Institut de physiologie et biologie cellulaires

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Institut de Physiologie et Biologie Cellulaires

From the

University of Poitiers

CNRS

March 2011

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

Section des Unités de recherche

AERES report on the research unit

Institut de Physiologie et Biologie Cellulaires

From the

University of Poitiers

CNRS

Le Président de l'AERES

Didier Houssin

Section des unités de recherche

Le Directeur

Pierre Glorieux

March 2011

Research Unit

Name of the research unit : Institut de Physiologie et Biologie Cellulaires

Requested label : UMR CNRS

N° in the case of renewal : UMR 6187

Name of the director : M. Frédéric BECQ

Members of the review committee

Committee chairman

Mrs. Cécile GAUTHIER-ROUVIERE, Université de Montpellier 2, Montpellier

Other committee members

Mr. Jean CARTAUD, Université Paris 7, Paris

Mr. Frédéric DARDEL, Université Paris 5, Paris

Mrs. Véronique DELMAS, Institut Curie, Orsay

Mr. Jean Pierre SAVINEAU, Université Bordeaux 2, CNU representative

Mr. Frédéric BOUILLAUD, Université Paris 5, Paris, CoNRS representative

Observers

AERES scientific advisor

Mrs. Catherine DARGEMONT

University, School and Research Organization representatives

Report

1 • Introduction

- Date and execution of the visit

The visit was held in the building of the "Institut de Physiologie et de Biologie Cellulaires" (IPBC). The visit started on March 9th at 10am and was completed on March 10th at 6pm. The whole committee listened to the presentations by the Director and the 3 team leaders. Separate sub-groups of the visiting committee also discussed with the different personnel categories (researchers, technical personnel, PhD students and Post doc). A meeting with the director and then with University and CHU representatives were held. No representative from INSB CNRS was present. The committee had closed-door meetings for organization of the visit and discussions. This visit had been carefully prepared by the Director and all IPBC members.

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

IPBC is a CNRS unit (UMR6187) of the Institute of the Biological Sciences (INSB). IPBC is in a single building with a working surface of 6699 m2 located on the campus of the faculty of Sciences of the University of Poitiers. IPBC is the largest laboratory in the field of biological sciences and health in the Region Poitou-Charentes-Limousin and it is highly connected with the University of Poitiers and the CHU La Milétrie. IPBC assembles about 110 people.

IPBC has a good expertise in the field of physiology and pharmacology of ionic channels, intercellular communication mediated by GAP junctions or by soluble factors of the vitamin K-dependent protein familly, calcium and Rho GTPases mediated signalling patways. IPBC is also actively engaged in the study of the cellular and molecular basis of pathologies such as cystis fibrosis, cardiac arrhythmias, muscular myopathies, leukemia, neuroblastomas and glioblastomas. The teams show a strong translational activity, which in the reviewed period led to a total of 10 patents.

- Management team

The current management team includes the Director and an administrative assistant who ensures effective organization and financial administration of the IPBC. The management team for 2012-2016 will include a Deputy Director.
Each month a directive committee consisting in the director, deputy director, the three team leaders and project leaders discuss the scientific organization and strategy for the laboratory. A laboratory council also meets once a month.
A health and safety committee has been held as well as a platform committee to coordinate the financial management and the functional organization of the six platforms created.

The committee recognizes the major contribution and efforts made by the current Director to reorganize the unit and better structure IPBC in view of the future contract (2012-2016).

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

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	39	44
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	9	6
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	4	5
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	23,30	24,30
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	3	0,70
N6: Number of Ph.D. students (Form 2.7 of the application file)	54	?
N7: Number of staff members with a HDR or a similar grade	33	34

2 • Overall appreciation on the research unit

• Summary

The IPBC will be reorganized around three teams which creates a new dynamics for this institute and have strong potential for collaborative synergies. IPBC covers broad scientific topics that extend beyond basic research by developing several initiatives of translational research and research valorisation. Beyond this apparent heterogeneity lies, however, a community of concepts and technical approaches, including molecular mechanisms of human pathologies (cystic fibrosis, myopathies, cardiopathies and cancers) with a special interest for the role of ionic chanels and intercellular communications. The IPBC succeeds in attracting scientists from the local environment : 1) a relatively large number of clinicians joined the unit to support the approaches dedicated to cancer research 2) a group from Tours will reinforce the field of ionic chanels 3) the merge of scientists of the past IPBC with newcomers leads to propose interesting projects on lipid droplets.

Overall, the research carried out at the IPBC can be qualified as medium to good. The committee noticed a substantial heterogeneity in the performance and the quality of the research of the various groups. The committee was unanimous that given the projects and the expertise of most groups, the scientific production should increase further in quality during the next five years period in order to remain internationally competitive.

IPBC is the largest public research laboratory in the field of biological sciences and health in the region Poitou-Charentes and it ensures the responsabilities linked to this by playing an important role in promoting valorisation and science teaching. 27 IPBC members have teaching responsibilities at the different academic levels of education (Bachelor and Master).

The Institute has organized and it is still operating several common services and platforms that seem to function satisfactorily, at least for those already running.

Discussion with tenured staff, technical and administrative staff and doctoral students revealed a large degree of cohesion and interaction within these groups and a general contentment in the way the Institute functions.

• Strengths and opportunities

IPBC is the most important research laboratory in the field of biological sciences and health in Poiters as well as in the Region Poitou-Charentes-Limousin and it is highly connected with the University of Poitiers and the CHU La Milétrie. An important strength of the research unit as a whole is its relationships with local authorities which guarantee a significant support from both University of Poitiers and the CHU.

Importantly, practical issues concerning the connections with the CHU and with the unit from Tours were raised during the visit. The answers were convincing : The medical analyses laboratories are located within the same building, the quality of connection and high commitment of people from Tours was confirmed by the meeting with university (including from Tours) and CHU representatives. Consequently, the objections initially raised by the committee with regard to these practical issues have been largely ironed out.

It is important to notice that IPBC members have an enormous involvement in teaching and therefore they are very well supported by the Universities. IPBC efficiently attracts PhD students, who recognize the IPBC as an excellent place for training.

The Director is dynamic and personally has a true international scientific recognition in his field of research (study of CFTR protein). He has made major efforts to restructure the research unit. When he started his leadership the unit was splitted in eight groups, which was reduced to five (including an INSERM « avenir »). The present project has reduced the number of groups to three, which guarantees groups with a stronger internal structure. Moreover, the director has been able to set up or reinforce facilities (Imaging and screening) to assist the research in the institute. Other facilities (proteomics, genomics, bioinformatics, animal surgery) are currently being set up. These facilities represent major tools for most of the current teams inside IPBC and offer services to the external communauty.

The IPBC has good local opportunities for interdisciplinary and translational research, for collaboration with the local hospital area to obtain relevant biological samples and informations. The IPBC has an important technology transfer activity leading to patents, one license and one clinical assay.

A member of the IPBC has set-up a regional council for cancer research, which allowed the connection with clinicians and favored the access to human biological samples.

The committee was convinced that people were happy to work in the unit and appreciated the supportive atmosphere and the strong emphasis on training. Students have the opportunity to present their work at national or international meetings.

Members of the unit play active roles in local and national committees and editorial boards. Some members of the IPBC have developed international collaborations (USA, Canada, Brazil, Liban). A Marie Curie fellowship has been obtained during the previous period.

There is a strong tradition of internal collaborations which reinforce and synergize the local expertise. This is a clear added value.

- Weaknesses and threats

There was a general consensus among the experts to notice a certain degree of self-effacement: i.e., few foreign post-doctoral trainees, limited attendance of the PIs and their younger colleagues to international meetings, a limited number of papers published in journals of broad audience and high impact factor. Some teams are doing better than others in this regard, but globally there is ample space for improvement of these items, and for induction of a virtuous circle that would lead to attract young investigators from all horizons.

The number of full time researchers is low since most of the IPBC members have teaching duties. There were few new recruitments over the past years. In this context, the committee noted the absence of open calls for the recruitment of new teams. This hinders promoting the national and international visibility and recognition of the IPBC.

A difficulty of assessing the general scientific level is the presence of some heterogeneity inside large teams. This was presented in some cases as the willingness to examine the proposed subjects from basic science to bedside (or the opposite). Nevertheless, the committee noticed that it led to include ongoing projects poorly related to the main themes of the team leader. This particular arrangement presents the risk of a dilution of forces and resources, and to reduce competitiveness of teams for funding and publications.

While the number of publications is high, the international recognition of some authors is probably not as good as it should be. This constitutes a threat because application of the « standards of excellence » as presently thought would jeopardize the unit, while its importance both in term of local policy and in terms of originality (relationships with chemists, applications, cutting edge projects proposed) deserves the highest consideration.

The current project also shows a significant emphasis on connecting their current biological projects to pharmacological and medicinal chemistry applications, for instance via drug-screening programs. This in itself is very positive, but care should be taken to secure collaborations and appropriate funding to make this whole endeavour feasible. Hit-to-lead improvement is a difficult track, which requires a lot of workforce and solid partnerships with expert medicinal chemists groups.

- Recommendations to the head of the research unit

The committee recommends that maximum efforts be made at all levels, particularly the Direction and PIs, to improve the visibility of IPBC outside. This may involve several tools:

The IPBC should try to attract new researchers, to promote new teams arrival through AVENIR/ATIP program or other attractive packages.

They have to promote a dynamic policy for recruiting workers on contracts (post-docs).

They should pursue the restructuration effort to focalize on the most promising projects in order to get better ressources.

The committee strongly advises scientists to remain focused on their most promising research projects and also add more mechanistic studies which should help in increasing quality of the journals that they publish in.

- Production results

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

A1: Number of permanent researchers with or without teaching duties (recorded in N1 and N2) who are active in research	44
A2: Number of other researchers (recorded in N3, N4 and N5) who are active in research	
A3: Ratio of members who are active in research among permanent researchers [(A1)/(N1 + N2)]	0,91
A4: Number of HDR granted during the past 4 years	9
A5: Number of PhD granted during the past 4 years	35

3 • Specific comments on the research unit

- Appreciation on the results

The relevance and the originality of the research are generally good, but not outstanding compared to the international level. While some groups are at the international standard, others experience some difficulties to reach a sufficient level of visibility and originality. The efficient collaborations with chemists as well as between biologists and clinicians were highly appreciated by the committee, and the developments of these collaborations are strongly encouraged.

Whereas the quantity of publications is high, their quality in general are not very good. The committee encourages team leaders to be more ambitious in their publication strategy.

Some PIs do not have enough international visibility since they are rarely invited to international meetings. The fact that the lab produces PhD theses was well appreciated. IPBC efficiently contributes to research training in Poitiers with an average of 4 to 5 PhD and many master degree students coming each year in the laboratoy.

On the research valorization side, several teams have filed patents. One has lead to a license (CNRS/Actelion Pharmaceuticals) and to phase 2 clinical trials, which is very positive.

IPBC benefits from an important and regular support on behalf of the University of Poitiers and the Region Poitou-Charentes-Limousin in particular in terms of funds and technicians' positions.

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

IPBC has a good national visibility as demonstrated by their ability to regularly raise funds from local and national charities (AFM, VLM, Mucovie, ABCF, Ligue contre le Cancer) and also from the national research agency ANR (2010-2012). Two teams are doing better in this regard. Funds were also obtained from Actelion Pharmaceuticals and Laboratoire Servier. The committee noticed a good integration into regional and national networks. Thus the visibility of IPBC at those levels is very good. A member of the IPBC has set-up a regional council for cancer research (GPRC) which allows the connection with clinicians and favours access to human biological samples. One drug (Miglustat) developped at IPBC leads to a licence (CNRS/Actelion Pharmaceuticals) and to phase 2 clinical trials.

From an international point of view, IPBC has a rather medium visibility. Some teams have ongoing international or european collaborations but no european or international grants have been obtained except a Marie Curie fellowship for a two-years post-doc position. Members of the institute participate to the EUROCARE network. Some members of the unit, especially the director, are regularly invited to national and international conferences. Whereas IPBC attracts many PhD students from Poitiers and abroad (20-25% of the Ph D student in biology granted by the government in this region), there is a clear deficiency in the recruitment of post-docs and young scientists. This might be attributed to the relative limited international visibility of IPBC. It should be mentioned that this is also

likely to reflect a regional problem independent from the intrinsic qualities of the unit as it appears reasonable to assume that scientists from abroad have a modest drive towards such a relatively small city in France.

- Appreciation on the strategy, management and life of the research unit

The general organization of the research unit relies on fully independent research teams (with collaborations between team members), shared core facilities and administrative service. The quality and organization of the governance of IPBC was considered to be good. In its overall description (both of past or project) the written report and presentations showed a realistic and reactive point of view. This might well be ascribed to the dynamism of the director, which constitutes a strength for the success of the future unit.

The action of the Director has been efficient in connecting the activity of the IPBC to the local tissue. The connection with the University of Poitiers is excellent. The positives outcomes of this strong interaction are the financial and technical supports from the university and the attractiveness of IPBC for PhD students, but its drawback is the heavy teaching load for IPBC members. Solutions are envisaged to alleviate the teaching load when requested.

The connection with the CHU and the School of Medecine is also excellent and again financial and technical supports from the CHU have been noticed.

IPBC is a major actor in the SFR project which aims to structure the « Biologie Santé » field in Poitiers.

The Policy of publication had the advantage to allow Ph D students and young tenured scientists to appear in leading positions (first, last). This authorizes the rising of future team leaders."

- Appreciation on the project

The proposed project, while in continuity with the activity during the previous period, shows a profound reorganization of the unit in three teams. The venue of two new groups, one from Tours and one from Poitiers appears as a good strategic choice. From the past records it is expected that the experience of team members will ensure expertise on specific domains amenable to grant applications. The link with chemists is to be mentionned as a very positive point for this unit, but deserves to be strengthened by appropriate co-funding.

A possible threat is that the unit could drift more and more toward application-driven research and progressively looses ground on basic science approaches. This balance will depend on how the director and group leaders will deal with this issue and find means to support « basic science », which is sometimes difficult, but creates the grounds for future progresses. In this respect the arrival of the group working on lipid droplet appears as a positive signal.

While the number of publications is high the international recognition of some authors is probably not as high as it should be. This constitutes a threat because application of the « standards of excellence » as presently thought would jeopardize the unit while its importance both in term of local policy and in terms of originality (relationships with chemists, applications...) deserves consideration and support.

4 • Appreciation team by team and/or project by project

4 - 1

Team : Physiologie, pathologie et pharmacologie des canaux ioniques
Leader: C. COGNARD

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

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	10	20
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)	0	2
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)	0	0,60
N6: Number of Ph.D. students (Form 2.7 of the application file)	21	6
N7: Number of staff members with a HDR or a similar grade	8	14

- Appreciation on the results :
- Relevance and originality of the research, quality and impact of the results

Axe1: The team has a longstanding experience in the study of chloride channels, in particular the CFTR , a Cl- channel, the mutation of which causes cystic fibrosis (also called mucoviscidosis). In the last few years, the team has contributed to the identification of several other key residues in CFTR, important for its pharmacology, has discovered several activatory or inhibitory molecules, and most importantly, has unveiled the mechanisms of retention of a misfolded mutant of the CFTR protein found in the majority of the patients. This latter discovery was the rationale for the identification of compounds that regulate the retention and compensate for the mutation. One of these drugs (Miglustat) led to a technology transfert (licence CNRS/Actelion Pharmaceuticals) and to phase 2 clinical trials.

Axe2: This medical genetic team already part of the IPBC will join the Axe 1 for the new project. In the last years, the team has, in close relationship with the molecular genetic laboratory of the CHU in Poitiers, developed a program in direct relation with the Cystic Fibrosis group. In particular, the group deciphered some new facets of CFTR trafficking.

Axe3: This group has a strong reputation in the study of calcium deregulation in dystrophin-deficient myocytes in Duchenne myopathy. In particular, the group showed that in the absence of dystrophin abnormal Calcium homeostasis in the muscle cells are implicated in the pathology, probably through Ca++ activated proteases.

Axe4: The group is primarely interested in the pharmacological study of ion channels considered as potential proarhythmic targets in remodeling of cardiac tissue. During the past years, the group identified the pacemaker channel HCN as the target of ivrabadine, a heart rate-lowering drug. The group also showed selective blocking of IKs in the prolongation of the QT interval in patients treated with the anti tumor drug doxorubicin.

Axe5 : The team located at the University of Tours is interested in the genesis of ectopic activity of pulmonary veins (PVs) cardiomyocytes responsible for atrial fibrillation (AF). The group has shown that at variance with atrial cardiomyocytes, PVs cardiomyocytes can generate a catecholamine-induced automatic activity that require the stimulation of both ¤ and ¤ adrenergic receptors. In the absence of efficient treatment for AF, these observations are important for future investigation.

The overall scientific production of the team is good with a high number of publications but too many are published in specialized journals. . Given the « axe » substructure of this team, a breakdown of the publications over the 2006-2010 period is given below:

- Axe1 has published 50 papers, 30 of which with first or last authorship, among which 1 JBC, 1 Mol Biol Cell, 2 Traffic, 2 Am J Respir Cell Mol Biol, 3 J Pharmacol Exp Therap.
- Axe2 has published 35 papers, 10 of which with first or last authorship, among which 2 Exp Cell Res.
- Axe3 has published 20 papers, 10 of which with first or last authorship, among which 2 FASEB J, 1 JBC, 1 Am J Physiol Cell Physiol, 2 J Gen Physiol.
- Axe4 has published 25 papers, 17 of which with first or last authorship, among which 1 Br J Pharmacol, 2 BBA, 1 J Neurophysiol, 2 J Cardiovasc Electrophysiol.
- Axe5 has published 25 papers, 12 of which with first or last authorship, among which 2 Br J Pharmacol, 1 J Med Chem, 1 Am J Physiol Cell Physiol, 1 Am J Physiol Heart Cell Physiol.

The team has several publications relative to collaborative works with foreign (through EUROCARE, USA) and local (IPBC) partners. The team is also actively involved in translational research, especially in clinical trials of compounds Licensing Miglustat and two phase II clinical trials (2008 & 2010).

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

The team has been successful to obtain fundings from a variety of institutions (Mucovie, VLM, ABCF, LNCC, Region Poitou-Charentes, European FP7, AFM, ANR) in the past and also in 2010. Pharmaceutical Industry Actelion Pharmaceuticals, Laboratoire Servier PhysioStim Company, Robert-Giffard). The funding is in good adequation with the scientific projects.

Members of the team gave lectures in several national and international meetings.

Most of the staff is engaged in teaching at the University of Poitiers

4 PhD students were formed during the last contract

- Appreciation on the project

Axe1: The current project is in direct line with the previous studies on CFTR: i) use of pharmacological and siRNA strategies to study the biogenesis and the degradation of the mutated F508del-CFTR protein, ii) research of molecular partners of CFTR that could account for the impaired Ca++ homeostasis in CF cells and iii) role of CFTR mutations in the perturbation of lipid homeosatsis and ER-stress. The questions are pertinent and interesting and the expertise of the scientists involved in adequation with these aims.

Axe 2: The current project is aimed at further analysing at the molecular and cellular levels new mutations in the CFTR gene and their implication in maturation, trafficking and activity. However, an important activity of the group is the genetic of rare diseases. This part of the program seems too far from the scientific interests of team 1.

Axe 3: The current project attempts to study calcium homeostasis at micro-domain level and to identify and characterize Ca++ channels using Scanning Ion Conductance Microscopy (SICM). Complementary approaches

(immunolocalization of membrane and cytoskeletal components, expression of various isoforms of TRP channels, siRNA etc…) are also planned. The main technique (SICM) is already available on site.

Axe 4: The current project is aimed at a better understanding of the role of ionic channels in the pathophysiology of cardio-myocytes and cardiac fibroblasts. Two aspects will be analysed : i) identification of molecular mechanisms involved in activity, trafficking and expression of mutated SCN5A (Brugada syndrome) and HCN channels in sick sinus syndrome. ii) Na+/K+ channels in cardiac fibroblasts : relevance for pathological remodeling upon pathological stresses.

Axe 5: The current project will be focussed on their discovery of the catecholaminergic automatic activity (CAA) associated with PV muscle cells. The project includes i) identification of cellular mechanisms underlying CAA (receptors, ion channels, signalling pathways) in pathophysiological conditions ii) resarch for differences in contractile and electrophysiological properties of atrial and PV cardiomyocytes iii) development and transmission of automatic activity from the PVs to left atrium.

- Conclusion :

— Summary

The activity of this team is focussed on ionic channels studies in physiopathological processes. The proposed future work is a logical extension of their projects.

— Strengths and opportunities

The team 1 has a well recognized expertise in ionic channels, originally from the electrophysiological aspects but now much broader, in particular on cellular and molecular aspects. Translational research from patient diagnosis to molecular studies is well developped particularly on CFTR. The team being involved both in fundamental as well as in clinical research, the results of their research will directly benefit to patients. Clinical trials of compounds are under way.

Successful approaches that have been developed for the CFTR studies will be applied to other projects, such as the cardiologic axis. The cooperation between scientific research and clinicians is a strong point. Original approaches have been developped (such as SICM). There are important exchanges with other IPBC teams. The funding is in good adequation with the scientific projects.

— Weaknesses and threats

It appears that they are too many projects in this team.

The quality of publications is of average level and should be greatly improved

To attract postdocs and young scientists from abroad does not appear as a priority of this team.

The committee was not convinced by the coherence of the non-CFTR topics of axis 2 with the rest of the team projects.

— Recommendations

The synergy between the different axis was not always apparent and should be improved.

Mechanistic analysis using cell biology approaches, such as intracellular trafficking analysis, should be further developed. Along this line, the projects on CFTR of axis 2 should be integrated with axis 1.

Fusion of axis 5 with IPBC makes sense scientifically but geographic implantation of axis 5 in Poitiers should be progressively envisaged (recruitment of a postdoc on this axis in Poitiers).

4-2

Title of the team: Croissance, mobilité cellulaire et cancer
Leader: O. BENZAKOUR

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

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	6
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	1,5
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)	0	3
N7: Number of staff members with a HDR or a similar grade	0	4

- Appreciation on the results

During the period 2006- june 2010, people now constituting team 2 were developing three distinct projects.

Project 3 in previous team 1: Regulation of calcium channels by scaffolding proteins. Implication in muscle physiology and myopathy

The group leader was previously working on complexes formed of calcium channels and dystrophin/syntrophin molecules in the membrane of skeletal muscle cells. He was studying their function in normal and dystrophic muscles. He has also a collaboration on the role of mutants of ¤-sarcomeric actin on congenital myopathies with a group in Belgium and collaborations inside the laboratory. He has a well internationally recognized expertise in the field of calcium signalling.

During the period 2006- june 2010, he published 17 articles (8 as co-author with other groups in the laboratory), of which he is last author on 3 research articles in medium to good impact factor journals (Matrix Biology, JBC and Faseb J).

For the new contract the group leader will move to another research field, the analysis of signaling pathways (in particular calcium signaling pathways) in leukeamia with two others members of IPBC coming from the former team 2 and team 4 of the period 2006-20010.

In previous team 4: GTPases signaling and cytoskeleton dynamics in Bcr-Abl-induced leukeamia

This group found that Bcr-Abl activates both Rac1 and RhoA. He studied the effectors involved in Bcr-Abl-induced migration and identified the pathways activated downstream Rac1 and RhoA.

During the period 2006- june 2010, he published 12 articles (8 as co-author with other groups in the laboratory), of which he is last author on 2 research articles (Oncogene and Leuk. Res.)

In previous team 3: Vitamin K-dependent proteins regulate angiogenesis and tumor growth, cell proliferation and phagocytosis

The work of this group was centred on the function of Vitamin K-dependent proteins (VKDPs) which regulates blood coagulation. The research activity is focused on two VKDPs, protein S and Gas6 which interact with tyrosine kinase receptors. These proteins play a major role in the angiogenis process, in neural stem cell biology and in regulating apoptotic membranes phagocytosis.

During the period 2006- june 2010, the team published 11 articles (4 articles from the group, 4 articles in collaboration, 3 reviews) and participates to 1 patent.

Moreover, an European Marie Curie project (2009-2010) implicating a collaboration with a Russian colleague has also been developed. This project dealing with the role of VKDP in non-professional phagocytosis constitutes a link between the different groups of that team.

This group has a good publication records with articles published in good quality journals (Oncogene, Stem Cells, Faseb J, JBC) and participates to 1 patent.

Given the « axe » substructure of this team, a breakdown of the publications over the 2006-2010 period is given below :

- Axe1 has published 43 papers, 8 of which with first or last authorship, among which 1 JBC and 1 FASEB J.
- Axe2 has published 25 papers, 3 of which with first or last authorship, among which 1 Oncogene, 1 Leuk Res and 1 Blood.
- Axe3 has published 11 papers, 7 of which with first or last authorship, among which 1 Stem Cells.

7 PhD students were supervised over the past 5 years and one Marie Curie fellowship for a two years post-doc position has been obtained (2009-2010).

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

The team has been successful to obtain fundings from a variety of institutions (LNCC, Region Poitou-Charentes, European FP7, INSERM etc) in the past and also in 2010. No funding was obtained from international funding agencies. The team obtained a Marie Curie fellowship for a two years post-doc position.

Members of the team contributed to national and international meetings and have also been invited to speak at international meetings.

One group leader has a collaboration with a belgian group (universty of Ghent). A member of the team will organize, in 2011, the VIIe national meeting “Small G proteins” in Poitiers.

The projects in the team are well connected.

Five members of the team are involved in teaching. 1 PR, 1 MCU/PH and 3 MCU. The group leader of the former project 3 axis1 is also actively involved in teaching especially at the master 2 degree.

One member of team is involved in the set up of the proteomic plateform.

- ## Appreciation on the project

There are three projects proposed. Two focus on the role of two vitamin K dependent proteins (VKDP) called Gas 6 and protein S and partners of TAM receptors in neural stem cell maintenance and on phagocytosis (axe 2) and on angiogenesis (axe 3). These projects are the continuity of the data obtained during the previous quadrennial period. However it was not clear in the oral presentation how the axis 3 will be conducted.

The third project (axe 1) aims at analyzing signaling pathways (Rho GTPases, calcium) involved in migration of hematopoietic cells and leukemogenesis.

These projects are well connected. Given the expertise of the scientists involved and the technical facilities requested the projects appear realistic.

These are challenging but feasible and very interesting studies, which should be strongly supported, as the team is in an ideal position to perform this cutting edge research.

- Conclusion :

— Summary

The team 2 “Cellular growth, mobility and cancer » results from the association of scientists coming from 3 original teams of the IPBC and with interest for working scientific scopes such as, VKDP-dependent signalling in neural stem cells, phagocytosis and angiogenesis, regulation of calcium channels by scaffolding proteins cell, GTPases signalling and cytoskeleton dynamics in migration of hematopoietic cells and leukemogenesis.

The new team 2 of IPBC will be composed of 7 staff members, 2 engineer/technicians and 4 PhD and post doc students.

The research was organized in 3 projects (groups) which appear well related to each others.

— Strengths and opportunities

The thematic cohesion is convincing. The committee appreciated the dynamism and competence of the project leaders of axe 1 and 2.

Several interesting projects have reached a state where the group can publish them and two publications are currently submitted.

— Weaknesses and threats

One of the potential weaknesses is the limited size of the team compared to the large number of projects proposed.

There are several senior scientists within this team, the reason of the choice of the proposed team leader does not seem obvious and appropriate to the committee.

No Post-Docs are actually mentionned in this team.

— Recommendations

Reinforcing the human potential (with staff scientist, postdoc and predoc) of this team would improve the feasability of the projects. The granting policy should be more agressive.

The committee is less supportive on the studies on the role of VKDPs on angiogenesis and recommends to focus the research on leukeamia and regulation of neural stem cells. The team needs to focus in the future on fewer projects so that they can have a stronger impact.

4-3

Title of the team: Communication, différenciation et cancer
Leader : M. MESNIL

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

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	13	18
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	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	3
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)	16	3
N7: Number of staff members with a HDR or a similar grade	11	16

- Appreciation on the results
- Relevance and originality of the research, quality and impact of the results

The research is mainly relevant to the domain of cancer as it addresses the regulation and activity of protein controlling cellular interaction during migration and invasion. When compared to the previous unit (2006-2010) the present team appears in continuity with the original team 3 (with the same leader). However the project proposes a significant re-shaping : ancient theme 3-3 will become autonomous creating the team 2 of the present project. The merging of « old themes (3-1 and 3-4) in the new axis 1. The VIP-hedgehog theme is conserved (axe 3 in project). Two new projects are proposed : 3-2 on prostate cancer which will be mainly driven by physicians and 3-4 (see below).

Accordingly past records will be evaluated according to people involved in the project proposed.

Axis 1: "Intercellular communications and glioma progression"

From 2006, the research activity was centered on studying the role of connexin 43 (Cx43) in cell differentiation and proliferation (functional regulation of Cx43-made channels, role of Cx43 in the differentiation of osteoblasts and in cell proliferation and invasion in glioma). Since 2008 the activity of the team was more focused on the involvement of connexin 43 in tumor development.

Another group (former 3-4) focused on semaphorin 3F asking how it functions as a tumor suppressor in the lung and how it is regulated.

Axis 2: "Mechanism of prostate cancer progression" new group with a large number of newcomers (clinicians)

Participants of team 3 axis 2 presented report about candidate genes on cancer cell proliferation, with special emphasis on prostate cancer (PCa). Their attention has been attracted by estrogen related protein such as BCAR1 (breast cancer anti estrogen resistance) and members of the EGF-Receptor family. It has to be mentioned that participants of team 3 axis 2 have produced joint publications on connexin 43 with present and future team 3 axis 1.

Axis 3: « VIP-receptor system, hedgehog pathway in cancer of the nervous system» in the future project.

The work of group 3-2 deals with the biological effects of the Vasoactive Intestinal Polypeptide (VIP) receptors system in cancer cells of the nervous system, such as neuroblastoma and glioblastoma. The group demonstrated that VIP decreased the expression of MYCN, an oncogene amplified in neuroblastoma. A collaboration with chemists (University of Poitiers) led to molecules targeting the hedgehog pathway in brain tumors.

Axis 4: “Lipid droplets in differentiation & proliferation in cancer”, new project associating people from the past unit to newcomers.

The past work of the members of this team was (1) to identify mutations that affect the formation of lipid droplets in yeast and (2) to analyze the pathways for differentiation of neurons and photoreceptors in the retina using a chicken embryo model.

The overall scientific production of the team is good with a high number of publication but too many are published in specialized journals. Given the « axe » substructure of this team, a breakdown of the publications over the 2006-2010 period is given below :

- Axe1 has published 53 papers, 37 of which with first or last authorship, among which 1 Antioxidants and Redox signaling and 1 Cancer Res.
- Axe2 has published 50 papers, 29 of which with first or last authorship, among which 1 Nat Rev Cancer and 1 Lancet Oncol.
- Axe3 has published 16 papers, 14 of which with first or last authorship, among which 1 Drug Discovery today, 1 Am J Hum Genet and 1 PNAS.
- Axe4 has published 17 papers, 4 of which with first or last authorship, among which 1 Free Rad Biol Med.

The reports indicates that 9 Ph D students were involved, out of them 7 did defend their thesis during the 2006-2010 period.

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

Members of the team contributed to national and international meetings and have also been invited to speak at international meetings. From past records it is concluded that 3-1 has a long standing collaboration with the University of British Columbia and University of South Carolina including prolonged stays of scientists. 3-2 participate in wide range national networks studying the factors relevant to prostate cancer. 3-3 collaborates with UCLA Los Angeles. 3-4 has settled a collaboration with the university of Cyprus.

If we consider the amount of resources communicated to the committee, the participants to the team 3 raised 22 200 Euros in 2008, 20 000 Euros in 2009 and 40 000 Euros in 2010. This seems not sufficient in regards to the projects presented. However, this negative statement should be balanced by the fact that not all resources were listed because of the important evolution between past unit (funding finally known) and the new one with incoming people whose past/ongoing funding was not detailed.

It must be emphasized that this team (like the rest of the unit) has developed a dense network of relationships with scientists, medics, or associations on a regional basis (West of France). This includes for example the fact that scientists from this team 3 are at the origin of a local network « GPRC ».

Members of the team are involved in teaching at the university and communication to a larger audience with conferences or events. One member is responsible of the license Sciences du Vivant.

- Appreciation on the project

The project proposes a significant reshaping of the team. The past team 3 has been split with scientists creating the team 2 of the project. The merging of past themes (3-1 and 3-4) in a new 3-1 while the original 3-2 project (VIP-hedgehog) is left autonomous. Two new projects are proposed: 3-2 on prostate cancer will be mainly driven by clinicians and involves nation-wide network (cohorts) for medical research, 3-4 is a cutting edge project which was highly appreciated by the committee.

There are four projects proposed (named axes).

3-1: This project aims at analyzing the role of gap junction (connexin 43), semaphorins and neurotransmitters in glioblastoma cell migration and invasion. They observed that CX43 expression in glioma cells increases the secretion of cytokines, proteases and extracellular matrix compounds. They want to analyze the mechanisms by which this occurs and its contribution to invasion of glioma cells. In collaboration with the CHU in Poitiers they will analyze whether molecules previously identified could be markers of tumor prognosis and progression. Since serotonin

mediates GJIC, they plan to screen for serotonin expression in glioblastoma cells lines and analyze whether serotonin impacts on CX43-dependent signaling pathways. Finally, the role of SEMA3F, which interacts wit CX43 in liver cell lines and control its localization and function, will be analyzed in glioma. These projects are well connected and focused around CX43 study in glioma. This axe benefits of the presence of researchers who has a long standing experience in gap junction. Scientists with long standing experience (connexin and semaphorin) will constitute a strength for success of the project.

3-2: In the past, genes expressed in PCa having strong clinical interest have been recognized. They propose a transition towards more mechanistic studies and to analyze the function of these genes in prostate cell lines and using mouse models.

ErbB3, member of the EGF-R family, can have a nuclear localization in PCa. Targets of ErbB3 will be identified and their contribution in PCa progression analyzed.

The function of Cx34 in PCa dissemination and heterotypic communication with endothelia and osteoclasts will be analyze (synergy with axe 1).

The projects are interesting and a translational part is proposed. However the committee had the feeling that this transition towards mechanistic issues will raise practical difficulties that have been largely underestimated.

Moreover, they would depend on facilities which are not settled yet and will require a strong financial support.

3-3: The project is the continuity of the activity during the previous period. They will analyze the function of VIP in glioblastoma. In neuroblastoma cell lines, they plan to analyze the VIP receptor and the signaling pathways involved in VIP-induced MYCN decrease.

In collaboration with a chemist team in Poitiers they have developed a pro-drug derived of cyclopamine, an Hh inhibitor. They will test the efficacy of this molecule in vivo. Moreover, they will analyze the connection between VIP and Hh signaling pathways in neuroblastoma and glioblastoma.

The committee rose concerns about the small size of the group.

3-4 Starting from their original expertise: lipid metabolism/dynamics in yeast and formation of photoreceptors which requires formation of a lipid droplet, the participants aim to address the question of lipid metabolism / dynamics in relation with cancer. They will analyze the genes induced after lipid droplet formation and screen chemical molecule for their ability to interfere with this process. Identified molecules will be analyzed for their anti-tumoral activities using Pca as a model system. This team brings together people having good expertise on the various aspects of the project.

The committee appreciates this very innovative and interesting project.

- Conclusion :

— Summary

During the 2006-2010 period the team 3 “Physiopathology of cellular differentiation and communication”, merged into a single team scientists coming from three teams of the previous IPBC working in cell differentiation and cancer. In the present project the original team 3 splits into a new team 2 (see above) and a new team 3 which in addition will host two new groups: One is headed by clinicians who join the IPBC to address more mechanistic issues starting from evidences coming from human genetics and the other presents a cutting edge project on lipids born from the merging between scientist from IPBC and newcomers bringing a « yeast approach ».

The general research theme of team 3 will be more cancer oriented in the future. The team 3 was composed of 17 staff members, many of them with teaching duties, 1 Post-Doc, 4 PhD students and 2 engineers. The size of team 3 will remain constant in the future and will be composed of 20 staff members 2 engineers/techs and 2 PhD students.

— Strengths and opportunities

Expertise in the connexin field is well recognized. The axis 2 has a strong past of medically orientated activities. Axis 4 represents a risky but original and well-designed project that has been appreciated.

— Weaknesses and threats

The association of the different axes into a single large team 3 may be questioned and the organisation of staff members in the different groups of team 3 appears sometimes rather artificial and not always supported by scientific criteria.

While the past record in terms of Ph D was satisfying the project presented to us includes very few Ph D students, another weakness is the absence of Post-Docs. The team involves only 2 staff CNRS scientists (1CR and 1DR) out of 20 staff members.

The feasibility of all the projects presented remains questionable in regards of resources

— Recommendations

Prioritize the projects as a function of financial and technical feasibility.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
INSTITUT DE PHYSIOLOGIE ET BIOLOGIE CELLULAIRES	**A**	**B**	**A+**	**B**	**A**
CROISSANCE, MOBILITE CELLULAIRE ET CANCER [BECQ-BENZAKOUR]	A	B	Non noté	A	A
PHYSIOLOGIE, PATHOLOGIE ET PHARMACOLOGIE DES CANAUX IONIQUES [BECQ-COGNARD]	A	A	Non noté	B	A
COMMUNICATION, DIFFERENCIATION ET CANCER [BECQ-MESNIL]	A	B	Non noté	B	B

C1 Qualité scientifique et production

C2 Rayonnement et attractivité, intégration dans l'environnement

C3 Gouvernance et vie du laboratoire

C4 Stratégie et projet scientifique

Statistiques de notes globales par domaines scientifiques

(État au 06/05/2011)

Sciences du Vivant et Environnement

Note globale	SVE1_LS1_LS2	SVE1_LS3	SVE1_LS4	SVE1_LS5	SVE1_LS6	SVE1_LS7	SVE2 _LS3 *	SVE2_LS8 *	SVE2_LS9 *	Total
A+	7	3	1	4	7	6		2		30
A	27	1	13	20	21	26	2	12	23	145
B	6	1	6	2	8	23	3	3	6	58
C	1					4				5
Non noté	1									1
Total	**42**	**5**	**20**	**26**	**36**	**59**	**5**	**17**	**29**	**239**
A+	16,7%	60,0%	5,0%	15,4%	19,4%	10,2%		11,8%		12,6%
A	64,3%	20,0%	65,0%	76,9%	58,3%	44,1%	40,0%	70,6%	79,3%	60,7%
B	14,3%	20,0%	30,0%	7,7%	22,2%	39,0%	60,0%	17,6%	20,7%	24,3%
C	2,4%					6,8%				2,1%
Non noté	2,4%									0,4%
Total	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%	100,0%

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

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

• SVE1 Biologie, santé
- **SVE1_LS1 Biologie moléculaire, Biologie structurale, Biochimie**
- **SVE1_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes**
- **SVE1_LS3 Biologie cellulaire, Biologie du développement animal**
- **SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie**
- **SVE1_LS5 Neurosciences**
- **SVE1_LS6 Immunologie, Infectiologie**
- **SVE1_LS7 Recherche clinique, Santé publique**

• SVE2 Ecologie, environnement
- **SVE2_LS8 Evolution, Ecologie, Biologie de l'environnement**
- **SVE2_LS9 Sciences et technologies du vivant, Biotechnologie**
- **SVE2_LS3 Biologie cellulaire, Biologie du développement végétal**

Institute of Cellular Physiology and Biology (IPBC, UMR 6187); Comments and responses to AERES report.

GENERAL COMMENT

We noted with satisfaction some recognition by the committee of the effort made to organize our laboratory into three research teams, services and platforms as well as to play an important role locally both for research and for teaching.
We appreciated most of the recommendation of the committee that should help us in improving the quality of our project. Thus, we have modified our project with three major modifications. First, we fused axes 1 and 2 of team #1. Second, we changed the team leader of team #2. Third, we fused axes 1 and 3 of team #3. These rearrangements will lead to reduce the number of research topics on more focused projects. We will pay a particular attention to preserve the balance between basic science and application-driven research.

Weaknesses and Threats

While the number of publications is high, the international recognition of some authors is probably not as good as it should be. This constitutes a threat because application of the « standards of excellence » as presently thought would jeopardize the unit, while its importance both in term of local policy and in terms of originality (relationships with chemists, applications, cutting edge projects proposed) deserves the highest consideration.

The director and most leaders are very much aware of this fact. We indeed need to pay a particular attention to the quality of our publications and to encourage our leaders and young scientists to better communicate through high IF publications and conference invitation and by any means to promote our research. On the other hand, we also have to take into account the number of publications for our PhD students because national instances such as CNU 66 impose 3 publications for qualification and most universities, including our, impose at least 2 publications to validate the thesis.

Recommendations

The IPBC should try to attract new researchers, to promote new teams arrival through AVENIR/ATIP program or other attractive packages.

This has been done in 2009 by attracting a young scientist with an ATIP program. This will be done in the next coming years by attracting new researchers. We will publish in 2011 an open call to welcome a new research group on our main research topics.

RESEARCH TEAM #1

Weaknesses and Threats

The quality of publications is of average level and should be greatly improved.
To attract postdocs and young scientists from abroad does not appear as a priority of this team.

We do not think that publishing in the best journal in Physiology like *Physiological Reviews*, *Journal of Physiology*, *Journal of General Physiology*, *American Journal of Physiology* can be interpreted as of "average level" given the fact that most of our colleagues physiologists worldwide also published in such journals and it is clearly established that the quality of the research is always excellent in those journals despite the medium IF (below 5) except for Physiological Reviews (IF: 37.7).

The second sentence is neither fair nor acceptable. In particular axis one (cystic fibrosis) is regularly attracting post-doc fellows among them ANR post doc (3 in 2010-2011).

We noticed a mistake. We indicated in the Table 4.1 page 9 that team #1 hosted a total of 21 PhD students during the past contract and not 4 as indicated page 10. Many of these students came from outside of our University.

Recommendations

Mechanistic analysis using cell biology approaches, such as intracellular trafficking analysis, should be further developed. Along this line, the projects on CFTR of axis 2 should be integrated with axis 1.

We decided to follow the recommendations of the committee by fusing axes 2 with 1 into a single research axis leaded by former axis 1 leader and focused on cystic fibrosis, from genetic analysis to molecular mechanisms of CFTR function, regulation and pharmacology. Other projects will be discontinued (Charge syndrome).

RESEARCH TEAM #2

Weaknesses and Threats

There are several senior scientists within this team; the reason of the choice of the proposed team leader does not seem obvious and appropriate to the committee.

The "proposed team leader" was initially asked by members of team2, leaders of axis 1 and axis 2 and the director of the IPBC to work towards setting up a new team. The "proposed team leader" initiated and implemented within the IPBC some of the topics that are major for team 2 such as **phagocytosis and VKDP,** opened up these topics to other team members and coordinated the European project proposal "PHAGOCYTOSIS". Within the last 2 years, the "proposed team leader" has worked with other team members in obtaining funding **for each** of the projects he is involved with: Angiogenesis-tumour growth/VKDP (LNCC/ Soutien Transfer CNRS), Neural Stem Cell/VKDP (LNNC, region PC), Phagocytosis (Europe/ ACI) and was therefore best placed to apply for "équipe labellisée LNCC". Moreover, "the proposed team leader" has worked and still works with other team members for promoting their research topics: (ERC starting grant application for axis 2 topics in 2010 and a project to re-apply in 2012; proposal on endothelial cell–neural stem cell interaction for our CR CNRS candidate that was granted over 80 000 Euros fund).

The committee noticed however that other senior scientist of the team should be proposed as team leaders.

After discussion with the director of the IPBC and with the members of the new team, we decided to follow the remark of the committee and to propose the group leader of axis 1 as the new team leader. In addition, he will connect axis 1 and axis 2 projects through his expertise on cytoskeleton, calcium signalling and cell motility.

Recommendations

The committee is less supportive on the studies on the role of VKDPs on angiogenesis.

Team 2, Axis 3, is focussed on the role of VKDPs in both angiogenesis and tumour growth. This project has already lead to a patent application and has been supported by a "soutien transfer CNRS" and special funds from University of Poitiers. Following the recommendation of the committee this project will be discontinued unless it benefits from support from an industrial partner or other funding bodies.

The work on VKDP and angiogenesis is part of a European project proposal on VKDP that includes several European partners and for which the group leader is the proposed coordinator. The team considers that this topic has a great potential both for fundamental and applied research. The European network should allow the development of the project through application for grants and for post-doctoral investigators.

RESEARCH TEAM #3

Weaknesses and Threats

The association of the different axes into a single large team 3 may be questioned and the organisation of staff members in the different groups of team 3 appears sometimes rather artificial and not always supported by scientific criteria.

We understand the statement as an apparent heterogeneity of the team. To prevent such heterogeneity, the number of axes will be reduced. Axis 3 will fuse with Axis 1, which will be entitled "Cellular communication in neural cancers".

The team will then be constituted of 2 major blocks dealing with invasive or metastasizing tumours (Neural tumours: new Axis 1 and Prostate cancer: Axis 2) and interfacing each with a third axis (lipid droplets: Axis 3) studying the role of lipid droplets in cancer cell behaviour for both models (neural tumours and prostate cancer).

While the past record in terms of Ph D was satisfying the project presented to us includes very few Ph D students, another weakness is the absence of Post-Docs. The team involves only 2 staff CNRS scientists (1CR and 1DR) out of 20 staff members.

The criticism about the lack of PhD students in the project is not funded. We have indicated in the Table 4.3 page 15 that team #3 hosted a total of 16 PhD students during the past contract. When we exposed future projects to the Committee, we only mentioned the permanent staff who will lead them. However, as it was in the past, PhD students will be the active components of the projects that have been presented. In fact, a PhD position will be already granted for the emerging Axis 3 (lipid droplets) from September 2011.

Moreover, as it was presented, a particular effort will be made for attracting post-docs and new CNRS staff to the Team 3.

The feasibility of all the projects presented remains questionable in regards of resources.

As mentioned in the report by the Committee, the resources of the new Team 3 were not well estimated (Page 16; Section "Appreciation on the impact"; 2nd paragraph; last sentence). This statement was the consequence of the difficulty to estimate precisely funding from people sorting out/coming in the new Team 3. Total of our resources for last 3 years were 197 200 Euros (2008), 213 450 Euros (2009) and 123 465 Euros (2010).

Part of resources from CHU was not taken into account in those estimations as well as facilities that will be opened to people of Axis 2 (Prostate cancer) and the rest of the Team 3. Moreover the implication of members of the team in regional glioma network (Axis 1; Canceropole GO) and in national prostate pathology network (Axis 2; CeRePP) will help getting funds as it was in the past. Finally, we will take advantage of this reorganization for applying to more ambitious grant sources (ANR, ARC, etc.).

About the feasibility of the project of Axis 2, it is mentioned in the Committee report that *"the transition toward mechanistic issues will raise practical difficulties"*. In response to such a

statement, we can say that cellular models are already available in the laboratory and some animal models will be developed locally or through collaborations. Moreover, the "In vivo" platform of Canceropole GO will permit the use of the model of orthotopic xenograft for prostate cancer.

Recommendations:

Prioritize the projects as a function of financial and technical feasibility

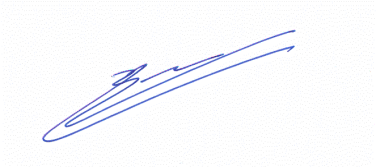
The projects will be developed according to the financial resources they will get.

Professor Frédéric Becq
Director IPBC

The University of Poitiers joins to all the observations made by the Director IPBC.

Poitiers on April 12th, 2011

The Vice-president in charge of the Research



Professor Olivier Bonneau