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Santé publique et épidémiologie moléculaire des maladies liées au vieillissement

Rapport Hcéres

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

Section des Unités de recherche

Evaluation report

Research unit:

Public health and molecular epidemiology of aging-
related diseases

University Lille 2



mars 2009



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

Section des Unités de recherche

Evaluation report

Research unit:

Public health and molecular epidemiology of aging-
related diseases

University Lille 2



Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

mars 2009



Evaluation report

The research unit :

Name of the research unit : Public health and molecular epidemiology of aging-related diseases

Requested label : UMR_S

N° in case of renewal : 744

Head of the research unit : M. Philippe Amouyel

University or school :

University of Lille 2

Other institutions and research organization:

INSERM

Institut Pasteur de Lille

Date of the visit :

4 December 2008



Members of the visiting committee

Chairman of the committee :

Mr Xavier JOUVEN, INSERM Paris, France

Other committee members :

Mrs Jolanda VAN DER VELDEN, Amsterdam, The Netherlands

Mrs Monique M.B. BRETELER, Rotterdam, The Netherlands

Mr Paul W FRANKS, Umeå, Sweden

Mrs Jane-Lise SAMUEL, INSERM Paris, France

Mrs Bernadette ALLINQUANT, INSERM Paris, France

CNU, CoNRS, CSS INSERM, (representant INRA, INRIA, IRD.....) representatives :

Mrs Sandrine ANDRIEU, (CNU representative)

Mrs Emmanuelle GENIN, (INSERM representative)

Observers

AERES scientific representative:

Mr Alexis ELBAZ

University or school representative:

Mr Alain DUHAMEL, Université Lille 2

Mrs Fabienne JEAN, Institut Pasteur de Lille

Research organization representative:

Mrs. Marie-Josèphe LEROY-ZAMIA, INSERM

1 • Short presentation of the research unit

- The Unit is formed by 3 teams, with 2 recently formed (team 2 and 3) entitled respectively :
- Team 1: Public Health and epidemiology of cardiovascular diseases;
- Team 2: Search for the molecular determinants of cardiovascular diseases via proteomics and candidate gene approaches;
- Team 3: Search for the molecular determinants of neurodegenerative diseases via transcriptomics and candidate gene approaches.
- Total number of lab members in the unit: 32 including
 - Researchers with teaching duties (5): team 1 (2), team 2 (2), team 3(1)
 - Full time researchers (4): team 1 (2), team 2 (1), team 3(1)
 - Research physicians (3): team 1 (1), team 2 (2), team (0)
 - Engineers (5): common to the unit (2), team 1 (1), team 2 (1), team 3(1)
 - PhD students (4): team 1 (1), team 2 (2), team 3(1)
 - Post-docs (3): team 1 (1), team 2 (0), team 3(2)
 - Technicians (5): common to the unit (4), team 1 (0), team 2 (1), team 3(0)
 - Administrative assistants (3): common to the unit (3)
- Numbers of HDR = 7
- Numbers of PhD students who have obtained their PhD : 9 including 3 for team 1, 3 for team 2 and 3 for team 3)
- Average length of a PhD during the past 4 years (3 years)
- Numbers of PhD students currently present in the research unit (4), all with fellowships (4)
- Numbers of lab members who have been granted a PEDR (1)
- Numbers of “publishing” lab members among researchers with teaching duties and full time researchers: 9 out of 9
- Total number of rank A papers published by the unit in the past 4 years : 200 (team 1: 100 ; team 2: 62 ; team 3: 38)

2 • Preparation and execution of the visit

The visiting committee received the documents and read them prior to the visit.

The visiting committee met for dinner the day prior to the evaluation and the AERES representative explained the evaluation procedures. The following day, after an overall presentation by the director of the Inserm unit, three scientific presentations were held, one by each team. At lunch time, the visiting committee was able to discuss with the PhD students and post-docs in front of their posters. In the afternoon, parallel meetings were organized and the committee was divided in three to meet the students, engineers, and researchers. Afterwards, the visiting committee briefly met the director of the Inserm unit, before meeting the representatives of the University Lille 2, Institut Pasteur de Lille, and Inserm. At the end of the day, the visiting committee met to perform the evaluation.

The visit was well organized and executed. We followed the schedule which was appropriate.

All the presentations and discussions were performed in English.



3 • Overall appreciation of the activity of the research unit, of its links with local, national and international partners

There is definitely a good level of activity, covering a wide and outstanding range of topics and expertises. The main objective is to “gain knowledge on the impact of the environmental and genetic determinants in the occurrence, the evolution and the prevention and treatment of two pathologies related to ageing ie cardiovascular and neurodegenerative diseases”. This research unit is effectively adressing all of these issues altogether trying to benefit from the permanent interaction between them.

The research unit has achieved considerable collaborations at local, national and international levels, with an excellent level of expertise. Although the publications are numerous and well ranked, the ratio of publications over publishers is not so high according to international standards. The highest ranked papers are not signed in first or last position.

The research unit has developed many and various types of scientific and medical know-how, from clinical research and epidemiological studies to the use of analytical techniques (genomics, transcriptomics, proteomics, bio-computing, cell biology). The visiting committee was impressed by the efforts deployed to adress every technical issue (mainly within the unit or at least with close collaborations). The research unit is also engaged in numerous data gatherings and different collections, maybe too many given the size of the unit and its analytical capacities.

The research unit has developed a front line and strategic position in two competitive areas: proteomics and genetic aspects of Alzheimer disease. They definitely require additional members to ensure and develop these strategic positions.

4 • Specific appreciation team by team and/or project by project

Team 1 is engaged in numerous data collections in regional, national and international levels, with adequate collaborations. MONICA, MONALISA, PRIME, MORGAM, EUROASPIRE, HELENA, REACH ... They have a good level of publication and expertise, they are involved in the development of Public Health policies, and are respected as international experts. Their projects are very good although not quoted as excellent by the visiting committee since they appear to be more the continuum of the past activity rather than cutting edge ones. As the main interest of the team members involves research, little effort is put into teaching duties.

Nom de l'équipe : Sante Publique Et Epidemiologie Des Maladies Cardiovasculaires

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A+	A+	A	A



Team 2 is devoted to the identification of molecular determinants essentially through proteomics, and is focusing on vascular and cardiac remodelling in abdominal aortic aneurysms and in post ischemic heart failure. The clinicians of the team are collecting the patient-cases through local or regional data bases and collaborations. They have recently extended their project to animal experimental domain through collaborations; albeit these collaborations already succeed in good publications and provide an excellent combination of human and animal studies, team 2 should be careful in avoiding a too large dispersion. As it is outlined by the team itself, the team is rather small and needs to be reinforced. If the level of publication is not outstanding (for the moment), it is clearly an innovative and promising topic.

Nom de l'équipe : Recherche des déterminants moléculaires des maladies cardiovasculaires

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A	A	A	A	A

Team 3 is mainly working on the genetic aspects of Alzheimer disease and is clearly positioned in front line of the scientific competition and is currently running a european collaborative project. The highest ranked paper of the unit is provided by team 3. They reach excellence in many items; however, in regards to the importance of the field and the actual leading position of the team, the size of the team is particularly small. One brilliant student should come back soon from a post doc. They would clearly benefit from the addition of different skills including statistical genetics, biostatistics, and bioinformatics.

Nom de l'équipe : Recherche Des Déterminants Moléculaires Des Maladies Neurodégénératives Par Analyses Transcriptomique Et Approche Gène-Candidat

Note de l'équipe	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	A+	A	A	A+

5 • Appreciation of resources and of the life of the research unit

The research unit succeeded to gain many contracts and to raise money and fundings. However the ratio publication/income funding is below the expected level. The members of the unit look very motivated and happy to work together and appreciate their interactions

The unit is engaged in cutting-edge projects and is collecting large volumes of data. A potential future problem will be organizing and analyzing this mass of data in order to translate the studies into high impact publications. The appointment of a bioinformaticist (dedicated to data organization and processing) and a statistical geneticist (focused on developing analytical methods for the analysis and integration of different types of "omics" data) seem to be important strategic objectives. Additional computing resources may also need to be identified if the analytical problems are particularly complex and involve very large volumes of data.



6 • Recommendations and advice

- Strong points :
 - Very large platform of capacities, skills and knowledge;
 - Good level of realization in terms of what has been achieved and publication
 - Good notoriety with many international collaborations;
 - Strong involvement in development of Public Health policies;
 - Strategic position in two emerging fields : techniques (proteomics) and applications (genetic aspects of Alzheimer disease).

- Weak points :
 - The research unit tries to encompass too many directions and topics;
 - There is too much heterogeneity and not enough synergy between the teams;
 - In several very competitive areas, two or three researchers involved in those specific areas will compete with foreign teams composed of > 50 people;
 - There is a lack in the field of teaching and PhD training.

- Recommendations :

This research Unit may have spread itself across too many areas of research and might benefit by narrowing its scientific focus. At present, the Unit focuses on several diverse areas and the connections between the projects is not always clear (in several cases, the projects appear completely disconnected). It seems that by choosing a smaller number of specific research areas and identifying how these link together, the Unit may improve its international ranking in these research areas. Explicitly identifying the connections between projects and increasing synergy between the teams within the Unit would likely improve continuity and productivity. It might also provide a better impression to those observing the performance of the Unit and its scientists (e.g. grant and manuscript reviewers, and research center evaluators), which could potentially result in improved funding and publication successes.

The research Unit would benefit from recruiting personnel in the bioinformatics and biostatistics areas, in particular with an expertise in statistical genetics.

The research unit would also benefit from recruiting additional full time reseachers in order to improve competitiveness. The unit has a good reputation at the international level but should increase its international visibility.

Note de l'unité	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Stratégie, gouvernance et vie du laboratoire	Appréciation du projet
A+	A+	A+	A	A



Université Lille 2
Droit et Santé

Lille, le vendredi 27 mars 2009

Monsieur Pierre GLORIEUX
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

N/Réf. : CS/PMR/SD/09/03/9
V/Réf. : EVAL-0593560Z-S2100012123

Objet : Observations sur le Rapport d'évaluation de l'Unité de recherche : Public health and molecular epidemiology of aging-related diseases dirigée par le Professeur Philippe AMOUYEL

Monsieur le Directeur,

Je m'associe aux remerciements formulés par l'ensemble de la direction du Laboratoire pour la qualité du rapport fourni à la suite de l'expertise de cette unité de recherche.

Au titre de l'établissement, le Vice-Président du CS et moi-même n'avons aucune remarque particulière à formuler en complément de celles exprimées par le directeur dont vous trouverez copie ci-jointe.

Veillez agréer, Monsieur le Directeur, l'expression de mes meilleures salutations.

Pr. Christian SERGHERAERT

Droit - Science Politique - Gestion - Santé - Sciences du Sport

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Section des Unités de recherche
20 rue Vivienne
75002 Paris

Nos réf. :
Vos réf. :

Lille, 6th March 2009

Dear Sir, Dear Madam,

First of all I would like to thank the AERES visiting committee for the time spent for the site visit and for the very helpful analysis of our laboratory activity. I would like also to take this opportunity to clarify two points raised by the expert committee that may have suffered from insufficient explanation in the report of our past and future activities:

1. Scientific project of team 1

As noted by the committee, parts of our activities are in the continuity of our previous projects. This may be seen as a strength for a team focused on epidemiology. Continuity is mandatory for prospective epidemiological studies such as the PRIME prospective study that has reached a follow-up of 17 years now. This is necessary to increase the number of events and reach sufficient statistical power to be able to analyse in depth the etiologic determinants of coronary heart diseases.

Our laboratory is involved in a number of national and international projects, the aim of which is to analyse the trends and determinants of cardiovascular risk. By definition these projects need repeated assessments of coronary heart disease rates and risk factors, through a series of studies that deserve a high level of quality to be maintained for more than 15 years with a permanent level of details. The calendar of the studies is imposed by the protocols of these collaborations : cross-sectional assessment of cardiovascular risk factors in population every 10

years (since 1985) for the WHO-Monica project and every 5 years (since 1995) for the EuroAspire European program. Thus, the strength of these projects relies upon continuity and repetition.

As a result of this epidemiological program, the last three years were devoted to the recruitment of more than 4,000 subjects. **This data collection phase needs large budgets, consolidated in the global funding of the unit that may explain the ratio publication/income.** The following periods will be devoted to the analysis of these data and will balance this budget over the next four years.

Another part of team 1 scientific activity is totally new, developed *de novo* during the past term, and centred around cutting-edge projects in the field of cerebrovascular diseases. One of the most prominent project is a **genome wide association study (GWAS) on Cervical Artery Dissections (CADISP study)** based on the largest case-control study developed in the world to date (1130 cervical artery dissection cases, 1100 ischemic stroke cases without cervical artery dissection cases and 2200 age and gender matched controls recruited in 9 European countries). This is the second GWAS developed in our unit, the other one being related to Alzheimer's disease. Since January 2009 we are in the final preparation of the DNA samples, that will be transmitted during the next month to the National Centre for Genotyping in Evry to be processed. Again it is important to note that this is a totally new program.

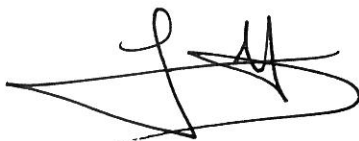
2. Teaching duties.

The second comment deals with our commitment in the field of teaching and PhD training. Concerning teaching, more than half of the lab members (5 out of 9) are researchers with daily teaching duties and *de facto* involved in the field of teaching. Moreover they perform their complete full time duties without any reduction in their teaching load. For instance we had to set up this last two years, the teaching program of critical article reading in public health and epidemiology for medical students. There has been on average one PhD/PostDoc per researcher during the whole term and 2 interns in Public Health are permanently hosted in the laboratory for their training. We always maintain a high level of selection of PhD students to ensure their best training with a dedicated researcher owning, as requested in France, an HDR

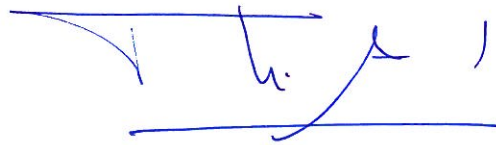
(accreditation to supervise research). Thus, during the last four years 9 students have obtained their PhD and 5 are currently preparing their PhD in the lab.

Hoping that these comments may help to clarify the strategy of our research unit,

Yours sincerely,



Prof. Christian Sergheraert
President of Lille 2 University



Prof. Philippe Amouyel
Director of UMR 744 Inserm-Lille2-IPL