CRBM - Centre de recherche de biochimie macromoleculaire

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Centre de Recherche de Biochimie Macromoléculaire

From the

University of Montpellier 1

University of Montpellier 2

CNRS

May 2010

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Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

May 2010

Research Unit

Name of the research unit: Centre de Recherche de Biochimie Macromoléculaire (CRBM)

Requested label : UMR CNRS

N° in the case of renewal: 5237

Name of the director: M. Paul MANGEAT (former director) and Ms. Anne DEBANT (future director)

Members of the review committee

Chairperson

M. Stéphane NOSELLI, Université de Nice-Sophia Antipolis

Other committee members

M. John G. COLLARD, Amsterdam, The Netherlands

M. Roger GOODY, Dortmund, Germany

M. Chris J. MARSHALL, London, England

M. René H. MEDEMA, Utrecht, The Netherlands

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M. Frank UHLMANN, London, England

Mrs. Pascale DURBEC, Marseille

Mr Moshe YANIV, Paris, France

Committee members nomminated by staff evaluation committees (CNU, CoNRS, INSERM and INRA CSS....)

M. Francis CASTETS, CoNRS representative

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M. Christian PERIGAUD, Université Montpellier 2

Research Organization representatives

Jocelyn MERE, Service Partenariat Valorisation, Délégation Languedoc-Roussillon

Report

1 • Introduction

- Date and execution of the visit

The visit took place from January 6th (12h30) to January 8th (14h30) at the Centre de Recherche en Biologie Macromoléculaire (CRBM), Campus CNRS, route de Mende in Montpellier. The whole committee was present and listened to the public presentations by current and future Directors, the scientific presentations by 20 group leaders and the presentations of 3 platforms by their representative heads. Separate sub-groups of the visting committee also discussed general matters with the personnel (Students/post-docs, technical staff, staff scientists). A meeting with University and local CNRS representatives was held. No representative from INSB CNRS was present. The committee also had closed-door meetings for organization of the visit and discussions.

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

CRBM is located on the CNRS campus, in a single building with a working surface of 2560 m2. This building is in a very bad general condition. Plans for moving CRBM in a new building started more than ten years ago. While moving was originally scheduled to take place at the beginning of the previous period, unexpected administrative complications have delayed the move. This led to an odd situation, where the Director and his team were located in a distant building away from CRBM. In 2010, all members of the CRBM will eventually move in a new building on the same campus (about 100m from its current location), and CRBM will remain physically connected to the neighboring IGMM (Institut de Génétique Moléculaire de Montpellier) with which CRBM has strong scientific and administrative interactions: CRBM and IGMM are associated into IFR122 and share common facilities; they are also co-founders of the spin-off company Splicos. CRBM will gain extra space in the new building (+ 1400 m2, total 3973 m2) and will share space and organization with CPBS (Centre d'études d'agents Pathogènes et Biotechnologies pour la Santé).

CRBM has a very good expertise in the fields of cell signalling with a strong focus on GTPase signaling in their biological context using different models systems (7 teams), cell cycle and cell division (6 teams), study of post-translational modifications (2 teams), drug design/delivery (2 teams) and bioinformatics (1 team). Other teams work on neurobiology (1 team), RNA metabolism (1 team) and ageing (1 team). Several teams show a strong translational activity, which in the reviewed period led to a total of 18 patents and the founding of a spin-off company in collaboration with IGMM (Splicos).

Over the past 4 years, CRBM recruited 5 groups, 4 through internal promotion and one external. No specific call for new group leaders was published and recruitment relied mostly on spontaneous applications. One particularly successful team will leave CRBM to join another institute in Paris in 2010; a current and promising post-doc fellow from this team applied for a position of group leader at CRBM, and therefore was evaluated by this committee.

In the next period, CRBM will have to develop a strategy to attract a number of new team leaders of high standard.

- Management team

The current management team includes Mr. P. Mangeat (Director) and Mrs A. Debant (Deputy Director). They are assisted by an administrative staff comprising a secretary, a financial manager and a person in charge of the logistics. Two candidates, one internal (Mrs. A. Debant) and one external (Mrs. C. Dargemont) applied for CRBM directorship for the next period (2011-2014). Following an internal vote by group leaders that clearly supported Mrs. A. Debant, she has been proposed as the future Director of CRBM. It is important to note that no Deputy Director has yet been identified for the next quadriennal period (2011-2014). Additionnally, there is no general administrative manager ('secrétaire général'). This administrative manager position represents a priority for CRBM future management team, a request supported by this committee. This is a key recruitment to maintain the Director's

scientific activity and ensure effective management and organization of CRBM, whose size will expand in the next few years. This position could be shared whith neighboring institutes (CPBS, IGMM).

The committee recognizes the major contribution and efforts made by the current Director to organize the moving of CRBM in the new building.

- 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	10
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	43	42
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	14	13
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	30	30
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	13	10
N6: Number of Ph.D. students (Form 2.7 of the application file)	18	15
N7: Number of staff members with a HDR or a similar grade	28	29

2 • Overall appreciation on the research unit

- Overall opinion

CRBM is a medium size biology institute currently comprising 22 teams (of which 19 have been evaluated for the next period). CRBM is located in a single building hosting 52 tenured scientists, 12 post docs, 18 PhD students (as of 06/2009; 15 in 2010) and 30 administrative/technical staff of which 22 work in the common services and 6 on the platforms to enable research. In total, 125 persons are working at CRBM with 82 having a permanent position and 43 on contracts (12 postdocs, 18 PhD students, 13 technicians/engineers). Over the years, CRBM has built up a good expertise in the fields of GTPases and cell signaling, cell cycle and division, molecular modifications and drug design/delivery. CRBM has also set up good platforms including photonic imaging (MRI), peptide synthesis and recombinant protein facilities. In addition, CRBM manages the La Valette Xenopus animal house, which is a renowned animal facility used by national and international groups working on Xenopus. One clear strength of CRBM is its ability to carry out translational research, with 18 patents and a spin-off company created in the past period. Overall there is a very good synergy internally between teams, with several ongoing collaborations (leading to a remarkably high level of shared publications). CRBM also shares common facilities and administrative organization with the neighbouring institute IGMM, through IFR122.

There is considerable heterogeneity among CRBM teams in terms of scientific production and management (funding, scientific focus, feasibility, attractivity, etc..), which will be detailed in the individual team reports. While some teams are leaders or have the potential to become leaders in their fields, others show too much dispersion, dilution of resources, modest attractivity and critically low level of funding. This led to the general feeling that some of the teams lack focus and realism. It also appeared that despite interesting observations and good ideas, several teams seem rather underperforming, and the competitivity and survival of some of them is therefore a concern. However, it has to be stressed that CRBM has a strong potential, and the institute could improve its general scientific output through changes in management, first by reconsidering the perimeter or keeping of some teams and by applying clear international standards for team definition (allocation of laboratory space and resources, scientific

focus), and importantly, the recruitment process. A clear challenge and objective for CRBM in the coming years will be to translate its expertise into excellence.

- ## Strengths and opportunities

CRBM has several strengths which provide great potential for the future of the institute, provided that in parallel actions are taken to correct some of its weaknesses.

Collectively, CRBM has very good expertise and a good critical mass studying cell cycle/division, the physiological role of GTPases, protein modifications and drug design/delivery. There is a strong tradition of internal collaboration and with neighboring institutes (IGMM) which reinforces and synergizes the local expertise. This is a clear added value and a situation not found frequently in similar institutes both in France and abroad. This is probably a positive consequence of several internal promotions over the history of CRBM.

CRBM has a high number of staff scientists indicating it is attractive to young scientists; however, CRBM has a high staff scientist/non permanent scientist ratio, indicating that CRBM has more difficulties in recruiting workers on contracts (PhD and post-docs) and therefore turnover is low. The proportion of foreign scientists is also relatively low.

Over the years, CRBM has been able to set up very good facilities, which are open to the surrounding community. These facilities represent major tools for most of the current teams inside CRBM but also outside, and a strong element for attracting groups to be recruited in the future. Efforts must be made to keep these facilities up-to-date and running effectively.

CRBM performs very well in terms of translational research, with a total of 18 patents in the past period. In addition, CRBM, in association with IGMM, has been able to set up a spin-off company (Splicos). Overall, the translational activity of CRBM is very good and has been recently recognized through an INPI award.

One major opportunity for CRBM is its long awaited move into a new building, to take place in 2010. The committee would like to stress that this is a unique occasion to reset the overall organization and scientific objectives of CRBM, and correct some of the critical weaknesses. In order to help the Direction to set these new standards, it is highly recommended that CRBM organises an external Scientific Advisory Board (SAB) as soon as possible.

Together with the new building, the recruitment of new international group leaders is a clear opportunity for CRBM to increase its critical mass in promising topics for example, protein modifications, structural biology, bioinformatics, etc… This will also help to increase the international visibility of the whole institute.

- ## Weaknesses and threats

Some of CRBM weaknesses and strengthes are interconnected. For example, team leader emergence from CRBM staff scientists generated a high proportion of internal collaborations (a positive point), but also led to a number of small groups with rather poor support and autonomy in their infancy, leading to modest contributions and questioning their role as independent groups. It is also important to note that some internal promotions backed-up by external independent funding have led to very successful young group leaders.

In addition, a high proportion of staff scientists is found in some teams. While this could generate momentum and stability to the group, this is often accompanied by a dispersion of projects and resources. Indeed, staff scientists of some groups work independently on projects poorly related to the main themes of the Group leader. This particular arrangement leads to a dilution of forces and resources, and reduces competitiveness of teams for funding and publications. It may also lead to ambiguous leadership and represents a threat for the long term contributions of the teams.

Overall, CRBM seems to favour internal or regional collaborations and recruitments, at any level. Although this may have some advantages, it appears to this committee that CRBM would benefit a lot from developing a strategy to significantly increase the proportion of group leaders recruited from outside CRBM including those from outside France.

The size of some groups is too small, which, added to a high ratio of projects/manpower limits scientific output and competitiveness. As a consequence of a small team size yet keeping a broad range of projects, funding appears problematic for a few teams, which clearly affects their ability to carry out research effectively, with a threat for their future survival.

Team management regarding scientific focus, allocation of resources and funding, seems quite variable among CRBM teams. It would be helpful if the Director of CRBM, with the assistance of a SAB, clearly identifies the requirements and standards for CRBM teams, in order to help teams to better manage current funding systems, human resources, attractivity, etc..

One weakness of the present situation of the institute is the lack of availability of an outstanding practical structural biology group(s), in particular crystallographic group(s). CRBM should consider hiring 1-2 crystallography groups in the new building, which would have the advantage of bringing together on the same site crystallographists and biologists, a situation encountered in renowned international institutions that prove to be highly effective. Alternatively, interested CRBM teams should find ways to better use local expertise, for example through crystallographically competent post-doc fellows shared with local protein structure groups.

Since chemistry is very strong in Montpellier, it should also be possible to find partners for synthesis. This project would offer the exciting possibilities of identifying compounds with potential therapeutic application that is of clear interest for several CRBM teams. There could be an extremely productive multi-group collaboration here, involving rounds of structure determination, prediction of better inhibitor structures based on these results and synthesis of new inhibitors.

- Recommendations to the head of the research unit

Establishment of a Scientific Advisory Board (SAB): it is recommended that an SAB is established as soon as possible for discussion and development of mid and longterm scientific strategy, setting up clear procedures for recruiting new teams, setting standards for evaluation and management of teams, policies for resource allocation, etc.. It is in the interest of all members of the CRBM and the future of the institute to set high standards and be successful in recruiting excellent external group leaders. In this respect, the allocation of laboratory space should be regarded as an important component of institute strategy.

Nominating a Deputy Director: for an expanding institute of the size of CRBM, it is strongly recommended to recruit a Deputy Director. The Deputy Director could be an active scientist, or, alternatively, a scientist who is not running a laboratory but who is interested in carrying out administrative work at a high level.

During the discussion with University representatives, the committee was informed that a new bioinformatics group from University of Montpellier 2 has been accepted to join CRBM. It is strongly recommended that the new rules for selecting group leaders should be applied right away and that this group should be evaluated before joining CRBM (in terms of quality of the research and overall synergy with other CRBM teams).

- Data on the work produced :

(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	53
A2: Number of other researchers (recorded in N3, N4 and N5) who are active in research	53
A3: Ratio of members who are active in research among permanent researchers [(A1)/(N1 + N2)]	1
A4: Number of HDR granted during the past 4 years	
A5: Number of PhD granted during the past 4 years A6: Any other relevant item in the field	26

3 • Specific comments on the research unit

- Appreciation on the results

The impact, originality and attractivness of the research can be assessed through a number of criteria, including the number and quality of research articles and invited reviews, invitations to international conferences, awards and distinctions, number of thesis defended, etc..

Collectively, CRBM members published 277 articles in the 2005-2009 period, among which 66 articles correspond to internal collaborations between CRBM teams. Of these 277 publications, 193 (70%) were authored by a CRBM group leader, of which the group leaders appear as last author on 92 ; the rest of the articles (84/277) correspond to collaborations or articles published by members of the groups without involving the PIs.

Of the articles authored by group leaders, 16 were published in journals with an impact factor higher than 10, and 2 were published in journals with an impact factor higher than 20.

In the 2005-2009 period, CRBM group leaders published 4 invited reviews in review journals (2 in EMBO Reports; 1 in Science STKE; 1 in the Trends series).

These figures indicate that, in the reviewed period, CRBM performed reasonably well quantitatively, however the general level and impact of publications could be higher.

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

Over the period under review, 26 theses were defended. The current number of PhD students is 18 (as of June 2009), and 15 PhD students will be trained at CRBM in 2011. The number of post-docs (12 total) is low compared to the size of the institute, the number of staff scientists and the number of independent groups. Overall, the number of students and post-docs is below the number of groups (i.e., on average not each group has a student and post-doc), and some teams rely largely or exclusively on staff scientists.

CRBM hosts 3 professors and 8 assistant professors ('Maitres de conference'), who are involved in organizing research and teaching at the university. One professor is in charge of the CBS2 Doctoral school ('école doctorale'), and two other professors are in charge of the 'BioMed' and 'Pharmaceutical Biotechnology' masters (master 2). De facto, this creates a proximity between members of the CRBM and local students, which could better stimulate PhD students to join the institute.

Collectively, CRBM has been awarded 3 distinctions: one group leader received awards from EMBO YIP and ERC (junior award)(this group will leave CRBM in 2010); one group leader was awarded a CNRS Bronze Medal.

In recognition of its strong translational activity, CRBM has been recently awarded a "Trophée de l'innovation" by INPI (Institut National de la Propriété Industrielle).

The total number of invitations to speak at international conferences is 66, with some heterogeneity from team to team. 14 of the current teams received such invitations, while 8 teams did not received any invitation to speak at international conferences.

The number of researchers coming from abroad is low and there is a general reduced attractivity for external group members. One possible explanation is the lack of maintenance of the current building and the high competition for recruitement of post-docs and students in Montpellier. However, some teams are succesful in generating funding including salaries and are doing well in attracting good group members at different levels (PhD and post-docs).

The funding situation at CRBM is summarized in the table below, describing the number of grants raised over different periods (source: written report):

NUMBER of GRANTS (based on written report Chapter 4 + update provided by group leaders):			
PERIOD	**2005-2009**	**2010**	**2011**
National	**66**	**22**	**12**
International	**6**	**1**	**0**
ERC	**1**	**1**	**0**
TOTAL	**73**	**24**	**12**

The recurrent funding from CNRS and Universities of Montpellier 1 and 2 (SE: subvention d'état) represents 30% of total CRBM running money (in 2007 and 2008; not including salaries), the rest originating from external funding (RP: ressources propres). During the past period, there has been a total of 14 contracts with private companies, of which 4 generated income for the Protein purification platform.

In 2009, 15/22 teams had a running grant. 11 national and 2 international grants ended in 2009.

Of 24 grants running in 2010 (see Table), 6 are 25 K€/year or less and thus do not represent major funding for the long term, and several teams do not have a grant.

These figures illustrate the difficulties that a few groups have to raise funding on a regular basis.

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

During the 2006-2009 period, the teams were organized into 3 different departments each headed by one of the group leaders. This organization will no longer be kept in the next period. Since this organization was largely set up for scientific interactions within the departments, the loss of departments should not dramatically change this aspect as meetings between groups with common interests will be maintained. However, considering the expansion of CRBM in the future, an organization into departments could serve management purposes and help the decision making process (e.g. by providing a 'Management Team' to assist the Director).

As already mentioned, it is recommended to hire a Deputy Director, to prepare the next period and have him/her participating directly in building up the future scientific projects of the institute. Active initiatives should be taken to identify the Deputy Director rapidly.

Discussions with the CRBM personnel indicate that internal communication can be largely improved, but it is fair to say that this is a common theme in many institutes. Some simple procedures for improving the flow of information, both top-bottom and bottom-up, should be implemented.

Except for common internal meetings held by departments, there is no clear scientific organization and animation.

Until now, emergence of new groups was achieved mainly through internal promotion and spontaneous applications. CRBM and CPBS (CPBS will share space with CRBM in the new building), have recently published a common international call for new group leaders. Of around 100 applications, CRBM has selected a couple of high level candidates, which will certainly build up the strengths of the institute.

- Appreciation on the project

CRBM has good resources and a strong potential, with a high level of expertise, good facilities and frequent and productive interactions internally. The goal of making CRBM a leading institute in biochemistry and cell biology is achievable and should represent a common objective for all members of CRBM. The move into the new building represents a major opportunity to set ambitious goals; this will probably involve actions to change some aspects of the organization, such as resource allocation, the process of selection of emerging group leaders and review of research team productivity.

CRBM can also expand on its interactions with neighboring institutes and increase international partnerships and recruitments. This could require changes to the current ways in which projects are allocated, taking more risks and developing ways of being more attractive. The possibility to merge with neighboring institutes to make a large biology institute provides an opportunity for making such changes and have greater impact.

4 • Appreciation team by team

Team 1 : " Rho GTPases : development, differentiation and physiopathologies"

Team leader : M. Phillipe FORT

- 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)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	5	3
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)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	
N7: Number of staff members with a HDR or a similar grade	2	3

The work is in a specialised field of the developmental role of less well studied members of the Rho GTPase family. The group has made significant observations on the developmental roles of the atypical GTPases RhoU and RhoV. A very interesting group of papers describes the use of a yeast based assay to identify inhibitors of GEFs but this area of work does not appear to be part of the PI's future programme. The work is of good quality and medium impact.

16 publications are listed in total; of these the PI appears to be the senior author on 6. 4 papers are in good quality journals (1 in Journal Cell Science, 1 in Dev Biol, 1 in Chemistry and Biology). 5 publications have been published in collaboration with other CRBM members indicating a good level of interaction within the institute. 3 patents have been registered over the last 4 years. There do not appear to be any theses at this time; the last one was defended in 2007. No post-docs have been recruited from abroad.

There is a long term collaboration with ISEM team on the genetics of mosquito adaptation (Culex pipiens). This collaboration is really productive leading to 3 publications and 2 patents, but represents a side project and does not seem to be part of future work.

The PI and members of the team have attended national and international meetings. It is not apparent from the activity report whether there were any invitations to speak at international meetings.

The PI has a reasonable track record of winning funding, and the team is a founding member of the GDR "GEF inhibitors". He has been a member of the CNRS National Committee and of the LNC scientific committee.

One team member is an associate professor at Montpellier II. The PI is co-organizer of the Cell fate program of BioMed Master at Montpellier II, and the team has trained Master students.

The future work is based around the role of RhoU, a Wnt regulated gene, in mouse development and SOX9 and miniSox9 in colorectal cancer. The latter seems a departure from previous work and have arisen from two CR1 from another institute joining the lab. Therefore the projects are not well connected. The projects are feasible but more thought needs to be given to aspects such as properly powered molecular pathology studies to relate expression levels of proteins to clinical behaviour. The studies make use of existing technologies such as mouse germ line manipulation. There does not seem to be any technological development.

The committee feels that the past work is of good quality, not at the highest level but making a decent contribution to the field. There is a good track record in GTPase signalling and strong interests in developmental biology.

However, the future plans present some departures from past work and it remains to be seen how productive the move into Wnt signalling, particularly in the mouse, will be. It is not clear whether this is a good move or how sustainable it will be if the two CR1s move on. The group should maintain strengths in GTPase signalling and show more focus and integration of projects. It is also crucial to develop a strategy for recruiting students.

Team 2 : Signal transduction of the Rho-GTPase exchange factors

Team leader: Ms Anne DEBANT

- 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	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	4
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	0
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)	1	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	1
N7: Number of staff members with a HDR or a similar grade	1	1

This team studies the function of activators of Rho GTPases, with a focus on different variants of the RhoGEF Trio. One TrioC variant has been found specifically expressed in the nervous system (Purkinje cells of the post-natal cerebellum). Furthermore an oncogenic isoform of Trio, termed Tgat, has been identified from adult T-cell Leukemia patients. The group found that Trio mediates axonal outgrowth induced by the attractive guidance cue Netrin-1. Peptide inhibitors have been developed that inhibit specifically the GEF2 domain of Trio or oncogenic T-gat. Another research line involves the function of the microtubule associated protein Zyg-8 in C-elegans neurons.

In particular, the Trio studies are original and interesting and will also have their impact on the general knowledge of RhoGEFs and their functioning. The availability of conditional Trio KO mouse makes it feasible to start in vivo studies on Trio in future research. The C-elegans studies on Zyg-8 are difficult to judge because this work has been initiated recently and no publications are available yet.

The publication record of the PI is reasonably good given the fact that she also acts as deputy director. Within the period 2005-2009, 8 publications have been published in which the PI was involved, two in which the PI is last author (Biol. Cell; Mol. Cell Biol.). Most papers are based on collaborations with different PIs within the Institute. The papers have been published in good quality journals such as Mol. Cell Biol., JCS and Mol. Biol. Cell. Additional papers have been published in more specialized journals.

The PI collaborates with various groups within the Institute but also nationally and internationally and the PI participates in the consortium CNRS GDR 2823. Clearly, The PI is a well known expert in studies of the function of the Rho-GEF, Trio.

The PI contributed to many national and international meetings and has also been invited to speak at international meetings. She organized recently a Jacques Monod Conference and is a member of various scientific committees.

The PI successfully applied for funding from different funding agencies. No funding was obtained from international funding agencies.

The PI is able to recruit high level scientists but these are recruited mainly from the region. 3 PhD students were supervised over the past 5 years. The research work resulted in 1 patent in 2003. Furthermore a patent on Peptidic inhibitors of the RhoGEF Trio and the applications thereof is in preparation.

Various members of the group did give lectures to Master II Biomed students.

The PI is deputy director of the Institute and thereby heavily involved in structuring the research at the local level (both the CNRS institute and collaborations with Universities I and II of Montpellier)

Future studies are mainly based on two different subprojects: (1) Function of RhoGTPases in neuronal physiology and cancer and (2) cytoskeletal and signaling roles of the MT-associated protein ZYG-8 in C-elegans. With respect to project 1, the preliminary data on a function of Trio in the aggressiveness of soft tissue sarcomas seems promising but need to be validated before studying the mechanisms involved. The studies on the function of Rho GTPases in cerebellum development are highly interesting and may reveal a function of Rho GTPases in cerebellar ataxia. Furthermore the availability of conditional Trio KO mice will allow studying the function of Trio in Purkinje cell differentiation and brain development in vivo. The studies mentioned above are highly relevant and feasible with the expertise of the group.

With respect to project 2, the committee is less convinced about the studies on the cytoskeletal and signaling roles of the MT-associated protein Zyg-8 in C-elegans. Although potentially of interest, this project is still vague and difficult to judge on its merits and feasibility because of lack of preliminary results. This project is not connected to project 1 and the committee does not see the added value of developing this particular project in this group.

The investigations on Trio in Purkinje cell differentiation and cerebellar development represent original and challenging research which may give new insight into the function of Rho-GEFs in the development of the brain. In particular the planned studies with Trio KO mice are of interest and may demonstrate the function of Trio in brain development in vivo. The team has an excellent background to perform the planned project. The proposed studies on the function of Trio in aggressiveness of soft tissue sarcomas are also of potential interest. It would be great if mouse tumor models could be used in combination with the developed TRIP inhibitory peptides that target Trio. The group is certainly internationally competitive with respect to the Trio work.

The committee is less enthusiastic about the studies on Zyg-8 in C-elegans neuronal development. The background of the group in this research field is low and convincing preliminary data are lacking.

The group has a strong background in research on GEFs (Trio) and Rho GTPases. They have identified a function of trio in brain development. Moreover, a potential funtion of Trio in aggressiveness of soft tissue sarcomas has been identified. A combination of in vitro work and in vivo studies using the Trio KO mice will allow to further unravel the function of trio in brain development and tumor progression.

The committee is less supportive on the studies on Zyg-8 in C-elegans neuronal development. This project is not connected to the main focus of the group, representing a threat for resource allocation, focus, leadership and competitivity. If the PI becomes the director of the Institute in the future, the research of the group should concentrate on the established strong points and expertise of the PI (Trio and Rho GTPase research).

Team 3 : RhoGTPase signaling in osteoclast biology

Team leader : Ms. Anne BLANGY

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

This team was created in 2005 by internal promotion (previously member of TEAM1) and aims to unravel Rho GTPase-mediated signaling pathways in osteoclasts. These haematopoietic cells are specialized in bone resorption and are involved in various pathological diseases including osteoporosis, rheumatoid arthritis and bone metastasis. The team identified novel genes involved in osteoclast differentiation and bone resorption that included Wrch1 and Dock-5. Wrch1 encodes a Cdc42 like Rho GTPase that interacts with the integrin $\alpha v\beta 3$ and interferes in osteoclast differentiation. Dock-5 encodes a Rac activator and is required for the formation of the sealing zone that is essential for bone resorption. Moreover, chemical inhibitors have been identified that inhibit resorption while having no effects on osteoclast precursor survival. These are very interesting and original studies that could have major impact in the treatment of various pathologies associated with osteopenia. The availability of conditional mouse models allows studying the signaling pathways involved using in vitro as well as in vivo models in future research

The publication record of the PI is very good given the fact that the group started in 2005. Within the period 2005-2009, the group published 6 papers in which the PI is first or last author. Furthermore the PI contributed to 8 additional publications, which included mainly studies together with other PIs of the Institute. Most publications have been published in good to very good journals such as PNAS and Mol. Biol. Cell. Additional papers have been published in more specialized journals.

The PI contributed to many national and international meetings and as a young investigator has also been invited to speak at international meetings.

So far the PI tends to focus on “home-grown” talents rather than to recruit scientists from abroad. When the PI becomes more established, she probably will be able to recruit researchers from abroad as well.

The PI has successfully applied for funding but at the regional level only.

There are strong collaborations with other teams at CRBM and the PI participates in the consortium CNRS GDR 2823.

The group leader has obtained very solid results based on fundamental biological and biochemical projects leading to 2 patents in 2008 and 2009. The proposed projects have high potential that may lead to a better understanding of normal and abnormal bone dynamics and may result in the development of successful treatments of pathologies associated with osteopenia.

The PI supervised 2 PhD students over the past 5 years. The group appears to be a good training environment based on the quality of the post-doctoral positions obtained by the PhD students working in the lab.

Future studies are mainly based on two different subprojects: (1) studies on Wrch1 and Dock5 functions and (2) the development of Dock5 inhibitors to treat osteolytic bone diseases.The PI will further investigate how Wrch-1 regulates integrin signaling and how this affects osteoclast precursor adhesion and fusion. Furthermore the function of the Rac activator Dock-5 in bone resorption will be investigated. Both Dock-5 and Wrch-1 conditional KO mice are available to investigate in vivo the function of both proteins as well. Identified Dock-5 inhibitors will be further characterized and tested on their anti-resorptive activities. 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.

The group has established ideal model systems to unravel the signaling pathways involved in osteoclast function. They have identified already key players in osteoclast differentiation and bone resorption, which can now be tested by using in vivo model systems. Furthermore the group started to develop chemical inhibitors that potentially are suitable to treat osteolytic bone diseasesors.

The combination of basal and translational research is a very strong point of this group. The development of drugs that inhibit bone resorption is a very interesting and promising line of research which is already supported by different patents.

The job change of one team member who is doing the mouse experiments is a potential threat for performing the interesting in vivo studies. However, the PI should be able to replace her by another Post-doc with expertice in animal experiments.

Collaboration with industrial partners should be set up to support the studies on the development of drugs that inhibit osteoclast-medaited bone resorption.

The PI of this young group should try to increase the visibility of the team. International collaborations could offer new opportunities and could increase the success to receive national and international funding for the proposed projects.

Team 4 : Adhesion, Rho GTPases and Physiopathology of Skeletal muscle

Team leader : Ms. Cécile Gauthier-Rouviere

- 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)	1	1
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)	4	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)	1	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	1
N7: Number of staff members with a HDR or a similar grade	1	1

This team studies the function of cadherins in cell-cell adhesion processes, myogenesis induction and myoblast fusion. In particular they aim to identify the signaling pathways activated by N-, M- and R-cadherin as well as

RhoGTPases during myogenesis. Major achievements are: (1) the establishment that N-cadherin-mediated Rho activation occurs in lipid rafts and is required for induction of myogenesis. (2) The identification of RhoE and M-cadherin controlled Trio-mediated Rac activation as regulators of myoblast fusion. (3) The function of R-cadherin in Rac-induced myoblast transformation.

In particular the functions of Rho GTPases and Trio in cadherin-mediated myoblast fusion are interesting findings. In addition the cadherin switches in rhabomyosarcomas and the function of R-cadherin and Rac in myoblast transformation are potentially of interest. R-cadherin expression could be a marker for or could be causally involved in the development of rhabdomyosarcomas.

The publication record of the PI is very good. Within the period 2005-2009, the group published 10 papers in which the PI is first or last author. Furthermore the PI contributed to 4 additional publications, which included mainly studies together with other PIs of the Institute. All publications have been published in good quality journals such as Cancer Research and Mol. Biol. Cell.. Additional papers have been published in more specialized journals. Two PhDs have defended their thesis during the last period.

The PI coordinates an INCa project and has permanent collaborations with other teams at CRBM. She was involved in the co-organization of various international meetings of the Société Française de Biologie Cellulaire (SBCF). The PI contributed to many national and international meetings and is member of the executive board of the SBCF.

The colleagues in the lab of the PI are recruitments from the region. Students that finished their PhD in the PI's lab obtained highly qualified Post-doc positions abroad.

The PI successfully applied for funding from different funding agencies. However, no funding was obtained from international funding bodies.

The PI supervised 2 PhD students over the past 5 years. No patents were realized.

Various members of the group did give lectures to Master II Biomed students (Signaling module). The PI, with a member of the group, also organizes yearly a training program for secondary school pupils.

Future studies are a logical extension of the earlier work of this group on the induction of myogenesis and myoblast fusion. To unravel the signaling pathways involved in cadherin-transduced induction of myogenesis, myoblast fusion and rhabdomyosarcoma development various approaches will be used. These are innovative and straightforward and include various screens. The PI studies the involvement of known pathways that are suspected to function in cadherin-mediated processes in skeletal muscle cells. Obviously the results of the screens are difficult to predict.

The PI is a well-known researcher in the field of myogenesis and myoblast fusion. The proposed new studies will certainly give more insight into the signaling pathways involved. In particular, studies on the potential function of R-cadherin in rhabdomyosarcoma development and progression may turn out very relevant and of high interest.

The proposed studies on unraveling the signaling pathways that regulate induction of myogenesis and myoblast fusion are straightforward and feasible. The additional studies of the function of R-cadherin in tumors originating of skeletal muscles are highly interesting. The proposed lines of investigation are very likely to generate important new knowledge on the physiology of skeletal muscles. The group has a strong background in skeletal muscle research which will facilitate the proposed studies. A potential function of R-cadherin in the development and progression of rhabdomyosarcomas makes these studies also cancer related.

The committee noticed that a number of screens have been proposed to identify new partners or molecules involved in skeletal muscle physiology. Obviously it is unknown whether these screens will lead to interesting hits. However, given the experience of the PI, the committee is convinced that methods and approaches will be adapted if not successful.

Team 5 : Morphologic alterations of transformed cells

Team leader : M. Pierre ROUX

- 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)		
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	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	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.7 of the application file)	2	1
N7: Number of staff members with a HDR or a similar grade	1	1

This team focuses on morphologic alterations of transformed cells. The research investigates the role of p53 not only in the control of cell proliferation but also in cell migration and invasion, which could contribute to metastasis. In particular, they propose that p53 inhibits epithelial-mesenchymal transition by regulating E-Cadherin expression. In addition, the team has found that alternative splicing of p53 could be associated with poor survival outcome of breast cancer patients. These results are of interest and could contribute to the development of new diagnostic or therapeutic tools in cancer.

The PI is author of 5 publications over the 5-year period. One research article is published in a very good journal (J. Cell Biol), others are more methodological papers (Meth. Enzymol., Protein Expr Purif.) or reviews published in minor journals (Med. Sci; Bull Canc.). Of note, there is a high level of valorization during the last 2 years with 4 patents registered and the founding of the Splicos spin-off with IGMM.

The team has some collaboration with other laboratories in the UK and with IGMM in Montpellier but none inside the institute. Many of these collaborations are long-term interactions that provide evidence of the value of this laboratory to the field. So far there are no publications from these collaborations although there are several patents.

The PI has been invited to speak at one international workshop during the last funding period.The group has recruited a previous PhD student back from a successful and productive postdoctoral position in the UK. New postdoctoral fellows have been recruited recently to work for the spin-off company Splicos. No contribution to teaching is described in the report.

The PI has been successful in raising funds from the Ligue contre le Cancer (at the regional scale) and from ARC although the laboratory depends mainly on income from the biotechnology start-up Splicos.

The laboratory is involved in international research, as indicated by joint patents with UK researchers, although it does not appear to participate in international (e.g. European Union) or national networks. The laboratory has recently increased its contribution to teaching through the arrival of an ATER.

Data from the team on p53 splicing and collaboration with another IGMM group led to the emergence of the Splicos start-up, which can be considered as cutting edge project. However, the success of Splicos strongly depends on the team's ability to develop innovative methodologies and therapeutical tools to inhibit cancer invasion and to manage cutting edge research projects on the basis of their expertise.

The projects will deal with the mechanistic roles of p53 in invasion and metastasis and the role of p53 isoforms in the microenvironment of invasive carcinomas. These are based on previously identified targets, which build on the strength and expertise of the team. The focus on regulators of Rho activity like GEFs and GAPs and the relationship with the regulation of migration through p53 isoforms should allow interesting collaborations with Rho GTPase experts within the institute.

The committee feels that this work is interesting but would gain extra value and visibility by actively promoting interaction and collaboration with other researchers (within CRBM and with national and European networks), leading to joint publications.

The team has interesting approaches that provide evidence of the dual role of p53 in regulating cell proliferation and participating in cell migration and metastasis. The main projects seem feasible in their scientific rationale and approaches. The team has a clear vision of the potential impact and value of their research results for industry and biomedicine, as illustrated by the 5 patents filed in the reporting period.

Weaknesses include a lack of interface with other areas of biological research in CRBM and the dependence on Splicos for funding and hiring non-permanent staff (post-doc positions) . There is also a lack of involvement in research networks at the national (i.e., InCa) or European level (FP7).

The team should aim to increase the level of high impact publications over the next few years and should improve the international visibility of their research by attending and participating to international meetings more frequently. The team should maximizes the interface with other teams within CRBM and outside, particularly with respect to Rho GTPases, for which there is considerable expertise in the CRBM.

Team 6 : Tyrosine Kinase oncogenic signalling

Team leader : M. Serge ROCHE

- 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	0
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)	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)	4	3
N7: Number of staff members with a HDR or a similar grade	1	1

This team is one of the most active groups in the biochemical and spatial analysis of Src Family tyrosine kinases signaling in normal and tumor cells. The team has made a number of significant observations for example in defining the role of the adaptor protein PAG in regulating Src activity by Csk. Some of the research appears narrow in focus but, within the institute, this program addresses basic biological questions of great interest for understanding oncogenic signalling.

The PI reports 13 primary publications from this group over the 5 year period, of these the PI appears to be the senior author on 7. On 4 articles the CR1 colleague from the group appears as the senior author. Many of these papers are in good quality journals (2 in Journal of Cell Science, 2 in Molecular and Cellular Biology, 2 in Oncogene, one in

Journal of Cell Biology and one in Cancer Research), testifying to the rigor of the published data. None of the papers involve collaborations with other groups in the institute. The papers do not show an exceptional high citation rate, but the field is specialized. It must be noted an increase in the quality during the 2 last years with publications in Blood, Canc. Res ., etc... Other outputs are reasonable but the number of invited presentations is quite low.

The team exhibits numerous collaborations with other labs in France and with outside collaborators. Many of these collaborations are focused interactions that provide evidence of the value of this lab to the field but it should be noted that the number of collaborative publications is low.

The research has not attracted the level of recognition or awards that would be consistent with the quality of the work. This may be a consequence of the SFK field being quite small.

The group tends to focus on "home-grown" talent rather than recruitment of scientists from abroad, although the research is truly international with some international collaborators.

The PI has been very successful in raising funds from external bodies (national agencies and industrial partnerships) although the group does not participate in many of the more influential European networks. The lab is engaged in international research, although we don't see it playing a leading role in the larger European network.

The team appears to be a good training environment with a high number of graduated students compared to senior scientist potential. The students and post-docs who leave the lab appear to go into independent positions, indicating the good training capacity of the lab.

The biochemical data are rigorous and of a high quality and it appears that the projects are driven by relevant biological questions. There is a strong emphasis on up-to-date phospho-proteomic techniques. This has led to some interesting results such as the demonstration of cross-regulation to other SFKs by activated Src. Probably, the work will remain relatively narrow in focus but well done in a highly competitive field. This holds promise for the future.

The projects are based on identified targets not on unbiased screens, which play to the strength of the team according to its expertise. Nonetheless these are valuable studies. More open-ended studies may result from the phospho-proteomic studies. The projects based on in vivo approaches are of interest and they represent more mainstream lines of research. Some of the projects in the team target a research field that is highly competitive and are being pursued elsewhere. This is a strength as long as the team ensures that they take an approach that exploits their skills.

The committee feels that this work is of extremely high quality but would gain in value and visibility by actively searching for interfaces with others (CRBM and national and european networks). However the work stands out in its own rights without extensive collaborations.

The projects are extremely rigorous with very interesting approaches, and the PI is an acknowledged expert in the field of Src signalling. However, the work deliberately focuses in the field of SFK signalling, which could limit the opportunity of generating interfaces with other areas of biological research.

The PI should improve the international visibility by attending and participating in international meetings more frequently. In addition, the PI should maximize the interface with other teams within CRBM and outside. This expertise needs to be sustained.

Team 7 : Cell signalling and morphogenesis

Team leader : M. Peter COOPMAN

- 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)	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)	1	
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	
N7: Number of staff members with a HDR or a similar grade	2	2

The team has a long-standing interest in the role of the Syk non-receptor tyrosine kinase. Their keynote publication was in 2000 when they showed that Syk may function as a tumour suppressor in breast cancer. Since then they have pursued mechanistic studies on Syk.

This group contributed to 18 publications during this evaluated period. Eight were loose collaborations in which a single member of the team was associated, not in first or last author. In the remaining 10 papers, senior members of the team were last author on 6. Among that latters, 3 appeared in good journals (one review in Seminar in Cancer Biol and 2 research papers in Oncogene and Cancer Research). The last 3 appeared in lower impact journals (C.R. Mechanique, J. Biomech, BBA). On only 1 research paper (Cancer Research), 1 review (Cancer Lett) and one book chapter does the PI appear as first or last author. Overall this seems a relatively poor output for a group of 9.

The PI received one invitation to speak at an international meeting. It does not appear that any members of the team received invitations to speak at international meetings.

The team was successful to obtain funding in the past (ARC, INCa, labellisation LNC), but for the 2010-11 period funding seems quite low (approx 25K€). The team has been active in coordinating networks on Syk but there does not seem to be any extant activity. There is no apparent participation to international or national scientific networks.

The PI has consulted for the Pharma industry on Syk. A patent has been issued on the use of Syk expression for detecting malignancy.

Members of the team participate in teaching, one as a full professor and other team members giving few hours per year of teaching. Two thesis came out of the lab. Noticeably, one member have heavy administrative duties (UMR Director).

For the projects, the focus remains on Syk. Interesting observations have been made on the relationship of Syk to epithelial-mesenchymal transition, therefore the involvement of Syk in intercellular adhesion and cell polarisation will be studied. Future work will study substrates of Syk by proteomic approaches and potential upstream activators. This latter project could be interesting if they find ITAMs on non-immunological signalling molecules. However, little detail is given on how this will be followed up. A final theme will be to use a conditional allele of Syk to test its role

in normal mammary development and in mammary tumorigenesis. Very little detail is given on the design of these experiments or how any results might be followed up. Some originality of the approaches comes from the planned use of phospho-proteomics.

This is a relatively large group that is focussed around one molecule: Syk. The case for Syk being important is not over-whelming and the work of the team over the review period has not been of high impact. Future studies may reveal more about Syk but it is likely that the results will be incremental rather than highly significant.

Team 8 : Polymodification of microtubules

Team leader : M. Carsten JANKE

- 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)		
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	1
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)		
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)	2	1
N7: Number of staff members with a HDR or a similar grade	1	1

This team is moving institutes and will not be part of the future CRBM. Work in this group focuses on the regulation of post-translational modification of microtubules. This is an important yet understudied area of research, which is relevant to fertility and neuronal development. The team has made major breakthroughs in the last few years, identifying a range of polyglutamylating and polyglycylating enzymes as well as those carrying out the reverse reaction, deglycylating and deglutamylating enzymes. They have also carried out functional studies on the physiological roles of these enzymes in Drosophila, and the effects of tubulin modification on interaction with microtubule-associated proteins.

The group has an excellent publication record in top level journals (12 publications in total, 8 involving the PI), including the PI as first or last author on 5 papers (Science, Cell, Molecular Cell and J Biol Chem). Team members have also written a review and contributed to top level publications in close collaboration with other groups (Dev Cell, Eukaryot Cell, J Cell Biol, EMBO reports, among others).

The team has established multiple national and international collaborations with other laboratories, several of which have led to joint publications. Some of these collaborations are long-term interactions that provide evidence of the value of this laboratory to the field.

The research has been recognised by the highly prestigous awards to the PI of an EMBO Young Investigator position and an ERC new investigator grant. He has also been invited to present at an international meeting in 2009.

The group has recruited an EMBO long-term postdoctoral fellow and other post-docs and a PhD student from abroad, indicating the high profile of the research.

The PI has been highly successful as a young group leader in raising funds from multiple sources, both national and international. Of particular importance is his role as coordinator of an international HFSP network, and

involvement in a new INCA project, indicating the ability to establish stable and productive collaborations with groups from other countries.

The PI is supervising four post-docs and two PhD students. He does not contribute to university teaching or local scientific committees.

The project takes multiple approaches to investigate the mechanisms of microtubule modifications and the functional relevance of these modifications. The project builds on the team's strengths in biochemistry and molecular biology, as well as increasing its expertise in cell biology. It is ambitious and innovative, and is likely to lead to high profile publications in the future.

The team has made major cutting edge breakthroughs in the last few years. The proposed projects build on the team's identification of enzymes that modify tubulin to now investigate the functional role of these tubulin modifications at both a cellular and organismal level.

The programme is very strong and has made a major contribution to our understanding of how microtubules are modified and how these modifications affect microtubule function in cells and organisms.

One particular strength is the identification and characterization of enzymes that regulate microtubule polyglutamylation and polyglycylation, giving the team a unique position worlwide in the microtubule research field. The main projects for the future are ambitious but feasible and involve a complementary range of approaches. The team has a clear vision of the potential impact and value of their research results and are actively involved in national and international collaborations.

The team did not make internal collaborations with other research teams in CRBM. The future proposals include 8 distinct projects and studies on multiple knockout mice, which could be too ambitious for a small team, particularly since they are moving institutes.

The team should focus carefully on the most productive projects for the future, and carry out other projects as part of collaborations. The team should also ensure that they continue to stay at the cutting edge of microtubule research by publishing team-centered papers as a priority above collaborative work. They should build up productive interactions with other teams within their new institute when they move.

Team 9 : Translational and p21-activated kinases (PAKs) regulation of mitotic progression

Team leader : Ms. Nathalie Morin

- 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)		
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)	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)	0	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	
N7: Number of staff members with a HDR or a similar grade	2	2

The main focus of this group in the last 4 years has been on the role of p21-activated kinases (PAKs) in Xenopus development. In addition, the group was involved in studies on the control of mitotic progression, and the regulation of mRNA polyadenylation. Altogether the group has worked on four rather divergent topics over the last four years:

1. The role of PAKs in early Xenopus development.

2. Regulation of mitotic events by the phosphatase Cdc14A in Xenopus.

3. Regulation of cytokinesis by wiskostatin in HeLa cells.

4. Regulation of mRNA polyadenylation in Xenopus oocytes.

Some of these research lines are only remotely linked to their primary research focus, resulting in a rather scattered research effort. The output can be classified as good, but not of the top level. The group is clearly competent in working with Xenopus and has build up significant expertise on PAKs, but work in other diverse areas has reduced its ability to contribute to this competitive field in a sufficiently comprehensive and timely manner necessary for major conceptual breakthroughs. Nonetheless, the group has definitely provided some novel and solid insights that are of interest within the respective research fields.

The group has contributed to 10 articles in the past period, among them the PI has published 5, of which 4 are signed as last author (Dev Biol; Exp Cell Res; BMC Cell Biol). The group has consistently published solid work, albeit of limited impact. In accordance with this, external funding is low, although the recent award of an ANR grant to the team is good. The group has trained only one PhD student in the last 4 years, in collaboration with another group at the CRBM. The group has initiated collaboration with Dr. Nelly Kieffer (CNRS-LIA124) that provides an essential component for their future research. In addition, members of the group have carried out collaborative research with other research groups locally and in Rennes and have thereby contributed to several research papers. The latter collaborations appear to be no longer active, as the subject of these is not part of the future plans.

Given the relatively small number of researchers in the group and the limited amount of external funding, the group will be more competitive and internationally visible if the different lines of research are more focused on a common theme, instead of the 4 rather distinct themes that were addressed in the last few years. The future aim of the group is to address the role of PAKs in cell cycle control and the regulation of cell morphology. The group aims to limit its efforts to two main lines of investigation; i) control of Ran by PAK-dependent phosphorylation, ii) control of integrin-dependent pro-platelet formation by PAKs. The strategy is clear, and should result in a more focussed research program. The group aims to shift part of its research efforts to a new area, namely pro-platelet formation. It aims to do so in close collaboration with ample expertise in this topic. Strong points of the plans concern the relatively strong focus on PAKs, and application of the acquired knowledge on PAKs to a new area of research. An active collaboration with a group with strong expertise in this particular field might allow the group to quickly execute experiments at the forefront of this field. The less convincing aspects of the proposal lie in the potential risk that the focus will once again drift away from PAKs. The current research plan does not go much beyond an attempt to demonstrate a role for PAKs in pro-platelet-like extensions, and a role for PAK in the regulation of Ran. Further plans, such as the regulation of Ran by other mitotic kinases, fall outside the area of expertise of this group and will cause the focus to shift to a more competitive area in which the group has little prior expertise. The intent is to focus on two entirely different areas of research, with a relatively small research group. Given the extensive competition and advanced research in Ran and platelet biology a careful identification of solvable and worthwhile goals (hypothesis-driven research) will be very important.

Team 10 : Chromosome separation and cytokinesis

Team leader : Ms. Ariane Abrieu

- 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)		
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	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	3	1
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	1	1

This group has a strong focus on regulation of mitotic progression, in particular on chromosome alignment, chromosome separation and cytokinesis. All of their research lines are coherently positioned around this common theme. During the past five years the group has worked on the role and regulation of kinases and kinesins that are important in these cellular processes. Their main achievements have been on three topics:

1. Auto-inhibitory properties of the kinesin Cenp-E and its regulation by the Mps1 kinase.

2. The role of Cdc14 in cytokinesis.

3. The role of ASAP in bipolar spindle assembly.

The first project was primarily executed by this group and led to a high impact paper. The other two projects were carried out in collaboration with other groups in the Montpellier area, one of which stationed in the CRBM. Overall, the success of this group can be described as very good, although the total number of publications over the last years has been limited. Nonetheless, the work that was published has been of high quality. The group has managed to obtain an international reputation with its original work, as is also exemplified by the fact that the group has participated in 2 major European network programs. This group is active in a highly competitive field, but continues to publish solid work in high impact journals. Over the last 5 years the group has managed to obtain a significant number of external grants, among which the aforementioned European funding.

Since 2005, the number of publications from this group has been limited, but the published work has had a significant impact on the field. The work was published in high-ranking journals: one collaborative work published in Proc. Natl. Acad. Sci. and one article in Mol. Cell where the PI is senior author. Their work on Cenp-E and Mps1 has been at the forefront of the field, and their work on MOB proteins has uncovered a group of understudied proteins that play important roles during mitosis. This combination provides them with an attractive line of research in future years. The group is active in important European networks and participates in a number of local and national collaborations. The group has supervised 4 PhD students in the last years, three of which have recently completed their thesis. One of the principle investigators has been elected to organize the upcoming Cell Cycle conference at Roscoff, a good demonstration of her high standing in the field. Collaborations at the international level have been extensive, and the group has secured a significant amount of financial support from European funding agencies. The group is also involved in teaching of the course "Regulation of cytokines" to the Master 2R BioMed students every year.

The group aims to continue to focus their future research on the processes of chromosome alignment, chromosome separation and cytokinesis. Again, this is a coherent theme in which the different subthemes can easily benefit from one another. The division of the responsibilities between the PI and associate staff scientist in this team is very clear. The PI will lead the research on Cenp-E and Mps1, while the second staff scientist will lead the research toward the role of MOB proteins and associated kinases in cytokinesis. Given the excellent track record of the PI in the field of chromosome alignment and separation, and the relatively understudied role of MOB proteins, this seems an excellent strategy. The proposed lines of investigation are very clear and straightforward and are very likely to generate important new knowledge and tools that will be of interest to many researchers working in this field.

Team 11 : Mitotic regulation of chromosome partitioning and cell division

Team leader : Simonetta Piatti

- 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)	2	
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		
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	2
N7: Number of staff members with a HDR or a similar grade		

The committee was delighted to see the new appointment to the CRBM of an internationally leading researcher from the University of Milano-Bicocca in Italy. The researcher has only recently arrived in Montpellier and the evaluation of the results is based mainly on the work performed over the last 5 years in Milan, where the PI maintained a group. The results show a consistent research output of outstanding quality, regularly published in excellent international journals, on the regulation of mitotic cell cycle progression in budding yeast. The PI published 12 articles, of which she is first/last author on 7 (3 in J. Cell Biol.; Mol. Biol. Cell; Cell Cycle). She also contributed to several collaborative research articles (EMBO J.; Exp. Cell Res.; Genetics). She is an internationally recognized expert in the field and has been an invited speaker at several important international conferences. The research group in Milan was well funded and last year included two postdoctoral fellows and four graduate students.

The group has in the past actively participated in collaborations with some of the best Italian research groups, on topics that intersect with her research and extended it into other model organisms, to additional aspects of mitotic regulation. In other collaborations the unit shared her expertise with other groups. Therefore the group will be a very valuable addition to the CRBM and to the greater Montpellier research area. Several research teams at the CRBM have already started to benefit and to collaborate.

The future research project is ambitious, yet well developed. Based on the past achievements there is a good chance of success. Two important aspects of mitotic regulation will be addressed that have so far remained poorly understood: 1) the phenomenon of checkpoint adaptation, which is an often described but not yet understood process with significant implications for chemotherapy of tumours; 2) The regulation of septin dynamics during cytokinesis, which despite its crucial importance for the finishing step of cell division has remained understudied. Around these two complementing topics the investigator presents a focused project that should keep the research group at the forefront of international visibility during the coming reporting period.

The research group is currently in the process of transferring from Milan to Montpellier and is housed in a very small space in the CRBM (< 15 m2). A first substantial grant to establish the research group has been obtained from the ANR and it appears likely that additional grant applications will be successful. The committee strongly endorses and recommends efforts from the CRBM and CNRS to facilitate the establishment of the research team at the CRBM with the required space and personnel. In particular, a technician position should be made available, since this is essential for this unit to operate efficiently and remain highly productive.

Team 12 : Controlling mitotic entry and exit

Team leaders : Ms. Anne Castro and M. Thierry Lorca

- 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)		
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4	3
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)	2	2
N7: Number of staff members with a HDR or a similar grade	3	3

This group has a strong focus on regulation of mitotic entry and exit, and all of their research lines are coherently centered on this common theme. During the past five years the group has worked on cell cycle regulation in G2 and mitosis, and their main achievements have been on three topics:

1. Greatwall-dependent regulation of Cyclin B/cdk1 substrate phosphorylation.

2. The role of Pin1 in stabilization of Cyclin B in G2.

3. Interaction of CHFR with TCTP on the mitotic spindle.

Despite the relatively small number of researchers in the group, they have been able to consistently publish papers of high impact, albeit that the numbers of papers has declined in the most recent years. Overall, the success of this group can be described as very good. The group has managed to obtain an international reputation with its original work and has build up significant expertise on the Greatwall kinase. This is a relatively understudied kinase, for which this group has convincingly shown that it plays an important role during mitosis. This has provided the group with a unique niche in this highly competitive field. Over the last 5 years the group has managed to obtain a limited number of external grants.

Since 2005, the group has consistently produced very solid work that has had a significant impact on the field, giving rise to a total of 12 publications. They published 8 original research articles, of these the PIs appear to be senior author on 3 that have been published in good journals (EMBO J; EMBO Reports; Oncogene). The team has also produced 2 review articles, 1 meeting report and 1 book chapter, in which the PIs are first and last author. Collaborative work has also been published in good to excellent journals (Nature Cell Biol; Cell Death Diff; J. Cell Sci)

Their work on Greatwall has been at the forefront of the field, and provides them with an attractive line of research in future years. The group has initiated a useful local collaboration with a clinical department in Montpellier

to survey expression of Greatwall kinase in tumor tissues. The group has supervised 2 PhD students in the last years, that have both completed their thesis, and another PhD student has recently joined the team. One of the PI's acts as a member of several scientific committees (Ligue Nationale contre le Cancer, ARC and CNRS). Collaborations at the international level have been limited, and there has not been any financial support from European funding agencies.

The group aims to focus their future research entirely on the Greatwall kinase, primarily in human cells. Given the relative void on this specific topic and the excellent achievements that this group has obtained in this area, this seems a good strategy. The proposed lines of investigation are very clear and straightforward and are very likely to generate important new knowledge and tools that will be of interest to many researchers working in this field. One potential risk to this project is the possibility that Greatwall will not play such an important role in mitosis in human cells, as it does in Xenopus. However, the preliminary work from this group suggests that Greatwall does play an important role in human mitosis, and therefore this risk can be considered to be small. Nonetheless, while the strength of this plan definitely lies in its strong coherence and focus, this also presents the group with the risk that their chances of success are limited to one single project. This is particularly noteworthy, given the fact that two of the principle investigators alternate as head of the team. In this case two clearly distinct research lines for each PI, and a more evident distinction of responsibilities would be preferred. In addition to the efforts to obtain chemical inhibitors, the group could consider the type of chemical genetics developed by the group of Kevin Shokat as a means to investigate late mitotic functions of Greatwall.

Team 13 : Cell Cycle targeting and Diagnostics

Team leader : May Morris

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

The biological focus of this group has historically been on cell cycle control (cyclin dependent kinases cyclins, phosphatases). The group has managed to publish a very reasonable number of medium impact papers in this area with the PI as last author. More recently the focus of the group has shifted towards the application of cell-permeable peptide-based inhibitors of cell cycle regulators. This part of the work of the group has to be considered together with that of the Divita group, since many of the developments were performed together. Several of the points made in discussing the work of the Divita group apply to the Morris group as well, but with the difference that Divita was senior author for most publications. The PI now appears to be moving towards a certain degree of independence. However, this has not yet led to many independently published articles in this area (despite an excellent recent single author review on enzyme biosensors), although this development appears to be in progress. Technologically the group appears to be developing the approach of fluorescent peptide-based biosensors as own project. The main aim of this project is stated to be for medical diagnostic procedures, but this view may be somewhat too narrow as well as

slightly naïve and ambitious. Also, the number of sensors under development appears to be more than a group of this size will be able to handle.

The PI has published well over the past few years, but it remains to be seen whether this trend will continue with papers for which she is the corresponding author. The PI published 20 articles (including reviews; 14 co-authored with Divita), of which she is the first/last author on 5 research articles in medium to good journals (NAR; BBRC; Biochemistry; Cell Cycle). However, in 3 out of these 5 articles, no other author works in her team

Her successes in obtaining funding have been numerous, although apparently not sufficient to achieve a level desired by the PI. There was a feeling after her presentation that she was tackling too many individual projects, particularly in the biosensor area, and she appears to share a perceived weakness of the Divita group with respect to applications of her work. This is a problem that might be resolved by more direct interaction at an early stage in specific projects with, for example, imaging groups and those doing in vivo experiments. The main challenge in the coming period for the PI is to show that she can develop and maintain at least one project at a high level in an independent manner.

The PI was involved in the organization of 3 international conferences, in which she presented her work. She was invited to give seminars in Belgium, Spain and USA. She has supervised 2 PhD theses and taught a total of 6 hours over the 5 years period

There is reason to expect good developments form this work, and the PI will presumably learn quickly what the scope and limitations of applications of her projects are. However, the PI has not yet shown that she can develop her own profile (backed up by independent publications) in her newly chosen area.

Team14 : Ubiquitin proteasome system and cell cycle control

Team leader : M. Olivier Coux

- 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)		
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	4	1
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	2
N7: Number of staff members with a HDR or a similar grade	2	3

The previous teams directed by Olivier Coux and Catherine Bonne-Andrea decided to combine their efforts in the study of the control of protein degradation with relation to cell cycle progression and cancer, a central research interest and strength of CRBM.

During this evaluated period, the team has contributed 10 publications, of which the PI is last author on 4 research papers. Among them, one appears in a good journal (Mol Biol Cell) and one in a excellent journal (Nat Cell Biol). In the Nat Cell Biol paper, in which a member of the team is first co-author and the PI is co-last author, they demonstrate that the HAT protein PCAF is also an E3 ubiquitin ligase that controls the degradation of Hdm2, the ubiquitin ligase that control p53 stability. Finally in another collaborative study (MBC) they reveal an unexpected role

of proteasome-PA28gamma complex in the intracellular traffic of SR proteins. The group also contributed to collaborative articles published in excellent journals (Cell; NCB; Mol Cell). In particular, two innovative studies concerning the control of p53 activity and stability have been published in collaboration with two different teams outside CRBM. In the first collaborative paper with a group from IGMM (Cell) they discovered that E4F1 is an atypical ubiquitin ligase that by ubiquitinating p53 does not drive it to degradation but rather increases its transcriptional activity driving the cell cycle arrest and not the pro-apoptotic programme. These are very good achievements for a rather small team. The team of Catherine Bonne-Andrea has been working on the role of Cdk/Cyclins and sumoylation in the control of the E1 papillomavirus replication protein. Two papers were published in the review period (J. Virol.; Cell Cycle).

The review panel was somewhat disappointed by the written report and oral presentation of the team leader. Too many research streams were presented and the preliminary data did not convince the panel that all should be pursued. The first involved the search for enhancers of proteasome activity (and stability), the ECM29 protein was identified but the biochemical and biological effects were not impressive. A second interesting collaborative project involves the better characterization of the bacterial-like proteasome present in the mitochondria of parasites and the development of specific inhibitors. A third subject concerns the Cdc25B dual-specificity phosphatase. The team showed that this critical cell cycle regulator is degraded during the metaphase-anaphase transition via the F-box protein bTrCP1 and that its over expression causes mitotic defects.

Future projects involve the pursue of the study of p53 ubiquitination, the potential role of p300 HAT/E3 a in K48 ubiquitination and not in chain elongation as well as a systems biology approach that uses protein chips to unravel the complexity of post translational modification in the p53 network. The panel was not convinced that even if the cost burden of protein chips can be overcome the information gained will be beyond descriptive level. A proof of principle experiment on a smaller scale, e.g. using an immobilized array of the known players would be a preferred first step if this approach was to be taken forward.

The second project concerns Cdc25B, the control of its turnover during interphase and the identification of additional mitotic substrates. This is a very competitive project with a possible advantage due to the collaboration with a very good mass spectroscopy laboratory in Strasbourg. A third project undertaken by C. Bonne-Andrea concerns the control of Cyclin E turnover by the interplay of Sumoylation and ubiquitination and the regulation of F-box protein Fbw7 by different covalent modifications. The other three sub-projects concern the proteasome: i- Imaging its sub-cellular localization in relation to its activity taking advantage of the use of GFP labelled subunits, imaging of p53 modification and degradation by FRET /FLIM technology, difficult technically. ii- Pursue of the search of cofactors with an uncertainty about financial support and meaningness of the results. iii- structure and inhibitor search for the parasitic forms of mitochondrial proteasomes. Again, this seems too broad for a rather small team.

The two groups had a number of very active collaborations in Montpellier, nationally and internationally with a number of excellent publications. The PI was involved in the organization of 2 lab courses, and 4 PhD students were trained in the team during the period. Therefore they have been successful in attracting students but the ratio between permanent staff and students/postdocs is too high tending to create subgroups. The projects/manpower ratio is also too high. Efforts should be done to avoid too much of dispersion.

Team 15 : Molecular genetics of ageing

Team leader : Simon Galas

- 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)	3	3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		
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)		
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	
N7: Number of staff members with a HDR or a similar grade	1	2

This team is studying the molecular regulation of the aging process using C elegans as a model. The group has taken a candidate approach and is analysing distinct pathways involved in this process, more specifically focusing on the role of Daf-2 and Klotho. In addition, previous work on Sfrp proteins done by a lab member who joined the group recently (2007) is now studied in the C elegans model. The phenotype of Sfrp worms is pleitropic, including longevity phenotypes, which may suggest indirect effects. Finally, a new project is developped to use C elegans as an integrated Biosensor using stress-response probes followed by imaging in collaboration with the MRI platform. The different activities of the group seem rather scattered and the rationale for investigating and choosing specific candidate genes (for example, klotho) was not clear to the committee, both from the report and oral presentation. The ageing field is very competitive and it appears very difficult for a small group with poor focus to get momentum and make significant and innovative outputs.

Three publications are listed in total over the last period, of these the PI is senior author on 1 (Exp. Gerontology). The other publication, in a very good journal (Mol. Cell), is from a collaborative effort on the greatwall kinase, neither related to the project of the group nor to the CRBM team working on this kinase. The overall publication level is below the level expected for a team composed of 3 senior researchers. Despite the fact that the team comprises 3 teaching researchers, one PhD student has been trained in the last four years (2004-2008).

The PI has attended international and national meetings and has been invited to 2 international conferences.

This group has a low track record of winning funding. There is currently no funding for the future projects.

The PI has national and international collaboration. No collaboration with other CRMB's members is reported. The PI is a full time professor of Montpellier I and is a coordinator of an ERASMUs program and associated coordinator of a DA Vinci program. The team also includes 2 assistant professors from Montpellier I and II.

The future work is in line of the previous project, scattered and with too many projects for a small size group. The originality of the proposed work is weak in a very competitive field, so it is not anticipated that the work would make a strong contribution. The design of large scale genetic screens is not productive according to the PI, although the literature demonstrates that such screens performed in other labs have yielded interesting new results.

The committee finds that the level and originality of the publication on the ageing project is too low regarding the number of permanent staff; the impact is not sufficient to make the group visible at the international level and for establishing a long term research program on this topic. The project for the future is scattered, not well focussed,

and seems to be relying on others's data. There is no use of the advantages of the system to identify novel molecules/pathways or concepts related to ageing, suggesting that the proposed research is not going to lead to innovative results.

The group is not convincing in its publication records, nor in its ability to attract young researchers at the PhD or post-doc levels. In addition, the load for teaching by each of the staff scientists is not a favourable situation to develop a strong scientific program. The funding being very limited, it is not helpful to the group to develop its projects and recruit new lab members.

Based on this evaluation and the fact that the team seem isolated at the CRBM scientifically, the committee recommends that ongoing projects being finalized and that the team does not make part of the future CRBM.

Team 16 : Molecular neurobiology

Team leader : M. Pierre Charnet

- 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)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	4
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)		
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	
N7: Number of staff members with a HDR or a similar grade	2	3

This team is specialized in the biophysical properties of voltage gated Ca2+ channels (VGCC). The group has made significant observations demonstrating the existence of a second permeation site in the pore-forming sub-unit of this channel. They have analyzed the mechanisms of Ca2+ and voltage inactivation of VGCC and regulation of channel properties by pH and small G proteins. In a collaborative effort with a bioorganic chemistry team, the group designed new photosensitive tools to follow rapid structural modification in VGCC. In conclusion in the past few years, results on the VGCC biophysics are of good quality and original approaches have been developed to dissect the molecular aspect of Ca2+ channel regulation. This structure-function analysis of VGCC is only a small part of the PI's project in the future.

The team contributed to a total of 15 publications. The work described is of good quality and medium impact. Since 2005, the PI signed 8 papers, of which 7 are signed as last author : 5 research articles in medium to good quality journals (FASEB J ; J. Gen. Physiol.; Prog Biophys Mol Biol; Pflugers Arch), 2 reviews (Med Sci, Sci STKE), and 1 method paper (Methods Mol. Biol). The scientific production increased significantly both in quality and number in the last years. Nevertheless the overall publication level is below the level expected for a team including four senior researchers. One PhD student was recruited in the reviewed period.

The PI and members of the team have attended national and international meetings. There are no invitations reported to speak at international or national meetings.

The PI has recently attracted 3 new researchers in his group. Some of them have excellent publication records. No post-docs or student have been recruited from abroad.

This team has obtained one financial support (ANR 2006-2009) in the last years. The group set up collaboration with other CRBM members and some international collaboration, which led to publications. There is one associate professor (MCU) with teaching duties, and two other staff scientists participating to M2 level courses.

The future objectives are to understand the various roles played by VGCC in neuronal physiology and pathophysiology. To do this, the group recently set up a protocol of cultured Purkinje cells (PC) differentiated from mouse embryonic stem (ES) cells. It is proposed to characcterize Cav2.1 signaling in these neurons and to perform a functional analysis. The mechanisms of the loss of PC described in spinocerebellar ataxia type 6 (SCA6) patients with poly-CAG mutations in the 3' end of the Cav2.1 gene will also be characterized. The project seem feasible thanks in particular to the expertise of a new researcher joining the team.

A large part of the project is based on the development and manipulation of a new cellular model (differentiated PC), which is not yet totally mastered by the team. The project is principally focused on the role of non-electrogenic function of CaV2.1 in PC and in cerebellar ataxia, a very competitive field, which is new for this team. It seems that the analysis of dysfunction of CaV2.1 in the context of the SCA6 would need more integrative models and neuro-physiological techniques that are not mastered by the team.

The past work on the biophysical aspect of CaV2.1 is of good quality even if the level of publication is low regarding the number of permanent staff. The arrival of new researchers in the team, with new expertise, is a good opportunity to strengthen the research output, which should lead to the development of more competitive projects.

The proposed projects show some departure from past work and is clearly based on the success of the team to master neuron differentiation from ES cells, which is a risky and demanding technique. Furthermore, this team is scientifically isolated in CRBM, both in term of the methodological approaches and conceptual background. It seems that this project would benefit from a more appropriate scientific environment.

It is recommended to maintain strengths in biophysical and molecular characterization of VGCC; and develop a strategy to raise financial support and attract students, as well as increasing scientific interactions with neuro-physiologists and neuro-pathologists.

Team 17 : Molecular biophysics and therapeutics

Team leader : M. Gilles Divita

- 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)	1	1
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)	5	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)	3	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	6	2
N7: Number of staff members with a HDR or a similar grade	1	1

This group is one of the leading groups in the world in the area of peptide mediated delivery of molecules to cells. This is not an easy area to evaluate, since many groups claim to have found "the" answer, and it often appears to work for the chosen cargo and in the particular situation described, but it then usually transpires that it does not

function in other situations, or at least not in the hands of others. It is therefore of great importance to investigate the mechanistic basis of effects seen in order to progress from the stage of interesting anecdotal episodes to a real scientific approach. The Divita group appears to be doing just this, which is highly commendable. However, it would perhaps be advisable to concentrate even more on this aspect, since a genuine understanding of the mechanisms of the effects seen would probably lead to significant further progress.

Over the years, the group has used covalently linked "helper" peptides with cell-penetrating properties, and more recently non-covalent complexes with such peptides. Peptide inhibitors of HIV-reverse transcriptase and of protein-protein interactions in cell-cycle control constitute a promising approach which could have advantages over more conventional strategies. Thus, for reverse transcriptase, there is a better chance of avoiding the development of escape mutations than with more classical approaches. For kinases, approaches not based on interaction with the ATP binding site could offer higher specificity.

The delivery work has been extended to transfer of nucleic acids into cells, which is particularly interesting in the case of siRNA. A recent publication suggests that this approach has therapeutic potential.

The combination of projects and methods used is very attractive and potentially of very high importance, both in terms of development of tools for biological research and for therapy. The group has been active in commercializing their results to make the delivery methods available to other groups. The Chariot system is probably the best known commercial delivery system worldwide. The group has published very well. In the last period, the PI has published 34 articles, of which he is last author on 16 (JBC; Biochemistry; BBA; J. Mol Biol; NAR; etc..). Other articles have been published in collaboration (PNAS; JBC; MBC; BBA; BBRC; etc..). The group has obtained substantial external funding. Teaching activities appear to be mainly concentrated on the substantial number of Ph.D. students in the team. There are significant national and international collaborations.

In conclusion, this team has functioned very well in a difficult but important area. The team has impressive strengths in basic biochemistry and biophysics, and adopts a fearless approach to challenging and important problems. One slight weakness is that the mechanisms of action of the cell-penetrating peptides has not been adequately determined, while at the other end of the spectrum there is a certain amount of naivety when it comes to in vivo applications. The team's ability to compete with the best groups internationally is by now well established.

Team 18 : RNA metabolism in S.cerevisiae and translational control

Team leader : Bruno Lapeyre

- 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	0
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	
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		
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)	1	1
N7: Number of staff members with a HDR or a similar grade	1	1

The group uses biochemical techniques to study tRNA and mRNA modification by methylation. Several RNA methylases that modify tRNAs were characterized. An interesting link was found between tRNA anticodon methylation and glutamine methylation of the translation release factor eRF1 that may mimic the tRNA structure. The same auxiliary protein participates in both reactions and may form a new link between tRNA metabolism and protein synthesis. The preliminary evidence that mRNA methylation at position 6 of an Adenine regulates meiotic gene expression is of great potential interest. Finally the PI collaborates on an unrelated project with a group in IGM to study the role of PKC in translation and polar growth, a potentially interesting system to study the function of PKC but may be a cause for dispersion. Concerns were raised that the ratio of projects/manpower was very high.

In the evaluated period, the PI published 1 review (2005) and 2 research articles, one as last author (Mol Cell Biol, 2005)., one in collaboration on a project not related to the main focus of the group (Biochem J). The committee is concerned that the last senior author publication from the group dates back to 2005. While that publication had some impact, the research output since then has lacked behind the expectations from groups at the CRBM. Noticeably, the last invitation of the PI to an international conference (Gordon Conference) took place in 2005. It was also noted with concern that the group currently comprises only one graduate student (with shared supervision) in addition to the group leader. The group was supported by an ARC contract in the past but no active grant income is currently available.

The group seems scientifically isolated in CRBM. It was noted that the PI has not established collaborations with other groups in Montpellier working on RNA (for example next building at IGMM), that would bring an interactive environment for developing projects.

In conclusion, the expertise in RNA biology and its specific methods was noted. Considering the available resources it is recommended that the group restricts the breadth of research suggested in the project. A focus on one clearly defined aspect of the investigation appears to provide greater potential for the group to finalize some results and regain productivity. The study of meiosis-specific mRNA modification emerges as an interesting subject with which the unit could regain a leadership status.

The committee recommends that the group focuses on finalizing the most interesting/advanced project. Future projects should then be considered in the context of an association with an existing group (either at CRBM or in another institute) working on RNA and/or yeast, but not as an individual group in the future CRBM.

Team 19 : Structural Bioinformatics and Molecular Modelling

Team leader : Andrey Kajava

- 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)	1	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)	3	
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		
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		

This group concentrates on understanding proteins with repeating structures, such as LRR (leucine-rich repeat) proteins, and on structures of amyloid proteins. The group has developed powerful methods for sequence-based detection of tandem repeats, and many new ß-solenoid proteins have been identified at the sequence level using these techniques. They have been very successful at structure prediction for proteins with repeating sequence elements and have proposed a new structural model for amyloid proteins (superpleated beta structure). They have made valuable contributions to our understanding of these areas, and the group´s work is well cited (ca. 2,500 times). There have been several fruitful collaborations with other groups in the CRBM. This type of collaboration could also be advantageous for a number of other groups in the institute, and they should be encouraged to look in this direction. In general terms, it is highly desirable to have a computational group of this kind in an institute dedicated to biochemistry/cell biology, and ways should be found to capitalize on having a highly competent group in this area. While it would probably be counterproductive to use such a group as a service function, mechanisms should be established that ensure the availability of state of the art biocomputing of this kind to the other groups of the institute.

The group has published well since 2005 and is recognized internationally amongst computational biologists. A total of 23 publications have been published by the PI, of which he is first/last author on 7, in medium to good journals (for example J. Mol. Biol.; J. Struct. Biol.; PLoS One). The PI also contributed to several excellent collaborative articles (Nature; Science; J. Mol. Biol.; J. Virol.; PLoS One). The group is doing work that is both valuable and relevant for basic research in biochemistry and cell biology. Teaching activities appear to be mainly in the area of post-graduate supervision, with some seminar activity which is not detailed in the report. The PI has been moderately successful in obtaining outside financial support, but improvement is definitely possible here, perhaps on joint projects of the type alluded to below.

One weakness of the present situation of the institute in Montpellier is the lack of availability of an outstanding practical structural biology group (see general comments). Overall, the group is considered to function very well, with the potential of making an even larger contribution to the general aims of the institute.

Team 20 : The role of tubulin modifications in ciliary functions

Team leader : Krzysztof ROGOWSKI

- 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)		
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		1
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)		
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
N7: Number of staff members with a HDR or a similar grade		

This is a new team proposed to be recruited from an existing CRBM group. The PI is currently a post-doc in Janke's team (Team 8) and proposes to set up a new group with 2 people also members of this team and not moving.

The new group will focus on the regulation of post-translational modification of microtubules. This is an important yet understudied area of research, which is likely to be important in multiple processes in cells and

organisms. The team has made major breakthroughs in the last few years, identifying a range of polyglutamylating and polyglycylating enzymes as well as those carrying out the reverse reaction, deglycylating and deglutamylating enzymes. They have also carried out functional studies on the physiological roles of these enzymes in Drosophila, and the effects of tubulin modification on interaction with microtubule-associated proteins.

The group has an excellent publication record in top level journals, including papers in Science, Cell, Molecular Cell and J Biol Chem. Team members have also written a review and contributed to top level publications in close collaboration with other groups (Dev Cell, Eukaryot Cell, J Cell Biol, EMBO reports, among others).

The team has established multiple national and international collaborations with other laboratories, several of which have led to joint publications. Some of these collaborations are long-term interactions that provide evidence of the value of this laboratory to the field.

Team members have been invited to give oral presentations at some international conferences and regularly attended scientific workshops and conferences.

The group has recruited a PhD student from abroad. Having been part of another group until now, they have not had the opportunity to raise funds independently yet.

The laboratory has multiple stable collaborations with groups in France and from other countries, which have lead to several high quality publications.

The PI is supervising a PhD student but so far does not contribute to university teaching or local scientific committees.

The project builds on the expertise of the team in studying mechanisms of microtubule modifications and recent work in Drosophila studying the functional relevance of these modifications in sperm flagella. The project takes 5 complementary approaches to study the involvement of tubulin modifications in cilia and flagella. It is also making use of Xenopus laevis (an area of expertise at the CRBM) to investigate how microtubule modifications affect microtubule-based transport of melanophores. The projects are ambitious and innovative, and are likely to lead to high profile publications in the future.

In conclusion, the past programme has made a major contribution to our understanding of how microtubules are modified and how these modifications affect microtubule function in cells and organisms. The future programme is focused on an important area – how microtubule modifications affect the function of cilia and flagella. It also uses an interesting cell model to study how microtubule modifications affect microtubule-based transport of organelles. The identification and characterization of multiple enzymes that regulate microtubule polyglutamylation and polyglycylation gives the team a unique position in the microtubule research field. The main projects for the future are ambitious, innovative and feasible.

The lack of interface with projects of other teams at the CRBM could limit the benefits of being in this institute. There is potential overlap of projects with the previous team leader who is moving to another institute.

Therefore the team should liase with the previous team leader to ensure that projects from each team are complementary rather than overlapping. The team should ensure they are recognised independently of the previous team leader by publishing team-centered papers on their chosen model systems as a priority. They should build up productive interactions with other teams in the Montpellier area, especially those working on the Drosophila model.

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

Nom de l'équipe : RHO GTPASES : DEVELOPMENT, DIFFERENTIATION AND PHYSIOPATHOLOGIES

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	B	Non noté	B

Nom de l'équipe :SIGNAL TRANSDUCTION OF THE RHO-GTPASES EXCHANGE FACTORS

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	A	Non noté	A

Nom de l'équipe : RHO GTPASES SIGNALING IN OSTEOCLAST BIOLOGY

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	A	Non noté	A

Nom de l'équipe : ADHESION, RHO GTPASES AND PHYSIOPATHOLOGY OF SKELETAL MUSCLE

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	Non noté	A

Nom de l'équipe : MORPHOLOGIC ALTERATIONS OF TRANSFORMED CELLS

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	B	Non noté	B

Nom de l'équipe :TYROSINE KINASE ONCOGENIC SIGNALLING

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	Non noté	A

Nom de l'équipe : CELL SIGNALLING AND MORPHOGENESIS

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	B	Non noté	B

Nom de l'équipe : POLYMODIFICATION OF MICROTUBULES

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+	Non noté	A+

Nom de l'équipe : TRANSLATIONAL AND P21-ACTIVATED KINASES (PAKS) REGULATION OF MITOTIC 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
B	B	B	Non noté	B

Nom de l'équipe : CHROMOSOME SEPARATION AND CYTOKINESIS

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	A	Non noté	A

Nom de l'équipe : MITOTIC REGULATION OF CHROMOSOME PARTITIONING AND CELL DIVISION

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	Non noté	A+

Nom de l'équipe : CONTROLLING MITOTIC ENTRY AND EXIT

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	Non noté	A

Nom de l'équipe : CELL CYCLE TARGETING AND DIAGNOSTICS

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	Non noté	B

Nom de l'équipe : UBIQUITIN PROTEASOME SYSTEM AND CELL CYCLE CONTROL

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	B	Non noté	B

Nom de l'équipe : MOLECULAR GENETICS OF AGEING

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	C	C	Non noté	C

Nom de l'équipe : MOLECULAR NEUROBIOLOGY

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	B	Non noté	B

Nom de l'équipe : MOLECULAR BIOPHYSICS AND THERAPEUTICS

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+	Non noté	A

Nom de l'équipe : RNA METABOLISM IN S.CEREVISIAE AND TRANSLATIONAL CONTROL

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	C	C	Non noté	B

Nom de l'équipe : STRUCTURAL BIOINFORMATICS AND MOLECULAR MODELLING

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	Non noté	A

Nom de l'équipe : THE ROLE OF TUBULIN MODIFICATIONS IN CILIARY FUNCTIONS

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	Non noté	Non noté	A+

Centre de Recherche de Biochimie Macromoléculaire ***(CRBM) UMR 5237***

Le Directeur

Madame Danièle HERIN
Présidente de l'Université Montpellier 2

Montpellier, le 16 Mars 2010

Objet : Réponse Scientifique à l'Evaluation AERES

Madame La Présidente, Chère Collègue,

Je vous prie de trouver ci-joint la réponse scientifique de la Direction du CRBM au rapport avant mise en forme d'évaluation de notre unité par le Comité l'AERES, que les services du Conseil Scientifique de notre établissement m'ont fait parvenir.

Veuillez agréer, Madame La Présidente, Chère Collègue, l'expression de mes sentiments distingués.

Pr. Paul Mangeat.

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Réponse de la Direction du CRBM (UMR 5237) au rapport de l'Evaluation AERES avant mise en forme

Nous voudrions d'abord remercier les membres du Comité AERES qui ont procédé à l'évaluation du CRBM du 6 ou 8 janvier 2010.

La Direction regrette l'absence au cours de l'évaluation du laboratoire d'un officiel de l'INSB du CNRS.

La réponse est notifiée en français pour le Président du Comité, la Représentante de l'AERES, et pour les Tutelles. Les réponses aux évaluations scientifiques des équipes sont en anglais pour être transmises aux membres du Comité, le cas échéant.

1. Remarques et Commentaires Généraux sur le rapport d'évaluation.

Nous nous félicitons de la reconnaissance par le Comité :

- du fort potentiel scientifique du CRBM

- de l'effort constant et productif du CRBM en matière de valorisation de la recherche

- de la très bonne synergie entre les groupes en interne et avec l'IGMM, institut voisin, à travers de nombreuses collaborations et publications, ce qui renforce la reconnaissance de l'expertise locale. Cette synergie est qualifiée par le Comité « de relativement unique en France et à l'étranger »

- de l'effort du CRBM dans le développement des plateformes, qui sont des outils majeurs pour le soutien de la recherche des équipes montpelliéraines, et qui représentent un élément stratégique pour attirer au CRBM des nouveaux groupes performants extérieurs à Montpellier.

Nous partageons l'opinion du Comité selon laquelle le déménagement du laboratoire dans un nouveau bâtiment représente une occasion unique et stratégique pour renforcer le potentiel scientifique du laboratoire en accueillant de nouvelles équipes et pour améliorer son organisation fonctionnelle.

Nous prenons acte des faiblesses du laboratoire perçues par le Comité, comme par exemple une certaine dispersion des thématiques scientifiques, l'hétérogénéité entre les différentes équipes en ce qui concerne les publications ou le fonctionnement, l'absence de procédure définie pour le recrutement des responsables d'équipe.

Le Comité souligne également l'absence d'un groupe de biologie structurale, en particulier de cristallographes, et souligne l'absence d'interaction avec des chimistes de Montpellier. Sachant que plusieurs équipes sont intéressées par le développement d'inhibiteurs, le Comité suggère une collaboration étroite entre biologistes, chimistes et structuralistes pour développer de façon synergique par une approche multi-disciplinaire des inhibiteurs efficaces.

Nous souhaitons répondre à un certain nombre de commentaires généraux et spécifiques exprimés dans le rapport d'évaluation, qui méritent ici des éclaircissements.

A - Remarques sur l'évaluation du bilan de l'activité scientifique.

Le Comité juge que l'activité globale du CRBM en termes de publications est raisonnablement bonne, mais aurait pu être meilleure. Le Directeur, au cours de sa présentation orale, a rappelé que le CRBM a augmenté le nombre de publications, de soutenances de thèses, de dépôts de brevets et de licences et ce dans des conditions où l'effectif et le budget annuel sont restés globalement

constants entre la période précédente et celle objet de l'évaluation. Il faut donc souligner que ce bilan est très bon au vu des conditions de travail qui ont continué à se dégrader au cours du temps, en particulier à cause de l'important retard pris par le chantier immobilier pour des raisons administratives. Nous voudrions souligner ici que ce retard a eu un réel impact négatif sur la dynamique scientifique du CRBM.

Par exemple, le Comité constate l'absence d'appel d'offres ouvert pour le recrutement de nouvelles équipes au cours des 4 dernières années, sans mentionner le contexte local défavorable à un tel appel d'offres. Vu l'exigüité et la vétusté des locaux, il était difficile dans ces conditions d'attirer des équipes extérieures, ce qui s'est traduit par le fait que 4 équipes sur 5 ont été recrutées en interne sur le dernier quadriennal. La Direction s'était formellement engagée (en 2003) auprès de la Direction Générale du CNRS de procéder à un appel d'offres pour l'accueil de nouvelles équipes extérieures à Montpellier dans les nouveaux locaux. La Direction voudrait souligner que l'engagement a été tenu (mai 2009) dès que la mise à disposition des nouveaux locaux était assurée et prévisible dans un délai raisonnable. Par ailleurs, malgré la critique de recrutements en interne, la Direction note que le Comité a jugé globalement très positive l'activité scientifique des 3 équipes émergentes (équipes 3,8,13) soumises à évaluation et de l'équipe recrutée à l'extérieur (eq. 11).

Le Comité, tout en reconnaissant l'attractivité du CRBM pour les jeunes scientifiques, estime, au vu du rapport chercheurs permanents/chercheurs non permanents que le turnover du laboratoire est faible et qu'il y a peu de chercheurs de nationalité étrangère. Nous voudrions moduler ces affirmations par des indications chiffrées sur la période considérée: i) le renouvellement des chercheurs statutaires a été de 25%, avec beaucoup de recrutements hautement compétitifs ; ii) le CRBM a recensé des personnels de 19 nationalités différentes, avec 20% des responsables d'équipe d'origine étrangère.

Le Comité souligne également que le nombre de doctorants est assez limité au vu de la taille du CRBM. De nouveau, ces critiques doivent être modulées par le contexte local défavorable, en particulier parce que les équipes montpelliéraines dont le nombre a considérablement augmenté ces dix dernières années, sont en compétition pour les doctorants et que l'état de délabrement du bâtiment actuel ne favorise pas les équipes du CRBM. Nous sommes persuadés que le déménagement dans le nouveau bâtiment et une politique scientifique dynamique et ambitieuse va permettre de recruter plus de doctorants dans le futur.

Commentaires sur l'évaluation spécifique des équipes :

Nous prenons acte que l'évaluation scientifique des équipes par les Comités AERES est fondée en particulier sur des critères quantitatifs d'activité. La lecture des rapports consacrée à l'analyse de l'activité des équipes fait apparaître une hétérogénéité dans l'utilisation de ces indicateurs, et un manque très clair d'homogénéisation dans la rédaction du rapport. Nous pensons que cette hétérogénéité est préjudiciable à l'évaluation équitable des équipes du CRBM.

Les remarques détaillées pour chaque équipe apparaissent plus loin dans le document, mais voilà quelques exemples représentatifs:

Le rapport comporte de nombreux oublis dans le nombre des publications (équipes 1,6,7,9,12,14,15,16,18,19), d'invitations à des congrès internationaux ou leur organisation (eq. 6,7,12,13,14,18), d'implications dans la formation et/ou l'administration de la recherche (eq. 1,6,7,12,13,14), du nombre de HDR dans les équipes (eq. 7,9,12,13,14) (toutes informations pourtant mentionnées et mises à jour lors de la visite). Parfois, il est fait état d'une distinction pour un responsable d'équipe (eq. 8) mais pas pour un autre (eq. 13). Une équipe, et une seule, voit son excellent niveau de publications tempéré par un indice de citations, tandis qu'une autre, et une

seule, se verra mise en valeur pour la formation de ses doctorants sur la base de la qualité du labo de stage postdoctoral. Pour le lecteur, l'absence de commentaires sur un de ces critères conduit inévitablement à une perception préjudiciable de l'activité de l'équipe. En outre pour certaines équipes des erreurs formelles sont à déplorer (eq. 1,7,14). Finalement, les efforts de restructuration de certaines équipes, qui conduisent inévitablement à un niveau plus important d'hétérogénéité dans la liste de publications (équipes 7,9,14,16) n'ont pas été pris en compte. En résumé, les équipes les plus citées ci-dessus ont souffert d'une étude bien moins complète et détaillée que les autres et qui a pu conduire à une réelle sous-évaluation de leur niveau d'activité.

Enfin, nous avons vérifié que dans le budget 2010 le nombre d'équipes rencontrant des problèmes de financement (ressources contractuelles inférieures à 25 keuros hors salaire) ne sont qu'au nombre de 4 et non de 12 comme le Comité en fait état.

B- Remarques générales sur l'évaluation du Projet scientifique

Nous prenons acte de l'évaluation scientifique des équipes 15 et 18. La Direction s'appuie sur les recommandations formulées par le Comité, et informe officiellement le Président du Comité et la Déléguée Scientifique de l'AERES que ces deux équipes n'apparaitront pas à l'organigramme du CRBM pour le prochain quadriennal. Une réflexion a été engagée concernant la réaffectation des personnels statutaires.

Nous suivrons les recommandations du Comité notamment pour l'identification d'un Directeur-adjoint et la mise en place d'un Comité scientifique international.

Nous notons que le Comité approuve la demande du porteur de projet auprès du CNRS pour un secrétaire général, poste indispensable au moment où le périmètre et l'organisation du CRBM vont considérablement changer. Néanmoins, nous voudrions préciser qu'il est exclu que ce poste puisse être partagé avec les instituts voisins (IGMM et CPBS) au vu de la taille importante des trois instituts et de l'importance stratégique de ce poste pour la Direction.

Nous voudrions revenir sur l'appel d'offres international lancé en mai 2009, et faire le point sur les candidats sélectionnés. Trois excellents scientifiques sont maintenant candidats au recrutement au CNRS et/ou à l'INSERM ainsi qu'aux appels d'offres ATIP/Avenir, (les trois candidats étant à l'étranger et deux sur trois étant de nationalité étrangère) : il s'agit d'un group leader de Dundee en Ecosse, qui est à l'origine de la découverte de la neddylation, un jeune chercheur qui a une expertise internationalement reconnue dans la régulation de la transcription du complexe SAGA chez S. pombe, et un jeune chercheur cristallographe qui s'intéresse à déterminer la structure de protéines participant aux complexes mitotiques. Ce dernier recrutement est proposé dans le cadre de la mise en place d'une collaboration à long terme avec le Centre de Biochimie Structurale, à Montpellier. Enfin, une discussion est toujours en cours pour l'accueil d'une équipe française internationalement reconnue dans la biologie du développement et des systèmes. La Direction voudrait souligner ici que les choix stratégiques du CRBM épousent parfaitement les recommandations du Comité AERES, en particulier sur l'attrait de chercheurs de renommée internationale, étrangers et extérieurs à Montpellier.

En conclusion, nous nous réjouissons de la reconnaissance du fort potentiel scientifique du CRBM. Nous sommes persuadés que le CRBM a tous les atouts pour devenir un laboratoire d'excellence internationalement reconnu grâce à l'association : i) d'un contexte immobilier favorable permettant d'être attractif pour des équipes extérieures; ii) d'une amélioration de son organisation; et finalement iii) d'une politique scientifique dynamique et ambitieuse avec un recrutement sélectif des meilleures équipes.

2. Remarques spécifiques du Directeur sur les conditions de la tenue du Comité.

Le Directeur du CRBM souhaite informer la Direction de l'AERES et les Autorités de Tutelle des circonstances qui ont présidé à la tenue du Comité d'Evaluation du laboratoire, et pour laquelle il n'a, à ce jour, reçu aucune notification officielle.

Ni la Représentante de l'AERES ni le Président du Comité n'ont personnellement contacté le Directeur avant la tenue du Comité. Le Directeur s'est donc tenu volontairement en retrait tout au long de la préparation et de la tenue de la visite. Le Directeur décharge totalement la Directrice-adjointe et porteur du Projet 2011-2014 de la situation créée.

Les membres du Comité ne se sont pas entretenus à huis clos avec le Directeur.

Le Comité n'a pas visité le laboratoire. Pour d'autres Comités, la visite des locaux représente un élément majeur d'information de la situation d'exercice des équipes de recherche.

Le temps de discussion avec les équipes a été trop court (30-40 min en fonction de la taille des équipes).

Le Directeur a été particulièrement surpris de recevoir un message la veille au soir de la tenue du Comité l'informant de la venue d'une représentante du Collège C de la section 23 du Comité National. Le Directeur a dû prendre en charge une situation devenue embarrassante à la suite du refus qui a été opposé à cette élue de participer à la réunion du Comité avec les ITA du laboratoire.

Answers to the AERES report on scientific activity of the different teams

This part is specifically devoted to reply to the scientific evaluation of CRBM individual research teams, in order to be forwarded to the foreign members of the committee, if applicable. A majority of teams has raised specific comments following their scientific evaluation by the AERES Committee.

On a general point of view, we want to stress again that there is an important heterogeneity in the overall evaluation of the different teams. Not to use the same items to weigh the overall contribution of each team is detrimental to the necessary equity of the evaluation. When certain comments (positive or negative) made for some teams are missing for others, this implicitly sends the message that when it is missing it's because it does not apply.

As stated before, the AERES evaluation system uses to take into consideration quantitative criteria and the importance given to some of them might turn in a somehow biased evaluation. For example, the committee has carefully counted how many publications PIs of different groups signed as last authors. We considered this as a secondary aspect of the evaluation because it is fair to acknowledge the investment of permanent staff scientists when they behave as leaders on a research project. Also, when some restructuration of teams occurs, it results in an unavoidable dispersion of authorship for a period of time.

Team 1

- The committee considered that *Sox9/Minisox9 and Rho signalling are not well connected*. Maybe the PI did not make it clear enough during his talk that RhoU/RhoV and Sox9 are encoded by Wnt response genes and in the neural crest, Sox9 induction requires RhoV activity. This represents strong enough a connection to study the interactions between these pathways in the Wnt signalling.

- The committee also concludes that *future plans present some departures from past work and it remains to be seen how productive the move into Wnt signalling, particularly in the mouse, will be.*

- The team wishes to emphasize that it has already shifted from the Xenopus to colon cancer cells, and that for the four scientists who will join the team, future plans do not present departure at all from their past work. How productive it will be is a general concern and could be opposed to any new project.

- The committee has omitted to mention the Mol Biol Evol paper, whose impact is 7.28.

- As stated in the written document, work on mosquito adaptation is a long term collaboration and as such will be continued.

- It seems that the implication of the PI in administrative boards has not been properly acknowledged, in particular for the CNRS national committee, the LNCC scientific committee and the Biology of the Cell Editorial board.

Team 2

- The reviewing panel acknowledges that the group has a strong and internationally recognized expertise in the Rho GTPase field via its publications on the Rho GEF Trio. Concerning the projects, the committee strongly supports the projects on Trio and on Rho GTPase signaling.

- However, the Committee is less supportive concerning the project on the role of the MAP Zyg-8 in C.elegans development. The statement *« Although potentially of interest, this project is still vague*

and difficult to judge on its merits and feasibility because of lack of preliminary results» is rather questionable as the project has already allowed the collection of numerous preliminary data clearly described in the document, data which will soon be published.

- However, the team agrees with the Committee that two separate projects in a group represent a risk for its productivity and competitivity, especially with the PI becoming the future director of the Institute. Consequently, the group will remain focused on the project concerning Trio and Rho GTPase signaling in cerebellar development and tumorigenesis, but will use the expertise it has in C.elegans development as a complementary approach to tackle the function of the RhoGTPase pathways *in vivo*.

Team 5

- The Committee pointed to *"Weaknesses include a lack of interface with other areas of biological research in CRBM"* and : *"The team should maximizes the interface with other teams within CRBM and outside, particularly with respect to Rho GTPases, for which there is considerable expertise in the CRBM."* and: "*The team has some collaboration with other laboratories in the UK and with IGMM in Montpellier but none inside the institute*." It is true that no internal collaborative work was published during the considered period. However it should be made very clear that the team is particularly active in the scientific discussions existing between groups at CRBM.

- The Committee sees *"Weaknesses include the dependence on Splicos for funding".* The PI has been successful in raising funds from the ARC and Ligue contre le Cancer.

- The Committee stated that "*No contribution to teaching is described in the report."* The team comprises 1 ATER and various members of the group did deliver yearly lectures to Master II Biomed students.

Team 6

- The team has published 4 additional articles in late 2009 and therefore the total number of publications is 17.

- The PI is highly involved in the management of the Canceropole GSO (member of the "Comité de pilotage scientifique", leader of the network "cellular signalling and therapeutic targets"). As a consequence, most collaborations of the team are made with labs of the CGSO. This has been illustrated by the support of 3 grants of INCa plus one currently under review, one PhD student co-supervised by the PI and Christian Recher, a team leader and clinician of the CPTP INSERM institute of Toulouse, one article published in *Cancer Res* and 3 manuscripts in preparation. This may explain the moderate international collaborations of the team mentioned by the Committee.

- Finally, the PI has been also involved in the organization of 5 national and international meetings within the 5 years.

Team 7

- The Committee did not take into consideration that the total number of publications is 18, which is not as low for the size of the group as stated by the Committee.

- However, it is true that the PI is involved with only a proportion of them. It is not certain that the Committee has well perceived the peculiar situation of this team, still located on the university campus, where it was part of another laboratory during the reported period. The group that effectively joined the CRBM as of Jan 1, 2007 is composed of members who have decided to reorient

their research projects on the study of Syk. It is therefore natural that a significant heterogeneity appears in the publication list.

- It should also be added that one member and former leader of the group, the Director, is involved in a long term collaboration with a former member of his team who started the Ciona's project.

- It is fair to say that the Syk project which is aimed at the understanding of the molecular basis of the anti-oncogenic properties of Syk is running at a slower pace than was expected. However it is felt rather important that a group in France keeps looking after this scientific and risky challenge.

- In addition, the Committee omitted to consider the huge administrative load of the Director, the implication of the team members in the formation of 4 PhD students, the invitation of the PI to an international conference, the capacity of the PI to raise significant research funds during this period, as well as the technological investment of the team to set up the SILAC approach at the local proteomics platform.

- Finally the funding of the team for 2010 is higher than 25 keuros.

Team 9

- The Committee expressed concerns that *« the less convincing aspects of the team proposal that lies in the potential risk that the focus will again drift away from PAKs"* and *« The current research plan does not go much beyond an attempt to demonstrate a role for PAKs in pro-platelet-like extensions, and a role for PAK in the regulation of Ran."* This is an ambivalent message since on one side the committee finds that the research is too narrowed on PAK functions in different mechanisms and finds on the other side that there is a risk to drift away from PAKs.

- Actually, two different projects involve studies of PAK functions. The first project is based on the understanding of the pathways that lead to proplatelet (PPL) formation. PAK is important in this process and the upstream regulators of the kinases and of their targets, involved in the regulation of actin and microtubule networks, during PPL extension need to be identified. The team has a solid expertise in studying transduction pathways, as well as cytoskeleton dynamics. This project will not drift us away from PAKs but is not either merely restricted to look at PAK functions in PPL extension. The second project consists in expanding the current work on Ran and PAK by studying the regulation of the GTPase by other mitotic kinases. This project appears to be of a concern for the committee who pointed out that « *the group is relatively small and that its expertise in this area is limited* ». The team has a longstanding expertise in manipulating egg extracts, in addition it was the first group to show that subgroup I PAK regulate G2/M transition and to demonstrate the coregulation of PAK with the amplification loop of cyclinB/Cdk1 (Faure et al, 1997, Cau et al, 1999, Cau et al, 2000). Finally the team will benefit of the very strong interactions existing with team 12 who are experts in mitotic kinases.

- Finally, it is right to say that if the size of the group does not increase, the team should concentrate on the development of project 1.

-The PI is highly involved in the management of the Canceropole GSO (member of the "Comité de pilotage scientifique" of the network "Genome, Structure and Function").

Team 12

- The Committee claimed that *the team project is mostly based in human cell model*- however, as it was shown in the report as well as stated in the oral presentation the project is based 50% in human

cells and 50% in Xenopus egg extracts where the team has already shown the importance of Greatwall in mitotic entry and maintenance.

- The Committee failed to mention the significant involvement of the PIs in teaching and formation, as well as organizing a conference, the publication of two additional book chapters, and the invitation of the PIs to four international meetings.

Team 13

- The PI has published 5 last author publications on projects developed within the team itself, funded by her own grants, indicating a certain degree of autonomy, aside from an established collaboration with team 17 on peptide-based delivery strategies, which has also produced publications in common.

- The PI was awarded a CNRS Bronze Medal in 2006 which recognizes the scientific value of her work and an encouragement to pursue it.

- Moreover the PI has been invited to two international conferences and co-organised an international conference. The group has supervised 2 PhD students over the past 4 years as well as 2 postdoctoral students, and is involved in teaching to Master BioMed students every year.

Team 14

- The Committee seems to have considered some publications of the group without fairness. First, the PI is co-corresponding author of the Nature Cell biology article, as mentioned in the front page of the published paper. This article should therefore be credited to him in the list of "papers of which the PI is last author". Second, the MBC paper strangely appears as" another collaborative study", as if the credit for this group should be questioned. The 4 first authors were from the group, as well as the last author. Indeed this project was elaborated and financed by the group.

The general tone of the report is rather pejorative, and here are some answers to specific comments:

- *"the ratio between permanent staff and students/postdocs is too high tending to create subgroups".* For the last period, the permanent staff was 2 scientists, while the lab constantly comprised at least 2 PhD students and 2 post-docs, not counting the short-terms students or visitors. The group is now in the process of fusing 2 teams and requests time to adjust to an appropriate balance between taking advantage of the complementary expertise of each permanent scientist and dispersion. It is strange that, while trying to join forces to become more competitive, this is not what is acknowledged in the report.

- *too many research streams for a rather small team*: (i) the objective is to expand the group: two grants are presently submitted that include salaries, the team applies for the MCF position open at the CRBM. (ii) It was made clear, both in the written report and in the oral presentation that, although different lines of research that would be logical to pursue have been presented, will be tackled only those for which appropriate funds and workforce are allocated. (iii) in the process of fusing 2 teams, some time is needed to finish what was undertaken.

- *preliminary data not convincing*:

> protein chips: The report states that the project is "*to use protein chips to unravel the complexity of post translational modification in the p53 network*" and that "*the information gained will not be beyond descriptive level*". The challenge presented was not to document further the complexity of post-translational modifications (PTM) in the p53 network which is already firmly established (Benkirane, Sardet and Coux (2010) *Biochem Soc Trans, 38: 98-103*)), but to develop innovative approaches allowing to monitor their dynamics. Actually, protein chips are one possible tool to tackle

this issue. The potential of this approach deserves to be explored, and the team is ready to take the risk. Finally, to find in this report the suggestion to start with a proof of principle experiment on a smaller scale is surprising, because it sounds again as a reproach, as if the team excluded such options.

> *proteasome biochemistry*: admitting that "*the present results are not impressive*", it could be acknowledged for equity that what was presented was a work in progress. This project is presently supported up to the end of 2010 (after a positive external reviewing of the progress done during the first year of funding (2009)) by a collaborative international grant obtained with an Israeli group who is among the leaders in the proteasome field. The PI has precisely mentioned in the written report that he was not sure that this project could be pursued over the next period (2011-2014), because of the exceeding challenging experimental aspects of the project.

- To conclude, there is a feeling when reading the comments regarding this team that, while acknowledging its past achievements, the committee did not trust the ongoing and future projects. If it is the actual message of the panel, then it is rather unjustified. If this is not the case, then amendments to the report are necessary to make it less negative.

Team 15

- There is a feeling that the Committee has misunderstood the proposed goals of the research team, especially regarding the project on Klotho gene function and involvement together with Daf-2 gene in aging.

-The Committee did not consider that:

- a pharmaceutical science peer reviewed paper as well as book chapters leading up to five the actual record of scientific production instead of the two reported for the considered period.

- one research team member joined the team as of Jan 1, 2007.

- one full-time researcher (CR1 Inserm) was planed to join the team to strengthen the workforce of the team.

- a new PhD student has joined the team and is financed through a scientific collaboration with IRSN.

-The scientific recommendation about genetic screens is definitively not applicable as a strategy in the present field of research on aging because measured pleiotropic effects have to be simply considered at more than a single gene suppressor screen level.

Team 16

- The total number of publications is 16 with 9 signed by the PI. One publication signed by unique members of the team has not been considered, as well as another collaborative work with team 17.

Team 18

- The evaluation of the team's scientific work has been excessively severe, particularly in its conclusion.

- The scientific production has been temporarily reduced, due to various factors including the fact that new ambitious projects were developed, however, the impact of the previous production and the importance of the current projects have been largely underestimated. For instance, counting the

published papers, only two have been retained here. However, a major paper was published in Molecular Cell, on November 19, 2004, only 6 weeks before the period that is considered here and therefore was not counted! Then, a review was published in Top. Curr. Genet. in 2005 by Lapeyre, which wasn't acknowledged at all. And now a manuscript on Trm112 is reviewed at JBC (February 2010, eight weeks too late ?). Therefore, it is not unreasonable to say there were 5 publications during the considered period of time, if it is extended 6 weeks upstream and 8 weeks downstream. Not an exceptional record, but a reasonable one considering the size of the group. It is below what the team published during the previous quadrennial evaluation, where the production of the group was judged to be excellent, but it is not insignificant.

- The Committee has not considered the PI's invitation at a Gordon conference. Nowhere the international collaborations were acknowledged with world-class groups. A PICS grant was recently awarded to support the collaboration with the polish group on the mRNA methylation project. Also, the board should be reminded that the group has always been independent financially, even though the budget may seem low compared to mammalian projects.

Team 19

- The total number of publications is 23 of which the PI is first/last author on 11. A collaborative work with team 8 failed to be acknowledged.

Montpellier le 16 Mars 2010

Professeur Paul Mangeat
Directeur du CRBM

UNIVERSITÉ MONTPELLIER 2
SCIENCES ET TECHNIQUES

La Présidente

Montpellier, le 18 mars 2010

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Monsieur le Directeur,

Je m'associe aux remerciements formulés par l'ensemble de la direction du "**Centre de Recherche de Biochimie Macromoléculaire (CRBM)**" pour la qualité du rapport d'évaluation fourni à l'issue de la visite du comité d'expertise.

Comme nombre d'autres sites universitaires en France, le site de Montpellier est en cours d'évolution avec la récente création d'un pôle de recherche et d'enseignement supérieur (PRES), ayant deux missions essentielles : accompagner les trois universités montpelliéraines dans un processus de fusion et assurer la mise œuvre de l'opération Campus.

Dans le respect de nos engagements, cette évolution s'est traduite récemment au sein de l'Université Montpellier 2 par la création de Pôles de Formation et de Recherche (PFR) permettant d'accroître la visibilité de notre activité scientifique à l'échelle nationale et internationale.

Le PFR Biologie-Santé, auquel le CRBM est rattaché, est l'un des cinq PFR créés par l'Université Montpellier 2 qui ont pour missions :

- de promouvoir l'excellence de la formation, de la recherche, de l'innovation et de la culture scientifique sur les champs thématiques qu'il porte, d'en renforcer la visibilité internationale et d'organiser les interdisciplinarités en interne et avec les autres PFR;
- de promouvoir la mise en cohérence des politiques de formation et de recherche en son sein ;
- de mutualiser en son sein, les plateaux techniques, les ressources documentaires, mais aussi d'harmoniser les services en charge de la communication, des relations internationales et de la valorisation, des structures de recherche impliquées dans le pôle, dans le cadre de la politique de l'établissement;
- de fournir aux services centraux de l'établissement les données pertinentes en matière de formation et de recherche, mais également d'insertion, de valorisation, et de gestion des ressources humaines, nécessaires au pilotage de l'établissement en matière de politique pédagogique et scientifique.

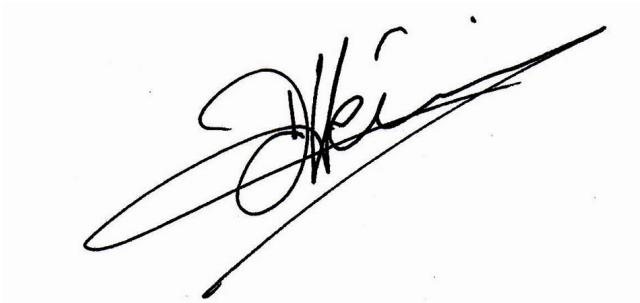
1809-2009
Bicentenaire de l'UM2

L'Université Montpellier 2 sera particulièrement attentive à ce que les recommandations formulées par le comité de visite soient prises en compte. Nous nous attacherons notamment à favoriser, par diverses actions, les relations de cette unité avec les autres disciplines scientifiques (chimie, physique), présentes au sein de notre établissement.

Il est bien évident que la relocalisation de cette unité dans un nouveau bâtiment (dont la construction touche à son terme), sur le site du CNRS, à proximité d'autres laboratoires de biologie (IGMM, CPBS), constitue une réelle opportunité pour le CRBM d'accroitre sa visibilité et son attractivité. L'Université Montpellier 2 accompagnera, dans la mesure de ses moyens, le CRBM dans cette évolution.

Il est à noter en réponse au comité d'expertise que l'absence d'évaluation d'une nouvelle équipe demandant son intégration au CRBM (page 7) est indépendante de notre volonté et relève de la seule responsabilité de la représentante de l'AERES. Cette équipe, dirigée par le Professeur Thérèse Commes est composée de deux Maîtres de conférences et d'un IATOS. Son intégration a été validée par la direction du CRBM et elle a vocation à rejoindre les nouveaux locaux sur le site du CNRS.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de mes respectueuses salutations.



Danièle HÉRIN
Présidente de l'université Montpellier 2