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Progression tumorale et microenvironnement. Approches translationnelles et épidémiologie

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

Research Units Department

AERES report on unit:

Tumour progression and microenvironment

Translational approaches and epidemiology

Under the supervision of the following
institutions and research bodies:

University of Strasbourg



January 2012



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

Section des Unités de recherche

Le Président de l'AERES

Didier Houssin

Section des Unités
de recherche

Le Directeur

Pierre Glaudes

Unit

| | |
|-------------------------------------|--|
| Name of unit: | Tumour progression and microenvironment. Translational approaches and epidemiology |
| Acronym of unit: | |
| Label requested: | University team - Equipe d'accueil |
| Present no.: | EA 3430 and a group of EA4438 |
| Name of Director (2009-2012): | Mr Georges NOËL (EA 3430) and Mr Bertrand LUDES (EA 4438) |
| Name of project leader (2013-2017): | Ms Dominique GUENOT |

Members of the committee of experts

| | |
|----------|--|
| Chair: | Mr Gilles FAVRE, Toulouse |
| Experts: | Ms Palma ROCCHI, Marseille |
| | Mr Carlo CATAPANO, Bellinzona, Switzerland |
| | Mr Frédéric JAISSE, Paris |
| | Ms Sylvie CHEVRET, Paris |

Representatives present during the visit

Scientific Delegate representing AERES:

Mr Jean ROSENBAUM

Representative(s) of the unit's supervising institutions and bodies:

Mr Eric WESTHOF - Université de Strasbourg



Report

1 • Introduction

Date and conduct of visit:

The visit took place on the 13th of January at the school of medicine. Dominique Guénot presented during 45 minutes the past activities of the previous teams and the project of the new team. The co-director of the team presented some clinical aspects emphasising on the future creation of the Institut Régional du cancer in Strasbourg. Then a discussion was held with the participation of all the team members. Thereafter the panel split and met separately students and post-docs, technicians, and scientists in the absence of the team leader.

History and geographical location of the unit, and overall description of its field and activities:

The project corresponds to the fusion of 2 university teams, EA 4438 (D Guénot) and EA 3430 and 2 small teams attached to the school of medicine, in the field of haematology and of biostatistics. The objective of the project is to gather the strengths in oncological translational research in a unique team. This new team will benefit of the molecular oncology platform labelled by INCa, which participates to the project and of clinical facilities of the CHU and Paul Strauss Comprehensive Cancer Centre. This demand of creation is part of and complementary to the ambitious project to set up in Strasbourg the "Institut Régional du Cancer d'Alsace", which will group in a new building in 2017 the oncological activities of Paul Strauss Centre and the CHU with research teams located in its vicinity.

Today, the teams are localized in different sites in Strasbourg; the Paul Strauss Cancer Center and the University Hospital. The biological part of the future team will aggregate on a single location at the hospital in 2013 and the biostatistics and epidemiologic part will rejoin the hospital site in 2015.

The team develops cancer research projects from basic to translational and clinical research including epidemiology. The research programs rely on biological resources and molecular oncology platform, bringing observations to basic research. The central theme of the team is the understanding of the role of hypoxia and the microenvironment in tumor progression and the response to treatment.

Management team:

The team is directed by Dominique Guénot, a Scientist at the CNRS and co-directed by Georges Noel, a radiotherapist at Paul Strauss Cancer Centre.



Unit workforce:

| Workforce | Number on 06/30/2011 | Number on 01/01/2013 | 2013-2017 Number of producers** |
|--|----------------------|----------------------|---------------------------------|
| N1: Professors or assistant professors | 10 | 10 | 10 |
| N2: EPST or EPIC researchers | 2 | 1 | 1 |
| N3: Other professors and researchers | 4 | 4 | 4 |
| N4: Engineers, technicians and administrative staff *on a permanent position | 5 | 5 | |
| N5: Engineers, technicians and administrative staff * on a non-permanent position | 2 | | |
| N6: Postdoctoral students having spent at least 12 months in the unit | 1 | | |
| N7: Doctoral students | 5 | | |
| N8: PhD defended | 5 | | |
| N9: Number of Habilitations to Direct Research (HDR) defended | 3 | | |
| N10: People habilitated to direct research or similar | 9 | 9 | |
| TOTAL N1 to N7 | 29 | 20 | 15 |

* If different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

<http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation>.



2 • Assessment of the unit

Overall opinion on the unit:

The project of creation of this new team is to gather 2 university teams that have developed common strategies in translational cancer research reinforced by 2 teams from the medical school in the domain of hematology, epidemiology and biostatistics. They brought relevant contributions in at least 3 fields; biomarker discovery for many cancers, discovery of determinants of the response to radiotherapy, and clinical trials. Each of these units has produced good quality work, has a high level of productivity overall, although not outstanding in terms of high impact publications and not sufficiently visible for providing an international recognition. They rely on the molecular oncology platform labelled by the INCa that provides access to biological samples and molecular technologies. The ambition is to create a reference research team in translational cancer research in the perspective of the creation of the Regional Institute of Cancer in Alsace, allowing the concentration of human, technical and financial resources. This is a great objective and it should be continued. They propose a scientific project, which considers the past project from each team, focusing on a relevant common theme on the role of hypoxia and microenvironment in tumor progression and response to therapy. However, it seems that the reflection was not conducted until the end because there are still too many projects for the team to be competitive at the international level. Moreover, the involvement of the biostatistics and epidemiology teams should be clarified, and possibly more directly related to the particular focus of this new research team. It seems necessary to focus on fewer projects to allow the development of more competitive programs in which basic research should be reinforced.

Strengths and opportunities:

They have a long experience in translational cancer research leading to contributions to the discovery of new biomarkers. They develop clinical research funded by grants obtained from competitive call for proposal (PHRC). It has been established effective and productive collaborations between the research groups, the molecular oncology laboratory including the Centre for Biological resources, the technological platforms and the clinics. This is facilitated by the participation of MD and PharmD to the team. They have a strong involvement in students teaching, medical training in research and academic promotions of their collaborators.

The main opportunity is the future creation of the "Institut Régional du Cancer d'Alsace" permitting to build a trans-institutional ambitious project in translational research. Integration of biostatisticians could be an added value to the team through a better definition of their implication in the project.

Weaknesses and risks:

The number of post-docs and full time researchers involved in basic project is too low. The location on 2 different sites is not favorable for building this new team.

The dispersion is a major risk for the competitiveness of the team by lack of resources allocated to projects, and it could ultimately impair the success in national calls, which are important providers for funding.

Recommendations:

Choose the most competitive projects and allocate to them adequate resources. This implies to continue the reflection on the building of an ambitious project for the team.

Prioritize the recruitment of post-docs to support experimental research programs and implement a strategy to attract or recruit permanent researchers in the next 5 years.

The regroupment on the same site of the different partners of the team should be realized in 2013 as mentioned.



3 • Detailed assessments

Assessment of scientific quality and production:

For the past activity, the group of Mr GUENOT (EA4438) has been focused on “molecular markers of tumor progression and sensitivity to anticancer drugs”. This group performed its research in epithelial cancer cells by conducting fundamental and pre-clinical approaches, which have led to a better understanding of some mechanisms of carcinogenesis in several models of cancer such as colon, lung adenocarcinoma in never smokers, pediatric brain and osteosarcomas.

The group from EA3430 has developed a research program on genetic alterations of cancer and modulation to the response to radiation therapy. They mainly focused their activities in metastatic progression, molecular basis of the response of cancer cells to radiation therapy, and its pharmacological modulation using both head and neck squamous cell carcinoma (HNSCC) and hepatocellular carcinoma models. They did make optimal use of availability of well documented tumor samples and do have translational relevance.

The other groups from the school of medicine, notably the epidemiologists, presented also a good record of publications, although weak in biostatistics.

The groups have produced good quality work. They have a high level of productivity overall, although not outstanding in terms of high impact publications. They published 132 publications in international journals and the average impact factor is 4.9. Overall, the impact factors of the publications are quite modest and could be improved. The number of publications with a present or past team member in a relevant position as first or last author is 43. The most important publications of the team are published in Int. J. Cancer, Clin Cancer Res, J. Proteome Res and Breast Cancer Res Treat. Only 3 biostatistical publications were found including one in Statistics in Medicine, which ranks 8th in the field.

Assessment of the unit's integration into its environment:

Economic valorisation does not seem to be the priority of the team and some efforts should be made on that direction, although they are concerned about the translation of their results into the clinic. Links to clinical activities is positive and particularly relevant for access to clinical samples and possibility to run clinical trials.

The team is really efficient to raise funds due the high number of clinicians involved in the team (1500 K€ coming from clinical PHRC projects (34%), private (18%) and INCA (39%). However, the financial support coming from the basic research part does not seem to be consequent, which raises the question of the team competitiveness in that regards.

Assessment of the research unit's reputation and drawing power:

There are no prizes and distinctions reported for the team regarding its significant contribution in the scientific national and international community. The recognition seems to be limited to the Grand Est Canceropôle mainly for their two platforms “xenograft for pre clinical studies” and “quality of life and cancer”.

Mostly local, regional and national collaborations are mentioned. There is none or minimal emphasis on international collaborations, despite the fact that these research topics are widely studied.

The capacity of the team to recruit researchers, post-docs and high-level students, in particular from abroad has not been mentioned by the team and does not seem to be easy.

The clinicians seem to have good national network as it is demonstrated by their PHRC and INCa's network projects. The recognition of the team in the international community is weak as it is reflected by the low number of collaborations and invitations with the international laboratories and institution. There is no mention to participation to international programs, visiting fellows or exchange programs. This also applies to the methodological setting of phase I clinical trials, with no scheduled collaboration elsewhere.

There is no visible national or international impact. This could be improved.



Assessment of the unit's governance and life:

The future director of the team has been able to set up discussions to propose a project regrouping 4 groups coming from different institutions with their own research themes and this must be noted. She is well accepted and recognized as the leader by the other members of the team. Moreover, they establish an organization that allows scientific communication and educational activities.

However, discussions should continue to select the most competitive projects and to prioritize those ones for the next 2 years.

Assessment of the strategy and 5-year project:

For the next 5 years, the team proposes to work on projects related to hypoxia and microenvironment in tumour progression and response to treatment. These projects are grouped into three main axes related to tumor adaptation to hypoxia (axis 1), hypoxia and microenvironment in tumour dissemination (axis 2) and hypoxia and chemotherapy/radiotherapy resistance: preclinical models (axis 3).

The project is fully relevant and of importance in the field. The access to clinical samples and the molecular biology platforms are clear added values.

The topics are articulated in a series of 12 sub-projects, certainly too many. Some projects are better defined than others, with clearly defined objectives and experimental plans. However, others are barely sketched and do not provide the essential information needed to understand what is specifically proposed to be done. A major criticism for some of them is the lack of originality and innovative approaches. While the relevance of the various projects sounds very good and well structured, the adequacy between manpower and real time implication for the clinicians to develop their research is questionable.

Assessment of the unit's involvement in training:

The involvement of the unit members in educational activities is pretty good due to the high number of professors (5) or MCU-PH (5). Student recruitment (PhD) is good (7 in 4 years) for the size of the team, no track of post-doc training.

They also seem to be quite well involved in regional animation as demonstrated by Canceropole Grand-Est certifications.



4 • Grading

Once the visits for the 2011-2012 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).

This score (A+, A, B, C) concerned each of the four criteria defined by the AERES and was given along with an overall assessment.

With respect to this score, the research unit concerned by this report (and, when necessary, its in-house teams) received the overall assessment and the following grades:

❖ Overall assessment of the unit :

Tumour progression and microenvironment. Translational approaches and epidemiology

Unité dont la production, le rayonnement et le projet sont bons, mais pourraient être améliorés. L'organisation et l'animation sont très bonnes.

Grading table:

| C1 | C2 | C3 | C4 |
|------------------------------------|---|---------------------------------|----------------------------------|
| Scientific quality and production. | Reputation and drawing power, integration into the environment. | Laboratory life and governance. | Strategy and scientific project. |
| B | B | A | B |



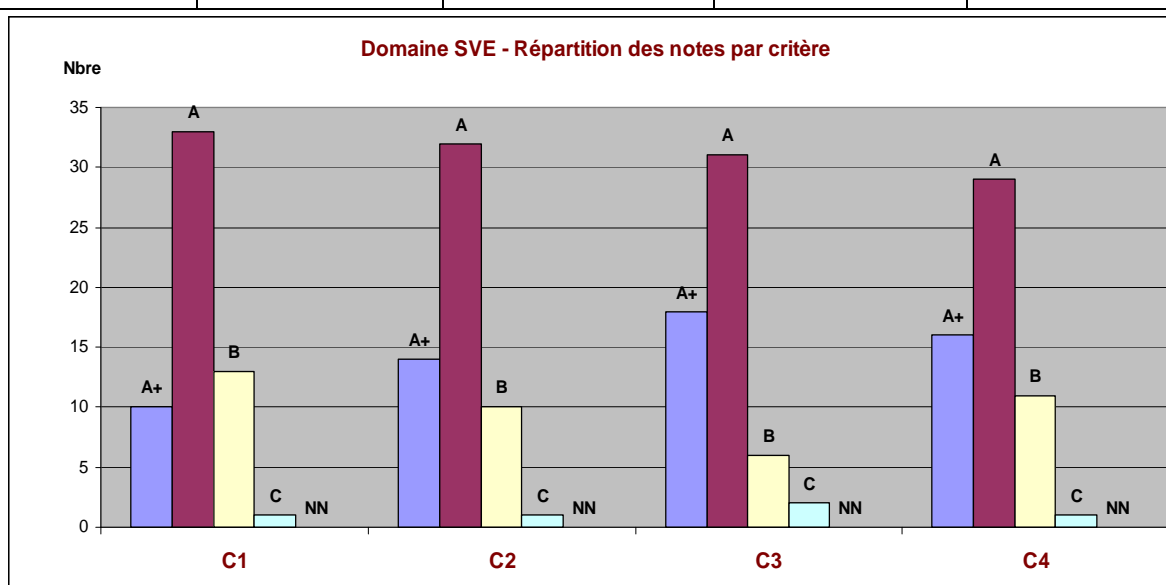
5 • Statistics per field : SVE au 10/05/2012

Notes

| Critères | C2 | C2 | C3 | C4 |
|----------|------------------------------------|---|---------------------------------|----------------------------------|
| | Scientific quality and production. | Reputation and drawing power, integration into the environment. | Laboratory life and governance. | Strategy and scientific project. |
| A+ | 10 | 14 | 18 | 16 |
| A | 33 | 32 | 31 | 29 |
| B | 13 | 10 | 6 | 11 |
| C | 1 | 1 | 2 | 1 |
| Non noté | - | - | - | - |

Pourcentages

| Critères | C1 | C2 | C3 | C4 |
|----------|------------------------------------|---|---------------------------------|----------------------------------|
| | Scientific quality and production. | Reputation and drawing power, integration into the environment. | Laboratory life and governance. | Strategy and scientific project. |
| A+ | 18% | 25% | 32% | 28% |
| A | 58% | 56% | 54% | 51% |
| B | 23% | 18% | 11% | 19% |
| C | 2% | 2% | 4% | 2% |
| Non noté | - | - | - | - |





6 • Supervising bodies' general comments

Monsieur Pierre GLORIEUX
Directeur de la Section des Unités de recherche
Agence d'évaluation de la recherche et de
l'enseignement supérieur (AERES)
20 rue Vivienne
75002 PARIS

Alain BERETZ
Président

Strasbourg, le 7 mars 2012

Objet : Rapport d'évaluation du projet de l'unité de recherche « Progression tumorale » (réf. S2PUR130004590-RT)
Réf. : AB/EW/N° 2012-102

Affaire suivie par
Eric WESTHOF
Vice-président Recherche
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Direction de la recherche

Cher collègue,

Je vous remercie pour l'évaluation du projet de l'unité de recherche « Progression tumorale » porté par Madame Dominique Guenot.

Vous trouverez ci-joint les réponses du porteur de projet concernant les erreurs factuelles et les remarques et appréciations du comité d'experts.

Je n'ai pas de remarque particulière à ajouter au nom de l'Université.

Je vous prie d'agréer, Cher Collègue, l'expression de mes sentiments distingués.



Alain BERETZ

P.J. :

- Une première partie corrigeant les erreurs factuelles
- Une seconde partie comprenant les observations de portée générale

EA 4438 de l'UdS
Physiopathologie et Recherche Translationnelle
Groupe « Marqueurs moléculaires de progression
tumorale et de sensibilité aux drogues anticancéreuses »
Bâtiment Inserm U682
3 avenue Molière
67200 Strasbourg

Response to the 2012 AERES report

Tumour progression and microenvironment Translational approaches and epidemiology – D. Guenot

Overall, we agree with the general comments of the AERES report but we have few points that we would like to discuss:

1- We feel that the committee expected a scientific report of the unified activity of our four teams, with aims consistent with each other. We would like to stress out that the project we submitted presents the strategic research axes as we envision them in the next five coming years. It must be precised that up to now, these four teams had little worked together and it is only recently that common projects have been built on.

2- Page 6: *“The team is really efficient to raise funds due the high number of clinicians involved in the team (1500 K€ coming from clinical PHRC projects (34%), private (18%) and INCA (39%). However, the financial support coming from the basic research part does not seem to be consequent, which raises the question of the team competitiveness in that regards.”*

We clearly emphasized that our projects – past and coming – are essentially translational projects rather than basic research and justified the fact that we were funded by the INCa but also by the Ligue Contre le cancer. We consider that our strength relies on the models that we developed to ensure a high quality translational research. However, we take the opportunity of several collaborations with teams of high quality for basic research, in Strasbourg, as with the IGBMC for instance.

3- Page 6 : *« Overall, the impact factors of the publications are quite modest and could be improved”.*

All publications consisted of 132 articles in international journals with peer-review. Consequently, it is not easy to publish as many articles in journals of high impact. On the other hand, there is in this list of publications, some relating to biostatistics and epidemiology. In these subjects, the journals concerned do not have high impact factors.

Madame Dominique GUENOT