Neurodegenerative diseases

Reclassifying neurodegenerative diseases to enable drug development and help patients

Neurodegenerative diseases are a growing global challenge as medical advances ensures more individuals live longer. By 2020 there will be more than 40 million individuals in the world with Alzheimer's disease and by 2040, without the development of truly disease modifying drugs this will be more than 80 million. Similar trends are also seen for Parkinson's disease. The annual treatment and social care of individuals with Neurodegenerative diseases is estimated to be more than $1 trillion by 2050, making it one of the most important socioeconomic challenges of this century. Discovering and developing disease modifying drugs i.e. those that prevent progression of the disease, has been very challenging with many programs failing. One of the reasons why the biopharmaceutical industry is having challenges in converting the emerging science in these diseases is the way we classify them. This is referred to as the disease taxonomy.

Disease taxonomy

The medical disease taxonomy is actually based on the work of William Farr in the 19th century. It has been refined since then as medical science has advanced, but it is still based on the signs and symptoms of the disease that the patients have when they see their doctor. This "phenotypic" based system has served us well for many decades but as it does not reflect the causes of the disease itself it is failing when used to develop treatments directed at the molecular causes of disease. The current phenotypic classification means that we cluster together individuals with the same symptoms even if the underlying cause of the disease is different and we separate individuals with the same underlying cause of their disease if the symptoms look different. This is resulting in patients getting treated with therapies where they have little or no potential to respond and similarly patients being denied treatments they would benefit from.

An indication as to the importance of this classification can be seen in 2 therapeutic areas where a more disease aetiological (causative) approach has been used. These are in antibiotics and cancer therapies. With regard to infection a movement from broad organ based classification e.g. pneumonia, UTI etc, to a pathogen based system e.g. Streptococcus, Klebsiella in the early and middle part of last century led to the development of treatments which could be based on treating the pathogens regardless of the organ that was affected. Similarly in oncology at present the latest personalised medicines which are transforming patients' lives are based on the molecular cause of the disease rather than the organ or tissue the cancer is in.

The lack of detailed understanding of the causes of neurodegenerative diseases in individual patients and a corresponding classification system is significantly impacting the discovery and development of true disease modifying therapies.

Aetionomy

Aetionomy is an Innovative Medicine Initiative (IMI) funded consortium established to develop an initial mechanistic based classification of neurodegenerative diseases focusing on Alzheimer's and Parkinson's disease. This public- private partnership is co-led by Duncan McHale from UCB and Martin Hofman-Apitius from SCAI Fraunhofer. The premise behind the project is that although large sums have been invested in research in neurodegeneration and a lot of data generated the co-ordination and integration of this data across the community has been less well addressed. The consortium has brought together experts in

informatics, computing, engineering, and mathematical modelling of disease, neuroscience and clinical neurology from leading academic centres, as well as, neuroscience, informatics and neurology drug development experts from the EFPIA Industry partners.

The project therefore is not focusing on generating more data but on bringing together all accessible data, curating it to ensure consistency and putting it into a knowledgebase which can be mined and used for disease modelling. Once finalised the knowledgebase will be available for both researchers to access, as well as being a curated and harmonised repository for the storage of future research datasets.

The Aetionomy researchers will use this database to identify sub-groups of patients with different molecular causes and will use this to develop a new taxonomy of disease.

The need to truly share data

The biomedical community has already spent over €10 billion in research into the causes and treatments for neurodegenerative diseases. This has led to a high quality evidence base but a lack of real progress for patients. One contributing factor is the fact that these projects often focus on individual technologies e.g. genetics or hypotheses e.g. the amyloid hypothesis in Alzheimer's disease. Aetionomy therefore decided that rather than generate another set of data it would look to create a framework where the currently available data could be brought together harmonised and stored so that researchers could look across 100s of millions of euros of research and develop new hypotheses.

The knowledgebase is now built and based in Germany and Luxembourg. It is currently being populated using data from publically available datasets, partner data sets including EFPIA company clinical trial datasets and datasets from collaborators. We are now reaching out to the whole neurodegeneration research community and asking for them to share their data so that we can integrate together all of the high quality science that has already been performed and enable drug discovery and developments for the millions of current

and future sufferers of this disease. This call to share data is being driven at the highest levels and was a key recommendation of the OECD meetings on meeting the Alzheimer's disease challenge, and was christened "unleashing the power of Big Data for Alzheimer's Disease and Dementia Research". A failure to share data will result in duplicating research or wasting resources on areas that have not been validated and delaying getting treatments to patients.

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The Future

The future will include a new way to classify neurodegenerative diseases based on the causes of the disease in each individual. We will have screening programs to identify patients at risk of developing neurodegenerative diseases and we will start treatment before symptoms occur. However before we get to this nirvana we must come together and share the data that is being generated across large numbers of publically and privately funded research programs to deliver on our common goal of discovering and developing treatments for neurodegenerative conditions.

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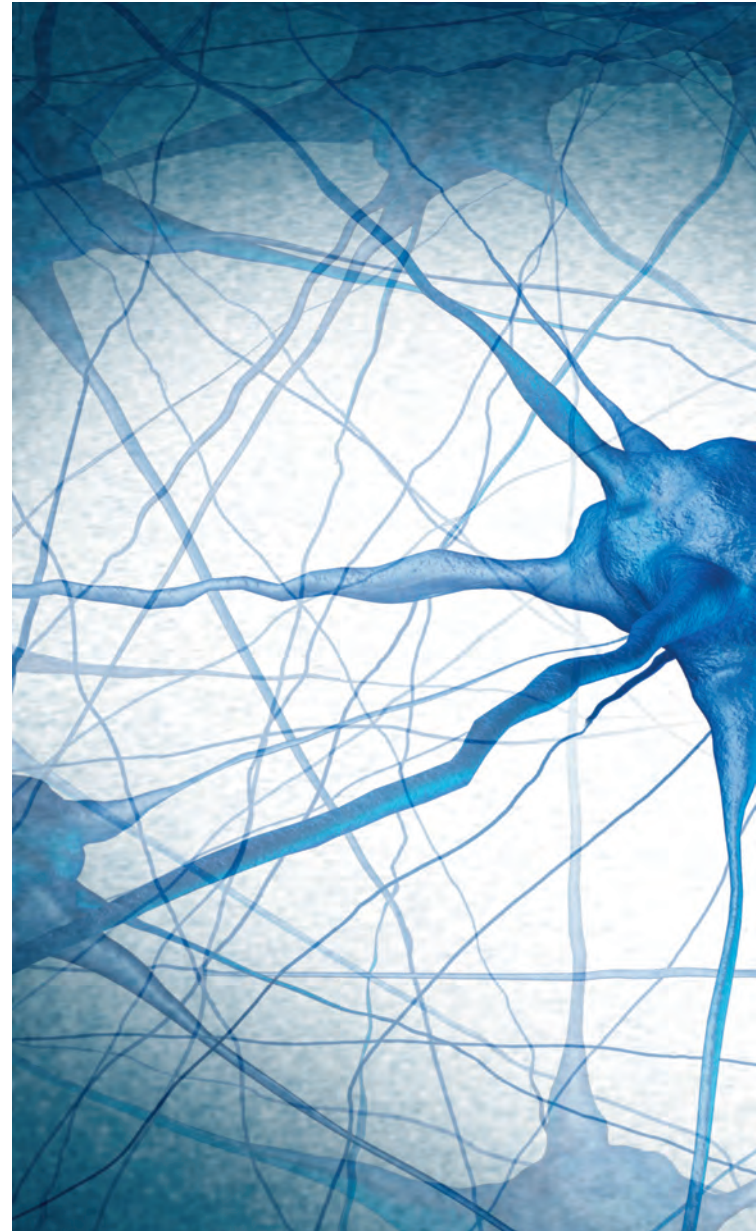# Dementia to become trillion dollar disease by 2018

Marc Wortmann, Executive Director of Alzheimer's Disease International (ADI), outlines the major impact dementia has worldwide and the urgent need for governments to help provide a better quality of life for people with the condition...

The World Alzheimer Report 2015 estimates that someone in the world develops dementia every 3 seconds. There are currently around 47 million people living with dementia globally, with numbers projected to nearly double every 20 years.

"ADI believes that the key to winning the fight against dementia lies in a unique combination of global solutions and local knowledge. As such, it works locally, by empowering Alzheimer associations to promote and offer care and support for people with dementia and their carers, while working globally to focus attention on dementia and campaign for policy change from governments."

In the report, 'World Alzheimer Report 2015: An analysis of prevalence, incidence, cost and trends' we highlight the global impact of dementia and its social and economic cost – currently estimated at $818bn. By 2018, dementia is set to become a trillion dollar disease. By 2050, it will affect over 131 million people. If global dementia care were a country, it would be the 18th largest economy in the world, exceeding the market values of companies like Apple and Google.

The report further illustrates the geographic prevalence and impact of a growing dementia crisis, showing that 58% of all people living with dementia today reside in low and middle income countries. As the unique challenges of dementia continue to pose a serious challenge to healthcare systems worldwide, it is these regions where dementia awareness and research is critical, and where the stigma attached to illnesses such as dementia poses a greater challenge.

The 10/66 Dementia Research Group, made of over 100 active researchers from more than 30 developing countries and supported by ADI, is a key part of effort to redress this balance. When the group was founded less than 10% of all population based research into dementia was directed towards the 66% of all people with dementia who will live in developing countries.

removing barriers to the involvement of people with dementia in everyday life.

The report findings demonstrate the urgent need for governments to implement policies and legislation to provide a better quality of life for people living with dementia, both now and in the future.

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You can read the full report on the ADI website at: www.alz.co.uk/worldreport2015

About Alzheimer's Disease International

ADI is the international federation of 83 Alzheimer associations around the world, in official relations with the World Health Organization. ADI's vision is an improved quality of life for people with dementia and their families throughout the world. ADI believes that the key to winning the fight against dementia lies in a unique combination of global solutions and local knowledge. As such, it works locally, by empowering Alzheimer associations to promote and offer care and support for people with dementia and their carers, while working globally to focus attention on dementia and campaign for policy change from governments. For more information, visit www.alz.co.uk .

The World Alzheimer Report 2015 was independently researched by King's College London and Karolinska Institute, Stockholm and was supported by Bupa.

As the only global federation, ADI works closely with Alzheimer associations worldwide, fostering twinning relationships, running Alzheimer University training events and supporting dementia care projects.

ADI is continuing to urge policy makers around the world to approach the issue with a broader agenda and a wider representation of countries and regions, particularly those in the G20 group of nations. A key call in the report is for a significant upscaling of research investment into care, treatment, prevention and cure, as well as to build on the success of dementia friendly community initiatives worldwide. These initiatives provide a key framework for integrating a better awareness of dementia needs in the community,

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