ERTICa - Equipe de recherche sur les traitements individualisés des cancers

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Equipe de Recherche sur les traitements individualisés du cancer

From the

Université d'Auvergne

February 2011

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From the

Université d'Auvergne

Le Président de l'AERES

Didier Houssin

Section des unités de recherche

Le Directeur

Pierre Glorieux

February 2011

Research Unit

Name of the research unit: Equipe de recherche sur les traitements individualisés des cancers (ERTICA)

Requested label : EA

N° in the case of renewal

Name of the director : Ms Frédérique PENAULT-LLORCA

Members of the review committee

Committee chairman

Mr Pierre BROUSSET, University of Toulouse, France, au titre du CNU

Other committee members

Mr Jos JONKERS, The Netherlands Cancer Institute, Amsterdam, NL

Mr Jacques BONNETERRE, CLCC Oscar Lambret, University of Lille, Lille France

Mr Thierry PETIT, CLCC Paul Strauss, University of Strasbourg, Strasbourg, France

Ms. Emmanuelle GENIN, Inserm U946, University of Paris Diderot, Paris, France

Observers

AERES scientific advisor

Mr Paul HOFMAN, University of Nice Sophia

University, School and Research Organization representatives

Mr. Philippe DULBECCO, Université d'Auvergne

Mr Patrice DETEIX, Université d'Auvergne

Mr Alain ESCHALIER, Université d'Auvergne

Mr SALAGNAC, CHU de Clermont-Ferrand

Mr Jacques DAUPLAT, directeur du Centre Jean Perrin

Report

1 • Introduction

- Date and execution of the visit :

The visit was organized on 9 February 2011.

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

The different teams listed below worked independently in different places (CHU, Cancer Center Hospital, University of Auvergne. The ERTICa's team is the merge of scientists coming from four different existing UMRs (UMR990 INSERM and (LMGE) - UMR CNRS 6023) or EAs (EA3846 UdA and 4233 UdA). ERTICa is composed of researchers from several backgrounds: cytogeneticists, oncogeneticists, cellular and molecular biologists, biochemists, pathologists, and clinicians. The starting point is cancer, a primary concern in the university's effort (Université d'Auvergne) to develop a strong cancer research axis. They focused on breast cancer, the most frequent cancer in female and the major disease treated in the Centre Jean Perrin, a comprehensive cancer center. They have chosen to focus particularly on triple negative breast cancer (TNBC) which represents an unmet medical need, a cancer frequently linked to BRCA gene alteration, with genetic instability.

- Management team:

The Head of the research unit is Ms. Fréderique PENAULT-LLORCA. M. Jean-Yves BIGNON, M. Andrei TCHIRKOV and JM Jean-Marc NABHOLTZ are in charge of the Exploratory axis of TNBC patients and tumors, the axis on the cellular biology preclinical models study of BRCA1 fucntions, and the axis on Clinical Research, respectively.

- Staff members

N1: Number of researchers with teaching duties (Form 2.1 of the application file)	13
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	16
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	23
N6: Number of Ph.D. students (Form 2.7 of the application file)	8
N7: Number of staff members with a HDR or a similar grade	11

2 • Overall appreciation on the research unit

- Summary

The ERTICa research unit is overall well structured, offering an opportunity to create a good synergy between existing local groups. The general direction of the project (early BC in particular BRCA-related) is highly competitive at national and international levels. It would be very risky to develop it without a very strong component of national and international collaboration. Frédérique PENAULT-LLORCA is an international opinion leader in breast pathology. JM NABHOLTZ is an international leader in drug development. The clinical network for collecting tumors in Clermont-Ferrand area seems well established. There is a great need to find new biomarkers that predict clinical response to treatment of BC. All tools for developing the project seem to be present (except for in vivo animal models). There is a strong support from the institution (University, Hospital, Cancer Center). The weakest part of this project is the level of the basic science which is not sufficiently competitive at national and international levels. The low level of the publications (impact factor and citation indexes) is a major weakness of a project in competitive fields such as DNA repair, genetics instability and high throughput sequencing. There are not enough strong working hypotheses and the presented hypotheses either lack novelty or are not competitive with regard to available expertise and publication records of the teams. In summary, there is a too diffuse spectrum of research hypotheses and projects with no real interaction between the different research subgroups. The general recommendation is to focus the project on biomarkers and drug development. This should be done by attracting new people (including students) with expertise and strong track records in DNA repair area.

- Strengths and opportunities

There is a great need to find new biomarkers (very competitive field). All tools for developing the project seem to be present (except for in vivo animal models). The clinical network for collecting tumors in Clermont-Ferrand and around area is well established. This initiative is strongly supported by the host institutions (University, Hospital, Cancer Center). Frédérique PENAULT-LLORCA is a national and international opinion leader in breast pathology. JM NABHOLTZ was the leader of a world-wide clinical investigator group and can be very active to recruit patients; even if there are many patients receiving neoadjuvant chemotherapy in Clermont-Ferrand, the number will not be enough to carry out an internationaly recognised scientific program; his connections with the pharmaceutical industry will be very useful to have innovative new drugs that will be studied in the neoadjuvant model (biomarkers evaluated before treatment at the time of biopsy and after treatment at the time of surgery). It will be important for the funding of research too.

- Weaknesses and threats

The quality of the basic science is not sufficiently competitive at the national and international level. The average level of the manuscripts in terms of impact factor and citation indexes is low. This is a major weakness of the project suggesting that the different groups are not able to address the several issues on DNA repair, genetics instability and high throughput sequencing. The working hypotheses lack strength and novelty. There is a too diffuse spectrum of research hypotheses and projects. There are no real links between the different subgroups. It looks as if this group wants to study everything in the field of genetic instability beginning with triple negative breast cancer. The biobank is a cornestone of the activity and should be reinforced. Stronger national and international collaborations are required in this highly competitive field. The number of students is too low to achieve the different goals.

- Recommendations

Focus on biomarkers and drug development. Attract new people with strong expertise and track records in the DNA repair area. It is mandatory to focus on some projects in which the group is well recognised, the translational and clinical research. The applicants have to position the project in a background of external collaborations. Regular joint meetings for students are necessary. More students need to be recruited.

- Production results

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	13
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	2
A5: Number of PhD granted during the past 4 years	16

3 • Specific comments

- ## Appreciation on the results

The relevance and the originality of the research, the quality and the impact of the result: Strong track report of two unit members. This program is risky because of national and international competition. There is a great need to find new biomarkers that predict clinical response to treatments of BC.

The quality and the number of the publications, scientific communications, thesis and other outputs: Average level for basic science. Many collaborative studies but no real landmark papers in the field in high impact factor journals. The papers in JCO by the project leader are either collaborative (national cohorts) or outside the scope of this project (gastric cancers).

The quality and the stability of partnerships: Important partnerships with pharmaceutical companies are apparently ongoing.

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

The head of the unit is frequently invited in international meetings concerning clinical trials. JMN has also a very good track record in this field.

The ability to recruit high levels scientists, post-docs and students, and more particularly from abroad: No specific information was provided. This could be a weakness of the project.

The ability to raise funds, to successfully apply for competitive funding, and to participate to scientific and industrial clusters: The translational research is quite good and attracts fundings from pharmaceutical companies (FPL, JMN) but this not the case for the basic science (INCa, ANR, ARC, Ligue..)

The participation to international or national scientific networks, existence of stable collaborations with foreign partners: No precise information. The head of the unit is an expert in the field of breast cancer pathology.

The concrete results of the research activity and socio-economic partnerships: A couple of patents was filed.

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

The contribution of the research unit staff members to teaching and to the structuration of the research at the local level: The students have no dedicated joint meetings

- ## Appreciation on the scientific strategy and the project

The existence, relevance and feasability of a long term (4 years) scientific project: Risky. No strong background in basic research, too low number of students.

The originality and existence of cutting edge projects: Yes for the biomarkers. Not for the basic research

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
ERTICA: EQUIPE DE RECHERCHE SUR LES TRAITEMENTS INDIVIDUALISÉS DES CANCERS	**B**	**B**	**Non noté**	**B**	**B**

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**

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Clermont-Ferrand, le 8 juillet 2011

Le Président

et

Le Vice-président du Conseil Scientifique

à

Monsieur Pierre Glorieux
Directeur de la section des unités de recherche
AERES
20 rue Vivienne
75002 Paris

OBJET : Rapport d'évaluation S2UR120001925 – ERTICa: Equipe de Recherche sur les Traitements Individualisés des Cancers – 0631262E

Direction de la Recherche

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N/réf. :DR-IR/AL/2011 N°216

Monsieur le Directeur,

Je vous prie de bien vouloir trouver ci-joint les observations de portée générale concernant le rapport d'évaluation de l'unité « ERTICa » dirigée par le Professeur Frédérique Penault-Llorca, envoyé le 4 mai 2011, observations que j'approuve bien évidemment.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de mes sentiments les plus cordiaux.

Professeur Philippe Dulbecco
Président de l'Université d'Auvergne

Professeur Alain Eschalier
Vice-président du Conseil Scientifique

UNIVERSITÉ D'AUVERGNE
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Reply to the AERES report concerning the project of creation of a research unit ERTICa (Equipe de Recherche sur les Traitements Individualisés du Cancer)

We thank the committee for their remarks and recommendations. We want to take this opportunity to address some points raised by the committee.

1. Introduction : No remark on the introduction
2. Overall appreciation of the research unit

• Summary

The ERTICa research unit is overall well structured, ……. It would be very risky to develop it without a very strong component of national and international collaboration.
We are aware that the area of triple negative breast cancer is highly competitive and it would be very risky to develop it without a very strong component of national and international collaboration.
Frédérique Penault-Llorca and Jean-Marc Nabholtz have developed a network of national and international collaborations providing the access to large cohorts of patients and discussions and exchanges around biomarkers. Yves-Jean Bignon also participates in a strong national network of oncogenetics departments. For basic research, we have already identified in the CLARA (our canceropole) a network of possible collaborations. Other collaborations (national and international) will also be examined.
"The weakest part of this project is the level of the basic science which is not sufficiently competitive at national and international levels"

We are creating a new research team and decided to work in the field of triple negative breast cancer for different reasons:
– The topic: the unmet medical need and the emergence of new therapeutic options such as DNA repair and EGFR targeting,
– A unifying topic: the triple negative breast cancer option was also the link between different skills of the merging teams, apart from clinical research and biomarkers: BRCA environment for the oncogenetic group, genetic instability (through telomere axis) and chromosomes interactions for the cytogenetic group, cellular biology, MDR phenotype (for which PARP inhibitors and EGFR targeted therapies have not yet been explored), and cell line models with controlled BRCA function.
– Gathering skills: to perform theses studies, different technological tools are already available through the different teams merging in this new research unit: *in vitro* models, high-throughput sequencing, array CGH, methylome and transcriptome facilities, as well as more classical tissue-based biomarkers studies.
– Access to relevant tumor samples: the most important thing is that our group will have access to patients in clinical trials (large ancillary studies have been planned and material already collected in the EGFR clinical trials). We also have a retrospective collection of tumours treated by neoadjuvant approach and of patients with familial history of breast cancer, which will be useful in developing our hypotheses.
– Our pioneering and strong role in clinical research in EGFR targeting: our international advance in the field of EGFR targeting (two neo adjuvant clinical trials have been developed: one is now completed, the other has already recruited half of the patients) and our previous expertise in the EGFR biomarker field (from colorectal and lung cancer),

So yes, we agree, that today the current state of basic science in the field of DNA repair is the group's weaker link, and might be considered as poor or unsufficient. Nevertheless, some members of the team have established expertise in DNA repair and DNA repair genetics that was not fully valorized in the dossier because the references antedate the 2006-2010 window requested. For instance Nancy Uhrhammer is coming from Richard Gatti (UCLA, Calidfornia, USA) worldwide known for his works on ATM gene.
Furthermore, our originality is a strategy "from the bedside to the bench and back to the bedside". Our research will first be clinical research and not basic science. In this context, where all the necessary tools are available (according to the report), an axis of basic research could be developed and be competitive only in the second half of the quinquenal project, based on the first results from the translational studies.

Management and choice of axis to develop on the theme of "biomarkers " will pave the way for the establishment of competitive basic research especially in the field of repair DNA and EGFR targeting.

Strengths and opportunities

... ; even if there are many patients receiving neoadjuvant chemotherapy in Clermont-Ferrand, the number will not be enough to carry out an internationally recognised scientific program;
The advantage of the neo adjuvant approach is that it is an excellent human *in vivo* model for tumor response (sensitivity and resistance). The answers are quick (maximum 6 to 8 months of treatment), and evaluation of the data for ancillary studies doesn't need large patient cohorts. The clinical trials that we have planned all involve networks of health care centers, either national (such as Unicancer, including 20 French comprehensive cancer centers), or international to ensure rapid recruitment and completion of the study. We recently completed a neo adjuvant trial (75 patients) for TNBC involving 13 centers in just one year, showing our ability to create networks and to enrol patients quickly in neoadjuvant clinical trials.

- Weaknesses and threats

The quality of the basic science is not sufficiently competitive at the national and international level. The average level of the manuscripts in terms of impact factor and citation indexes is low.
It is important here to stress the point that the teams have worked in different backgrounds and on separate and very different subjects. The creation of the ERTICa team will potentiate our ability to improve our research projects and publication levels. We do not plan, in the first part of our research program, do develop basic science hypothesis apart from the cellular models, and some specific genes for which we have some knowledge (in somatic but also germinal samples of patients from the trial and few controls), the majority of the studies will be pure biomarker development programs.

Taking the cumulated H index of the groups merging for ERTICa it is not so low and poor overall.

Team	all years		2006-2010	
	number	H	number	H
Pathology	288	35	112	15
Cytogenetics*	189	25	57	9
Oncogenetics	270	34	57	7
Clinical Research	324	42	99	14

*In this area, some members worked previously on non cancer or xenobiotics, the highest journals ranks are at 3. Nevertheless, past four years, two patents with international extension have been filed in this group.
This is a major weakness of the project suggesting that the different groups are not able to address the several issues on DNA repair, genetics instability and high throughput sequencing. The working hypotheses lack strength and novelty.

High throughput sequencing « 454 Roche » platform got a recent national label IBISA in 2009 working for different other teams (mainly in Lyon) is not producing yet publications ; nevertheless two papers have been submitted in 2011, one on BRCA sequencing in breast and ovarian cancer, and the other one on deep sequencing of ovarian epithelial carcinomas, screening for therapeutic targets. This underlines our expertise with the recently acquired high throughput sequencer.

For N Uhrhammer, YJ Bignon and A Tchirkov, these additional selected references may be cited:
- Varon R, Gosse-Brun S, Bignon Y-J, Sperling K, Uhrhammer N. Nijmegen Breakage Syndrome gene (*NBS1*) is not the tumor suppressor gene at 8q21.3 involved in colorectal Carcinoma (CRC). *Oncol. Rep*. 9: 709-11, 2002.
- Uhrhammer N, Bay JO, Gosse-Brun S, Kwiatkowski F, Rio P, Daver A, Bignon YJ. Allelic imbalance at *NBS1* is frequent in both proximal and distal colorectal carcinoma. *Oncol. Rep.* 7: 427-31, 2000.
- Bay JO, Uhrhammer N, Stoppa-Lyonnet D, Hall J. Role of the *ATM* gene in genetic predisposition to cancer. *Bull. Cancer* 87: 29-34, 2000.
- Bay JO, Uhrhammer N, Pernin D, Presneau N, Tchirkov A, Vuillaume M, Laplace V, Grancho M, Verrelle P, Hall J, Bignon YJ. High incidence of cancer in a family segregating a mutation of the ATM gene: possible role of *ATM* heterozygosity in cancer. *Hum. Mut.,*14: 485-492, 1999.

- Pernin D, Bay J-O, Uhrhammer N, Grancho M, Bignon Y-J. Intermediate sensitivity of *ATM* heterozygote cells after streptonigrin and etoposide exposure. *Eu. J. Cancer* 35: 1130-1135, 1999.
- Uhrhammer N, Bay J-O, Grancho M, Gosse-Brun S, Pernin D, Rio P, Daver A, Bignon Y-J. Loss of heterozygosity (LOH) at the *ATM* locus in colorectal carcinomas. *Oncol. Rep.*, 6: 655-658, 1999.
- Uhrhammer N, Fritz E, Boyden L, Meyn MS. *ATM* antisense confers an A-T phenotype on normal fibroblasts. *Int. J. Mol. Med*., 4: 43-47, 1999.
- Bay J-O, Grancho M, Pernin D, Presneau N, Rio P, Tchirkov A, Uhrhammer N, Verrelle P, Gatti RA, Bignon Y-J. No evidence for heterozygous *ATM* mutation using protein truncation test in breast/gastric cancer families. *Int. J. Oncol*. 12: 1385-1390, 1998.

In addition to this published work, Ms Uhrhammer taught the eukaryotic DNA repair section of the "Genome Dynamics" module, part of the 2nd year courses for the Genetics and Physiology Masters program (University D'Auvergne aand Blaise Pascal)from 2004 to 2007, and will take up this course again for the upcoming 2012-2015 quadrennial.

Pr Tchirkov is involved in many networks on telomerase : at the national level with Dr J.L. Mergny, Laboratoire ARNA (ARN : Régulations naturelle et artificielle), INSERM U869, Institut Européen de Chimie Biologie, Université de Bordeaux, Pessac, France, Dr M.P. Teulade-Fichou. UMR176 « Conception, synthèse et vectorisation de biomolécules », Institut Curie, Laboratoire Raymond Latarjet, Orsay, Pr J.M. Lehn. Laboratoire de Chimie Supramoléculaire, Institut de Science et d'Ingénierie Supramoléculaires, CNRS UMR 7006 et Université de Strasbourg, Strasbourg and international level with Dr A. Petitjean. Department of Chemistry, Queen's University, Kingston, Canada and Dr. Chetan G K, National Institute of Mental Health and Neurosciences, Bangalore, India (French-Indian Medical Research Cooperation, INSERM-ICMR Program)

To facilitate experimentation concerning radio-biology, the "Pavirma" platform has recently been funded at the University Blaise Pascal, and is currently under construction. This platform will provide both an X-ray generator (before the end of 2011) and a neutron cannon (in 2012) for irradiation of cultures, materials, plants and small animals. Ms Uhrhammer and Pr Bignon have been involved with this project since its inception in 2007, and Mr Bidet joins them on the planning committee as the facility takes form. These ERTICa team members, and possibly others, will participate in the scientific committee overseeing the platform. Interactions with other committee members constitute a local network of DNA repair-related researchers (C. White, P. Vernet, S. Alziari...) and physicists (G. Montarou...). This developing platform was not previously mentioned.

There is a too diffuse spectrum of research hypotheses and projects. There are no real links between the different subgroups.

We will be able after gaining results from the clinical trials to focus our basic research on one or two basic research programs. We repeat that this is a new merger, and the links between the groups will deepen and broaden with time as we work together and share results and ideas.

It looks as if this group wants to study everything in the field of genetic instability beginning with triple negative breast cancer. The biobank is a cornestone of the activity and should be reinforced. Stronger national and international collaborations are required in this highly competitive field. The number of students is too low to achieve the different goals.

Our project does not "want(s) to study everything in the field of genetic instability beginning with triple negative breast cancer" ! First of all our research will be focused on the patients in clinical trials, and some controls (35 tumors from BRCA positive patients, and post chemotherapy patients without response to treatment, as one of the clinical trial planned is for non responders). Second, the clinical trials are either targeting EGFR or genetic instability (via some special design of chemotherapy and/or by adding PARP inhibitors).

- Recommendations

Focus on biomarkers and drug development.

We will clearly focus on drug development through biomarker studies and when necessary go to the bench to confirm some of the hypotheses. For the patients in clinical trials we will explore both germinal (focused on 30 genes) and somatic alterations, mainly concerning the EGFR pathway when relevant and DNA repair and telomere function. The results from aCGH will correlated with the germinal and biopathological alterations, aiming to find surrogate markers. For the other patients, they will be part of the IBCSG program and of other collaborative programs.

Attract new people with strong expertise and track records in the DNA repair area.
We are a new team, not even created, so recruiting senior scientists is for the future, when our program is established. It will not be possible to attract a senior scientist so early in our project.
It is mandatory to focus on some projects in which the group is well recognised, the translational and clinical research. The applicants have to position the project in a background of external collaborations. Regular joint meetings for students are necessary. More students need to be recruited.

Our students come principally from two masters programs: "Génétique et Physiologie" et "Cancérologie et Nutrition" But as of 2012, we will add our own source of students through the new Master "Biomedical technology and biomedical specialty" (M1 & M2).
As the new ERTICa team develops and becomes known, additional doctoral students and post-doctoral researchers will be recruited. Regular meetings among these junior scientists are planned as part of their training.

Production results

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	13
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	2
A5: Number of PhD granted during the past 4 years	16

We have granted 16 PhDs during the last four years, and currently have 10 PhDs and five post docs in training. This number is not so low for 13 researchers with teaching and heavy clinical duties, and in absence of permanent researchers without teaching duties.

3 Specific comments

Appreciation on the results

The relevance and the originality of the research, the quality and the impact of the result: Strong track report of two unit members. This program is risky because of national and international competition. There is a great need to find new biomarkers that predict clinical response to treatments of BC.
The quality and the number of the publications, scientific communications, thesis and other outputs : Average level for basic science. Many collaborative studies but no real landmark papers in the field in high impact factor journals. The papers in JCO by the project leader are either collaborative (national cohorts) or outside the scope of this project (gastric cancers).
The JCO papers are from large biomarkers studies or clinical trials conducted by the project leader, showing the experience in the field of breast cancer and also the networks. The other papers are not outside the field because the colorectal (JCO, Lancet Oncology, clinical cancer research), and lung studies are in the EGFR biomarker field, which is completely in the scope of the project. The gastric cancer papers are in fact international guidelines, showing the networks and the experience in biomarkers determination.

The quality and the stability of partnerships: Important partnerships with pharmaceutical companies are apparently ongoing.
They are ongoing.

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

The ability to recruit high levels scientists, post-docs and students, and more particularly from abroad: No specific information was provided. This could be a weakness of the project.

As part of the upcoming quadiennal plan, the University of Auvergne will open a new, two-year undifferentiated (Research and Professional) Master, entitled « Biomedical Technology », and including a Biomedical Diagnostics specialty. This specialty was developed by Mahchid Bamdad of the ERTICa team, and recruits biology students as well as interested medical doctors and pharmacists. Within this masters program, Frédérique Penault-Llorca, the director of ERTICa, is responsible for the M1 Anatomo-pathology module, and several team members will be involved in teaching. We will train medical students, in particular, oncologists, genetic counsellors and pathologists. For instance, for the pathologists, for 2 years we have one student per year, and we have already planned additional M2 students in 2011-2012 and in 2012-2013, on the TNBC subject and in collaboration with the Gustave Roussy Institute and the department of pathology in University of Sydney (Westmead hospital….).The principal laboratory on which the Biomedical Diagnostic module of this Master program depends is ERTICa, which facilitates the recruitment of doctoral students.

ERTICa members are also involved in teaching specific modules in other Master programs (notably Genetics and Physiology).
We have a long tradition in the formation of students from abroad, often in the form of short (< 6 months) stages, for both basic science students and medical specialists. For example, between 2006 and 2010, the Bignon group hosted 11 foreign students from seven countries, at levels from Master to post-doctoral/post-medical studies, with two Chinese students staying a full year.

The ability to raise funds, to successfully apply for competitive funding, and to participate to scientific and industrial clusters: The translational research is quite good and attracts fundings from pharmaceutical companies (FPL, JMN) but this not the case for the basic science (INCa, ANR, ARC, Ligue..)

Ability to raise funds for basic research

- programme européen Lifegrid 159 K € : Système d'Information pour l'étude de la genèse et du développement de la maladie cancéreuse
- FEDER Région (bourse innovation) 110 000€
- CNRS (demande de soutien au transfert CNRS) 30 000€
- FEDER région (programme opérationnel Compétitivité régionale et emploi) avec Clermont Communaté : Convention n° 31355-2008 « projet de coopération en recherche développement avec l'université médicale de Chine en dépistage et prévention des cancers » 373 800 € /2 ans
- reinforcement of the diagnosis laboratory from INCa in 2010 40 000K€
- Coopération INSERM- CNRST Franco-Marocain (Marrakech) Génétique moléculaire du cancer du sein au Sud du Maroc. Over 3 years (budget de mission 2000€ par an)
- FEDER région (programme opérationnel Compétitivité régionale et emploi) avec Clermont Communauté : Convention n° 31355-2008 bourse post-doctorale un an « oncogénétique » 36K €
- FEDER région (programme opérationnel Compétitivité régionale et emploi): Convention n° 32641-2009 système d'expertise en diagnostic et thérapeutique des cancers d'origine génétique » 247 611 €
- IBISA label : 101 695 €
- ANR (Adelbio project) for the center Jean PERRIN, 40K€ per year for 3 years
- Ligue contre le cancer for the different groups every year between 30 and 45K€
- PHRC 2008-2009: 210K€

The participation to international or national scientific networks, existence of stable collaborations with foreign partners: No precise information. The head of the unit is an expert in the field of breast cancer pathology.
We participate to the IBCSG program
The cytogenetic team is involved in the national network on array-CGH analysis (ACPA).
Already developed earlier for the rest of the activities with a focus on DNA repair

The concrete results of the research activity and socio-economic partnerships: A couple of patents were filed. Six international patents were filled

Appreciation on the management and life of the research unit

The contribution of the research unit staff members to teaching and to the structuration of the research at the local level: The students have no dedicated joint meetings

Since the start of our project, students from the different units have gotten to know each other (and also the different senior researchers) through the monthly journal club and a variety of research meetings such as the "Journée Scientifique Régionale de Cancérologie d'Auvergne". Additional regular meetings will be organized, and they will have a dedicated area at the university in the future team.

Appreciation of the scientific strategy and the project

The existence, relevance and feasability of a long term (4 years) scientific project: Risky. No strong background in basic research, too low number of students.
The competition is high, but our originality is the choice of the clinical research on drug development as the core of the project. It is a truly multidisciplinary team. The tools are in place, the skills are real, collaborative axes through the CLARA and the different clinical and pathological networks are in place. The project is focused only on the clinical trials and the biomarker research (early response, resistance etc…). Collaborations are in place also locally with the metabolic imagers and radiation therapists. The tumor bank is well organized, and adapted to our clinical trials in terms of authorizations, labelization and consents.

The originality and existence of cutting edge projects: Yes for the biomarkers. Not for the basic research
In the medium term, the basic research will be based on hypotheses derived from the clinical trial biomarker studies. We do not have the pretension to re-do studies performed at a larger scale and by large groups such as the IBCSG. Our strength is the access to the patients in our clinical trials.

Pr Frédérique Penault-Llorca, on behalf of the ERTICa group.