JPND NEWS

September 2014 Edition

Check out our SAB Interviews on pages 2-4

Professor Philippe Amouyel, Chair, JPND Management Board updates us on JPND progress:

2014 continues to be a remarkable year for Neuro-degenerative Diseases, with increased awareness and support coming from initiatives such as the Global Summit on Dementia. 2014 also witnessed a scaling-up of the implementation of the JPND Research Strategy with partnership options being investigated with the European Commission (through Horizon 2020), other relevant pan-EU initiatives and the United States of America.

At the end of August 2014, the initial JUMPAHEAD-FP7 support to JPND management ended. From September 2014 JPND Member Countries are supporting JPND management activities for a one-year transition phase prior to developing a sustainable structure, able to support our long-term fight against neurodegenerative diseases and dementia in particular.

2014 JPND highlights to date:

Reports from several JPND Alignment Actions

JPND is promoting strategic alignment of research activity related to neurodegenerative diseases across Europe. Several parallel actions are on-going, and a number of JPND Action Groups have reported with their recommendations in areas such as:

- Extracting the value of nationally-funded longitudinal cohorts
- Identifying new lines of intervention for Animal and Cell Models
- Assisted Living Technologies (with the AAL Joint Programme)

These reports have been submitted to the JPND Management Board for consideration as part of the implementation of the JPND SRA.

Read more

Results of Call for Working Groups in Longitudinal Cohorts

Ten proposals are to be funded under the new JPND "rapid action" call related to longitudinal cohorts (call closed on June 16th, 2014). The funded proposals are a series of community-led working groups of leading experts in the neurodegenerative disease (ND) field who have come together to provide advice on how to address the most pressing issues that are preventing the full exploitation of longitudinal cohorts for ND research. The groups will provide outputs such as 'best practice' guidelines and methodological frameworks of use to the ND field within a 6 month timeframe.

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Palliative and End-of-Life Care Research

The JPND Action Group on Palliative Care organised an expert-led work-shop in Amsterdam airport on June 25th, 2014 to identify capacity-building and integrative research opportunities in this area, and to recommend future JPND actions and activities. The report to the JPND MB is currently being drafted by the JPND Action Group.

Read more

Participants at the JPND workshop on Palliative and End-of-life Care, Amsterdam, June 25th, 2014

Acting Globally

Through its strong global dimension, JPND has quickly become the reference for European and global knowledge and innovation in the area of ND research. JPND was consistently highlighted during the 2013 high-level G8/G7 summit on dementia and is aligned with the summit recommendations. Philippe Amouyel has since been nominated to the World Dementia Council that has emerged from this initiative.

Moreover, several JPND members are working with the OECD on the mapping of e-infrastructures and big data for ND research, using the JPND mapping exercise as a reference point.

Philippe Amouyel at the first 2014 Global Dementia legacy event on Finance and Social Investment, London, June 19th.

JPND Advisory Board on Patient and Public Involvement (PPI)

The JPND Action Group on PPI has recently been expanded to form a JPND PPI Stakeholder Advisory Board, with the addition of senior leaders from relevant parts of the international scientific, clinical, healthcare and social care systems. The primary aim of the Board will be to provide rapid and frank feedback and early advice from the broad stakeholder community to JPND in relation to implementation of PPI in ND research.

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2013 Annual calls for proposals — Results of Stage I

Two JPND calls closed in February 2014 in the areas of "Preventive strategies" and "Cross-disease analysis of pathways", the final results of which will be announced in Autumn 2014. The stage I (pre-proposal stage) attracted a significant interest from the research community, with a number of proposals being invited to submit full proposals for stage II.

2013 Call	Pre-Proposal Submissions	No. of Research Groups (countries)	Total Budget Application	Submissions selected for full proposals	Full Proposals Funding Application
Cross-disease analysis of pathways	92	418 (16)	€112 Million	35 (39%)	€46 Million
Pilot studies on Preventive Strategies	35	160 (16)	€36 Million	22 (63%)	€25 Million

Read more

Updates from JPND-supported projects

Check out the websites of a number of JPND-supported projects:

- BIOMARKAPD - biomarkers for Alzheimer's and Parkinson's Disease (www.biomarkapd.org)
- RHAPSODY - research and strategy for dementia in the young (www.rhapsody-project.eu);
- ACTIFCare - Access to timely formal care (www.actifcare.eu).

Also, the world's largest piece of genetics research focusing on early-onset Alzheimer's is a JPND-supported project entitled "PERADES". PERADES recently benefited from £388,920 of additional funding from Alzheimer's Research UK, thanks to a generous donation from Iceland Foods Charitable Foundation.

Read more

JPND research
EU Joint Programme – Neurodegenerative Disease Research

Martin Rossor

University College London and Vice-Chair of JPND SAB

MARTIN ROSSOR

"Neurodegenerative dementia, exemplified by Alzheimer's disease, is the most obvious and tragic example of cognitive impairment. However, there are numerous causes of dementia and less severe cognitive impairment which we need to take seriously. Cognitive health, and healthy brains, are essential to meet the global challenges that we now face. Engaging in research is everybody's responsibility".

Martin Rossor

In your opinion, what is the single biggest challenge for researchers investigating neurodegenerative disorders like Alzheimer's or Parkinson's?

I feel that a big challenge if not the biggest challenge for researchers investigating neurodegenerative disorders is the difficulty of disease definition and the overlap with ageing. It is worth restating the obvious fact that diseases as such do not exist although clearly unwell people exist. The diseases are merely classifications that we use to help us understand disease in general and to manage patients individually. Thus we use many different dimensions to classify neurodegenerative diseases. Clinicians tend to view post mortem examination as the gold standard for diagnosis but in each case neuro-pathologists also have great difficulty in deciding what is out with the common ageing process. We need greater clarity about which dimensions we are talking about, for example whether it is a particular molecular pathway, a constellation of histological features or a variety of functional deficits. As our understanding increases it may well be that we learn to distinguish a number of different processes within the Alzheimer rubric. How we then relate these processes to the processes that occur to us all as we get older will remain a major challenge.

At the moment, what area of your own personal research gets you excited?

My interest has always been in the younger patient, in particular those with familial dementias as this reflects clinical practice in the UK where it is the rare and younger patients that tend to be referred to neurologists. It has been a fascinating area of research to see how a rare type of Alzheimer's disease, or of the other degenerative dementias that are familial, can be very informative. What has remained has been the interest in the problems that are presented in the neurology clinic and with experience the increasing appreciation of the heterogeneity of patients which in itself must hold important clues.

How can people with neurodegenerative disorders contribute to the prioritization of research?

Each individual with a neurodegenerative disorder and their family brings a unique experience. The prioritisation needs to be a partnership and a dialogue around what is important and what is a tractable problem. It can be easy to forget though that there are an enormous number of skills in the patient community that ensures that it is a very rich partnership.

What kind of impact do you think JPND has had to date on the ND research community in Europe?

JPND has had a major impact on neurodegeneration research in Europe and is looked upon as a model around the world. Although competition to ensure funding goes to the best sciences is essential, collaboration is the future. JPND has provided the infrastructure for safe and creative collaboration.

All JPND Scientific Advisory Board member interviews are available on the JPND website - www.jpnd.eu

JPND research
EU Joint Programme – Neurodegenerative Disease Research

Eric Karran

Alzheimer's Research UK and JPND SAB member

ERIC KARRAN

"I am confident that we will find effective therapies for many neuro-degenerative diseases. We need to continue to focus on increasing the research base and to provide mechanisms to ensure that basic research is translated into patient benefit."

Eric Karran

Why do you think there has been so little progress, if any, in developing a drug that can slow the progression of neurodegenerative disorders?

A major problem remains the preclinical to clinical translation. For some of the drugs that have failed in phase 3 clinical testing, it is clear that from the preclinical data it would have been very surprising if they had worked. Another big issue is that we now have far better insight into how the pathology of Alzheimer's disease progresses some 10-15 years in advance of the clinical symptoms – or at least those symptoms that can be detected using clinical measurement instruments such as the ADAS-cog. The drugs that have failed were all tested in mild-to-moderate AD, at a stage in the disease when the pathology is already well-advanced. So, it is likely that we shall need to test drugs much earlier in the disease process. Another issue is that many of the therapeutics that have been tested did not have an appropriate separation of safety and efficacy for the medicines to be tested at doses that might have shown efficacy. Finally, patient ascertainment – ensuring that the patients that you recruit really have Alzheimer's disease - needs to be markedly improved to remove 'noise' in the clinical efficacy signals.

Are you discouraged by the progress that has been made, particularly after the failure of recent drugs?

Disappointed? Yes. Discouraged? No. As I have explained above, many of the clinical failures can be explained. With each avenue tested, the field moves forward to new avenues and one of these will be successful. Compared to other diseases of the brain, such as schizophrenia for example, I think we understand neurodegenerative diseases comparatively well. Now is the time to redouble our efforts and keep going. Many new approaches are being tested and innovative trial designs, including prevention studies, are underway.

What needs to happen before we can successfully treat the individual causes of neurodegenerative disorders?

We need much more research into fundamental disease mechanisms. For example, the field still does not have a good description of how a neuron dies in neurodegenerative diseases. The field needs to start to translate the genetic findings into cell biological experiments and ultimately into preclinical in vivo studies so that we can draw a more complete picture of the disease. Some of the systems biology approaches looking at patterns of gene expression are starting to do this as well. I think that, for Alzheimer's disease for example, it is not far-fetched to believe that we will be able to intervene so as to delay the onset of the disease by decades so as to effectively prevent the disease.

If we lived an ideal scientific environment and your organisation had unlimited resources to do a single experiment, something you could not afford right now, what would you do?

I would enrol thousands of people into a longitudinal study that would follow their cognitive performance, lifestyle, medical events, and so on in a frequent and detailed manner. I would have blood samples taken for genome analysis. I would measure their brain function in a multimodal manner – MRI, amyloid PET, FDG-PET etc – and take CSF for biomarker measurement and discovery. This cohort could be used as appropriate for clinical trials, and because of the detailed pre-analysis, very well defined cohorts could be used for specific clinical experiments.

In your opinion, what would the benefits be for ARUK by partnering with JPND?

ARUK wants to be able to fund the best research into neurodegenerative diseases, and to ensure that there is collaboration between different research groups. Finding treatments for these diseases is a massive challenge, and it seems like we need to co-ordinate our scarce resources effectively to make optimal progress.

JPND research
EU Joint Programme – Neurodegenerative Disease Research

Thomas Rooney

Sanofi and JPND SAB Member

THOMAS ROONEY

"There are many talented and committed scientists and clinicians in both academia and industry who are all working to better understand the underlying causes and pathophysiology of neurodegenerative disorders and to identify new therapies that will provide significant benefit to patients and their families. While we are not yet where we want to be in terms of providing new therapies, there has been real scientific progress in the past few years that can allow us to anticipate some possibilities for real breakthroughs in the next 5-10 years".

Thomas Rooney

In your opinion, what is the single biggest challenge for researchers investigating neurodegenerative disorders like Alzheimer's and Parkinson's?

To identify the pathological mechanisms that are causally linked to the onset and progression of neurodegenerative disorders and to identify dynamic biomarkers that can be used to follow disease progression and to evaluate therapy intervention within a short timeframe.

Why do you think there has been so little progress, if any, in developing a drug that can slow the progression of disorders such as Alzheimer's or Parkinson's?

The development of disease modifying therapies for Alzheimer's and Parkinson's disease has proved extremely challenging, at least in part, due to the fact that these are complex multifactorial neurodegenerative disorders that start to damage the brain several years before patients develop symptoms. Together with the lack of diagnostic biomarkers and measures to monitor disease progression, this has led to drugs being tested in clinical trials where there was inappropriate patient selection, high patient heterogeneity and where the treatment was started when the disease was too far advanced, thereby making it difficult to demonstrate therapeutic efficacy and contributing to the high attrition rate. In addition, although there have been major advances in our understanding of the pathophysiology of neurodegenerative disorders, such as Alzheimer's and Parkinson's, the cause of these diseases is still largely unknown which has probably led to the testing of some drugs targeting a hypothesis or mechanism of action whose role in the cause of the disease has not been sufficiently validated in preclinical and clinical studies.

What are the current research priorities for Sanofi?

Immune system modulation, neuroprotection and brain metabolism are some of the approaches being investigated. Within these approaches there are novel research programs specific to Alzheimer's and Parkinson's, as well as projects that have potential application for several neurodegenerative disorders.

In your opinion, what would the benefits be for Sanofi by partnering with JPND?

By collaborating with the JPND and its European wide key stakeholders, the goal is to "de-risk" and accelerate drug development for neurodegenerative disorders by addressing some of the key challenges mentioned above.

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