Breakthrough Studies Confirm Brain Plaques
Can Help Predict Alzheimer's Disease

An international consortium – supported by Professor Harald Hampel of Pierre and Marie Curie University, Paris, France – performed the largest analysis to date of amyloid plaques in people's brains confirms that the early presence of the substance can help predict who will develop Alzheimer's and determine who has the disease.

Two linked studies, published on Tuesday, the 19th of May, in the worldleading medical journal **JAMA** (*The Journal of the American Medical Association*), also support the central early role in Alzheimer's of beta amyloid, the protein that creates plaques. Data from nearly 9,500 people on five continents shows that (1) amyloid can appear 20 to 30 years before symptoms of dementia, (2) the vast majority of Alzheimer's patients have amyloid, and (3) the *APOE ε4* gene, known to increase Alzheimer's risk, greatly accelerates amyloid accumulation.

These findings also confirm that amyloid screening, investigated by Positron Emission Tomography (PET) scan or cerebral spinal fluid tests, can help identify people for clinical trials of drugs to prevent Alzheimer's. Such screening is increasingly used in research. Experts say previous trials of anti-amyloid drugs on people with dementia failed because their brains were already too damaged or because some patients, not screened for amyloid, may not have had Alzheimer's.

The researchers scrutinized data from numerous studies. One analysis involved people without dementia who had normal cognitive functioning or subjective cognitive impairment (a sense of memory loss despite normal memory tests) or mild cognitive impairment (MCI) a condition often considered a precursor to Alzheimer's.

"These are truely outstanding and important studies", commented **Professor Harald Hampel of Pierre and Marie Curie University in Paris**, one of the investigators. *"The lag between the appearance of amyloid and the onset of dementia is a bit longer than previous estimates"*, **Professor Hampel wrote**. He also cited limits on interpreting the results—such as the study's cross-sectional design and the idea that people with high cognitive reserve may stave off dementia longer than others. *"The final answer will come from large longitudinal studies"*, **Professor Hampel stated**.

Reference:
"**Prevalence of cerebral amyloid pathology in persons without dementia: a meta-analysis**"
JAMA. 2015 May 19;313(19):1924-1938. doi: 10.1001/jama.2015.4668.
Available at: **http://www.ncbi.nlm.nih.gov/pubmed/25988462**

The Journal of the American Medical Association (**JAMA**) (http://jama.jamanetwork.com/journal.aspx) is an international peer-reviewed general medical journal published continuously since the year 1883. JAMA is presently the most widely circulated medical journal in the world and its **Impact Factor** is **30**.

Voicing out the silent markers of Alzheimer's

Alzheimer's disease is one of the most significant risks for the growing population of elderly individuals and their families, with an estimation of 35.6 million people presently affected in the world. These numbers are expected to almost double every 20 years, to 65.7 million in 2030 and 115.4 million in 2050. As the most frequent neurodegenerative disease and a major worldwide epidemic, Alzheimer's presents a global challenge, with increasing strain on health-care systems and our societies.

The recently evidenced existence of a decade-long silent stage of the disease, with no clinical symptoms expressed, yet biological markers observable, creates opportunities for improving and accelerating early detection. To meet the need for diagnosis of Alzheimer's from the beginning, the AXA - UPMC Chair on Alzheimer's has been created with the aim of developing and validating new biomarkers to increase diagnostic accuracy at the totally asymptomatic stage and to better assess drug efficacy.

Hosted by the highly specialized Institute for Memory and Alzheimer's Disease (IM2A) using the latest cutting-edge genetic, biochemical and neuroimaging technology available, the Chair will utilize the combined resources of several first-class scientific research teams in a rich variety of related research fields—from cognition to neuroimaging to genetics—working from bench to bedside. It will use quality and exhaustive cohorts of patients from all disease stages, managed through the IM2A infrastructure, which is a national reference center for several Alzheimer's and neurodegeneration-related clinical research programs and a leading institution worldwide. It will also benefit from a unique platform for integrating and processing multimodal biomarker information in order to extract specific algorithms for early presymptomatic detection.

The Chair and full university professorship will be permanently held by **Prof. Harald Hampel**, who is a word-leading researcher with vast expertise and reputation in neurology, psychiatry and cutting-edge neuroscience research. With 20 years of experience, he has successfully developed international research programs dedicated to Alzheimer's diagnosis and therapeutic algorithms.

Hampel's findings will provide significant new understanding of Alzheimer's Disease and related disorders, while building upon the scientific capabilities of biostatistical modeling, leading to breakthrough advances in improving both diagnosis and treatment using innovative biological markers.

It will aim at validating new biomarkers to increase diagnostic accuracy at the totally asymptomatic stage, and allow to better assess drug efficacy.

To do so, the Chair will rely on the unique combination of resources of several first class scientific research teams in the variety of related fields – from cognition to neuroimaging to genetics. It will use quality and exhaustive cohorts of patients - from all disease stages-, managed through the highly specialized IM2A infrastructure that is national reference center of several Alzheimer and neurodegeneration related clinical research programs and a leading institution in France, Europe and worldwide. It will also benefit from a unique platform to integrate and process multimodal information – taking into consideration the variety of markers & data characteristics-, to extract specific algorithm for early pre symptomatic diagnostic.

The Chair will be permanently held by **Prof. Harald Hampel**, who benefits worldwide experience and reputation in neurology, adult and psychiatry of later life and neuroscience research, with more than 15 years of experience in transdisciplinary and translational international research programs dedicated to Alzheimer's diagnostic and therapeutic algorithms.

With the large 3.0 Million Euro AXA endowment, University Pierre et Marie Curie, the first French University in Science & Medicine and a global leading in the field of brain research, will provide new significant insights on Alzheimer's Disease, related dementia disorders and neurodegenerative diseases, while building upon the scientific capabilities of statistical modeling, potentially leading to essential advances in diagnosis and treatment using innovative biological markers **Prof. Harald Hampel** is currently the scientific coordinator of the Institut Hospitalo Universitaire (IHU) and industry

funded French flagship research program INSIGHT (INveStIGation of AlzHeimer's PredicTors in Subjective Memory Complainers) that is currently ongoing at the IM2A, Hôpital de la Salpêtrière and the Institut du Cerveau et de la Moelle (ICM). The major goal is to indentify and validate biomarkers, genetic risk factors and neuroimaging methods in at risk subjects for Alzheimer's disease before the onset of clinical symptoms.

Prof. Hampel and his multi-disciplinary research team in Paris endeavours to characterize the full disease "roadmap" in the brains of living people with all available biological indicators to provide effective early solutions for diagnosis and therapy for affected patients.

Biosketch Professeur Harald Hampel, MD, PhD, MA, MSc

After a post-doctoral fellowship at the National Institute of Health, Bethesda, he became professor of psychiatry and founding director of the Alzheimer Memorial Center at Munich University before being appointed professor and chair of psychiatry at Trinity College, Dublin. In 2010 he was appointed as professor & chair of psychiatry at the University of Frankfurt and in 2013 as professor and AXA Research Fund Chair at Pierre and Marie Curie University, Départment de Neurologie, Institut de la Mémoire et de la Maladie d'Alzheimer, Hôpital de la Salpêtrière, Paris. He published more than 500 peer-reviewed research papers and edited 8 books, won multiple awards for his research focusing on brain health & disease, biomarker and therapy discovery in Alzheimer's disease. He holds international research grants and is principal investigator of research consortia. He is senior Associate Editor of the journal of the Alzheimer Association Alzheimer's & Dementia.

The activity of the AXA-UPMC is located at the:

1) **Institute of Memory and Alzheimer's Disease** (*Institut de la Mémoire et de la Maladie d'Alzheimer*) [IM2A]);

2) **Brain & Spine Institute** (*Institut du Cerveau et de la Moelle Épinière* [ICM]). The Brain & Spine Institute (http://icm-institute.org/menu/actualites) is the leading neuroscience institute in France and a widely renowned research centre of excellence of international dimensions. It brings together scientists from various horizons and countries in order to develop innovative and cutting-edge research in the area of brain research.

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