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Institut national
de la santé et de la recherche médicale

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Communiqué de presse

AgedBrainSYSBIO, a medium-scale research initiative against neurodegenerative diseases

A European group of academic laboratories and industrial scientists from SMEs will combine integrative systems biology & comparative genomics for studying human brain ageing and/or most common age-related diseases with a special emphasis on late-onset Alzheimer Disease for identifying and validating new molecular targets and biomarkers. This four-year research programme is coordinated by Inserm (Pr Michel Simonneau).

March 2013 - The AgedBrainSYSBIO project on systems biology of synapse proteins & ageing was officially launched March 18th in Paris, France. AgedBrainSYSBIO is a European collaborative research project funded by the European Commission under the Health Work Programme of the 7th Framework Programme. This multidisciplinary consortium assembles 14 academic and industrial internationally renowned research teams from Belgium, Estonia, France, Germany, Israel, United Kingdom and Switzerland.

Ageing is undisputedly a complex process because it affects the deterioration of most (if not all) aspects of life. Cognitive decline is emerging as one of the greatest public health challenges of the old age, with nearly 50% of adults over 85 afflicted by Alzheimer's disease, the most common type of dementia.

As other chronic and neurodegenerative diseases, Alzheimer's disease develops slowly and gradually; but is distinctive in that it forces patients to endure many years of steadily-lessening contact with others, because of memory loss, difficulty with orientation, loss of language and speaking abilities, judging things and depression amongst numerous other symptoms. In 2013, it is estimated that there are worldwide more than 24 million people with Alzheimer's disease, with 4.6 million new cases each year, which means a new case each 7 seconds. It is thus one of the greatest challenges in public health for modern societies, in terms of costs but also in terms of cause, cure and care. To address all these issues, European Commission-funded research effort is crucial as there are still no curative drugs, with only symptomatic treatment able to delay the disease progression.

Over the last years, Genome-Wide Association Studies (GWAS) have been instrumental to identify genes that mediate genetic risk associated to Late-Onset Alzheimer Diseases (LOAD). These approaches based on the genetic comparison of large cohorts of patients and healthy aged persons, and for which three academic partners have been involved (Inserm U894; Institut Pasteur Lille, University of Antwerpen), have been largely funded by Europe. Additionally, a variety of new sets of data have been built and have delivered the state-of-the art of protein-protein interactions, their localisation in subregions of human neurons and genome-wide transcriptome analysis of human neurons derived from aged patient fibroblasts. In another field, new drosophila and mouse models have also been generated via academic partners involved in European Commission-supported large-scale programmes. Finally, the analysis of genes displaying an accelerated evolution in as well humans as non-human primates do not display these human-specific neurodegenerative diseases and has opened interesting research paths. So far however, in spite of a huge amount of data available and existing *in vitro* and *in vivo* models, these approaches have not been successfully translated into the clinic.

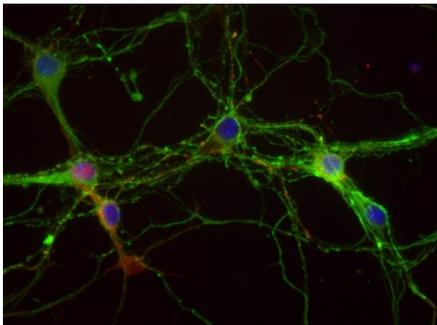
The AgedBrainSYSBIO will take advantage of these large set of data, will cross them to other large-scale ageing databases and will include all this know-how, technologies and results. Thanks to the involvement of four European SMEs, this program is expected to get results readily translated into preclinical studies.

The AgedBrainSYSBIO project assembles 13 well-established research teams both from academia and industry. The scientists will share results and know-how on LOAD GWAS gene discovery, comparative functional genomics in mouse and drosophila models, in mouse transgenic approaches, research on human induced pluripotent stem cells (hiPSC) and their differentiation *in vitro* and modelling pathways

with emphasis on comparative and evolutionary aspects. Importantly, the four European SMEs involved will bring their complementary expertise. QURETEC (Estonia) will be a key partner for data management solutions and bioinformatics data analyses; HYBRIGENICS (France) is a world leader in comparative proteomics and protein-protein interaction analyses; GENEBRIDGES (Germany) is marketing novel strategies for DNA engineering in mammalian cells; reMYND (Belgium) drives the development of treatments against protein misfolding-diseases, both through its Contract Research activities (Alzheimer's disease) and Drug Discovery and Development (Alzheimer's disease, Parkinson's disease, Diabetes)..

Together, researchers will address the basis of brain ageing by studying the pathways involved in Late-Onset Alzheimer Diseases combining integrative systems biology and comparative genomics. One of the first steps will be to identify the interactions through which the ageing phenotype develops in normal versus disease conditions; on this basis, novel pathways and their evolutionary properties will be modelled and experimentally tested in order to identify druggable targets. This work will finally allow the validation of new druggable targets and markers as a proof-of-concept towards the prevention and cure of aging cognitive defects.

Michel Simonneau, MD PhD, Professor at Ecole Normale Supérieure de Cachan, who coordinates this effort states that *"this ambitious project integrates the numerous European initiatives, such as JPND¹, as well as national research programmes, which address the scientific and societal challenge of neurodegenerative diseases. This project receives the decisive input of 4 small to medium size enterprises (SMEs) allowing us to get candidate solutions for curing and preventing common age-related diseases. The links between academia and industry is the driving force of this work program and in the end will hopefully benefit to all of us."*



Cortical mouse neurons 7 div labeled with AUTS2 (red); Tau(green) and Dapi(blue) (10µm)
© Inserm, Malik Khelifaoui (U894)

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L'Inserm est le premier porteur de projets européens « Santé » avec 28 projets coordonnés par l'institut dans le cadre PC7.

Créé en 1964, l'Institut national de la santé et de la recherche médicale (Inserm) est un établissement public à caractère scientifique et technologique, placé sous la double tutelle du Ministère de l'Enseignement supérieur et de la recherche et du ministère de la Santé.

Ses chercheurs ont pour vocation l'étude de toutes les maladies, des plus fréquentes aux plus rares, à travers leurs travaux de recherches biologiques, médicales et en santé des populations.

Avec un budget 2011 de 905 M€, l'Inserm soutient quelque 300 laboratoires répartis sur le territoire français. L'ensemble des équipes regroupe près de 13 000 chercheurs, ingénieurs, techniciens, gestionnaires...

L'Inserm est membre de l'Alliance nationale pour les sciences de la vie et de la santé, fondée en avril 2009 avec le CNRS, le CEA, l'Inra, l'Inria, l'IRD, l'Institut Pasteur, la Conférence des Présidents d'Université (CPU) et la Conférence des directeurs généraux de centres hospitaliers régionaux et universitaires. Cette alliance s'inscrit dans la politique de réforme du système de recherche visant à mieux coordonner le rôle des différents acteurs et à renforcer la position de la recherche française dans ce secteur par une programmation concertée.

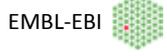
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¹ JPND, for EU Joint Programme – Neurodegenerative Disease Research ; see <http://www.neurodegenerationresearch.eu>



AgedBrainSYSBIO

The AgedBrainSYSBIO consortium is coordinated by the French National Institute for health and medical research (Inserm, Prof. Michel Simonneau) and brings together scientists with internationally recognized expertise in systems biology of the synapse and four small to medium size enterprises (SMEs) with a leading role in the project. The SME partners will assure translation of project results to clinical application.

Country	Participant organisation legal name		Principal Investigator
France		Institut National de la santé et de la recherche médicale (Inserm)	Michel Simonneau
		Institut Pasteur de Lille (IPL)	Jean-Charles Lambert
		Centre Européen de Recherche en Biologie et Médecine (CERBM-GIE)	Yann Herault
		HYBRIGENICS SA	Jean-Christophe Rain
		Inserm Transfert SA (IT)	Christiane Dascher-Nadel
Belgium		VIB	Christine van Broeckhoven
		reMYND NV	Dick Terwel
Germany		Heinrich Heine Universität Düsseldorf (UDUS)	James Adjaye
		Gene Bridges GmbH	Harald Kranz
		European Molecular Biology Laboratory -European Bioinformatics Institute (EMBL-EBI)	Henning Hermjakob
Israel		Tel-Aviv University (TAU)	Tal Pupko
Estonia		OU QURETEC	Jaak Vilo
Switzerland		Swiss Institute of Bioinformatics (SIB)	Ioannis Xenarios
United Kingdom		The Babraham Institute (BI)	Nicolas Le Novère

www.agedbrainsysbio.eu

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