Facteurs de risques et déterminants moléculaires des maladies liées au vieillissement

Rapport Hcéres

agence d'évaluation de la recherche
et de l'enseignement supérieur

Department for the evaluation of research units

AERES report on unit:

Risk factors and molecular determinants of aging-related diseases

RID-AGE

Under the supervision of the following institutions and research bodies:

Université Lille 2 - Droit et Santé

Institut National de la Santé Et de la Recherche Médicale - INSERM

Institut Pasteur Lille

December 2013

agence d'évaluation de la recherche
et de l'enseignement supérieur

Department for the evaluation of research units

On behalf of AERES, pursuant to the Decree of 3 november 2006[1]*,*

- Mr. Didier HOUSSIN, president
- Mr. Pierre GLAUDES, head of the evaluation of research units department

On behalf of the expert committee,

- Ms Florence DEMENAIS, chair of the committee

[1] The AERES President "signs [...], the evaluation reports, [...] countersigned for each department by the director concerned" (Article 9, paragraph 3 of the Decree n ° 2006-1334 of 3 November 2006, as amended).

Evaluation report

This report is the result of the evaluation by the experts committee,the composition of which is specified below.

The assessment contained herein are the expression of independent and collegial deliberation of the committee.

Unit name:	Risk Factors and molecular determinants of aging-related diseases
Unit acronym:	RID-AGE
Label requested:	UMR_S
Present no.:	UMR_S 744
Name of Director (2013-2014):	Mr Philippe AMOUYEL
Name of Project Leader (2015-2019):	Mr Philippe AMOUYEL

Expert committee members

Chair: Ms Florence DEMENAIS, INSERM

Experts:

Ms Jane ARMITAGE, University of Oxford, United Kingdom

Ms Virginie GARDETTE, MCU-PH (representative of CNU)

Mr Dominique GAUGUIER, INSERM

Mr Tobias KURTH, INSERM (representative of INSERM)

Mr Frank LEZOUALC'H, INSERM

Scientific delegate representing the AERES:

Mr Emmanuel LAGARDE

Representatives of the unit's supervising institutions and bodies:

Mr Regis BORDET, Université Lille 2 – Droit et Santé

Ms Christine GUILLARD, INSERM

Ms Fabienne JEAN, Institut Pasteur Lille

1 • Introduction

History and geographical location of the unit

The UMR-744 entitled "Public Health and Molecular Epidemiology of Aging-Related Diseases" was created in 2006 and renewed in 2010. The current application is for the creation of a new unit entitled "Risk factors and molecular determinants of aging-related diseases". The unit has expertise in epidemiology, genetics, molecular biology and clinical studies. The research program focuses on cardiovascular and neurodegenerative diseases. The unit is supported by Inserm, Lille 2 University Medical School, the Pasteur Institute of Lille and the University Hospital. It is located on the Pasteur Institute of Lille campus. The laboratories are located in three different buildings.

Management team

The unit is composed of three teams:

1) team 1: Public Health and molecular epidemiology of cardiovascular diseases (team 1 leader: Mr Philippe AMOUYEL who is also the director of the unit);

2) team 2: Molecular determinants of heart failure and cardiac remodeling (team 2 leader: Ms Florence PINET);

3) team 3: Molecular determinants of neurodegenerative diseases (team 3 leader: Mr Jean-Charles LAMBERT).

The administrative and scientific management of the unit is planned and executed through weekly meetings that are attended by all researchers of the unit, one student representative and one or two representatives of the technical and administrative staff. The functioning of the unit is regulated by internal rules.

AERES nomenclature

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	6	9
N2: Permanent researchers from Institutions and similar positions	6	6
N3: Other permanent staff (without research duties)	21	19
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	3	2
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	10	9
N6: Other contractual staff (without research duties)	2	1
TOTAL N1 to N6	**48**	**46**

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	4	
Theses defended	11	
Postdoctoral students having spent at least 12 months in the unit*	12	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	9	13

2 • Assessment of the unit

Strengths and opportunities related to the context

The unit develops an ambitious program in a highly topical field of clinical and biomedical research. It integrates epidemiological, genetic and "omics" approaches together with functional studies in animal and cell-based models to characterize the molecular mechanisms underlying cardiovascular and neurodegenerative diseases. It also includes an excellent translational research program.

The unit has an outstanding scientific production including publications in excellent journals.

The unit has developed many collaborations nationally and internationally with a leading position in international consortia.

It shows an excellent ability to raise funds nationally and internationally.

It demonstrates excellent interactions with both the economic and social environment.

The unit shows a good capacity for attracting new scientists and has strong involvement in teaching and training.

Weaknesses and threats related to the context

The committee has noted the difficulty of retaining experienced post-doctoral fellows and engineers.

There are not enough methodologists in epidemiology and biostatistics at the senior level.

Generating exome and whole genome sequenced data requires very significant data storage, computing power and bioinformatic skills that are not currently available.

Recommendations

Interactions between the three teams should be optimized.

Improve the exploitation of the high quality data the unit has collected.

Attract senior scientists in epidemiology and biostatistics.

Face the Big Data issue by having access to large-scale IT facilities and by attracting a bioinformatician.

Improve international visibility for attracting international post-doctoral fellows and visiting scientists.

3 • Detailed assessments

Assessment of scientific quality and outputs

Scientific achievements are excellent. The scientific production is clearly outsanding with more than 345 publications and a number of them in excellent journals including the New England Journal of Medicine, Nature Genetics, Cell (34 articles are in journals with IF ≥10). The scientists of the unit often have leadership positions in these publications (as first or senior authors). The unit has constituted large collections with high quality data and biological resources. The main achievements include:

- the characterization of new risk factors for stroke and the understanding of the underlying molecular mechansims,

- the identification of new molecular determinants of heart failure and cardiac remodeling through

- omics aproaches and the characterization of their pathophysiological role in animal and cell based models,

- the identification of new genetic factors associated with the risk of Alzheimer's disease together with the assessment of these factors in Alzheirmer's disease process and the development of diagnostic tools.

Assessment of the unit's academic reputation and appeal

The unit is engaged in many collaborations at the national and international level. It has international visibility through the coordination of international consortia and contribution to other ones in both the cardiovascular and neurodegenerative fields. It demonstrates a capacity of raising funding nationally and internationally. The team coordinates the Labex DISTALZ, funded by the competitive "Investissement d'Avenir" program. The unit has been able to attract 6 new scientists with permanent position and post-doctoral fellows during the last five years. Members of the unit contribute to national and international scientific committees in which they most often occupy a leading position. They have also participated to the organization of international meetings and have been invited to make presentations at international conferences.

Assessment of the unit's interaction with the social, economic and cultural environment

The unit has excellent interactions with both economic and social environments. The research projects have conducted to 3 patent applications over the last five years. The unit contributed to the development of a small company (Genoscreen SAS) and formed the MEDIALZ consortium with two startup companies (Genoscreen and Alzprotect) to develop diagnostic tools and therapeutics targeted towards Alzheirmer's disease. It has several contracts with the pharmaceutical industry. The unit has contributed to public health programs and to dissemination of knowledge through various media.

Assessment of the unit's organisation and life

The visiting committee has appreciated the very good atmosphere in a well organized and structured unit. Students and support staff are strongly involved in the research projects and they can interact easily with their surpervisors. There is a weekly meeting for the overall unit, a weekly meeting within each team, and there are frequent contacts between the members of each team. There are shared Information Technology (IT) and biological resources. The unit receives strong support from the local environment (Institut Pasteur, Université Lille 2 and University Hospital in Lille).

Assessment of the unit's involvement in training through research

The unit is strongly involved in teaching and training. It includes seven scientists with University and/or hospital positions. Teaching activities cover various disciplines including epidemiology, biostatistics, clinical and public health research, molecular and cell biology and medical specialties in cardiology and neurosciences. The unit has trained a total of 119 students over the last five years (including 30 Master 2 and 18 PhD students). There are frequent contacts between the students and their supervisors. Students appear satisfied with the policy regarding publications and presentations at meetings. The unit plans to develop a European and International training program, as part of the Labex DISTALZ (participation to an advanced Erasmus Mundus European Master program, development of an international summer school, organization of thematic workshops).

Assessment of the strategy and the five-year plan

The scientific questions are ambitious and relevant to characterize new risk factors and to get better insight into the molecular mechanisms underlying cardiovascular and neurodegenerative diseases. The projects are based on large and very well characterized collections with extensive phenotyping and biological resources. The main assets of these projects rest on the integration of various approaches in epidemiology, biostatistics and molecular biology using animal and cell-based models. One of the goals is to pursue the identification of genetic and other determinants of cardiosvascular diseases (stroke, heart failure) and associated traits (obesity) and of neurogenerative diseases (Alzheimer's disease) using new sequencing and omic technologies. Other aims include the characterization of molecular mechanisms involved in the pathophysiology of these diseases and identification of biomarkers for diagnostic and prognostic purposes based on a variety of approaches.

The unit has the expertise to conduct these projects and can benefit from its established links with international consortia. Prioritization of the research questions would be desirable. The recruitment of senior methodologists in epidemiology and biostatistics and highly-qualified post-doctoral fellows would favor the achievement of this high quality program.

4 • Team-by-team analysis

Team 1: Public health and molecular epidemiology of cardiovascular diseases

Name of team leader: Mr Philippe AMOUYEL

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions	3	3
N3: Other permanent staff (without research duties)	9	8
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**17**	**16**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended	2	
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	5	7

• Detailed assessments

Assessment of scientific quality and outputs

This is a coherent body of excellent work on the various causes and manifestations of cardiovascular disease. The program of work of team 1 has produced information on coronary heart disease trends in incidence and determinants which has been very valuable for the scientific community. It is, however, not clear how this has fed local public health policies and strategies (for example tackling the mentioned increase in coronary heart disease incidence in young women). The data from these well phenotyped cohorts are also a very valuable contribution to various international collaborations. The diet and socio-economic factor work is illustrative of the difficulty of studying this area to develop relevant public health policies with huge amounts of observational data that the team have valuably summarized. Significant efforts have been made to translate healthy diet messages into public health policy but it is not entirely clear how successful this has been. The stroke work is very innovative and has already provided new insights. The case-control study of stroke due to cervical artery dissection has been an outstanding addition to the literature. The team members need to ensure that they exploit their own high-quality data as much as possible. The exploration of the PROX1 gene has been interesting and produced high quality publications.

Team 1 has an outstanding scientific production with 187 published articles as follows: 8 in journals with IF >20, 15 in journals with IF between 20 and 10 and 39 in journals with an IF between 10 and 5, as well as 60 collaborative papers.

Assessment of the unit's academic reputation and appeal

This group has developed expertise in identifying trends in risk factors for cardiovascular diseases, based on knowledge of metabolic pathways (focusing on excess body weight and type 2 diabetes) and abnormalities in dietary behavior. As a result of long-term national and international collaborations, the team has gained a substantial scientific reputation and is considered a leading group in the field. Collaborations exist specifically with the following projects: WHO-French MONICA network, Euroaspire network, PRIME, BiomarCaRE, GenomEUtwin, CHANCES, HELENA, ENGAGE, GIANT, EGG, and CADISP.

The team leader is regularly invited to present the unit’s work at high profile national and international meetings. Three major recruitments (1 CR2, 1 MCU, and 1 MCU-PH since 2009) have taken place.

Assessment of the unit's interaction with the social, economic and cultural environment

The work of the group on dietary patterns has led to specific expertise and recommendations. Particularly these include: recommendations for fatty acid intake; Expert panel Human Nutrition. ANSES 2011; Collective Expertise in Dietary behavior (INRA 2009-2010); Implementation and economic challenges and barriers of risk guided therapy (Risk Stratification Guided CV Preventive Drug Therapy Symposium); European Stroke Conference Working Group on Cardiovascular Pharmacology and Drug Therapy.

Assessment of the unit's involvement in training through research

This team has a good training record with long standing expertise in mentoring and supervising PhD students and postdoctoral fellows. Compared to participation of team 3 in new innovative and international teaching programs in Alzheimer’s disease, specific modules for cardiovascular and cerebrovascular-related topics are lacking.

Assessment of the strategy and the five-year plan

The 5 year plans are ambitious for this team. The future work on genetic and other determinants of obesity is particularly interesting and (perhaps in collaboration with other groups) has the potential to provide new insights into genetic determinants of eating behaviors and obesity. The expansion of the stroke surveillance is also potentially valuable and we would urge the team to investigate further subtypes of ischaemic stroke (lacunar, small artery and large artery) as well as cervical artery dissection. The use of the coronary heart disease cohorts to investigate cognitive function and the overlap between cerebrovascular and coronary disease is interesting but requires careful epidemiological analysis. It is not clear whether there is sufficient expertise currently within the group for this sort of work and expansion of the epidemiologically trained personnel is recommended. The value of the continuing

molecular investigations into the PROX1 and other genes needs to be carefully balanced against all the other demands on the team. It is important that the data sharing of the valuable information from the existing cohorts, which can require considerable resources, does not detract from the work that the team wants to pursue.

Conclusion

- **Strengths and opportunities:**

- renowned research team with excellent international collaborations;

- well established local cohorts in coronary heart disease and newly established in stroke;

- extensive experience of managing prospective collaborations;

- ability to respond to collaborative projects from elsewhere;

- experienced team with good training record;

- working with other teams within the unit and cross-fertilization of ideas.

- **Weaknesses and threats:**

Cohorts are not very large and competing with large-scale studies such as planned large cohort studies in France or the UK Biobank. However, maintaining the excellent clinical information and focus on specific aspects should allow this team to continue to play a leading role in the field.

Team thinly spreads between laboratory based and epidemiological studies which require very different sets of skills and intra-laboratory communication.

Moving into exome and whole genome sequencing requires substantial computing power and bioinformatics, which is currently not available.

- **Recommendations:**

Continue with the planned work on developing the stroke prospective studies and include detailed phenotyping to allow further subtyping of ischaemic stroke.

Continue to focus on high quality clinical data to allow evaluating categories that are not easily addressable in larger cohort projects.

Consider concentrating more on “just” the epidemiology rather than on both epidemiology and molecular biology.

Consider contributing to or initiating a EUROASPIRE type study for secondary prevention of stroke.

Team 2: Molecular determinants of heart failure and cardiac remodeling

Name of team leader: Ms Florence PINET

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	3
N2: Permanent EPST or EPIC researchers and similar positions	1	1
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)	3	2
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**9**	**10**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	4	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

During the last quadrennial period, the team successfully developed translational research programs in close collaboration with cardiologists at Lille University Medical Center, for identifying novel biomarkers of cardiac remodeling diseases (namely abdominal aortic aneurysm and left ventricular remodeling). The final objective is to improve risk stratification and patient management. The approach is based on the use of omic technologies (proteomics, transcriptomics (RNA and miRNA) for the screening of human sample collections that the team has constituted. The group has acquired a solid expertise in omic technologies and has optimized them to human samples. In addition, the team has also developed molecular approaches and animal models for deciphering the disease mechanisms underlying changes in proteins and miRNA targets in these pathological conditions. The major scientific breakthroughs include the following:

- protein levels secreted by pro-inflammatory macrophages as potential new biomarkers of abdominal aortic aneurysm;

- right ventricular systolic function for risk stratification in patients with stable left ventricular systolic dysfunction;

- identification of the level of phosphorylation of troponin T and hepatocyte growth factor as biomarkers for left ventricular remodeling post-myocardial infarction;

- miR 22-3p as risk marker associated to early death in heart failure patients.

The scientific production of the team is very good with 70 original articles published since 2008, out of which 40 were signed by team members as either first or senior authors, and some of them are published in major cardiovascular journals including 3 European Heart Journal (IF ≥ 10), 1 Circulation (IF ≥ 10), 1 ATVB (Arteriosclerosis, Thrombosis and Vascular Biology), 1 Circulation-Heart Failure.

The team leader and members of the team are also authors on 9 review articles and 2 patents.

Assessment of the unit's academic reputation and appeal

The group is very well funded: Members of the team participate in various European and French networks: 2 FP7 (FAD, HOMAGE), Euro-observational research program from European Society of Cardiology (heart failure, post-partum cardiomyopathies) and French networks (PAH, PH-HF, OFICA). In addition, the group is very active and successful in obtaining grants from national agencies and foundations (team labelled FRM, 3 ANR granted projects in collaboration with UMR Inserm 1096 (Rouen), SFC/FFC, Foundation “Coeur et Recherche”).

The team members participate in many scientific societies (European Council for CV research, Fondation de France, GRRC, SHFTA, SFC, …).

One member of the team is an associated editor of the European Heart Journal (IF>10).

70 invitations to give lectures in national and international congresses (European Society of Cardiology: 2009, 2011, 2012).

Recruitment of one Research Engineer (Université Lille 2) in 2010.

Assessment of the unit's interaction with the social, economic and cultural environment

The team has filed 2 patents on “Post-translation modified cardiac troponin T as a biomarker of a risk for heart failure, 2010” and “Methods and kits for predicting the survival time of post acute MI, 2013”. Of note, the team developed an ELISA for the analysis of the phosphorylated form of troponin T (project financed by an ANR Emergence grant, 2012-14) which could be used as a predictive biomarker for left ventricle remodeling.

One industrial contract is mentionned in the report (with Pfizer, 2011).

Team members participate actively in numerous public dissemination activities (Forum Santé La voix du Nord

(Lille), conferences « 5 to 7 IPL » Lille, the General European day of heart failure (since 2011), PAH day (in association with patients) and has been involved in the writing of many didactic publications.

Assessment of the unit's involvement in training through research

The team is actively involved in teaching at Master 2 level (Lille 1, Lille 2, Paris 7 Universities) and DU of heart failure, DU of general medicine and DU of geriatrics (Lille Faculty of medicine).

The team is also very active in training students. Altogether 7 PhD students and 5 Postdoctoral fellows have been trained in addition to 15 Master students, which is a remarkable and successful commitment to training young scientists.

Assessment of the strategy and the five-year plan

The five-year plan is in line with the previous year activities but with a focus on cardiac remodeling. The project is structured according to 4 main axes:

a) to validate the previously identified targets for diagnostic and prognostic purposes in dedicated clinical studies and in population samples;

b) to identify by omic approaches, new circulating biomarkers that are associated with early cardiac mortality in chronic stable HF (Heart Failure) patients, in order to establish a predictive score for the stratification of HF patients;

c) to screen circulating microRNAs and long non-coding RNAs in post-MI LVR patients;

d) to understand the pathophysiological mechanisms underlying changes in the identified targets.

The team possesses all the required expertise and the project looks feasible within the next 5 years.

Conclusion

- **Strengths and opportunities:**

- excellent translational research;

- strong background data accumulated over the past 5 years;

- team members are working together in the same direction towards convergent objectives;

- high expertise of the team in differential omics approaches and constitution of human sample collections with cardiac disorders;

- active involvement in national and international research programs;

- the project is feasible;

- ability to raise funds.

- **Weaknesses and threats:**

There may be issues with bioinformatic/biostatistical analysis of omic datasets that have been and will be generated.

There are strong concerns regarding limitations in the recruitment of both permanent and contract staffs at all levels, which will hamper the positive momentum of the research and the team productivity.

Even though the project is strong, highly topical, competitive and well-structured, it should seek additional alliances and collaborations with national groups to enhance the visibility of this line of research and establish its leadership.

There are apparently logistic issues that may affect the performance of the team, which is physically separated from the other two teams of the unit.

Team members should aim at increasing the team's visibility by publishing in high impact multidisciplinary scientific journals targeting a broad scientific/clinical audience.

- **Recommendations:**

A tenured clinical scientist has joined the team to strengthen its structure and contribute to supervision of staffs and students. This looks a little limited when considering the strong scientific and editiorial activities of team members. Therefore, a young researcher in basic science should be recruited.

The team should increase its international visibility.

The team should work out a platform for omic data analysis with other groups at the Lille Pasteur Institute and seek collaborations with emerging/structured national and international networks.

Team 3: Molecular determinants of neurodegenerative diseases

Name of team leader: Mr Jean-Charles LAMBERT

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	2	3
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	6	5
N6: Other contractual staff (without research duties)	2	1
TOTAL N1 to N6	**13**	**12**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	5	
Postdoctoral students having spent at least 12 months in the unit	6	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	1	3

• Detailed assessments

Assessment of scientific quality and outputs:

Team 3 research program aims at identifying the genetic factors involved in dementia and more specifically in Alzheimer Disease and at characterizing the biological function of these genes and their role in Alzheimer disease pathophysiology. The work conducted by team 3 has led to major achievements in the field and placed this team at the cutting edge of the research on this topic internationally. These achievements include:

1) the identification of new genetic determinants of Alzheimer disease through genome-wide association studies (GWAS), meta-analysis of GWAS and genome-wide haplotype analysis;

2) the coordination of an international consortium on the genetics of Alzheimer disease which has allowed the identification of 11 novel susceptibility loci;

3) the demonstration of a role of BIN1 gene related to Tau protein through functional studies;

4) the characterization of a new pathway involving ADAM30 gene in APP (amyloid precursor protein) metabolism;

5) the development of a diagnostic tool.

The team demonstrates an excellent scientific production. Among 78 original articles, 38 have the team members as first or senior authors and 21 are in journals with IF≥10 (such as the New England Journal of Medicine, Nature Genetics, Cell, Molecular Psychiatry). Additional publications (10) include contributions to large collaborative international groups and review articles.

Assessment of the unit's academic reputation and appeal

The international visibility of the team is attested by the coordination of European and International consortia on the genetics of Alzheimer disease. Team 3 is also co-coordinating the national Three-City study and is involved in many national and international collaborations. The team is very successful in obtaining funding at the regional, national and European levels. The team is the coordinator of the LABEX DISTALZ, a highly competitive Investissement d'Avenir programme in France.

The team leader and the director of the unit contribute to many scientific committees with most often a prominent position: the scientific committee of France Alzheimer and Fédération pour la Recherche sur le Cerveau (team leader), Fondation nationale de coopération scientifique Maladie d'Alzheimer et maladies apparentées (the unit director is the Scientific Council Director), the European Joint Programming Research Initiative of neurodegenration and Alzheimer's disease (the unit director is the Chair). Members of the team have been invited to make presentations at national and international conferences. The team leader has been awarded the Adrienne and Herbert prize from the Fondation de la Recherche Médicale.

The attractiveness of the team is also demonstrated by the recruitment of two young research scientists (CR2 Inserm and "Chaire d'excellence" Inserm-Université Lille 2).

Assessment of the unit's interaction with the social, economic and cultural environment

The team is very active in the dissemination of their results through Intellectual Property protection and industrial partnership. They filled one patent (in partnership with the CEA) and have obtained funding from the pharmaceutical industry (several contracts). The team contributed to the development of Genoscreen SAS, a small company dedicated to genomics and diagnostics focused on AD. They formed the MELDIALZ consortium with two private companies (Genoscreen and Alzprotect) and this is funded by the Fonds Unique Interministériel (FUI) for the development of diagnostic tools and therapeutics targeted towards AD. Team 3 is also partner of the steering group for European Innovation Partnership on Active and Healthy Ageing of the European Commission. Team 3 members have contributed to dissemination of their work through various media.

Assessment of the unit's involvement in training through research

Over the past five years, the team has played an important role in the training of undergraduate (7), master and doctoral students (16) and post-doctoral fellows (7). Team 3 researchers are involved in teaching in Université de Lille. As part of the LABEX DISTALZ, an international education and training program is planned including a European Master program, summer schools and thematic workshops in social sciences. The students appear satisfied of the policy regarding publications, their relationships with their supervisors and life of the unit.

Assessment of the strategy and the five-year plan

The proposed research for the next five-years will be developed along the three following lines:

(1) the pursuit of the identification of the genetic component of Alzheimer disease;

(2) the characterization of the function of Alzheimer disease-associated genes at the cellular and molecular levels in order to better understand the underlying mechanisms:

(3) the assessement of the relationships between cognitive impairments and cardiovascular factors at both the genetic and epidemiological levels.

The scientific questions raised are very relevant. Regarding the first axis, members of this team have access to large cohorts of Alzheimer disease patients and coordinate European and international consortia. Identification of new genetic factors involves moving to exome and whole-genome sequencing, which requires bioinformatic skills that need to be developed. The proposed functional studies of Alzheimer disease-associated genes are of major importance. These studies are based on a series of well-defined in vivo and cell-based models that are complementary. The drosophila model for fast screening of normal and altered gene function is unique and very promising. This work is linked to the LABEX DISTALZ which can favour its success. The last axis will be done in close collaboration with team 1 and is of interest to better characterize the relationships between cardiovascular diseases and dementia.

Conclusion

- **Strengths and opportunities:**

- internationally renowned expertise in Alzheimer disease genetics (coordination of the Alzheimer disease International Consortium);

- constitution of exensive biological collections and associated data;

- development of a unique animal model for functional studies;

- excellent productivity with a high proportion of high IF publications;

- capacity for raising funds nationally and internationally;

- ability to attract new research scientists and training of many students;

- partnership with the private sector to translate the research findings into clinical applications;

- relevance of the research plan.

- **Weaknesses and threats:**

- difficulty to get enough support to maintain a cutting-edge research in a highly competitive field internationally;

- difficulty of attracting and maintaining high-level post-doctoral fellows and potential decrease of contractual staff in the future;

- the Big Data issue is a major problem the team will have to face with currently insufficient IT resources and staff in bioinformatics.

- **Recommendations:**

- continue to have a leadership position in the genetics of Alzheimer disease.

- attract a senior biostatistician and a bioinformatician in the group as well as highly-qualified post-doctoral fellows.

- maintain and possibly increase the level of funding from European and International sources.

- get access to large-scale IT resources.

5 • Conduct of the visit

Visit date: 19th December 2013

Start: 19th December 2013, 08.00 am

End: 19th December 2013, 06.15 pm

Visit site:

Institution: UMR

Address: Institut Pasteur de Lille
1 rue du Pr. Calmette
59019 Lille

Conduct or programme of visit:

08.00 am — Welcome to the committee

08.50 am — Preliminary meeting of the committee (closed hearing)
Attending: expert committee members and AERES scientific delegate (DS)

Scientific part

08.35 am — Presentation of AERES evaluation and of expert committee members
(DS: Mr Emmanuel LAGARDE)

08.45 am — Presentation of the unit project: Mr Philippe AMOUYEL (discussion)
Attending: expert committee members, DS, representatives of institutions and unit members

09.45 am — Scientific presentation team 1 - (discussion)
Attending: expert committee members, DS, representatives of institutions and unit members

10.45 am — Break

11.00 am — Scientific presentation team 2 - (discussion)
Attending: expert committee members, DS, representatives of institutions and unit members

12.00 pm — Scientific presentation team 3 – (discussion)
Attending: expert committee members, DS, representatives of institutions and unit members

Lunch with representatives of Institutions

01.00 pm — *(discussion with committee members)*
Attending: expert committee members, DS, representatives of Lille 2, representatives of Institut Pasteur of Lille, CHRU de Lille and of INSERM (Ms Christine GUILLARD) (without the direction of the unit and without team leaders)

Meeting with representatives of the doctoral school

02.00 pm — *(discussion with expert committee members)*
Attending: expert committee members and doctoral school representative

Meeting with researchers, technicians, doctoral students and post doctoral fellows

02.15 pm *(in parallel the committee splits into three groups)*
Meeting with researchers
Meeting with technicians
Meeting doctoral students and post doctoral fellows
Attending: expert committee members, DS (without representative of institution, the direction of the unit and team leaders)

Meeting with the unit director

03.00 pm *(discussion with the expert committee members)*

Close-door meeting of the site visit expert committee with AERES scientific advisor

03.30 pm Deliberation of the committee (closed hearing)
Attending: expert committee members and DS

06.00 pm End of the site visit

Specific points to be mentioned:

Besides those already mentioned, the committee also met other representatives of the insitutions:

Prof. Patrick BERCHE, conseiller scientifique Institut Pasteur de Lille

Prof. Antoine CORTOT, représentant la direction du CHRU de Lille

Mr Samir OULD-ALI (administration Déléguée Régionale de l'INSERM)

Mr Jacques RICHIR, administrateur délégué Institut Pasteur de Lille

6 • Supervising bodies' general comments

Université Lille 2
Droit et Santé

Service de la Recherche, de la Valorisation
et de l'Information Scientifique (SeRVIS)
Affaire suivie par Christophe BOUTILLON
Directeur du SeRVIS
christophe.boutillon@univ-lille2.fr / 03.20.96.52.16

Le Président de l'Université

à

Monsieur le Professeur Pierre GLAUDES
Directeur de la Section des unités de recherche
Agence d'Evaluation de la Recherche et de l'Enseignement Supérieur (AERES)
20 rue Vivienne
75002 PARIS

Lille, le 20 mars 2014

V/Réf. : E2015-EV-0593560Z-S2PUR150007714-005653-RT

Objet : Observations de portée générale sur le rapport d'évaluation de l'unité *Risk factors and molecular determinants of aging-related diseases (RID-AGE)*

Monsieur le Directeur,

Considérant le rapport que vous m'avez récemment transmis, je vous remercie au nom de l'Université Lille 2 et en particulier du directeur et des membres de l'unité *Risk factors and molecular determinants of aging-related diseases,* pour la qualité de l'évaluation effectuée le 19 décembre 2013 par votre comité d'experts.

Les appréciations et recommandations formulées seront soigneusement prises en considération et discutées avec le directeur de l'unité dans le cadre de la structuration de notre recherche pour le prochain plan quinquennal (2015-2019).

Vous trouverez ci-dessous les observations de portée générale sur le rapport d'évaluation de l'AERES, émises par le Directeur de l'unité *Risk factors and molecular determinants of aging-related diseases.*

Je vous prie d'agréer, Monsieur le Directeur, l'expression de ma considération distinguée.

Pr. Xavier VANDENDRIESSCHE

Institut Pasteur de Lille

Université Lille 2 Droit et Santé

Inserm
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Directeur

Monsieur le Professeur Pierre GLAUDES
Directeur de la Section des Unités de Recherche
AERES
20 rue Vivienne
75002 PARIS

Nos réf. :
Vos réf. :

Lille, 17 mars 2014

Objet : Compte rendu de visite d'unité, projet RID-AGE

Monsieur le Directeur, Cher Collègue,

L'Université de Lille 2 m'a transmis le 3 mars dernier le rapport d'évaluation du projet d'unité "Risk factors and molecular determinants of aging related diseases (RID-AGE)" que j'ai l'honneur de conduire dans le cadre de la vague E en cours d'évaluation.

Je tenais à vous faire savoir combien mes équipes et moi-même avons apprécié la rigueur de la préparation et la qualité de la tenue de la réunion d'évaluation sur site qui a eu lieu le 19 décembre dernier. Aussi voulais-je remercier très sincèrement les personnalités composant le Comité de Visite et leur Présidente pour le temps consacré à ce travail et pour les recommandations constructives qu'elles ont bien voulu nous transmettre.

Nous ne manquerons pas de suivre leurs conseils et avis qui viendront renforcer les axes et la stratégie scientifique de notre projet. Je vous prie de croire, Monsieur le Directeur, Cher Collègue, en l'expression de ma considération distinguée.

Philippe Amouyel

Le Président de l'Université

Pr Xavier VANDENBRIESSCHE

Université Lille 2 Droit et Santé