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Letters

Boosting translational research on Alzheimer's disease in Europe: The Innovative Medicine Initiative AD research platform

Alzheimer's disease is becoming one of the most serious societal challenges with the increasing average life expectancy across the globe. The Alzheimer's Disease International (ADI) Report "The Global Impact of Dementia 2013–2050" shows convincingly that between now and 2050 there will be a steep increase in the number of Alzheimer patients from currently 44 million patients affected worldwide to 135 million patients in 2050. Alzheimer's disease will become a societal challenge, not only in the aging societies of the Western world, but also—and even more—in the developing countries. Without a cure or preventative treatment, Alzheimer's disease will substantially impact the future of entire societies.

Developing drugs for Alzheimer's disease has proven to be an enormous challenge, many candidate drugs have failed at high cost to the pharmaceutical industry and several companies have withdrawn from the field. Sharing of risk (and of course rewards and opportunities) between pharmaceutical companies and academic research groups is a way to lower both the entry barrier for the industry and to boost research and innovation in Alzheimer's disease in a precompetitive environment. The Innovative Medicine Initiative (www.imi.europa.eu), a public-private partnership between the European Union and the pharmaceutical industry association European Federation of Pharmaceutical Industries and Associations (EFPIA) responded to this combined societal and scientific challenge with a dedicated research program of three highly complementary projects.

1. EMIF (coordinated by Bart Vannieuwenhuyse and Simon Lovestone; EMIF-AD led by Johannes Streffer and Pieter Jelle Visser)

Acknowledging the existence of huge volumes of data underutilized for research, the European Medical Information Framework (EMIF, http://www.emif.eu/) was established to facilitate the use of data from research cohorts and population studies and routine care data. EMIF does this first by making data sets more "visible" by cataloguing the metadata or variables collected in these various data sets, second by pooling suitable data sets on a common platform, and third, especially for routine care or "real-world" data, by enabling distributed analysis of huge data sets. EMIF has two use cases: Alzheimer's disease and metabolic disease. Both are focused on biomarkers. In the first 18 months EMIF has assembled data sets for research including more than 30,000 participants in the catalog browser, approximately 5000 pooled individual data from five separate cohort studies and data from routine care from up to 50 million Europeans. EMIF supports research on Alzheimer's disease with a focus on search and validation of biomarkers, on the comparison of diagnostic criteria, and on the exploration of risk factors in relation to therapeutics development.

2. Aetionomy (coordinated by Duncan McHale and Martin Hofmann-Apitius)

The goal of aetionomy is to generate a "mechanism-based taxonomy of Alzheimer's Disease and Parkinson's Disease". The project pursues a "Big Data" approach in neurodegenerative disease research: heterogeneous information is integrated into disease models and made available for dedicated mining approaches aimed at identifying disease candidate mechanisms. This program exploits the very large amount of data currently available. The mechanistic context is represented through graph-based modeling of causal and correlative relationships between entities known to play a role in the pathophysiology of AD. In addition, information extracted and abstracted from -omics data and clinical data is integrated into the disease models. Candidate mechanisms identified will be validated in biomaterial banks and a prospective cohort. For the Alzheimer's disease mechanisms, this prospective cohort will be part of the much larger European Prevention of Alzheimer's Dementia (EPAD) cohort providing an even larger, independent validation cohort.

3. EPAD (coordinated by Serge Van Der Geyten and Craig Ritchie)

The EPAD Initiative started in January 2015. It is a 5-year program to create a pan-European platform for the delivery of a standing phase 2 Proof of Concept study for the secondary prevention of Alzheimer's dementia. Over the last 15 years there have been no phase 3 successes of agents seeking to

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modify the course of Alzheimer's disease. There is now consensus that Alzheimer's disease pathology starts many years before dementia develops but we need to be able to identify the high risk population with accurate risk models, identify them from the general population, and then measure the success of a drug (or combination of drugs) against clinically meaningful endpoints. EPAD will achieve this by working with existing parent cohorts across Europe and entering 24,000 of these individuals into a virtual register. This register will feed into a "n = 6000 EPAD Cohort" which has the dual utility of generating the most accurate disease models in the predementia phase of Alzheimer's disease and identifying subjects for a series of different interventions using EPAD cohort as a trial-readiness cohort. The EPAD trial (n = 1500) will accommodate multiple arms for proof of concept. EPAD involves 35 partners and will be delivered at 30 Trial Delivery Centres in 15 countries across Europe.

Together, these projects create the IMI Alzheimer's Disease Research Platform. The Platform establishes a critical mass and a coherent set of translational research activities that span from biomarker characterization in patient cohorts and the identification of candidate mechanisms for personalized, mechanism-based therapy to the first adaptive prevention trial in Alzheimer Research so far.

In July 2014, the second phase of IMI, IMI2 was launched. With a €3.3 billion budget for the period 2014 to 2024, IMI is the world's biggest public-private partnership in the life sciences. Neurodegenerative disorders and in particular Alzheimer's dementia are one of the key strategic areas for the funding activities of IMI2. A key priority will be to further foster knowledge management and output value for Alzheimer's research via the integration of the public and private sector researchers in the IMI Alzheimer's Disease Research Platform and seeking collaboration and coordination in Europe and globally, across the different regional research networks and activities and their respective funding agencies. This will represent a unique opportunity for researchers to see the impact of their work amplified and channeled beyond individual initiatives for the benefit of patients and society at large.

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