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Carcinogenèse épithéliale : Facteurs prédictifs et pronostiques

Rapport Hcéres

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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

Epithelial Carcinogenesis: Predictive and prognostic
factors

From the

Université de Franche-Comté

March 2011



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Le Président de l'AERES

Didier Houssin

Section des unités
de recherche

Le Directeur

Pierre Glorieux

March 2011



Research Unit

Name of the research unit: Epithelial Carcinogenesis: Predictive and prognostic factors

Requested label: EA

N° in the case of renewal: 3181

Name of the director: Mrs Christiane MOUGIN

Members of the review committee

Committee chairman:

M. Juergen SIEPMANN, Université de Lille 2, Lille

Other committee members:

M. Thomas BRUNNER, Universität Konstanz, Konstanz, Germany

M. Laurent DUBUQUOY, Université de Lille 2, Lille

M. Pierre LEHN, Université de Bretagne Occidentale, Brest

M. Michael OTT, Medizinische Hochschule Hannover, Hannover, Germany

M. Michel PLOTKINE, Université de Paris Descartes, Paris, CNU representative

M. Stéphane ROCCHI, Université de Nice Sophia Antipolis, Nice

Observers

AERES scientific advisor:

M. David DOMBROWICZ

University, School and Research Organization representatives:

M. Jacques BAHY, Université de Franche-Comté



Report

1 • Introduction

- **Date and execution of the visit:**

The visit took place on 2nd March 2011 and included presentations of the director of the research unit as well as of some of her collaborators. The presentations were followed by discussions with the review committee. In addition, separate discussions were held with the review committee members and the following three groups of personal: (i) PhD students and postdoctoral fellows, (ii) engineers, technicians and administrative assistants, and (iii) researchers with permanent position, all in the absence of the director of the research group. Furthermore, posters were presented and allowed for an exchange between the review committee members and team members. The review committee also met the vice-president for research of the University of Franche-Comté as well as other representatives of the Faculty of Medicine and Pharmacy, University and University hospital.

- **History and geographical localization of the research unit, and brief presentation of its field and scientific activities**

The EA 3181, entitled "Epithelial Carcinogenesis: Predictive and prognostic factors" was created in 1996. It is located at the Faculty of Medicine and Pharmacy at the University of Franche-Comté in Besançon. The research group works on the fundamental and clinical aspects of cancer treatment. In particular, the team focuses on the following two types of cancerogenesis: (1) human papillomavirus (HPV)-associated cancerogenesis, with the following sub-topics: understanding the role of anti-TNF (anti- Tumor necrosis factor) in resistance to apoptosis, understanding the mechanism of horizontal transfer of viral oncogenes, expression of HPV genes and their regulation by epigenetic mechanisms, (2) urothelial carcinogenesis, with the following sub-topics: identification of molecular markers, understanding the role of PPAR (Peroxisome Proliferator-Activated Receptor) in regulating the expression of these markers, understanding the mechanisms by which PPARgamma ligands act.

- **Management team:**

The management team is limited to the director of the group.



- **Staff members**

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	11	11
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)	6	6
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3	3
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.8 of the application file)	8	
N7: Number of staff members with a HDR or a similar grade	13	13

2 • Overall appreciation on the research unit

- **Summary**

The clinical research of the group is very strong, with a considerable number of publications in journals with very high impact factors. The entire team covers the whole range from fundamental to clinical research and is well managed. The director of the group is an opinion leader in the field of human papillomavirus (HPV)-associated cancer, several other members are also very well visible at the international level. The group considerably contributes to European organizations, such as the EORTC (European Organisation for Research and Treatment of Cancer) and is actively involved in the organization of national and international scientific meetings. The impact of the research is very significant with respect to the clinical treatment of cancer and addresses a field of great interest for the public health. The quality/originality of the fundamental research of group should be improved in the future, including more risk-driven, cutting edge projects. The publication activity of this relatively small group in the field of clinical research is remarkable. This includes articles in general journals with very high impact factors. The group actively collaborates with the University hospital and industrial/academic partners on the local, national and international level.

- **Strengths and opportunities**

- The research unit covers the whole range from fundamental research to clinical research. Thus, it allows the transfer of new findings in more basic biological/medical science into practical applications for the patient.
- The director of the research group manages this highly interdisciplinary team very efficiently.
- The clinical research of the group is very strong.
- The director of the research unit is recognized as an opinion leader in the field of human papillomavirus (HPV)-associated cancer. Also other team members have clear international visibility.
- The group actively contributes to European organizations, such as the EORTC (European Organisation for Research and Treatment of Cancer) and intensively interacts with national regulatory authorities, such as the "Institut National de Prévention et d'éducation pour la Santé" (INPS).



- The team very actively publishes in peer-reviewed, international journals, including very high Impact Factor (IF) journals. 184 peer-reviewed articles in international journals in the field of cancer, 16 in journals with impact factors higher than 10: 3 in the New England Journal of Medicine (IF = 50, one first authorship), 1 in Lancet (IF 28), 7 in the Journal of Clinical Oncology (IF 17), 4 in Lancet Oncology (IF 13) and 1 in the American Journal of Human Genetics (IF 10).
- The group intensively interacts with industrial partners, allowing for the transfer of new findings in more fundamental biological/medical sciences into practical applications.
- The group intensively works together with the University hospital.
- The team works on a highly relevant research topic, an important health issue of great public interest.
- The group has a strong epidemiological research activity and is involved in major European studies, including EURO CARE (EUROpean CAncer REgistry-based study on survival and CARE of cancer patients).
- The team actively and fruitfully collaborates on the local, national and international level.
- The scientific animation of the research group is well established and effective.

- **Weaknesses and threats**

- The fundamental research is - compared to the clinical research - less developed, being mainly oriented to translational research.
- The animal models used are not always optimal for the given purposes.
- The supervision of the PhD students can be improved/intensified.
- Caution should be paid with respect to the retirement of several leading researchers in the team. Highly active and well recognized researchers, publishing in journals with very high impact factors will leave the group in the next few years. Their successors should be very carefully selected (the maintenance of the permanent positions in the group was confirmed by the Vice-president of the University of Franche-Comté).

- **Recommendations**

- To install an external advisory board, which could for instance once a year evaluate the progress of the team and give recommendations for the future.
- To improve the quality of the basic/fundamental research of the group, ideally up to the high level of the current clinical research. For example, more relevant animal models could be developed and the primary material available from the University hospital could be more intensively used. Furthermore, special tools might be developed in collaboration with the clinical and epidemiological researchers, e.g. using innovative biomarkers. It would be good to develop more risk-driven basic/fundamental research projects.
- To further increase the number of articles published in very high impact factor journals, eventually by decreasing the total number of articles (increased quality, decreased quantity).
- To better inform the young scientists in the group about their future carrier options.



- **Production results**

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	11
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	0
A3: Ratio of members who are active in research among staff members $[(A1 + A2)/(N1 + N2)]$	1
A4: Number of HDR granted during the past 4 years	3
A5: Number of PhD granted during the past 4 years	7

3 • Specific comments

- **Appreciation on the results**

- The research - in particular the clinical research - is of very high quality and has considerable impact in the field. It is a highly relevant research topic with great interest for the public health: cancer, in particular human papillomavirus (HPV)-associated cancer. This work allowed evaluating quality of life of the patients and identifying: (i) risk factors taking into account socio-economic and demographic determinants, (ii) factors predicting treatment response and (iii) new therapeutic strategies (phase II-III trials).

- The team very actively publishes in peer-reviewed, international journals, including very high Impact Factor (IF) journals. Between 2006 and the proposal submission date in 2010, the group published 184 peer-reviewed articles in international journals in the field of cancer, with only 6.5 "Full time researcher equivalents". Sixteen of them were published in journals with impact factors higher than 10: 3 in the New England Journal of Medicine (IF = 50, one first authorship), 1 in Lancet (IF 28), 7 in the Journal of Clinical Oncology (IF 17), 4 in Lancet Oncology (IF 13) and 1 in the American Journal of Human Genetics (IF 10).

- The contribution of several team members to international organizations, such as the European Organisation for Research and Treatment of Cancer (EORTC) is highly remarkable. For example, one team member is responsible for studies on cancer of the digestive system at the EORTC, serving on consensus conferences and coordinating several national and international clinical trials leading to recommendations. Furthermore, the team contributes to the EUROcare (EUROpean CANcer REgistry-based study on survival and CARE of cancer patients) work group. The latter is a cancer epidemiology research project on survival of European cancer patients.

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

The director of the research unit is an opinion leader in the field of HPV-associated cancer. Also other team members are very well visible on the national and international level. A considerable number of young scientists (master/PhD students/post-doctoral fellows) is trained in the group. For instance, 7 PhD degrees and 3 "Habilitation" degrees ("HDR") were obtained by team members since 2007 until the proposal submission in 2010. Some among the young scientists come from abroad, however, the majority is recruited locally. The team successfully applies for external, competitive funding. For instance, projects are funded by the "National Ligue contre le Cancer" (French organization supporting cancer research).



The group successfully collaborates with other research teams on a local, national and international level. This includes also collaborations with industrial partners, including big pharmaceutical companies. These are either “real” collaborations, or “research services”, which help funding the group’s general research activities and allow for the transfer of new knowledge obtained in more fundamental sciences into practical applications. The group works fruitfully with international partners, in long term stable relations, for instance with the “Deutsche Krebsforschungszentrum” (German center for cancer research). Furthermore, the team successfully contributes to international clusters, such as the IARC (International Agency for Cancer Research) CLARA cancer competitive cluster. The group is actively involved in the organization of national and international scientific meetings. For example, they organized the 4th International Meeting of the Cutaneous HPV Consortium “HPV & Skin Cancer” in 2007 in Besançon. Team members intensively serve as experts for various institutions, including InVS (Health Monitoring Institute), HAS (French Health Authorities), AFSSET (French Agency for Health Safety for the Environment and for Work), INCa (French National Cancer Institute), Cancéropôle IDF, Cancéropôle GO, (Cancer competitive cluster for Paris and for the west of France), Ligue contre le Cancer (League Against Cancer). The group actively and regularly participates at national and international scientific meetings in their field. Covering the range from fundamental to clinical research, the group facilitates the transfer of new findings in more basic sciences into practical applications.

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

The group is very well managed by its director. A particular challenge is the broad range of backgrounds and activities of the group members (including teaching duties and services provided at the hospital). The scientific animation is very well established and intense. Regular meetings allow for an efficient exchange between the group members. The guidance of the PhD students can be improved: the supervision can partially be intensified and future career options should be more clearly explained. Yet, there is no external advisory board, which could give advice on future directions and strategies. The encouragement of cutting edge projects in the more fundamental sciences could be intensified. Several team members are actively involved in the local “Federative Research Structure”, and significantly contribute to the interactions of the local research players, in particular the University hospital.

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

The research project is solid and feasible. The quality of the clinical research is very high. This includes for example therapeutic trials of phases 2/3, epidemiological research on the evaluation of diagnostic and therapeutic management, quality of care and quality of life, the implementation and coordination of the “Quality of life and cancer” platform of the CGE (competitive cluster for cancer in the east of France), approved and funded by the “Ligue Nationale Contre le Cancer” (“National Ligue Against Cancer) as a clinical research platform as well as the coordination of institutional clinical studies (e.g. by the EORTC -European Organisation for Research and Treatment of Cancer). However, the fundamental research is not very risk-driven and its originality could be improved for instance by the development of innovative and more relevant animal models as well as the more intense use of primary material from the University hospital. The group could more benefit from the fact that they have direct access to such primary material, which could render this part of their research activity more innovative and allow them to perform work at the “cutting edge” of the current state of the art. Most of the allocated resources are bound to specific projects. The recurrent, basic funding is relatively limited and appropriately distributed within the group.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
CARCINOGENÈSE EPITHÉLIALE : FACTEURS PRÉDICTIFS ET PRONOSTIQUES	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