CRCT - Centre de recherches en cancérologie de Toulouse Nouveau projet UMRS

Rapport Hcéres

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

Section des unités de recherche

AERES report on the unit :

Centre de Recherches en Cancérologie de Toulouse

University :

University Toulouse 3

May 2010

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et de l'enseignement supérieur

Section des Unités de recherche

AERES report on the research unit

Centre de Recherches en Cancérologie de Toulouse

From the

University Toulouse 3

Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

May 2010

Unit

Name of the unit : Cancer Center of Toulouse

Requested label : UMR_S INSERM, UMR CNRS

No. in case of renewal :

Unit director : M. Jean-Jacques FOURNIE

Members of the expert committee

Chairperson:

Mrs Karin TARTE, Inserm U.917, Université Rennes 1, Rennes

Reviewers:

Mr Georges UZAN, Inserm U.972, Hôpital Paul Brousse, Villejuif (co-chairperson)

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Reviewer(s) nominated by the staff evaluation committees (CNU, CoNRS, CSS INSERM ...):

Mrs Cécile FAIRHEAD, CoNRS

Mr Pierre LAURENT-PUIG, CNU

Mrs Jane-Lise SAMUEL, INSERM

Representatives present during the visit

Scientific delegate representing AERES:

Mrs Marie-Annick BUENDIA

University and Hospital representatives :

Mr A. MILON, representative of University Toulouse 3

Mr J.J. ROMATET, representative of the Centre Hospitalo-Universitaire (CHU) of Toulouse

Mr C. CAZAUX, representative of the Toulouse Cancer Campus

Mr G. FAVRE, representative of the « Reseau Thematique de Recherche et de Soins » (RTRS)

Research organisation representatives :

Mrs Mireille BLANC, INSERM

Mrs Christine TUFFEREAU, Inserm

Mrs Catherine LABBÉ-JULLIÉ, Inserm

Mrs Urzula HIBNER, CNRS

Mr Y. SEGUI, CNRS

Report

1 • Introduction

- Date and conduct of the visit :

The review took place during two days (November, 19-20) at the INSERM unit U563. The future director presented the overall scientific project and the organization for the 4 next years, *i.e.* before the opening of the new CRCT building, as well as the perspectives for the future. The 15 team leaders presented thereafter their achievements and projects before a discussion with the visiting board. Unfortunately, due to time limitation, the first afternoon was organized in two sub-committees. At the end of the presentations, the committee could discuss with institutional representatives (INSERM, CNRS, University, Faculty of Medicine) and with representatives of the Toulouse Cancer Campus and the RTRS RITC. The committee was then splitted again for two parallel meetings with (1) Researchers; (2) PhD students/post-doctoral fellows. The technical staff could discuss separately with an ITA representative from Inserm. Finally, after discussion with the director, the committee had a short door-closed meeting. Overall, the evaluation was well prepared and organized and the execution of the visit went smoothly even if the general feeling was a lack of time for the final discussion.

- History and geographical location of the unit and brief description of its field of study and activities:

The CRCT is a new exciting project integrated in a vast campus dedicated to cancer research and care (Toulouse Cancer Campus) that will include a Comprehensive Cancer Care (Clinique Universitaire du Cancer, CUC), several pharma companies, an interdisciplinary research center dedicated to innovation in biology (ITAV), and probably the French Blood Bank (EFS). The CRCT building is planned for the end of 2012, with a total area of 8700m^2 including 5200m^2 for research teams and 2700m^2 for core facilities. The initial settling for current applicant teams has been designed to leave about half of the lab space for new external research groups that will be recruited according to the CRCT scientific priorities. The applicant teams are currently located on three main sites and belong to the INSERM U563 (CHU Purpan, 3 teams), the INSERM U858 (CHU Rangueil, 7 teams), or the Claudius Regaud Cancer Care Institut (3 teams) but two of them reside outside of these units, within the UMR CNRS 5089 (Team 1.1) and 5088 (Team 1.2).

Despite this important geographical scattering, it is obvious that efficient scientific and organizational discussions have been conducted for about 2 years, leading to a fully integrated proposal in which all the applicants are actively involved. Jean-Jacques Fournié has been elected by the funding team leaders as head of the CRCT project in March 2009. The goal of the CRCT is to unravel the processes underlying oncogenesis and host/tumor interface through a strong basic research, but also to develop high quality translational programs in order to delineate new markers predictive of the response/toxicity to treatment and to design and evaluate new anticancer drugs, through contracted partnerships with private companies. Accordingly, the initial structure of the CRCT comprises 4 scientific departments: 1) Genetic and cellular oncology; 2) Tumor Biology; 3) Hematology and Immunology; 4) Experimental Therapeutics.

- Management Team:

The CRCT director will be assisted by a direction board comprising 6 scientific vice-directors that have already been appointed and an administrative director to be named. The whole direction board will be renewed at a 4-year period. The CRCT direction board constitutes the CRCT Scientific Council that manages the CRCT scientific life including issues relative to the functioning of shared services. The CRCT has an external Scientific Advisory Board (SAB) composed of three to four persons named by the CRCT direction. This SAB meets once per 4-year period to evaluate the CRCT research activity and produces a report for the CRCT direction board.

- Staff: (according to the dossier submitted to AERES):

	In the report	In the project
N1: Number of professors and assistant professors (see Form 2.1 of the unit's dossier)	46	46
N2: Number of EPST, (Public scientific and technological institution) or EPIC, (Public industrial and commercial institution) researchers (see Form 2.3 of the unit's dossier)	30	31
N3: Number of other professors and researchers (see Form 2.2 and 2.4 of the unit's dossier)	32	32
N4: Number of engineers, technicians and tenured administrative staff members (see Form 2.5 of the unit's dossier)	23	23
N5: Number of engineers, technicians and non-tenured administrative staff members (see Form 2.6 of the unit's dossier)	7	8
N6: Number of doctoral students (see Form 2.8 of the unit's report dossier and 2.7 of the unit's project dossier)	51	51
N7: Number of persons accredited to supervise research and similar	54	55

2 • Assessment of the unit

- Overall opinion:

The CRCT project is a beautiful and fully integrated cancer-dedicated multidisciplinary project that covers all the scientific aspects from bench to bedside, is closely linked to major pharmaceutical companies and patient care, and is strongly involved in teaching in both faculty of science and medical schools.

The 10 state-of-the-art core facilities are essentially already existing and running, and they will be relocalized to the new buiding. They will be further developed with the help of the two foundations that are supporting the project. When opening, the new building will be interconnected to a new cancer care hospital and will integrate a campus completely devoted to cancer.

The CRCT project is clearly a unique opportunity to build a competitive cancer research pole in France, based on well-recognized research teams and with a good potential to attract some international scientific and clinical leaders in a coordinated manner.

- Strengths and opportunities:
  - The project results from the gathering of proactive teams that are strongly implicated in the initial definition and further developments of the whole project.
  - The research project shows a good coherence that could reinforce the visibility of Toulouse as a major cancer-devoted place in France and Europe.
  - The CRCT will be integrated within the Toulouse Cancer Campus. This convergence is a unique opportunity to create a highly attractive research pole, able to recruit international scientific leaders, to favour the attraction or the local development of biotechs and to initiate truly original clinical trials.
  - The future Cancer Center will have free space to attract new teams according to their scientific excellence and because they have developed recognized expertise in complementary and/or previously uncovered research fields.
  - The candidate director demonstrates a good leadership.

- High-quality translational research is based on strong interactions between clinicians and scientists.
- Unique sample collections are available for the teams.
- Leadership has been recognized in pancreatic cancer research, and there is a critical scientific mass in the field of angiogenesis with some original approaches including IRES and lymphangiogenesis.
- Very strong connections have been established with industrial partners leading to efficient valorisation of new tools, targets, and molecules.

- Weaknesses and threats:
  - The common building is far from opening and the CRCT will remain virtual until at least 2012.
  - The CRCT lacks eminent scientific leaders with outstanding publication record that could reinforce the visibility of the whole project.
  - The Scientific Advisory Board appears somewhat small and ideally, it should include essentially foreign experts and give more regularly strategic advices concerning for example the new teams that will integrate the CRCT.
  - Several important topics are not currently covered, in particular epigenetic, cancer stem cell biology, and tumor immunology. Concerning the last one, whereas many teams introduced "immune cells" or "immune response" in their presentations, the CRCT project is essentially devoid of tumor immunologists, except the team of the Director which is expert on □□T cells and NK cells.
  - Even if the University of Toulouse clearly supports the CRCT program, no fully defined budget, including technician positions or attractive PI positions (PU-PH), has been specifically assigned to date to this project.

- Recommendations for the unit director:
  - A strong basic research should be maintained (all projects should not necessary deal with translational aspects).
  - A clear policy to coordinate team expansion should be defined as soon as possible. These rules should ideally preserve free space for new external teams but should also allow the emergence of young promising local scientists.
  - The size of the teams has to be regularly adapted to the scientific projects and objectives.
  - The links between core facilities and research teams should be reinforced. Restructuration of the biobanking, in particular the gathering of the two current core facilities, should be carefully prepared and coordinated by the pathologists and, since these resources are limited, rules should be defined to avoid any competition for the same samples when the CRCT will further enlarge.
  - A great effort should be done to guarantee that the relationships between the CUC and the CRCT will be as close and easy as possible, at both scientific, medical, and organizational levels. Combined or coordinated recruitments of scientists and clinicians focusing on the same cancer type/reserach area would have obvious positive impact on the project.

- Data on work produced :

(see http://www.aeres-evaluation.fr/IMG/pdf/Criteres_Identification_Ensgts-Chercheurs.pdf)

A1: Number of *produisants* (professors and researchers whose names appear in a minimum number of "publications" over a 4-year period) listed in N1 and N2 in the project column	72
A2: Number of *produisants* among the other staff listed in N3, N4 and N5 in the project column	22
A3: Proportion of *produisants* in the unit [A1/(N1+N2)]	72/76
Number of theses for accreditation to supervise research defended	52
Number of theses defended	45
Any other data relevant for the field (please specify)	

3 • Detailed assessments

- Assessment of work produced and scientific quality :

Overall, the applicant teams have developed successful research over the past four years with a very good balance between basic and translational research as outlined by: several high rank publications (Embo J, Mol Cell Biol, Blood, J Exp Med, PNAS...), more than 10 patents/licenses, major studies on biomarkers and drug pharmacokinetic/pharmacogenetic, and original clinical trials including multicentric phase II/III trials. The connections between scientists and clinicians are obvious and efficient in the vast majority of the teams and the relationships with pharmaceutical companies have been strongly developed. A wide range of cancers are targeted, including in particular hematologic malignancies, with a potentially fruitful interaction between two well-recognized teams and a new one, and pancreatic/digestive cancers, a specific field in which the CRCT could be considered as an international leader. As already discussed, when considering all the teams, the publication track record is good to very good but not outstanding.

- Assessment of the influence, appeal and integration of the research unit in its environment :

Several team leaders have long lasting experience in their specific research fields, are fully recognized and are regularly invited as speaker or chairman in international conferences. They have established international collaborations with Germany, US, Japan, UK, Australia, and Spain.

The applicant teams successfully obtained numerous important national grants (INCa, ANR, Labellisation Ligue, ARC) as well as European grants and industrial contracts. One of the PI is the president of the RTRS-RITC and another co-PI is the vice-president of the Canceropole Toulouse Cancer Campus and the vice-president in charge of partnerships at the University of Toulouse 3. Overall, the financial feasibility of the different projects seems guaranteed.

- Assessment of the strategy, governance and life of the unit :

The CRCT director is elected by a vote of the CRCT assembly including the direction board, scientific council, and all group leaders. He/she presides the Scientific Council, takes decisions and represents the CRCT for a period of 4 years. The team leaders are responsible for organizing the life of their research groups and asking for financial support. Even if the CRCT director was designed only few months ago, its leadership is obvious, and no management problem could be detected by the committee.

The CRCT includes 51 professors/assistant professors that display teaching activities at both the faculty of Sciences or the two Medical Schools, and encompasses the president of the scientific committee of the Ecole Doctorale Biologie-Sante, one vice-president of Toulouse University 3, the Dean of the Purpan Medical School, and the president of the UFR Sciences de la Vie et de la Terre, thus ensuring strong relationships with the different authorities of Toulouse University.

- Project assessment :

See Team by team analysis.

4 • Team-by-team and/or project-by-project analysis

Name of the team : CDK Inhibitors in Tumor Suppression & Oncogenesis

Name of team leader : Mr Arnaud BESSON

- Team staff or staff allocated to the project (according to the dossier submitted to AERES):

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	1
N7: Number of staff members with a HDR or a similar grade	1	1

- Assessment of work produced and scientific quality:

This young team was created in 2007 under an ATIP-CNRS structure. The aim of the research is to define the molecular mechanisms involved in the potent oncogenic activity independent of Cyclin-CDK of CDK inhibitors of the Cip/Kip family, and then to determine their impact on tumorigenesis. The originality of the work comes from murine models generated by the PI during the ATIP-CNRS obtained in 2007 (p27 knock-in) and during his

PhD at the University of Calgary (p27 knock-out). This is a high rank quality project with expected high quality results and a wide spectrum of collaborative programs (some are already ongoing) with the other teams of the CRCT.

No scientific paper has been published since the PI post-doc that led to very good papers (Genes Dev 2006; Genes Dev 2007), several reviews and 2 licenses. High level papers are currently in preparation, derived from the mouse model work.

The team leader is well appreciated through the French institutional organisms (CNRS, University) and an ATIP plus has recently been obtained from the CNRS to support financially his team.

- Assessment of the influence, appeal and integration of the team or the project in its environment:

Two prizes were obtained during his thesis at the University of Calgary: Cooper Award and Government of Canada award (2001). Another prize was obtained during his post doctoral fellowship at the Howard Hughes Medical Institute (Seattle): Leukemia Lymphoma Society Special Fellow Award.

A technician and a post doctoral fellow joined the team in mid-2008.

In addition to the financial support by the ATIP-CNRS programme, the PI has obtained financial supports from associations (ARC) and grant applications to the ANR (program Genopath) and AICR are pending. The CNRS delegate has advised the committee of the attribution of an ATIP-plus support for two years. Since its creation the team has obtained more than 400K€ of grants.

An active collaboration with the Team 1.3 is ongoing and multiple partnerships with other members of the CRCT are envisioned.

- Assessment of the strategy, governance and life of the team or project:

The PI has the good expertise and strategy to conduct his project and is well supported by the CNRS and the Toulouse University 3. However, the team is very small with only one researcher, one post-doc, one PhD student, and one technician.

The team is part of the Ecole doctorale Biologie-Santé. No teaching activity is reported.

- Project assessment:

The long-term scientific project of the team contains 3 main axes: 1/ deciphering the molecular mechanisms by which p27 regulates Rho-B signalling and tumorigenesis, 2/ understanding the role of p27 in bronchio-alveolar stem cell regulation and 3/ studying cyclin-CDK independent functions of $p57^{Kip2}$. The force of these tasks comes from their originality and from the novelty of the tools generated by the team, in particular the very interesting mouse models (p27 knock-in and p27 knock-out). This aspect renders the project greatly feasible and promises publications with high impact factor.

The PI has a strong capacity to obtain financial supports (ATIP-CNRS, ATIP-plus, ARC).

- Conclusion:

  - Opinion:

This young team carries a real potential and has already made important progress in mouse models. Several papers are in preparation.

The team will serve the interest of a number of other teams from the CRCT and develops very good basic science.

  - Strengths and opportunities:
    - Due to these models and the expertise of the team in cell cycle study, a fruitful collaboration with the Team 1.3 has already emerged. The support from the other teams of the CRCT is strong.
    - The PI of this new and dynamic team has good leadership.
    - Fruitful links have been established with prestigious foreign laboratories.
    - The project is solid and original.
    - The team develops interesting tools and skills that could be very useful for several CRCT teams in a near future.

- Weaknesses and threats:
  - The geographic localisation of the team (currently in the laboratory of the CNRS LBCMCP, Toulouse) needs to be solved as soon as possible, even if the CRCT director and the CNRS representative have both comfort the committee concerning the possibility to house the team with its ATIP grant within one of the three main INSERM partners of the CRCT project.
  - This team should focus on its main projects in order to fill the gap in publications associated with its recent installation in Toulouse. The number of new projects/collaborations, even within the CRCT, should probably be restricted at least for the next few years, until this team has been strongly secured.
- Recommendations:

It is of importance for this team to have a geographic situation in close contact with the other CRCT partners, to recruit other technical staff members, and to obtain high financial supports. It could perhaps be considered that this team could join temporarily another team from the CRCT, possibly the Team 1.3. This would allow the team leader to have more time to focus on his project and to build a more stable structure.

Name of the team : DNA Replication & Genetic Stability in Cancers

Name of team leader : Mr Jean-Sébastien HOFFMAN

- Team staff or staff allocated to the project (according to the dossier submitted to AERES):

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	4
N7: Number of staff members with a HDR or a similar grade	2	3

- Assessment of work produced and scientific quality:

The group has an international reputation in the field of DNA polymerases and cancer. In particular, its contribution to demonstrate the role of Pol beta in cancer has been seminal in the field, and has been followed by many other groups. This team was the first demonstrating that increased levels of Pol beta or Pol kappa correlate with increased genetic instability, and accelerate tumorigenesis in nude mice. Using DNA-combing technology this group showed that a moderate overexpression of Pol beta or Pol kappa is sufficient to impede replication fork progression and to promote the activation of additional replication origins, proposing that this mechanism contributes to genomic instability and to cancer development.

They also showed that Pol kappa is required for the intra-S Checkpoint signalling, and that Pol eta is required for processing structured non-B DNA, and for the common fragile sites stability during unperturbed S-phase. More recent work demonstrated the *in vivo* role of human Pol lambda and Pol mu in NHEJ-mediated DSB repair. In a large-scale study participated by 25 research French groups, it was found that most of the TLS polymerases are down-regulated in colon and breast cancers, by comparing with normal tissues, with the exception of two of them, Pol beta and above all Pol theta, whose up-regulation emerged as a marker of poor prognosis and genetic instability in breast cancer.

The team has published 27 papers including **13 main publications** and 10 joint publications. The publications are of high quality with main papers in Mol Cell Biol (2009), Nucleic Acids Res (2006, 2007), Cancer Res (2005), and Oncogene (2007, 2009). One CNRS patent was recently launched (2009). The team trained 4 PhD students during the last 5 years.

- Assessment of the influence, appeal and integration of the team or the project in its environment:

The work is internationally recognized and appreciated, since the PI and co-leader are frequently invited to important international events (Gordon Conferences; Jacques Monod Conferences; International Environmental Mutagens Society Meeting). Moreover, the team contributed to the organization of important international meetings (Cell Cycle and Cancer; INSERM workshop; European Workshop of Molecular Cytogenetic in Human Solid Tumours; European Summer School of Medicine)

For the last 5 years, besides 3 PhD students (including the major from National Institute for Applied Sciences (INSA)), the team recruited foreigner Post-Docs (Norway; Brazil) and 1 outstanding foreign PhD student from Germany.

The team successfully obtained for the last 5 years important national grants (Labellisation program from the Ligue contre le cancer; INCa Libre 2007, projet libre ARC), the PI coordinated an INCA-DAAD (French-German collaboration) program and the co-PI headed the INCa ACI-GSO network "Genetic instability as a negative outcome in cancer" (25 groups, 2003-2007 and 2008-2011). Important collaborations were established with US, Japan, UK and Spain.

The PI and co-leader were experts during several years for National Research evaluation (INSERM/CSS6 and CNRS/S22), participated to AERES evaluation, and were members of scientific committees for "La Ligue Contre le Cancer". They also exert different responsibilities at the University of Toulouse (Vice-President for partnership; President of the Scientific Council of Life Science department). The co-leader contributed to several articles in national newspapers (Le Monde) and interviews for national TV and radios. He is vice-president of the Cancéropole Toulouse Cancer Campus and is setting up an institution dedicated to broadcast health sciences.

- Assessment of the strategy, governance and life of the team or project:

The recommendation would be to continue with the current governance and the scientific strategy for this internationally highly visible team. The implication of the team members in different aspects of the scientific project (technologies, grants, communication) was appreciated, as well as promising collaborations already set up with other groups at the CRCT.

The existing scientific coordination between the PI and co-leader will facilitate risk taking decisions.

The co-leader is highly involved in teaching and administrative activities. The PI organized an INSERM Workshop aiming to teach the use of the DNA Combing powerful technology. Finally, the PI is one of the 6 scientific vice-directors of the CRCT.

- Project assessment:

The project and the scientific strategy are ambitious and present excellent future potential. Feasibility at both medium- and long-term is guaranteed as genome instability projects are internationally well appreciated, and the one presented here must be considered highly original and relevant in both basic science and cancer translational research.

- Conclusion:

  - Opinion:

An excellent group pioneering the study of the impact of genetic instability associated to DNA replication and DNA repair in cancer development. The team has been successfully working for many years and is consolidated, constituting one of the reference groups in this area of expertise, both at national and international levels. The project is very original, with a marked translational research potential. This group will contribute to the necessary basic research core of the CRCT project.

  - Strengths and opportunities:
    - International visibility is remarkable in the field of specialized DNA polymerases.
    - The scientific project is ambitious and original with high viability and feasibility.
    - Methodological strategies such as cutting-edge DNA combing technology are innovative.
    - A recently filed patent is potentially important.
    - Expected benefit will come from the scientific environment of the CRCT research groups, especially the expertise of Team 1.3 for the signalling pathways and Team 1.1 for the cell cycle mediators.

  - Weaknesses and threats:

There is lack of a MD pathologist within the team, to improve the quality and the efficiency of the translational approaches, and the interaction with clinical researchers.

  - Recommendations:

The committee recommends recruiting a new scientist to reinforce the team and developing the study of the biochemistry aspects related to the mechanisms of the new functions of specialized DNA polymerases.

Name of the team : GTPases in Tumor Progression

Name of team leader : Mr Gilles FAVRE

- Team staff or staff allocated to the project (according to the dossier submitted to AERES):

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	6	4
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	5	4
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	4	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	6	4
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	5	5
N7: Number of staff members with a HDR or a similar grade	8	5

- Assessment of work produced and scientific quality:

The former team has obtained an international recognition mainly due to its work on deciphering the molecular pathways by which several anticancer agents affect cell proliferation and induce apoptosis in many cancers. Moreover, during the past four years, the unit has brought significant contributions to the role of Rho-GTPases in cancer initiation and progression in different cancer models, mainly lung and melanoma but also breast cancer. While the roles of Rho-A and -C are studied by a number of laboratories over the world, that of Rho-B is much less studied and the novelty of the team's work was to show that it negatively controls tumorigenesis, plays a critical role in UV-induced cell death in skin cancers, breast cancers, and glioblastomas. The data argue for a role of Rho-B as a tumor suppressor gene and a regulator of EGFR signalling. Moreover, Rho-B is a multifaceted gene regulating the expression of MHCI in melanoma cells. Thus Rho-B has emerged as a potential target in cancer therapy. Together with other laboratory data obtained with farnesyl transferase inhibitors (FTI), these findings lead to clinical trials associating FTI with radiation and/or antiestrogens in glioblastomas and breast cancer.

The total number of publications is 70 including **28 in house publications** and 17 joint publications. The publication track record is good, in particular with papers in Cancer Research (2006, 2009, 2009), Cell Death and Diff (2005), FASEB (2005), and J Biol Chem (2005, 2008). One should note the very high rank publications of the members that joined the team (25 papers including Nat Biotech, Nat Methods, Cell Death Diff, EMBO Rep), which is a sign of judicious recruitments.

One new INSERM patent and two licenses to Millegen have been launched. A newly recruited member is also involved in a license transferred to Algenex. 9 PhD theses were defended since 2002.

The team exhibits very strong capacity to obtain support from private companies (Sanofi-Aventis, P. Fabre, PhD fellowships, financial supports), from Foundations (Innabiosanté, RTRS-RITC), from associations (ARC, Ligue Nationale contre le Cancer) and from institutional agencies (ANR, INCA).

- Assessment of the influence, appeal and integration of the team or the project in its environment:

The participants in the project have organised international meetings and one newly recruited researcher obtained the Outstanding Innovation 2007 Technology transfer Award for GFP Research Tool (Los Alamos, USA). The team leader coordinates a network in melanoma research and is the scientific director of the Claudius Regaud Institute. He heads the Foundation of Scientific Cooperation which supports the Toulouse Cancer Research and Therapeutic Network (RTRS-RITC). He has been invited to 2 international congresses during the last 2 years.

In 2008, a CR1 INSERM issued from the NCI was recruited, and a MCU (Toulouse Univ) from EMBL was also recruited the same year. In September 2009, a CR2 INSERM with high level publications (Nature Biotech., Nature Methods) joined the team. Three team members were upgraded to full professorship. Actually, 2 post-doc are on the team listing. These recruitments constitute a strong added value to the project in term of feasibility. It proves the existence and the effects of an efficient recruitment policy, widely externally opened.

In addition to institutional grants from INSERM, external financings are obtained from the most prestigious national agencies, ANR, Cancéropole du Grand Sud-Ouest, INCA, ARC, Ligue Nationale contre le Cancer, foundations.

Major collaborations have been undertaken with several international teams, for example, one team at MOFFITT Cancer Center Tampa and another at Lankenau, Wynnewood in the field of farnesyltransferase inhibitors and Rho proteins, leading to co-authorship publications; and a team at Garvan Institute, Sydney (Australia), giving rise to several good papers describing the potential therapeutic activity of FTIs. A recent collaboration was initiated with a laboratory in Dundee on the relationships between RhoB and p53. Recruitment of the new researchers will give the opportunity to collaborate with different teams at Los Alamos, au NCI et à l'EMBL, Heidelberg.

Several clinical trials are ongoing (association of FTI to radiotherapy in phase I-II trials, design of a multicentric phase III trial funded by a PHRC). Another multicentric phase II clinical study (tamoxifen plus FTI) in metastatic breast cancer is in progress. The recorded benefit (55%) combined with identification of a potential therapeutic biomarker lead to study opportunity of a new patent. These activities highlight the efficient implication of the team in translational research.

- Assessment of the strategy, governance and life of the team or project:

The working strategy is well organised around three main tasks (Rho-B in tumor progression, molecular determinants of melanoma progression, and translational research) to which are dedicated different senior participants from which emerges a leader. Strong interactivity of each participant to one sub-task with the other members of other sub-tasks is obvious from the oral presentation of the PI. Moreover, strong interactions with the other members of the CRCT (Team 1.1 on the p27 RhoB interaction, Team 2.1 on the role of microenvironment on melanoma progression, Team 3.3 on Rho and NKG2D ligands and Team 1.2 on genetic instability and melanoma) have been developed. Local collaborations are ongoing mainly with two senior scientists at INSERM U 563. A recent collaboration was established with LAAS CNRS on biomarker discovery with nanobiotechnology and mathematic methods. Lastly, the team collaborates with companies such as CEPHEID (morphological studies and research on the involvement of microRNA in lung cancers), Metagenex (Circulating Tumor cells), P Fabre Laboratories (Drug targeting RhoB expression), Sanofi-Aventis (determinants of the micro environment), and Roche (RhoB in the response to TKI).

The team does not hesitate to built its own tools and develop new imaging strategies (split-GFP technology, new sensors...), revealing coordination and coherence of the governance and vitality of the team. In addition the emergence of young researchers is clearly encouraged as underlined by the appearance of the autonomous Team 4.4 in the CRCT project.

The PI has a strong activity in organising research in the region Toulouse-Midi Pyrénées (director of Clinical and Genetic Oncology Laboratory Medicine at the Institut Claudius Regaud Cancer Center, Director of the department “Signalisation, oncogénèse et innovation thérapeutique”, Scientific director of the Claudius Regaud Cancer Center, Director of Toulouse Cancer Research and Therapeutic Network, and president of the RTRS-RITC). He is responsible for one Master 1 teaching unit and member of the scientific and pedagogic committee of the Master 2 “Cancer”. The other PU and MCU are all teachers in the doctoral school.

- Project assessment:

There is no doubt that this is a long-term and reasonably ambitious scientific project. It associates a number of skills and complementary competences (molecular biologists, chemists, oncopneumologists and oncodermatologists with a contract of interface from INSERM, clinical chemists…). All the tools (transgenic mice, 3D culture and organotypic cultures) have been obtained and those which are actually lacking (specific antibodies against the GDP- and GTP-binding forms of Rho-B) are in the project, with preliminary data. Members of the team have access to the platforms of the different campus. The team has a long-time support of two pharmaceutical companies and each senior member of the team competes for the calls from the national institutes in France giving financial support in cancer research. This is decided in meetings establishing priority policy for the applications.

The team emerges from the former department “Signalisation, oncogenèse and innovation thérapeutique" of the Centre de Physiopathologie Toulouse Purpan renewed in 2007. It was decided to focus mainly on lung and skin cancers leaving aside a developmental research on anticancer drugs in breast cancer. This future team will be smaller than the previous one with a well defined strategy. This team is the only one in the consortium dealing with lung cancer and melanoma while several others are dealing with hematopoietic diseases.

- Conclusion:

  - Opinion:

The project is very strong and original, including young researchers besides well experienced seniors. It shows solidity in the human forces, pertinence and an evident coherence with the resources and appears with no doubt feasible in a period of 4 years. The project has emerged as a priority from those ongoing in the former team, leading to reorganisation and strong recruitment of young researchers with required skills. This recruitment policy together with the originality of the project and its strong translational research capacity constitutes a marked added value.

  - Strengths and opportunities:
    - The team has great potential to attract very good young researchers and to obtain contracts with the pharmaceutical industry.
    - A strong translational research capacity is based on the integration of clinicians and clinical biologists.

- A new aspect of the signalisation triggered by potent anticancer drugs has promising developments with opportunity to discover new biomarkers.
- The team demonstrates good capacity and strong potential to communicate and shares tools/expertise with the other teams of the CRCT.

- Weaknesses and threats:
  - The DR INSERM will retire in 2012 and caution must be taken to replace him.
  - It is expected an increased level in the publications as already revealed by the latest published.

- Recommendations:

The team should recruit another CR and encourage the young CR1 to obtain his HDR as soon as possible. Efforts should be made to improve the international recognition and it is suggested to cooperate with a foreign laboratory with strong international reputation.

Name of the team : Sphingolipids, Cell death and Tumor Progression

Name of team leader : Mr Thierry LEVADE

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

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	3	3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	4	4
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	5	5
N7: Number of staff members with a HDR or a similar grade	4	4

- Appreciation on the results:

This group displays a long standing expertise in two fields: i) biochemistry and cell biology of lipid mediators and ii) signaling pathways of death receptors and cell death in general. Sphingolipids play a crucial role in the apoptotic signalling pathway induced by death receptors, The modulation of the apoptotic signal and the subsequent modulation of the sphingolipid metabolism is envisioned as a tool to resensitize tumor cells to death inducing signals. The group belongs to the leaders in the sphingolipid metabolism field and their results are internationally recognized.

In the last 4 years, 23 main papers of the team have been published in high-rate journals (3 JBC, 1 JI, 2 Leukemia, 1 Cell Death Diff, 1 J Leukoc Biol etc.) in addition to 26 clinical papers. Overall, the team has published 74 papers.

The team has strong international collaborations. They have developed long standing research collaborations with chemists and pharmaceutical companies to achieve their ultimate goal: generation of new sphingolipid analogs and inhibitors of sphingolipid metabolism enzymes, which could be of great interest for the oncology field.

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

The PI has been invited as speaker, chairman or discussion leader at the Gordon Research Conferences on Glycolipid and Sphingolipid Biology, the Charleston Ceramide Conferences and the Sphingolipid Club Conferences.

This team and especially the PI have the opportunity to attract scientists from abroad due to the high quality of the publications. Furthermore, the contribution of lipids in cancer development and in the battle against tumor cell growth is a new exciting topic to be developed. Since this PI has the unique opportunity to be at the forefront of this new research line, he has the opportunity to attract a top-level scientist who could create a niche for him/herself.

This team has raised a total of more than 550 k€ of contracts (ARC, Labellisation program by the Ligue contre le Cancer, research funding contract with Pierre Fabre) and 30 students were graduated. For this team it is not and it will not be a problem to raise funds on multiple topics (e.g. lipid metabolism disorders, cancer etc.).

This team already has strong collaborations with scientists from other research fields, with scientists from abroad and with industry.

- Appreciation on the strategy, governance and life of the research unit:

This team seems well-balanced mixing clinicians, researcher with teaching duties and full time researcher. Each of them focus their work on what we could call atypical apoptotic signaling pathways (sphingolipid- and lysosomal-mediated cell deaths). This team is stabilized by an experienced staff.

The PI can rely on young searchers to run and develop new projects and also on one Ingeneer and one research technician.

The three professors/assistant-professors are important animators of the teaching on molecular biology and cancer at the University.

- Appreciation on the project:

The proposed research program is partly an extension of running projects that are long lasting and have shown to be successful. In addition, the PI presented new very promising axes that will be started soon.

This project is divided in three major parts: i) the influence of sphingolipids on the death of cancer cells, ii) the role of these lipids in the communication between tumor cells and the surrounding environment and finally iii) the generation, in strong collaboration with a chemist, of sphingolipid analogs to modulate death of malignant cells.

Overall this project is very original. As stated above, the PI aims to be at the forefront of a reseach field that recently gained much interest from the scientific community.

- Conclusion:

  - Overall opinion :

This team is headed by a senior researcher who possesses a strong reputation in the field of apoptosis and a very strong one in the field of sphingolipid metabolism. He runs a team with a CR1 INSERM position and 2 researchers with teaching duties. The team is attractive with the recruitment of 2 young permanent researchers (1 CR and 1 MCU), and 1 post doc. It has also access to various sources of funding.

The group works in the field of apoptosis and more accurately on the role of sphingolipid generation in the modulation of the cell death program. The project sounds very coherent with a good ratio between the project ambitions and the investigators involved in each process. In addition, a strong link exists with the clinic since the PI is in charge of the department of lipid metabolism disorders, which include Gaucher disease, patients with a significant risk to develop melanoma, multiple myeloma, etc.

- Strenghts and opportunities :
  - The work is strongly focused on the sphingolipid metabolism for which the team has international visibility and obtained good funding from pharmas and academics.
  - Innovative projects are supported by interesting tools and skills including relevant murine models.
  - There is a good opportunity to bring this strong experience in lipids to the surrounding teams and to extend the study of sphingolipids to the immunological field. The skills of the group will take advantage of the oncology environment with numerous collaborations.
  - Very good publication record of the team members was noted.

- Weaknesses and threats :

At the initiation of the CRCT, this group will be the only one working on apoptosis mechanisms used by malignant cells to escape recognition by effector immune cells and chemotherapy.

- Recommendations to the head of the research unit:

Identification of the links between death receptor signaling pathways and sphingolipid metabolism is an uncommon area of research and it is highly promising in oncology. Therefore this group should spare no effort on the different parts of their project focusing on these points to maintain their leadership on this promising niche.

Name of the team : (Lymph)angiogenesis, translational control and gene therapy in digestive cancers

Name of team leader : Mrs Anne-Catherine PRATS

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

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	4
N7: Number of staff members with a HDR or a similar grade	2	2

- Appreciation on the results:

The lymphangiogenesis project developed by this small team is original as only few groups address actually the role of these vessels in tumor growth and dissemination. The study of the role of IRES as an alternative translational regulation for FGF is also innovative and the group has already obtained significant results about this non classical cap dependent mechanism. This IRES structure is present on the mRNA coding for numerous angiogenic growth factors, among which FGF2 and VEGF, playing a crucial role in tumor angiogenesis. The team leader was a pioneer on that field. The effort of this group to develop IRES based technology vectors for anti-angiogenic therapy may also have broad application for bicistronic vectors. AAV vectors coding different anti-angiogenic molecules (FGF, fibstatin, PF4-V1) have already been generated. First published study on the use of this vector to correct ischemia demonstrates the potential clinical value of this approach.

The level of publications is good in regards to the size of the team (total number of team publications: 29). During the last four years, the group published in dominant position (1st, 2nd, last and before last) **6 papers** in journals with IF equal or superior to 5 (Circ Res, Faseb J, J Biol Chem, Mol Ther, Nucleic Acid Res, RNA). This level of publication is over the average, but not outstanding.

A long-standing collaboration has been developed with the Team 2.3 on IRES. The PI has strong partnerships with other academic partners (*ie* cooperation with a laboratory in Dundee) involving co-shared PhD studients. The project also displays strong translational aspects.

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

Some invitations in European (Dundee Toulouse conference) and National meetings (J Monod Conference 2006-2009) as well as many scientific communications in international conferences (Embo 2005, 2007, 2009, Cold Spring Harbor Laboratory Conference 2006) are mentionned. The PI organized the J Monod Conference in 2009.

The team leader obtained the INSERM Award of therapeutic research (2000), the Award of the Concours Regional de l'Innovation (2003) and an Interface Contract with the Toulouse University Hospital Center (2004).

It is mentioned that the PI raised funds from INCA, ARC and Association Française contre les Myopathies) but without more precisions (date and duration of contract, coordinator, amount of fund raised).

The team contributes to the creation of a European Associated Laboratory with a laboratory in Dundee and with two PhD students shared. However, they don't yet have joint publications. Another collaboration with a team in Japan should be noticed with two joint publications. The team includes two post-doctoral fellows.

- Appreciation on the strategy, governance and life of the research unit:

This small team relies on the dynamics and efforts of the team leader. The lymphangiogeneis project will be supervised by a post-doctoral fellow coming back from the US. The PI seems to favour emergence of young researcher.

The team leader plays also a governance role as a director of the IFR 31 and in the direction committee of the CRCT project. She is co-founder of a master of vectorology, gene therapy and vaccination and co-responsible for the cancer gene therapy module in the research master of pathophysiology. Number of teaching hours is not mentioned.

- Appreciation on the project :

The project on the role of IRES in mRNA translation relies on high expertise from the team leader. The goal to identify IRES trans-acting factors (ITAFs) is ambitious, risky and internationaly competitive but if successful, it may represent new breakthrough in the understanding of IRES regulation. The lymphangiogenesis project is also innovative as most groups focused on tumor angiogenesis. The aim to better understand lymphangiogenesis regulator factors is important but it will be difficult and risky as many molecules (FGF2, some VEGF isoforms) seem to contribute to both lymphangiogenesis and angiogenesis. The specificity of some lymphangiogenesis marker (Lyve 1) used by the team has been challenged during the audit. Effort of the team for developing translation research projects based on IRES technology has to be encouraged.

Overall the projects are ambitious and various questions addressed are relevant. However, the team has a small size with only one full time scientist and a PU-PH. The recruitment of a full time scientist will help for the success and implementation of all the projects developed.

The team seems attractive and competitive for external resource funding.

- Conclusion:

- Overall appreciation :

The team has a well known and recognized expertise on the IRES role in alternative translation mechanism, thanks to pioneer work on that topic. It represents an emergent field in gene regulation with some important applications in the field of angiogenesis. The lymphangiogenesis project is a new field introduced in the lab. Some tools and approaches have still to be validated and international collaboration on that topic encouraged. The effort of the team to develop translational research on vectors based on IRES technology has to be mentioned as they have all the expertise and results may have some impact on gene therapy in general.

The group has to be reinforced by a full time scientist to remain competitive and for the implementation of all the projects in good conditions. The creation of an European associated Laboratory with Dundee with two shared PhD and the support of a post-doctoral fellow as a project leader, and search for a permanent researcher may help the team to reach a critical size.

- Strengths and opportunities :

- Projects are original, ambitious and competitive and the PI is a well known scientist in that field.
- The team seems attractive for PhD and post-doctoral fellows reflecting a good local and international recognition.
- The goal to identify ITAF is innovative although risky and may lead to some breakthrough in this important emerging field.
- The lymphangiogenesis project showed that the team engaged itself to new risky field with potent application in oncology.
- Efforts to create new bicistronic vectors based on IRES technology will allow clinical valorisation of the expertise of the team.

- Weaknesses and threats :

- Due to the ambitious projects developed by the team, its size may represent a limit for their implementation in the best conditions.
- The lymphangiogenesis project has just been introduced in the team. The experimental models and tools have to be improved to allow better specificity of its analysis compared to angiogenesis.

- Recommendations :

The lymphangiogenesis project is promising but tools have to be validated and it will benefit of an integration in a network or supported by international collaboration.

It will be important during the next four years to reinforce the structure by recruiting a full time scientist. The delegation of responsibility to the post-doctoral fellow for the supervision of the angiogenesis project is a good point.

Name of the team : Tumor angiogenesis and control of gene expression

Name of team leader : Mr Hervé PRATS

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

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	6	6
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3	3
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	2
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	2
N7: Number of staff members with a HDR or a similar grade	3	2

- Appreciation on the results:

The team has developed interesting strategies for studying the post transcriptional regulation of key transcription factors such as FGF2 and VEGF. FGF2 is translocated in the nucleus via its direct interaction with different molecules, including FIF (FGF-2-interacting-factor). Interestingly, FIF/FEGF2 also interferes directly with the initiation factor EF2F1. For this project, the group has developed specific tools, such as FIF knock out mice. An important part of this project is the study of a FGF-2 binding chemokines, CXCL4, for which a variant, CXCL4L1 was discovered. This molecule is differentially expressed in some tumors, such as in kidney and pancreatic cancers. Its biological role and its value as cancer biomarker are currently under investigation, in cooperation with several groups.

The other main project which is developed concerns the post-transcriptional abnormalities observed in several key genes controlling tumor angiogenesis. Two main directions are taken, one on the unfolded protein response (UPR), a mechanism occurring under endoplasmic reticulum (ER) stress conditions, and the other on the identification of a specific miRNA interfering with HIF1-alpha.

These research projects are original, and use up to date technologies. The activity of the team ranges from basic high level academic research to translational research with potential clinical applications in the domain of cancer.

The level of publications is good (Total number of papers: 71). During the last four years, the group published **19 main papers in dominant position** (1st, 2nd, last and before last) including several publications in high-rank journals, and 41 clinical papers. The PI has published 11 papers during this period (Nucleic Acid Res, RNA, J. Biol. Chem, Cir. Res., J. Cell Science...). One joint INSERM/Millgen patent and 2 other INSERM patents have been filed (one license in discussion).

- Appreciation on the strategy, governance and life of the research unit:

The team has recently encompassed local groups, which resulted in an increase in the team size that is composed now of 16 staff members, among wich 2 young investigators with permanent position (Inserm and CNRS). This fusion has considerably increased the strength of the team, by providing a much stronger working force. Moreover, the team has gained in dynamism with the recruitment of 2 young permanent scientists and 2 post-docs. This new team has the capacity to attract competitive PhD students and post-docs, since the number of researchers/professors with management capacity (HDR) has significantly increased. Animated by the PI and experienced researchers/professors, the team has a good international visibility, based on solid publications and participation to national/international congresses and could develop new projects. The steam also relies on one engineer and one research technician. The group has developed numerous productive collaborations with important academic laboratories (ie in Bordeaux and in Villejuif) and with high level clinical groups working on cancer (ie at IGR, Villejuif).

The team is an important element of the global CRCT project. The group has many links with other teams, in particular the Team 2.2. The reputation of the PI is very good, both in France and abroad and he has been awarded by prize of the "Concours Général de l'innovation en Midi-Pyrénées" 2003. The PI papers have a very good citation index, showing its international visibility.

The team is funded by the Agence Nationale de la Recherche, by INCA, by the regional Cancerople, by the Pôle de compétitivité Cancer Bio-santé and by ARC.

The PI is Professor, and he is an important animator of the teaching on molecular biology and cancer at the University. Other members of team are involved in teaching (1 PUPH, 3 MCUPH and one MCU).

- Appreciation on the project:

The 2 main projects of the team are based on long term experience of the PI, first on the factors regulating FG2 activity, and second on the molecular mechanisms regulating the post-transcriptional fate of main pro-angiogenic factors. The team has developed tools and models to adress these 2 projects, and has access to indispensable technical platforms. The team also collaborates with main actors of cancer research. The team also makes efforts for developing translation research, such as for the project on CXCL4L1. The project on the post transcriptional control is original, and contains a part of risk, mainly in the part concerning the miRNAs.

Overall the projects are ambitious and feasible. This feasibility is much increased by the fusion of previously independent teams, resulting in reaching a decisive critical mass.

This team is attractive with 2 young permant researchers, and 2 post docs. It is stabilized by experienced staff, including professors and technician/enginneer. The team has also access to various sources of funding.

- Conclusion:

  - Overall appreciation :

The team has a solid reputation, based on the good publication record, the long lasting experience of the PI on the domain, and on the durable and fruitfull collaborations that have been established.

The project on FGF2 has contributed to reputation of the PI. This project is renewed by new perspectives, concerning the role FGF2 interating Factor (FIF), with access to important tools such as FIF deficient mice. The role of a variant of CXCL4 which may be involved in the regulation of tumor angiogeneis is another interesting emerging topic.

The study of post-transcriptional regulation of key factors inducing tumor angiogenesis is a novative approach. The discovery of miRNA interfering with the mRNA of these genes is of peculiar interest.

  - Strengths and opportunities :
    - The projects include main stream classical approaches and more innovative/risky approaches.

- The team has reached a critical mass, which makes it attractive for post-docs and PhD students. Attractivity is peculiarly important for PhD students, since several members of the team are importantly involved in teaching and teaching organization.
- The team has also access to critical technical platforms, and seems to have easily access to local/national grants.

- Weaknesses and threats :
  - Few pieces of information are provided concerning the international collaborations of the team, and on its participation to international grants.
  - The recruitment of young scientist seems to rely on local network. Opening post-docs coming from abroad will certainly increase the international visibility of the team.

- Recommendations :

The team should improve its international collaborations and networking. Recruitment of post-docs coming from other countries should also be searched.

The young permanent staff should be encouraged to develop its own emerging projects.

Name of the team : PI3K-signaling and translational control in pancreatic and pituitary tumors

Name of team leader : Mr Stéphane PYRONNET

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

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	3	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		4
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		2
N6: Number of Ph.D. students (Form 2.7 of the application file)	5	3
N7: Number of staff members with a HDR or a similar grade	3	3

- Appreciation on the results:

Over the last 4 years, this team has developed cellular models which have allowed the identification of an original role of the somatostatin receptor subtype 2 (sst2) in the regulation of PI3K in pancreatic cancer. In particular, this work has demonstrated that sst2 regulates the expression of the translation initiation factor 4E-BP1 as well as cell-cell interactions by restoring the expression of connexins 26 and 43. This knowledge is important for predicting the therapeutic response to somatostatin and for identifying new anti-tumor strategies.

The team has published over the last 4 years **26 publications from the laboratory**, 16 publications in collaboration and 13 clinical publications or during team member post doc. The quality of these publications is excellent, for example in 2009: PNAS; EMBO J , and MCB. One patent has been filed.

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

The PI is regularly invited abroad (7 times in the last 4 years). A researcher was recruited as CR2 INSERM last year. Furthermore the team have been joined by a MCU in the same year, and this team has recruited two post-docs. This team has multiple funding sources including Cancéropôle Sud Ouest, ANR (several programs), ARC, Ligue contre le cancer, and 2 industrial contracts (Pfizer, Novartis). This team collaborates with the Team 4.3 of the CRCT and also with several international groups, in particular for the development of original mouse models targeting 4E-BP1 (a well-known team at Mc Gill University, Canada) and p110 (another team in London).

- Appreciation on the strategy, governance and life of the research unit:

Teachers-scientists and researchers are actively involved in organizing local and regional meetings (GSO and RTRS-RITC). They participate in the teaching of Biology Graduate School of Health. They have mentored 12 students during the last term of office. The PI is one of the 6 scientific vice-directors of the CRCT.

- Appreciation on the project :

The project presented by this team is a continuation of previous work. This project focuses mainly on the function and role of PI3Kinase in pancreatic carcinogenesis and also in pituitary tumors. This project makes use of biochemical, cellular and animal models. This project is structured into three well-articulated and logical themes from basic research to translational research. The skills of individual team members can ensure a high probability of success. This in an original and long-lasting project but with little risk-taking.

- Conclusion:

  - Overall appreciation:

This team is dynamic and powerful. It is on the rise, the project is well structured including a field ranging from fundamental to the clinic. The project and the team rank among the best in the center.

  - Strengths and opportunities:
    - Young team with PI of a great scientific value with an international dimension.
    - The integration of this team in the center will provide a central conceptual and technical expertise at a very good level.
  - Weaknesses and threats:
    - The ratio of technical staff versus researchers seems a bit weak and should be strengthened.
    - The study of the pituitary should be more precisely defined.
  - Recommendations :

This project warrants support without any restriction. Some more risky projects could be undertaken by this efficient team in order to remain at the front line also in the future.

Name of the team : Gastrin precursors: functions and therapeutic perspectives in gastrointestinal cancers

Name of team leader : Mrs Catherine SEVA

- Team staff or staff allocated to the project (according to the dossier submitted to AERES):

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		0
N6: Number of Ph.D. students (Form 2.7 of the application file)		2
N7: Number of staff members with a HDR or a similar grade		3

- Assessment of work produced and scientific quality:

The project developped by the team concerns gastrin precursors and their role in colon and pancreatic cancers. This team has shown that mutations of Kras and APC in early steps of carcinogenesis lead to an increase of gastrin precursors expression. They also found that these precursors induce proliferation and decrease cell adhesion, which facilitates invasion and metastasis processes. Moreover, whereas the receptor for gastrin precursors is not known, this team recently found that these precursors were able to interact with a membrane receptor. Overexpression of these precursors was found in the early steps (precancerous lesions) of colon and pancreatic carcinogenesis. The work developed by this team should allow identification of new targets to develop targeted therapies against cells responsible for tumor development and recurrence.

This team has published over the 2005-2009 period 11 main publications, 10 publications in collaboration and 26 clinical publications or publications during post-doc by team members. Publications have been published in good general journals: JBC, Cancer Research, Oncogene, BBA Mol Cell Res (x2), Physiol Rev, Cancer Lett (x2) and in gastrointestinal/clinical reviews : World J Gastroenterol (x2), Br J Surg. One PhD thesis led to recruitment of one researcher. Four PhD theses were defended since 2005.

- Assessment of the influence, appeal and integration of the team or the project in its environment:

The PI is regularly invited as speaker and/or chairman in international congresses.

One Inserm researcher was recruited in the group in 2008. One post-doc is recruited for 2 years as of January 1st, 2010. One clinician (PUPH) joined the team in january 2009.

The project is already funded by caritative associations (ARC), by local institutions (Région Midi-Pyrénées) and by french (ANR) and international (Medical Research and Technology, Australia; Austin Hospital Medical Research Foundation, Australia) agencies. In total 380 k€ have been raised by this team.

The team participates every year to french congresses about intestinal epithelial cell biology (CECED) and French pancreatic club (CFP) and to international meetings. The PI has participated in organization of one international meeting. They stably collaborate with several other teams of the CRCT and with national (Montpellier, Bordeaux) international (U of Melbourne Australia, Harvard Medical School Boston, New York University) research laboratories.

The team has developed stable relationships with several companies (Bioréalité Montpellier, Novaptech Bordeaux, Rotta Pharma Italy) with the aim to develop new drugs and biomarkers.

- Assessment of the strategy, governance and life of the team or project:

The team is very well organized with 2 full-time researchers and one clinician, allowing the development in this team of both basic science and translational research. The PI is young, dynamic and has already national and international recognition. She belonged to a bigger team in the previous research center (I2MR), and she has developed over the years her own research. She is now in the situation to direct her own team and to emerge as a major scientist in the future CRCT. Several tools were already created by the team and presently the main goal is to develop progastrin molecules as anticancer targets. The team, although small at present, has established interesting national and international, public and private collaborations that will permit to carry out the project under optimal conditions.

The PI is actively participating in teaching activities, she is part of the scientific committee of the Master "Innovation pharmacologique" (University Paul Sabatier, Toulouse) and participates in student selection, organization of lectures, teaching and student evaluation. The clinician of the team is teaching at the Medical faculty.

- Project assessment:

The PI started this project within the Team 4.3 and published several original papers. After that time, several other teams, located in France or elsewere, have been inspired by her results. Presently, the PI focuses its interest in developing anticancer therapeutic approaches using the progastrin-dependent pathway as a specific target. This project is interesting and original and already converted into one publication in 2009 (Int J Cancer). Results presented sound very promising.

- Conclusion:

  - Opinion:

This new dynamic team that emerges from a local team (Team 4.3 of the CRCT project) succeeded in that goal and is already fully working on its own, presenting with an important potential for the future CRCT.

  - Strengths and opportunities:
    - Strong basic science is presented using in vitro (cell lines), in vivo (animal models) and ex vivo (patient material) approaches.
    - Research includes basic science, preclinical studies and translational research with good opportunities in the near future to patent some of the tools developed of markers identified.
  - Weaknesses and threats:

Few high-rank papers have been published so far.

  - Recommendations:

The team should develop even more valorization of its research and publish in journals with higher impact factor.

Name of the team : Molecular genetics in hematopoietic tumors

Name of team leader : Mr Pierrre BROUSSET

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

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	4	4
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)		5
N7: Number of staff members with a HDR or a similar grade	5	5

- Assessment of work produced and scientific quality:

The team is well-known in the world for its work on ALK-positive lymphoma. The group has had a very consistent scientific production over the years and is very well rooted in National networks. For example, it provides the leadership in a national consortium on the classification and pathophysiology of T-cell lymphomas. The group is very well embedded into the clinical setting. The work decisively influenced classification of anaplastic large cell lymphoma and is very relevant for the search for novel targets in the treatment of T-cell lymphomas. Moreover, the team is an international leader in the identification and characterization of Pax5-related genetic abnormalities in B-ALL. The project ideas are solid; the strategy of the lab seems to be logical succession of successful running projects. This promises a relatively smooth road to further high-quality publications. The novel project concerning miR125b is presented and has convincing results leading to a major publication in J Exp Med.

The whole team is very actively publishing. Constant, excellent publications (IF around 10) over the last 5 years, very often with team members as either first or last author (1 J Exp Med, 3 Blood, 2 Mol Cell Biol, 1 Cancer Res, 3 Leukemia...). Overall, the team has published over the 2005-2009 period 31 main publications, 43 publications in collaboration and 14 clinical publications or isolated publications by team members.

Four PhD theses have been defended since 2005.

- Assessment of the influence, appeal and integration of the team or the project in its environment:

The team is very well embedded clinically, scientifically and in collaborative groups in France. Therefore, the ability to recruit excellent scientists seems evident. Accordingly, the group has 2 post-doc fellows and has recruited recently two young researchers on CR1 positions.

The team exhibits a strong capacity to successfully obtain grants from several associations (ARC, Ligue Nationale contre le Cancer, Fondation de France) and from national (INCa) and European institutional agencies.

- Appreciation on the strategy, governance and life of the research unit:

The constant flow of data from the lab illustrates that the quality of management of the lab. Also, there is clear evidence that the members of the lab are very well integrated in the mission of the lab and the strategic planning of the experiments. The projects are convincingly discussed by different scientists of the group and it is clear that they are on top of their projects, providing a strong hint for a good, productive atmosphere in the lab with lively exchange of scientific ideas.

Several team members have important teaching activities at the faculty of medicine and the leader of the ALCL project is one of the 6 scientific vice-directors of the CRCT.

- Appreciation on the project:

The scientific project is relevant, feasible, well-focused, and with a good mid- and long term perspective. The new axis on Pax5 isoforms in B-cell differentiation is very interesting and promising. The programs are meaningful and well-funded but not overtly risky except the more recent orally-presented project dealing with chromosomal abnormalities targeting non coding RNA.

- Conclusion:

This group is excellent, with a very strong publication record, well-organized, and with a well-balanced, smart project. The project and the team rank among the best in the center.

- Strengths and opportunities
  - Relevant topics are developed.
  - Good story in the past prdicts good story in the future.
  - A good balance may be noted between very good basic science and more translational approaches.
  - Interesting hypotheses and adequate technical approaches are proposed, including fully original, conditional mouse models of tumorigenesis.
  - The team appears to be well-managed, with nice interactions of the PI and the staff.
  - The publication track record is very good.
- Weaknesses and threats

No real high risk/ high gain project is presented.

- Recommendations :

It will be important to further develop the emergence of strongly innovant projects on small nucleolar RNA and, owing to the size and quality of the team, to start additional long-term, more risky projects to get a chance to publish not only in very good, but also in outstanding journals.

Name of the team : Signaling, Cell cycle and Therapeutics in Myeloid malignancies

Name of team leader : Mr Stéphane MANENTI

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

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)		
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		
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		4

- Appreciation on the results:

This team is a novel group that applies for the first time. The group was put together very thoughtfully, as researchers interested in basic cell cycle machinery came together with signalling specialists and clinicians treating myeloid malignancies. The cooperation among team members seems to be good. The new group will be very well embedded, since clinical and basic scientists already work together and since the patient recruitment is extremely good (150 AML, 120 MDS per year). The collaboration between clinicians and basic scientists seems to be perfect here. Also, a very nice partnership with the industry to build a model of preclinical evaluation of drug effects is being built. The scientists of the group are well-rooted in their respective fields. The output of the group cannot be judged since the group is freshly formed. The members of the group are well established in their fields. The field of research is relevant, since myeloid malignancies are still very difficult to treat.

Previous publications in the field of application are very good, many of them jointly. The team members have published over the 2005-2009 period **22 main publications** (including 4 Blood, 4 Leukemia, 1 Cancer Res, 1 MBC, 1 Oncogene, 1 Cell Death Diff...), 10 publications in collaboration and 23 clinical publications or isolated publications by team members. 4 PhD theses have been defended since 2005.

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

As one of the largest AML and MDS center, national visibility will be high. The group has high potential to be internationally renowned, once it has constituted.

The group is young and dynamic, has a good publication record and seems quite attractive for junior scientists to join it.

- Appreciation on the project:

Translation into clinical application is self-evident. The program is highly interesting, methodology well-designed and utilizing central structures and interesting hypotheses.

Collaborations with other cell cycle groups, especially the team 1.1, are encouraged. The group should make sure that they analyze subpopulations of leukemias for cell cycle regulation (Collaboration with split-GFP group recommended).

- Conclusion:

Overall, a very able group has been formed with basic scientists and clinicians very well connected. The projects are well-founded on existing work of the participating scientists that have very well published in their field. They focus around a disease, for which excellent clinical expertise exists in the group and for which many samples will be available. The group has formulated well thought-through projects that focus around aberrant cell cycle control in myeloid malignancies.

- Strengths and opportunities :
  - This freshly formed group has been created because of common interest.
  - Good publications are presented by the team members.
  - The project is well-focused.
  - The topic is relevant.
  - Excellent transfer from and to the clinic is noted.
- Weaknesses and threats :

The group has to be formed first.

- Recommendations :

The group should make sure to analyze not only bulk disease, but also to develop assays for analyzing cell cycle control in specific leukemic subpopulations. The group should be encouraged to aggressively search cooperation in the center. The group is not yet first grade internationally visible – however, this could rapidly change.

Name of the team : Therapeutic immunotargeting of B-cell tumors

Name of team leader : Mr Jean-Jacques FOURNIE

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

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	4	3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	4
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	4
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	7	5
N7: Number of staff members with a HDR or a similar grade	5	5

- Assessment of work produced and scientific quality:

The reported activities results from the merge, by mid-2006, of two previously independent groups working on different aspects of immunotherapy and microenvironment.

The PI is an international leader in the field of innate immunity with both solid basic programs and translational projects that have led to the development of clinical trials dealing with NK and □□□T cell activation and to the creation of a successful private company (group 1). The second group has developed original and productive projects aiming at unraveling the mechanisms of the direct cytotoxic activity of the anti-CD20 antibody Rituximab (group 2). The collaboration between the two groups has already been validated at the scientific level but also through the design of a multicentric phase II clinical trial combining rituximab and □□ T-cell-targeting phosphoantigens. Besides these well-recognized projects, the group of the team leader described few years ago a fully original trans-synaptic transfer system called trogocytosis that is in particular involved in the crosstalk between stromal cells and malignant carcinoma cells. The question of tumor microenvironment was also investigated in multiple myeloma by a third small group that proposes to join the team in the CRCT (group 3). They recently demonstrated that mesenchymal stem cells (MSC) are abnormal in this disease and identified GDF-15 as a new potential tumor marker. This third group is small and mostly recognized for its implication in the design and coordination of multicentric clinical trials.

Overall, the team made significant scientific contributions and developed an outstanding translational program with potential impact at clinical and valorization levels.

The team has a long standing track record of very good works on innate immunity, Rituximab-mediated signal, and trogocytosis (> 5 Blood, 3 JBC; 2 J Leukoc Biol; 1 Cancer Res, 2 J Immunol...). The team has published over the 2005-2009 period 29 main publications, 21 publications in collaboration and 43 clinical publications or isolated publications by team members. The work on myeloma microenvironment was less productive to date (Leukemia 2007). 6 PhD theses were defended since 2005. Four patents were filed by INSERM, among which one was licensed to Innate Pharma.

- Assessment of the influence, appeal and integration of the team or the project in its environment:

The PIs are regularly invited in national and international conferences and the team leader has organized a congress in 2008. The team leader is the candidate director of the CRCT.

The team includes two post-doctoral fellows and exhibits strong capacity to successfully obtain grants from private companies including big pharmas, from several associations (ARC, Ligue Nationale contre le Cancer, Fondation pour la recherche médicale) and from national (coordination of an INCa program) and European (participation to a FP6 program) institutional agencies. The leader of the group 2 steers a multicentric international phase II clinical trial.

The valorization program is outstanding and includes contracts with pharma companies to investigate the activity of new drugs or new drug combinations on malignant B cells.

- Assessment of the strategy, governance and life of the team or project:

The leader and the co-leader have developed complementary approaches and all the scientists are clearly involved in the management of their programs. This successful fusion was strongly appreciated. The myeloma group is less visible at a scientific level but will probably benefit from the integration in this very well managed team. Several members of the team are professors or assistant professors and are strongly involved in teaching activities. Some team researchers have organized Canceropole GSO days and participate actively in the scientific life in their region and at a national level.

- Project assessment:

The project has been focused on B-cell malignancies and is strongly relevant. The main tools are already available or are in development with preliminary data (3D spheroids) and the team aggregates all the complementary expertise required for this ambitious translational project.

The group leader has good experience in the partnership with private companies and the team have obtained substantial resources from national and international funding agencies.

There is a good balance between solid, already running projects (NK/T□□, mAb bioactivity, BCR signal) and more recent risky projects (trogocytosis and tumor escape, nurse-like cells).

- Conclusion:

  - Opinion:

The team has an internationally recognized expertise on innate immunity and B-cell targeting mAb thanks to pioneer works and important contributions in these fields. The team is very solid, based on several fully independent and highly productive researchers and the future position of the team leader as the CRCT director will probably not be deleterious for the scientific development of the team and will ensure good collaborations with the other groups of the CRCT. New projects are promising and should be encouraged.

  - Strengths and opportunities:
    - Large body of past work presents with very good balance between basic and translational research
    - The publication track records are very good.
    - Efficient links with private pharma companies
    - The fusion of two well-recognized research groups creates a unique opportunity to develop joint innovative programs on B-cell neoplasias
    - Strong interactions between clinicians and scientists are noticeable.
    - Interesting new projects are being developed on nurse-like cells/TAM in B-CLL
  - Weaknesses and threats:
    - The myeloma project should be defined more precisely at both scientific and organizational level (people involved, dedicated grants...)
    - The availability of primary cell samples in some cancer models could be a restrictive factor for the relevance of some specific studies
  - Recommendations:

The recruitment of another team focusing on "classical" cancer immunology in the CRCT will allow the development of new synergistic projects on tumor microenvironment. It will be important to maintain a strong effort on basic/mechanistic science in order to develop new innovative translational projects in the future.

Name of the team : Markers and targets for digestive cancer biotherapy

Name of team leader : Mr Louis BUSCAIL

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

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	6	6
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3	2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)		
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	4
N7: Number of staff members with a HDR or a similar grade	7	7

- Appreciation on the results:

The research presented by the PI deals with the identification of new biomarkers in digestive cancers and with the development of biotherapy dedicated to the treatment of pancreatic cancer. During the last four years, this group developed a research focused on the identification of biomarkers using different transcriptomic and genomic approaches in different digestive cancers, mainly in pancreatic cancers. This research is based either on human samples or animal models, and covers the fields from fundamental research to the patients. The weak efficacy of current treatments of pancreatic cancer justifies largely the relevance of the research subject in its both aspects. The biomarkers are developed in two ways: i) first to identify new biomarkers that can allow the early diagnosis of pancreatic cell transformation; ii) second to determine new cell products that could be targeted by drugs. Among the first results obtained, the role of miRNAs is the most promising. Concerning the second aspect -trying to develop biotherapy for pancreatic cancer-, the preclinical phase allows starting in March 2010 a first clinical trial testing the role of 2 previously identified genes in association with a biotechnology company.

The group have published 67 publications: 20 are main publications by the team, and 9 are identified as joint publications, the remaining publications are identified as clinical and independent publications. The quality of the main publications is good with a high impact factor in specialized journal (Journal Clinical Oncology, Gut, Human Pathology, Cell Death Differentiation, Oncogene, Human Gene Therapy, Journal of Biological Chemistry).

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

The PI is regularly invited in international congresses on pancreatic diseases and also on human gene therapy at european and international level.

The team has recently recruited a post-doc and a second one is under recruitment.

It is clear that the ability to raise funds is a strong point of this group which interacts with biotechnology companies to develop biotherapy in pancreatic cancers. The team has also multiple sources of academic/caritative grants (INCA, Ligue Nationale contre le Cancer).

The team participates to the project ONCOSPIM-Innabiosanté on the realisation of spheroid pancreatic cell culture. It also developed collaboration with two international groups in Dartmouth (NH) and Rochester (USA).

This research field leads to start in the next months a biotherapy trial in pancreatic cancer.

- Appreciation on the strategy, governance and life of the research unit:

The group comprises several professors and assistant professors and organizes the annual workshops on oncology for M2 students. In addition, the team is strongly involved in the local research organization (Coordination of the Canceropole GSO axis "Biotherapy and Innovative treatment for cancer", RTRS-RITC). Of note, two out of four PhD students are not funded.

- Appreciation on the project:

The research project on digestive cancer includes 4 axes: molecular analysis, identification of the markers, characterization by using specific animal model and prospective clinical validation. This is an ambitious project since it covers three cancers (pancreatic, liver and colorectal). The most promising and relevant at mid-term is the exploration of miRNAs expression and methylation status in PanINs (precursor to invasive pancreatic cancer). In addition this subproject is led by the only full time researcher of the team. This project will provide new relevant markers to accurately predict pancreatic cancer initiation and progression. Moreover translational research is ongoing with highly promising results. Subproject 2 on splicing variant of KLF6 (KL6-SV2) in liver tumor is highly risky since the role of this variant in tumor cells is not well established. Subproject 3 on colorectal carcinomas is a more long-term scientific and applied research. Preliminary results are convincing, the project has been funded by both LNCC and INCa, clearly the subgroup involved in this project needs to be reinforced.

Targeted biotherapy of pancreatic cancer by using non integrative lentiviral vectors is an original and risky project that includes in particular the choice of the most relevant target before the long process of transfer to clinic.

- Conclusion:

  - Overall appreciation :

This is a good team with one leading project on pancreatic cancer.

  - Strengths and opportunities :
    - Interdisplinarity and real continuum between basic and applied research should be emphasized.
    - Medical practitioners are strong involved in the project.
    - Translational research is well developed.
    - This is a very attractive field for pharmaceutical companies.
  - Weaknesses and threats :
    - Ambitious projects are conducted in parallel in three cancer types.
    - There is apparently no synergy between the different goals of the team's project.
  - Recommendations :

Given the strong and recognized expertise of the team in both basic and translational research in pancreatic cancer, a better synergy with other teams of CRCT involved in this field (teams 4.3 and 2.5) would lead to a very competitive pole dedicated to pancreatic cancer.

Given the weakness of the subproject 2, the strategy should be re-defined in order to either rapidly validate KLF6-SV2 as a potent prognostic marker or focus research activities on subprojects 1 and 3.

Name of the team : Individualization of anti cancer treatments

Name of team leader : Mr Jean-Pierre DELORD

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

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	9	9
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)	2	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	3	3
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	4
N7: Number of staff members with a HDR or a similar grade	7	7

- Appreciation on the results:

The proposed team brings together a research unit, a clinical investigation unit and an experimental laboratory. The research unit is dedicated to clinical pharmacokinetics of anticancer agents, with a recognized experience in pharmacokinetics and pharmacogenetics studies, and in pharmacologic modelling by population approaches in children and adults. This unit has been a reference for individual dosing and pharmacokinetics of platinum compounds. The clinical investigation unit has experience in early phase clinical trials, and the experimental laboratory aims at providing preclinical data and cellular investigations.

The objectives of the team, such as improvement of intra operative detection of tumor cells, personalized drug administration, better selection of patients, are relevant to cancer research and useful for the improvement of patient treatments. There is a strong interdisciplinarity within the team. The impact of previous findings is important for medical practice. Several recommendations have been issued from recent research and published in good level journals. However, the approaches presented remain global, and there are no scientific hypothesis clearly defined.

The research related to the role of stromal cells in ovarian carcinoma, developed in the experimental laboratory unit is original. This group has described and patented specific stromal cells (Hospicells) able to transfer cell surface proteins to tumor cells (oncologic trogocytosis). However, the projects related to these potentially important findings are not described, and there is no elaboration on the strategy of development within the projected team.

The scientific level of the laboratory's activity is quantitatively good with 57 publications including 34 main publications. Most of them involve either the pharmacology field or the reporting of early phase clinical trials. During the last four years, the group driven by the pharmacologist had a regular production in good level scientific journals and in dominant position (1st, 2nd, last or before last): 3 Clin Cancer Res (IF 6.5) , Br J Cancer (IF 4.8); Ann Surg Oncol 3.9) and third author in J Clin Oncol (IF 17.1). The molecular biologist published in dominant position in Gene Therapy (x2) (IF 4.5) and Cancer Gene therapy (x2) (IF 3). Most publications of the PI are clinical publications in good journal of speciality: Clin Cancer Res x2 (IF 6.5); Annals oncology x 2 (IF 4.9), Br J Cancer (IF : 4.8).

Overall, due to the size of the team (9 senior scientists), the juxtaposition of publications involving separate fields and authors (80% of the publications do not overlap), the presence of many publications reporting large clinical trials with one single member of the team, and not addressing specific scientific questions, and the lack of an individualized scientific originality, the estimation of the overall quality and of the output of the proposed research should be average.

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

Invitations to international conferences are mentioned, but no post-doctoral staff is noted.

The team is sponsored by institutional grants from ARC, Ligue contre le cancer and national (INCA, PHRC) and international funding agencies, without precision about the amount and the duration of sum raised. Some contracts exist with pharmaceutical companies but are not detailed. Globally, the team has experience and has been successfull in raising funds.

The team is leader in several domains (such as clinical pharmacokinetics of anticancer drugs) within collaborative groups. It belongs to large, cooperative clinical research groups: European organization for research and treatment of cancer (EORTC), pharmacology and molecular mechanisms (PAMM Group). It has numerous, stable national (one PI is president of the Groupe de pharmacologie clinique en oncologie, GPCO) and international research collaborations. This confers to clinical research and to the pharmacologic parts of this team a large national and international visibility.

The team leader is vice-director of the industry and trade activities branch of the University Paul Sabatier. He acts as a scientific advisor for several drug pharma. He has experience in intellectual property. Finally, the PI is one of the 6 scientific vice-directors of the CRCT.

- Appreciation on the strategy, governance and life of the research unit:

The proposed research team is currently scattered into different research units, and the evaluation of its organization is not possible. Moreover the strategy considered in the project remains vague and this appears as a weakness.

The PI has experience in setting up and conducting innovative clinical trials. During these trials, pharmacological issues are addressed with the pharmacologist team. However, the link between scientists and other medical doctors is less clear. The proposed team's organization has to be better defined, even if most scientists previously belong to the same research unit, since the scientific coordination does not appear clearly.

All members of the team have teaching activities and participate in the organization of research. They belong to several scientific committees and coordinate teaching courses in medical or pharmacological sciences, at the undergraduate, or Master (professional or research) and Doctoral levels at the University of Toulouse. Most of them are involved in doctoral training. They coordinate locally the European exchanges of students (Erasmus). Several members of the team belong to the local ethic committee. The team leader is the director of the clinical research unit.

- Appreciation on the project:

Various projects have been presented in different fields. The project relying on pharmacological studies to better individualize dose drugs is well constructed with recognized expertise. However, the presentation of other themas (head and neck cancer classification to better predict response to Her1 inhibitor, role of hospicells in the growth of ovarian cancer…) remains descriptive and not sufficiently elaborated. Research program often use integrative biology (omics) without scientific hypothesis. The scientific leaders for the various projects do not always appear clearly. Several projects with potential clinical interest would be more appropriate in a transfer laboratory.

The number of projects, some of them very ambitious, contrasts with the absence of full time researcher or post-doctoral student. Resources allocated to each project and how the project will be funded were not clearly stated. It may be that pharmaceutical support play a role in their development but it is difficult to appreciate that point.

The projects present some original aspects (role of hospicells, individual dosing of chemotherapy…). However, in most cases, the approaches rely on the use of common integrated biological platform. Some special cohorts of unique samples may have been derived from the various innovative clinical trials developed but this important point is not defined enough.

- Conclusion:

  - Overall appreciation :

The team presents a translational project closely linked to innovative clinical trials. Pharmacological studies for individual dosing of chemotherapy are competitive and have to be supported. However, although scientific issues addressed by many other projects may have interest, there is no precise definition of resources and manpower allocated to each of them. In addition, lack of an identification of a principal investigator for each project makes them weak and risky in their feasibility. This team has clearly a place to find in the overall project including the CRCT and the CUC. Based on the presentation of the project, a translational research laboratory or department would be more appropriate than an INSERM scientific team to successfully implement them.

  - Strengths and opportunities :
    - High quality of clinical research should be emphasized.
    - The expertise of this group is recognized and is important for the CRTC at several points of view, including access to samples derived from innovative clinical trials, support for clinical development of molecules originating from the research projects of the CRCT teams.
    - The development of new tools for individual dosing of drugs is original and competitive.
  - Weaknesses and threats :
    - The team appears as a juxtaposition of three units with little interactions and without any clear integrating strategy.
    - Many projects have been presented covering a large field without clear hierarchization and priority. The size of the team (part time researchers) does not fit with that of the projects. Several aspects of the projects remain vague and the PI for each projects are not identified.
  - Recommendations :

The projects have to be more focused with a clear definition of the resources and manpower allocated to each programs. The recruitment of full time researchers will help for the structuration of the team. The strength of the team in terms of cohort of patients and collection of samples has to be better presented for international recognition. Caution has to be taken not to develop only common integrated biology techniques, where the specificity and competitivity of the team could be questioned.

Name of the team : New targets and pharmacological tools in pancreatic pre-neoplastic lesions and cancer

Name of team leader : Mr Daniel FOURMY

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

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	3	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	6	4
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	4	2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	3
N7: Number of staff members with a HDR or a similar grade	6	4

- Assessment of work produced and scientific quality:

This team is very well known for its work on the role of gastrin, via its receptor (CCK2R), and its precursors (G-Gly, Pro-G), in the formation of preneoplastic pancreatic and colonic lesions as well as in tumoral progression. The data produced over the past 4 years are considerable and various.

The team showed the role of amidated gastrin and CCK2R in the development of pancreatic cancer, alteration of expression of PFT1a transcription factor in pancreatic cancer in parallel with acino-ductal transdifferentiation, the role of apelin in tumour neoangiogenesis and the role of gastrin precursors in colorectal cancers. All these studies allowed this team to become expert in pre-clinical murine models (KRasG12D) of pancreatic cancer and laser-captured microdissection. The team has provided important data to better understand tumour initiation, tumour progression as well as tumour behaviour and its environment (neoangiogenesis).

The team has published over the past four years **28 main publications**, 7 joint publications and 13 independent publications by team members for a total of 48 publications. The quality of the publications is very good (J Biol Chem, Endocrinol) to good (Int J cancer, BBA, BBRC). The ratio publications/researchers is however low and the quantity seems to decrease.

- Assessment of the influence, appeal and integration of the team or the project in its environment:

The PI and researchers of the team have been regularly invited as speakers in national and international meetings. The team includes two post-doctoral fellows, another one should be recruited.

The team has regularly obtained funding from caritative cancer associations (ARC, LNCC, FRM), regional institution (région Midi-Pyrénées) and from national (ANR) and European research funding agencies. It is also supported by pharmaceutical companies through partnerships with Inserm-transfert.

Active collaborations exist with other teams of CRCT and external teams at both national (Marseille, Beaujon, Strasbourg) and international (Berne) levels.

The team has developed stable relationships with two pharmaceutical companies (Rotta Pharma Italy, GSK in negociation) with the aim to develop new drugs and biomarkers and patents are in progress.

- Assessment of the strategy, governance and life of the team or project:

The team participates every year to French congresses on intestinal epithelial cell biology (CECED) and French pancreatic club (CFP) and international meetings to present their work. PI is a consultant for 2 pharmaceutical companies. Two permanent researchers of the team are members of Club Français du pancréas steering committee and one is member of the council of the European Pancreatic Club. The team will organize in 2010 the next international conference on gastrin and the 1st on apelin. As the team is developing translational research, the networking with clinician is in progress.

Using genomics, molecular signatures will be established at the different stages of the disease in order to identify new early markers. Development of new ligands and aptamers should also be done in collaboration with private companies and give a good opportunity for the team to patent these molecules.

Permanent investigators in the team are involved in teaching. Master and PhD students are regularly formed in the team with an excellent employment rate of these students.

- Project assessment:

The project is the continuation of the previous research led by this group. Using genomics, molecular signatures will be established at the different stages of the disease in order to identify new early markers. Development of new ligands and aptamers should also be done in collaboration with private companies and give a good opportunity to the team to patent these molecules.

The team is composed of several researchers leading each theme so the aims should be reached. However, the risk is that too many directions are followed and focus on one or two themes may reveal positive in terms of increasing the level of publications and the development of efficient private partnerships.

The project is quite original and the risk is high as several animal models have to be developed in the coming years.

- Conclusion:

  - Opinion:

This team is a large one with 4 full-time researchers and one clinician. The organization of the different projects between researchers may have to be reconsidered to fully optimize data collection and publications. Scientific priorities may have to be identified in order to get stronger visibility.

- Strengths and opportunities:
  - The team has developed strong and recognized expertise in animal models, laser-microdissection of PanINs, proteomics and genomics.
  - The team presents an innovative project which includes transfer and valorisation (drug design with pharmaceutical companies).
  - Active collaboration with pharmaceutical companies has been established.
- Weaknesses and threats:
  - The ratio publications/researchers remains low and the impact factor of reviews is also average.
  - The large amount of animal models to be developed may keep the team away from publishing for several more years. The team may be careful as to publish from the other themes developed.

- Recommendations:

The team has to increase level and amount of publications, to develop international collaborations and networking. A reorganization of the team may have to be discussed as it will evolve in the coming years so that the size fits the scientific output. The team should be careful as to stay independent from pharmaceutical companies it collaborates with. The apelin group has to be reinforced by one researcher recruitment, if this theme is maintained.

Name of the team : Tumor radioresistance, from signalling pathways to therapy

Name of team leaders : Mrs Elizabeth COHEN – Mr Jonathan MOYAL

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

	In the report	In the project
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	2	2
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)	5	5
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	3	3
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	1
N7: Number of staff members with a HDR or a similar grade	3	3

- Appreciation on the results:

The team developed an original, translational research in radiotherapy. The type of research is experimental, and applicated. It aims at translating experimental results obtained in the current laboratory (Inserm U 563) into preclinical data and into clinical trials. It belongs to the field of radiosensitization of tumors. The quality of the approach is remarkable in that the concepts that have been generated within the laboratory as a result of a fundamental program, have already been translated into high quality clinical research. Also, this has already led to the identification of new predictors of radioresistance.

Specifically, the team has identified several molecular mechanisms involved in the radioresistance of tumor cells. It has made the link with secondary changes occurring in the tumor microenvironment like angiogenesis and hypoxia. It has individualized molecular changes (overexpression of adhesion molecules as integrins, of growth factors as FGF-2) on the basis of the observation of patients (analysis of predictive factors of radioresistance in biopsies of patients). Using rodents models of glioblastoma (orthotopically xenografted tumors) the team has carried out studies with biological modifyers (farnesyltransferase inhibitors) to evaluate the in vivo relevance of their findings. They have extended their results to other molecular pathways (avb3/avb5 integrins/FAK/RhoB), and demonstrated the clinical relevance by showing an association between the radiosensitivity of the tumor of patients and the level of expression of these molecules thus individualizing original tumor indicators of radiosensitivity.

On the basis of preclinical studies and clinical observations, the team conducted several early phase clinical trials of radiosentitization of glioblastoma and also lung cancer by inhibition of these pathways, some of them already published, other going-on.

The impact of the results is potentially high, in that very few radiosensitizer have been available or are currently into development.

The number and quality of publications are quite good, with 9 main publications including 3 papers in good journals (2 Cancer Res, 1 Cell Death Differ). The team leader is the last author of the two Cancer Res. published in 2009. In addition, there are 3 joint publications in good journals and 15 clinical publications by other team members. Only one student is currently beginning a PhD.

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

The proposed team leader has a wide national and international scientific recognition. This is highlighted by invitations of the PI as speaker at the ECCO meeting in Berlin (2009), at ICTR 2009 in Geneva, and at 3 other international meetings. The PI is the co-organizer of the next session of an international meeting on translational research in radiotherapy, to be held in the near future.

A researcher with teaching duties has joined the team. Three post-docs are already involved in the team and a new post doctoral student is expected to arrive shortly.

The team has been succesfull in obtaining competitive fundings from multiple sources. These include ANR (740 k€), INCa (170 k€), Régions Midi-Pyrénées, Fondation InaBioSanté (264 k€); associations such as ARC, Ligue Contre le Cancer. The group is also specifically supported by the Institut Claudius Regaud. It has relationships with the pharma industry, as shown by its succesfull application to ANR for a jointed grant with Sanofi-Aventis Toulouse and its multiple contracts with pharmas.

Overall, there is no doubt that the proposed team will be able to generate appropriate funding for its projects.

The development of contrast agents for MRI, to visualize with nanoparticules, radioresistant tumor cells on the basis of the targeting of FGF-2 receptors or avb3/avb5 integrins has led to a stable collaboration with a laboratory (LPCNO) at INSA in Toulouse.

- Appreciation on the strategy, governance and life of the team:

One of the strength of the scientific strategy is the translation of observational data extracted from clinical practice into scientific knowledge through the use of experimental systems both in vitro and in vivo. Such strategy has been able to translate some results back to the clinic by designing and carrying out 3 clinical trials.

The team's organization fits optimally with the project by taking into account the transversality of the members' expertise: clinical care, access to the cancer centre resources (biopsies), and technical platforms. The previous performance of the members assess that the team in the proposed configuration has the ability to reach its objectives.

The governance of the group emerges adequate, with the size and the position of the group within the research centre and clinic department. The initiative of emerging as an independent team with a well focused and defined project is a positive risk. The PI has structured a local network of laboratories in Toulouse, involved in biological aspects of improvement of radiation therapy or imaging. She is the coordinator of this network. The PI, along with 3 other teaching researchers of the team, is involved or responsible of several teaching formations for students at the undergraduate or master levels, in scientific formations or medical students (2e and 3rd cycles). They also belong to scientific committees, and held responsibilities at the university or at the faculty of medicine. Finally, the PI is one of the 6 scientific vice-directors of the CRCT.

- Appreciation on the project:

The project belongs both to fundamental and applied research. It aims at getting new insights into mechanisms controlling the sensitivity of tissues to radiations, along the lines previously developed. The other goal is to translate the results to radiation therapy. The strategy involves validation steps of the identified targets based on their study as potential predictive factors of clinical response to radiotherapy, and early phase clinical trials.

This is a long term project perfectly relevant, where each step prepares the ground for the following. The feasability is elevated, as can be judged by the ability of the team to carry out succesfully such a research in the past. The project is original. Few teams around the world are able to carry out such a translational research with a productive fundamental part and a direct translation from patients to cognition and from fundamental results to clinical applications, both in terms of prediction, imaging and therapeutic improvements. The risk taken is elevated, but diluted into the multiplicity of scientific spin-offs. There is an adequate allocation of resources, both in terms of access to technical facilities or clinical wards. There is adequate funding of the projects. The PI has experience of the relationship with the pharma industry.

- Conclusion:

  - Overall appreciation :

A highly interesting ambitious project is carried out by an homogeneous team characterized by its overlaping and complementary experience, and success in previous results as a consequence of an adapted research strategy. The project associates high level fundamental research and efficient translation to the clinic. This is further supported by a complete fit between an appropriate scientific and medical environment, with access to the technical plateforms and clinical facilities.

  - Strengths and opportunities :
    - The team members, and specifically the PI, have translational scientific and medical culture and experience.
    - Appropriate logistics are used with high quality facilities.
    - The previous research strategy has been efficacious.
    - Quality of the collaborations, specifically with pathologists, will benefit of the Research Center organisation.
    - Abundant and adequate funding could be collected.
  - Weaknesses and threats :
    - Few collaborations with foreign teams.
    - The team has no full time researcher.
    - High rate publications are lacking.
  - Recommendations :

The team should maintain strong relationships with the fundamental research teams. The quality of the research would help the PI to recruite full time researcher with a permanent position. An adequate growth of the team will help the PI to propose publications in the top ten journals more in adequation with the financial supports obtained until now.

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

Team 1: CDK Inhibitors in Tumor Suppression & Oncogenesis

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

Team 2: DNA Replication & Genetic Stability in Cancers

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

Team 3: GTPases in Tumor Progression

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

Team 4: Sphingolipids, Cell death and Tumor Progression

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

Team 5: (Lymph)angiogenesis, translational control and gene

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

Team 6: Tumor angiogenesis and control of gene expression

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

Team 7: PI3K-signaling and translational control in pancreatic and pituitary tumors

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

Team 8: Gastrin precursors: functions and therapeutic perspectives in gastrointestinal cancers

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

Team 9: Molecular genetics in hematopoietic tumors

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

Team 10: Signaling, Cell cycle and Therapeutics in Myeloid malignancies

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

Team 11: Therapeutic immunotargeting of B-cell tumors

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

Team 12: Markers and targets for digestive cancer biotherapy

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

Team 13: Individualization of anti cancer treatments

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

Team 14: New targets and pharmacological tools in pancreatic pre-neoplastic lesions and cancer

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

Team 15: Tumor radioresistance, from signalling pathways to therapy

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

Université Paul Sabatier
TOULOUSE III

Direction de la Recherche

Toulouse, le 16 mars 2010

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Le Président

au

Président du comité d'experts de l'AERES

Objet : Observations de portée générale sur le rapport d'évaluation de l'unité **« Centre de Recherches en Cancérologie de Toulouse » - CRCT -** UMR en création portée par **Jean Jacques FOURNIE**

Monsieur le Président,

Nous remercions vivement les experts de l'AERES pour leur travail d'évaluation de notre projet, le **Centre de Recherche en Cancérologie de Toulouse** et nous nous réjouissons de l'évaluation globalement très positive du centre et de ses équipes constituantes.

La direction du projet et l'ensemble des chefs d'équipes ont lu avec attention le rapport du comité d'experts et pris bonne note des suggestions constructives y figurant. Nous approuvons le volet général de ce rapport. Par conséquent, le Centre de Recherche en Cancérologie de Toulouse s'appuiera sur les jugements scientifiques et recommandations stratégiques formulés par l'AERES pour se développer durant les quatre prochaines années. Conformément à ces suggestions et pour renforcer les liens CRCT-CUC, notre équipe 4.2 (J.P. Delord) quitte donc le projet CRCT pour demander sa création en tant qu'unité de recherche translationnelle au sein de la Clinique Universitaire du Cancer. La présence sur site de cette équipe de recherche préclinique et clinique en pharmacologie des traitements anticancéreux est en effet absolument indispensable à l'objectif du traitement personnalisé qu'ambitionne le Canceropôle de Toulouse et dynamisera les liens entre nos deux établissements.

Hormis ce principal changement et quelques informations complémentaires (en anglais, page suivante), le volet équipe du rapport est approuvé par les chefs d'équipe et n'appelle aucune autre remarque.

Je vous prie d'agréer, Monsieur le Président, l'expression de ma sincère considération

Jean Jacques FOURNIE

Supplementary Informations for AERES report on CRCT teams

-Team 1.1 is a new CRCT junior group recently awarded with ATIP-Plus. Its current geographical localization issue will be solved within the next few months by the CRCT direction and hosting institutions (INSERM, CNRS, Univ. Toulouse 3). This group has 3 manuscripts currently submitted on its highly promising project.

-Team 2.2 is presently reinforced by B. Garmy-Susini who currently applies for CR1 2010 positions at INSERM and CNRS. To reach its new endeavours, this group not only allies competences on both translational control of gene expression and lymphangiogenesis, uses fully validated tools(LYVE-1, Prox-1 and podoplanin are lymphatic vessel-specific markers, *Wigle etal.,1999, Wicki etal.,2006*), but also collaborates with P. Carmeliet, one of the most outstanding scientists in the field, with two grant applications pending at INCA (preselected) and ANR.

-Team 2.3 actually established not yet visible but highly effective international collaborations: with S. Teshima-Kondo (Japan) on VEGF expression (a collaborative paper currently submitted to Nature Medicine) with G. Melillo and G. Semenza (USA) on HIF-1□; with P. Krejci (Csech Republic) and D. Wilcox (USA) on FGF-2. They also plan to promote an emerging group within the next 4 years.

-Team 2.5 is a new CRCT junior group able to rapidly increase its publications in high-ranking journals, as they very recently *1°)* succeeded in identifying the progastrin receptor and its novel mechanism of action; *2°)* confirmed progastrin as prognostic factor for colon cancer recurrence; 3°) now assess therapeutic activity of aptamers to progastrin in colon cancer. So their highly valuable tools are now considered by INSERM Transfert.

-Team 4.1 has all skills and tools to find prognostic and surrogate markers on different cancer types. So the KLF6 SV2 subproject will be stopped if not a reliable marker for hepatocellular carcinoma. Since their scientific interactions with other CRCT teams will create a very competitive "pancreatic cancer" pole in France, these groups started sharing resources, models, projects and will have joint lab meetings in this aim.

-Team 4.2 is one of the very few research units in the world that are dedicated to pre-clinical and clinical assessment of cancer treatment pharmacology. Its presence on the Toulouse's global project site is therefore absolutely required to its fully integrated "bench to bedside" philosophy. Since AERES recommended its implementation as on-site translational research laboratory rather than as an CRCT's INSERM team, we changed our initial plans accordingly. These changes are:
-former Team 4.2 quits the CRCT project to join a distinct project in the CUC
-former Team 4.2 will ask University of Toulouse-3 to be created as a new Translational Research Unit in the new Centre d'Investigations Cliniques of the CUC.
-former Team 4.2 will examplify the CRCT-CUC links by collaborating with the CRCT teams.

-Team 4.3 will comprise 4 full-time researchers and not 6 full-time researchers as stated by the AERES report. They recently produced a large amount of data to be published in 2010: two new papers have yet been accepted (Mol Pharmacol, Int J Cancer), eight manuscripts are in preparation and the discovery of an apelin receptor antagonist is currently undergoing patenting.

-Team 4.4 is a new CRCT junior group which recently integrated two European clusters of basic and clinical research applying for the IMI and SUDOE fundings. This team will not only attract a full-time researcher (contacts taken) but they will also present N. Skuli, currently post-doc fellow investigating hypoxia in stem cells (USA) for CR2 position at INSERM.

UNIVERSITE PAUL SABATIER

Gilles FOURTANIER

Inserm

Unité 563
Centre de Physiopathologie de
Toulouse Purpan

Toulouse , le 09/03/10

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Objet : Observations de portée générale sur le rapport d'évaluation de l'unité
Centre de Recherches en Cancérologie de Toulouse
UMR en création portée par **Jean Jacques Fournié**

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