.

Others focus on **broader challenges in drug development** like drug and vaccine safety, knowledge management, the sustainability of chemical drug production, the use of stem cells for drug discovery, drug behaviour in the body, and the creation of a European platform to discover novel medicines. IMI also supports **education and training** projects.

IMI finances

IMI has a budget of **over €5 billion** for the period 2008-2024. Half of this comes from the **EU's research and innovation programmes**.

The other half comes from large companies and organisations, mostly **EFPIA companies**. These do not receive any EU funding, but contribute to the projects **'in kind'**, for example by investing their researchers' time or providing access to research facilities or resources.

Get involved

IMI regularly launches new Calls for proposals, giving scientists and experts from universities, small to mid-sized companies, patient groups and more to get involved in multi-disciplinary, cross-sector projects. Details of forthcoming Calls for proposals are published on the IMI website and promoted through Twitter and our newsletter.

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