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

Section des Unités de recherche

AERES report on the research unit

Cancers et Préventions – EA 3936

From the

University of Caen Basse Normandie

INSERM

November 2010



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Le Président de l'AERES

Didier Houssin

Section des unités
de recherche

Le Directeur

Pierre Glorieux

November 2010



Research Unit

Name of the research unit: Cancers et Préventions - EA 3936

Requested label : UMR INSERM

N° in the case of renewal: ERI3

Name of the director: M Guy LAUNOY

Members of the review committee

Committee chairman

M Florent DE VATHAIRE, University of Paris

Other committee members

Ms Hélène SANCHO-GARNIER, University of Montpellier, France

Mr Vincent J COGLIANO, IARC, Lyon, France

M Francis GUILLEMIN, University of Nancy, France

M Max PARKIN, Cancer Research UK, London, United Kingdom

M Paul LANDAIS, University Paris Descartes, France, (CNU)

Observers

AERES scientific advisor

M Jean ROSENBAUM

University, School and Research Organization representatives

Mrs Marie-Josèphe LEROY-ZAMIA, INSERM representative

Mrs Josette TRAVERS, University President

Mr Pierre DENISE, Vice-President, Scientific Council

Mr Jean-Louis GERARD, Dean of the Medical School

Mr Pierre FORMSTECHE, Director of Canceropole Nord-Ouest

Mr Alain LAMY, Directeur Adjoint chargé de la Recherche CHU Caen

Mr Emmanuel DOIZY, représentant Khaled Meflah, Directeur CRLCC F. Baclesse

Mr Xavier DROUET, Délégué Régional à la Recherche et à la Technologie Basse- Normandie

Mrs Christine MAZINGUE, Déléguée Régionale INSERM, Lille.



Report

1 • Introduction

The evaluation visit had been very well prepared by the Unit. The visit took place on November 2nd 2010. All presentations were in French, with the slides in English. Both written documents and oral presentations were of high quality, complete and giving a detailed description of the scientific activities. A hand-out of the slides was given to the Committee. The committee was able to ask questions to technicians, assistants, students, post-doctorates and researchers in separate meetings, the interaction with the team being immediate and straightforward. The Committee also met various authorities responsible for local cancer prevention and control, research, and the university. The evaluation began at 9h00 and finished at 16h15.

The research Unit is located in Caen, and its members come from two cancer epidemiology research groups, as well as from the biostatistics department of the Regional Cancer Center (CRLCC François Baclesse) and of the University Hospital of Caen (CHU of Caen). The research unit includes also the research activity of 3 cancer registries: the general cancer registry of the Calvados department, the specialised cancer registry of digestive tumors of Calvados and the multicentric mesothelioma registry.

At the time of the visit the Unit was located in 2 places, in the CHU and the CRLCC.

The Unit works on various aspects of cancer epidemiology : cancer risk factors, cancer screening, quality of life, and social inequalities in cancer.

The head of the Unit is Mr Guy Launoy. He is assisted by a co-director.

- Staff members are the following (on the basis of the application file submitted to the AERES) :

| | Past | Future |
|--|------|--------|
| N1: Number of researchers with teaching duties (Form 2.1 of the application file) | 7 | 12 |
| N2: Number of full time researchers from research organizations (Form 2.3 of the application file) | 0 | 0 |
| N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file) | 4 | 4 |
| N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file) | 4 | 5 |
| N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file) | 15 | |
| N6: Number of Ph.D. students (Form 2.7 of the application file) | 4 | |
| N7: Number of staff members with a HDR or a similar grade | 5 | 8 |



2 • Overall appreciation on the research unit

- Summary

The unit has a strong track record and occupies a solid position in the field of epidemiology of cancer in France. Its activities are divided into 4 main topics.

Topic 1: Occupational and environment cancer risk factors. The activity is mainly focused on the management of a large scale cohort of farmers (AGRICAN), which includes about 180,000 French farmers and aims to study the effects of agricultural occupational exposures on the risk of cancers. A biological resource center on about 1,000 individuals is associated with this cohort, and it is planned to extend this group to about 6000 individuals in view to study some biomarkers of genotoxicity. Up to now, and due to the cohort experimental design, the scientific production in this research area is still quite limited. Another research area of the team is asbestos related cancers, in which the unit has historically a specific epidemiological experience and develops also some biological investigations, in relation with pathological modifications linked with abestosis and possibility of screening for lung cancer in the exposed population.

Topic 2: Cancer screening The unit investigates various aspects of lung, colon and prostate cancer screening. This research is mainly guided by local or national screening committee considerations; the approach is global and multidisciplinary and concerns both choice of screening techniques, and organizational and economical aspects. In particular, the team has conducted several prospective studies, including tens of thousands of individuals, and demonstrated that immunological fecal occult blood tests are superior to gaitac haemocult tests for colon cancer screening, by having a higher sensitivity without decreasing significantly the specificity. Lung cancer screening projects are related to automated cytological screening of asbestos-exposed workers. Prostate cancer screening investigations are used to study population behavioural aspects concerning participation to screening.

Topic 3: Living with cancer: quality of life. The projects of the Unit are mostly focused on prostate cancer and benefit from the experience of the clinicians in the Unit, who are involved in all of the projects. The projects are original in concept, of very high level, and will provide new information on this topic, in order to offer a better quality of life to the cancer survivors.

Topic 4: Studying social and geographical inequalities in the management care of cancer patients The Unit investigates social inequalities in several aspects of the care and management of cancer patients, in order to understand the mechanisms responsible for these inequalities and the possible answers. The investigations are supported by their interconnections with cancer registries, and aim to identify the mechanisms responsible for the emergence of social and territorial inequalities, as well as to elaborate a geographical index of social deprivation. A specific projet is to evaluate the relevance in France of "screening guide," similar to the "patient navigator" in United States, in order to reduce the social inequalities in access to cancer screening .

- Strengths and opportunities

The Unit has a portfolio of high level applied and interventional research in public health, and is one of the few in France having this profile. The good representation of biologists and clinicians in an epidemiological unit is one of the most important strengths, and the deep and effective involvement with the National Cancer Plan is another. The committee has noted the current dynamic in the increase in human resources, particularly in the number of PhD students, and of HDR. The capacity of the Unit to adapt to local opportunities as well as national priorities is also a manifest strength. Amongst the projects, the AGRICAN cohort is clearly of major international importance, and therefore of exceptional interest. Additionally, the excellent integration of the Unit with the local deliverers of health care, public health and biomedical research, as well as its strong support by the local partners, are considered as of value. Lastly, the strong involvement of the Unit head with the North-West Canceropole, as co-cordinator of the Axis "Cancers, Individuals and Society" is a very positive feature.



- Weaknesses and threats

The project presents two limitations.

1) There are no full time researchers from national research structures, and probably as a consequence, no post doctoral research staff. This is one of the major weaknesses of the present projects, and means to resolve this should be investigated as a priority.

2) The international visibility of the unit exists, but is still limited, and greater participation in international scientific meetings, notably for doctoral students, should be developed

- Recommendations

The Committee considers that AGRICAN is a major feature of the French epidemiological landscape, and strongly recommends the creation of an international scientific committee, in order to support the investigators in charge of the cohort. The Committee strongly recommends that support in the the long term is needed, so that the full benefits of this large scale project can be realised. The committee also recommends the establishment of a biological databank including all or most of the AGRICAN participants. A more specific suggestion from the committee is to investigate also biological risk factors for cancer, rather than only the chemical ones.

One of the most urgent point to correct is the lack of full time researchers and post-doctoral fellows. The Committee supports the creation of a Master of Epidemiology and Public Health, which is planned, as being one of the way to resolve this limitation.

The committee recommends that the research unit investigates different ways to increase its international visibility, which it considers to be insufficient

The consolidation in one unique geographical location of the Unit, which is now located in two different places, is planned. The Committee strongly endorses the importance of this issue, which needs to be addressed with minimal delay. This consolidation should help the integration in the Unit, comprising as it does researchers with different backgrounds and experience.

| | |
|---|-----|
| A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research | 10 |
| A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research | 3 |
| A3: Ratio of members who are active in research among staff members [(A1 + A2)/(N1 + N2)] | 83% |
| A4: Number of HDR granted during the past 4 years | 1 |
| A5: Number of PhD granted during the past 4 years | 2 |

3 • Specific comments

- Appreciation on the results

The scientific productivity of the researchers who participate in the proposed Unit is of excellent quality. A total of 205 articles have been published for the last 5 years, for a full time equivalent of 7.5 researchers, corresponding to an annual average of 5.4 articles per full time position, and an average of 3.4 articles per year and per researcher. 74 out of the 205 involved a lab member in first and/or senior position. More than 22% of the articles were in the top 10 according to the JCR classification. This includes articles in Gut, Int J Cancer, Br J Cancer. Of the researchers, 2 have an average Index Factor, corrected by the position, superior to 10 during a 5 years period, with, respectively 2 and 3 articles each year, really rather exceptional in epidemiology.



A total of 7 theses are on going, for 7 researchers holding an HDR, what can be considered acceptable, given the lack of full time researchers.

- **Appreciation on the impact, the attractiveness of the research unit and of the quality of its links with international, national and local partners**

The scientific activity of the Unit puts it at the top level, with an excellent scientific quality of research, an high applicability to the national and local framework, and with a potential for a strong impact on public health policy in France, and in particular on the National Cancer Plan. The international visibility is nevertheless insufficient at present, in part because of its focus on national public health issues. This will probably change in the coming years, when the follow-up of the AGRICAN cohort will be sufficient. Another reason to be optimistic is the fact that the Unit is well implicated in European and international research networks.

The capacity of the Unit to obtain funds is excellent, as it obtained several large grants from the National Cancer Institute (INCa). Funding is however mostly limited to the national level.

The findings of the Unit with respect to technological aspects of colon cancer screening directly inspired measure 16.3 of the Cancer National Plan, which aims to gradually extend the use of the immunological test for colorectal cancer screening to the entire country, replacing the gaiac hemocult test. The results of this research are of major importance and this unit is considered as one of the two best research teams working on colon screening in France. The fact that the international visibility of the Unit in this area is not very developed is considered by the Committee to be a consequence of focusing its activity on national public health issues.

- **Appreciation on the management and life of the research unit**

In general the management of the Unit by the director and co-director was considered to be of very good quality in all aspects of organisation and leadership. The Unit is well embedded in the medical faculty and in the university environment, and tightly supported by the university and the actors of the regional research.

Most of the PhD students have a background in science (a positive point), and some have co-directors of their theses. It has been noted by the Committee that the PhD students frequently share their questions and experience with others, rather than being isolated. However, none of the students has made a presentation at an international meeting, which is a clear weakness in their training, although they do participate in international consortia. PhD students are well integrated within the Unit, and they are aware of the major issues, including the origin of fundings.

Most of the researchers come from France, of whom about half from the area of Caen, from the medical and pharmacy faculties, where they have also teaching duties. Researchers participate in the definition of scientific policies of the Unit and in funding issues.

- **Appreciation on the scientific strategy and the project**

Topic 1. The AGRICAN cohort is of exceptional interest, as being one of the most important cohorts in France, and will be one of the most important resources worldwide for evaluating the risk associated with chemical and biological risk factors specific to agricultural activity. To evaluate the consequences of agricultural practices is of specific relevance to France, which is one of the most extensive users of pesticides internationally. The interest of this cohort goes well beyond oncology and concerns many other areas of medical and biomedical research. Additionally, this cohort is included in an international consortium; the Committee considered that this was an indicator of past, and a guarantee of future quality and efficacy. However, the Committee expressed regret that there is no international scientific committee in AGRICAN, and that the planned size of the subcohort for the biological bank seems to be only of about 6000 individuals. Concerning the second area of research within this theme, the Committee considers that, although the study on pleural plaques is quite innovative, the overall activity is still determined by local and historical constraints, and lacks international visibility.

Topic 2. Overall the investigations of the Unit on this theme were considered by the committee as translational research of a high level of quality, very relevant to, and integrated with present local French considerations, and the medical context, which interacts with them. The major public health problem represented by the wide spread of individual prostate cancer screening creating deleterious effects without clear benefit on mortality is also one of the important topic studied by this unit. The Unit has to be careful not to extend too much the number of different on going projects, in order to maintain a high capacity of innovation



Topic 3. The projected work in the area is of high quality. The major source of strength derives from the tight interaction between epidemiologists, clinicians and psychologists with good experience and a real knowledge of the problems faced by cancer survivors. Again, here the application to prostate cancer may be useful to decide above a public health decision on this problem. Despite the very high level and diversity of experience within the Unit, which guarantees quality of investigations and results, the Committee was concerned about a possible lack of coherence within the whole topic.

Topic 4. The projects are well structured and conducted. The committee had some concerns that the focus of the studies on geographical inequalities might not be sufficient to answer questions concerning the underlying mechanisms of inequality, and that more thought should be given to collection of data on more proximal variables, for more detailed studies.

| Intitulé UR / équipe | C1 | C2 | C3 | C4 | Note globale |
|----------------------------------|-----------|-----------|-----------|-----------|---------------------|
| CANCERS & PRÉVENTIONS | A+ | A | A+ | A+ | A+ |

C1 Qualité scientifique et production

C2 Rayonnement et attractivité, intégration dans l'environnement

C3 Gouvernance et vie du laboratoire

C4 Stratégie et projet scientifique



Statistiques de notes globales par domaines scientifiques (État au 06/05/2011)

Sciences du Vivant et Environnement

| Note globale | SVE1_LS1_LS2 | SVE1_LS3 | SVE1_LS4 | SVE1_LS5 | SVE1_LS6 | SVE1_LS7 | SVE2_LS3 * | SVE2_LS8 * | SVE2_LS9 * | Total |
|--------------|--------------|----------|-----------|-----------|-----------|-----------|------------|------------|------------|------------|
| A+ | 7 | 3 | 1 | 4 | 7 | 6 | | 2 | | 30 |
| A | 27 | 1 | 13 | 20 | 21 | 26 | 2 | 12 | 23 | 145 |
| B | 6 | 1 | 6 | 2 | 8 | 23 | 3 | 3 | 6 | 58 |
| C | 1 | | | | | 4 | | | | 5 |
| Non noté | 1 | | | | | | | | | 1 |
| Total | 42 | 5 | 20 | 26 | 36 | 59 | 5 | 17 | 29 | 239 |
| A+ | 16,7% | 60,0% | 5,0% | 15,4% | 19,4% | 10,2% | | 11,8% | | 12,6% |
| A | 64,3% | 20,0% | 65,0% | 76,9% | 58,3% | 44,1% | 40,0% | 70,6% | 79,3% | 60,7% |
| B | 14,3% | 20,0% | 30,0% | 7,7% | 22,2% | 39,0% | 60,0% | 17,6% | 20,7% | 24,3% |
| C | 2,4% | | | | | 6,8% | | | | 2,1% |
| Non noté | 2,4% | | | | | | | | | 0,4% |
| Total | 100,0% | 100,0% | 100,0% | 100,0% | 100,0% | 100,0% | 100,0% | 100,0% | 100,0% | 100,0% |

* les résultats SVE2 ne sont pas définitifs au 06/05/2011.

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

- **SVE1 Biologie, santé**
 - SVE1_LS1 Biologie moléculaire, Biologie structurale, Biochimie
 - SVE1_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes
 - SVE1_LS3 Biologie cellulaire, Biologie du développement animal
 - SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie
 - SVE1_LS5 Neurosciences
 - SVE1_LS6 Immunologie, Infectiologie
 - SVE1_LS7 Recherche clinique, Santé publique
- **SVE2 Ecologie, environnement**
 - SVE2_LS8 Evolution, Ecologie, Biologie de l'environnement
 - SVE2_LS9 Sciences et technologies du vivant, Biotechnologie
 - SVE2_LS3 Biologie cellulaire, Biologie du développement végétal

Monsieur le Directeur
Section des Unités de Recherche AERES

Caen, le 28 février 2011

V/Réf. : Evaluation - S2UR120001220 - Cancers & Préventions - 0141408E

I - Unit location

The review committee "strongly endorses the importance of a one unique geographical location of the Unit, which is now located in two different places". The all local partners (University, Hospital, Cancer care centre) of the Unit are fully aware that this point is essential. The unique location for the Unit is for the University the first priority in its present thought on the restructuring of its cancer research units.

II - Limitations, weakness and threats

The review committee has identified two limitations: lack of full time researcher from national research structures and the weakness of the international visibility.

1- Lack of full-time researcher:

The Unit fully agrees that the lack of full-time researcher represents the main threat for the development of the unit project. The Unit had identified on its own this point as a major weakness in its proposal report. The Unit aims at developing its scientific projects, especially topics with national and international originality and excellence, as well as its activities in national and international networks in each of Unit topic (see below) to enhance its international visibility, its competitiveness and attractiveness with young researchers and post doctoral students. The "excellent integration of the Unit with local delivers of health care, public health and biomedical research, as well as its strong support by the local partners" as mentioned by the AERES committee will facilitate the reception and the integration of full-time researchers in coming years. Moreover, the Unit is involved in the creation of a Master in "Epidemiology and Clinical Research", which is considered by the AERES committee as a way to resolve the lack of PhD students and post-doctoral researchers. As a matter of fact, the coming integration of full-time researchers is strongly linked with the presence of high-level post-doctoral researchers in the Unit.

2- Weakness of the international visibility

The Unit did not valorize its international activities as it should in its presentation even though they exist in each topic. The all activities listed below were not well-mentioned in the Unit proposal report.

Topic 1 : Occupational and environmental risk factors

The investigators of the AGRICAN cohort constituted an international Scientific Council with 8 members (2 US Americans, 1 German and 5 French) which met for the first time at IARC in Lyon the 21st of October 2010 just after the last meeting of the International Consortium of Agricultural Cohorts (AGRICOH). The members are L Beane Freeman, one of the 4 Principal Investigators of the Agricultural Health Study conducted by the US NCI and NIH, A Blair, Emerit Scientist in the NCI and previous Head of the Department of Occupational and Environmental Epidemiology of the NCI, F Clavel-Chapelon as one the two principal investigators of the E3N cohort, J Godet as a genetician, S Hercberg as a specialist on nutrition and one of the principal investigator of the nutrient program, N Le Moal as a specialist in the respiratory diseases, K Straif on behalf of the IARC, Head of the Monographies program and P Vasseur as a specialist on epigenetic and environment.

A part of research on mesothelioma is organized around the activity of the international centre of excellence for mesothelioma diagnosis (MESOPATH, IM@EC) which develops an international collegial examination for histopathologic diagnosis supported by the American Pathologists Society. This international network is constituted of 17 French pathologists and 20 pathologists from United Kingdom, Belgium, Austria, USA, Canada and Japan. Several workshops have been held last years, latest in Hiroshima on November 2010 and in San Antonio on February 2011.

Topic 2 : Cancer screening

The AERES Committee considers that researches in this topic were mainly guided by national screening committee considerations. Actually, the national screening committee is concerned by immunochemical faecal occult blood test since the Unit have established the superiority of these tests comparing with guaiac test. The evidences established by our studies have not only a national repercussion with the spreading of immunochemical test on the whole national territory but also international influence. American Societies promoting colonoscopy rather than fecal occult blood test, our results have a limited influence in USA. On contrary, our results have a significant influence in Europe. In November 2008, we were invited with S Halloran (Londres, NHS) by the Slovenian government (J M Zakotnik, health ministry) to plan the national screening program which is conducted since that time with the immunochemical test (Svit Programm). The director of the team, Pr G. Launoy, was asked to be co-author in the new EU Guidelines on Colorectal Cancer Screening and Diagnosis which has been just published (press conference of the European commission on 3th February 2011). In collaboration with S Halloran (Londres) and M Zappa (Florence), he was in charge of the chapter on "Faecal Occult Blood Testing".

Topic 3 : Living with cancer

The project "impact of cancer and treatment on cognitive functions", one of the main projects of the "Cancéropole Nord Ouest", is coordinated by the Unit since 2008 at an international level with the International Task Force on cognition and cancer: The ICCTF (International Cancer Cognition Task Force) with J Vardy (Sydney), S Schagen (Amsterdam), J Wefel (Houston), and T Ahles (New York) as steering committee members and P Ganz (Los Angeles), J Tannock (Toronto), J Holland (New York), C Meyers (Houston) and F Van Dam (Amsterdam) as advisory board. Involved in this task force, our team participated to the last international Workshops (Venice, Amsterdam, New York) and is in charge of the organization of the next one, planned for March 2012 in Paris. Our team also participated to the international guideline for trials on cognitions in Oncology (in press).

Topic 4 : Social inequalities in care management and survival

The project ISSUE (Social Inequalities in Health in European Union), supported by INCa, aims at investigating the difference in impact and mechanism of social inequalities on survival for patients with cancer in different European countries. It is based on a close collaboration with English and Italian colleagues expert in geographical, demographical and epidemiological aspects of this topic : M. Coleman and B Rachet from London School of Hygiene & Tropical Medicine, D Gordon from Townsend Centre for International Poverty, D Foreman from Northern and Yorkshire Cancer Registries Information System, R Haynes, and A Jones from the School of environmental Sciences of University of East Anglia, and M Vercelli and R Lillini from Genoa University. Two international workshops were held in Caen on January 2009 and June 2010 with respectively 18 and 55 participants. A third international workshop on this topic will be organised at Caen on June 2011 where the Unit is in charge of the 36th meeting of the European Cancer Registries (130 participants expected). The last two workshops are focused on the construction of a European Aggregate Index for deprivation, a topic for which the team is involved in work package "information and data" of the European Joint Action : "European Partnership for Action Against Cancer (EPPAC)" since January 2011.

III - PhD Students Presentations

The AERES Committee mentioned that "none of the students has made a presentation at an international meeting". We think this remark is not justified since Unit Ph D students made 17 communications in international scientific meetings since 2008 such as those of World College of Gastroenterology (WCOG Londres 2009), European Society for Medical Oncology (ESMO Barcelone 2009, Milan 2010), United States and Canadian Academy of Pathology (USCAP Washington 2010) and American Society of Clinical Oncology (ASCO San Fransisco 2011).

La Présidente de l'Université
de Caen Basse-Normandie



Josette TRAVERT