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

Section des Unités de recherche

AERES report on the research unit

Institute of Biology of Rennes

From the

University of Rennes 1

CNRS

December 2010

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Le Président de l'AERES

Didier Houssin

Section des unités de recherche

Le Directeur

Pierre Glorieux

December 2010

Research Unit

Name of the research unit: Institute of Biology of Rennes

Requested label: UMR

N° in the case of renewal: UMR 6061

Name of the director: PRIGENT Claude

Members of the review committee

Committee chairman

P. CHAVRIER, Institut Curie, Paris, France

Other committee members

K. NIERHAUS, Max Planck Institute, Berlin, Germany

R. MELKI, CNRS, Gif s/Yvette, France

C. JANKE, Institut Curie, Orsay, France

A. GERBER, ETH, Zurich, Switzerland

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Observers

AERES scientific advisor

C. DARGEMONT

University, School and Research Organization representatives

A. LE BIVIC, CNRS

P. DELAVAL, University Rennes 1

Report

1 • Introduction

- Date and execution of the visit

The site visit took place in Rennes on the premises of the School of Medicine of University Rennes 1, Health Campus of Villejean, on December 7, 8 and 9th, 2010. It was conducted by an international evaluation panel of twelve experts in the scientific fields represented by the nineteen teams evaluated. The visit started by a very short introductory speech by the Director of the future Institute of Biology of Rennes that will result from the fusion between CNRS/UR1 UMR6026 and UMR6061. Then, the Directors of UMR6026 and UMR6061 presented the activities and projects of each unit. The organization scheme of the Institute of Biology of Rennes into two Departments (Cell Biology & Development, Biology & Expression of Genomes) and two Transverse Programs (Biology of Human Pathologies, Biology & Interdisciplinarity) was presented by one Department Head. The principal activities of the various platforms were also presented (although not evaluated here). Then, each group leader (or co-leader) presented the activities and projects of their team during two and a half days of the visit. During the afternoon of the second day, the committee divided into different groups in order to have separate closed-door meetings with the different categories of personnel of the Unit (three meetings with the students, technician/engineers and post-docs/permanent scientists). The committee also met with the representatives of University Rennes 1 and CNRS. The visit ended with a closed-door meeting with the Director and the Deputy Director of the research Unit.

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

UMR6026 was created in 2000. It is composed of about 120 people in ten teams, nine located in one building of the Science Campus of Beaulieu, one located on the Health Campus of Villejean. UMR6061 was created in 2000 and renamed Institute of Genetics and Development of Rennes in 2008. It is composed of about 150 people, including 48 permanent researchers in eleven research teams including two ATIP CNRS and one AVENIR INSERM teams. It is located in two buildings of the School of Medicine on the Health Campus of Villejean in Rennes, close to the Pontchaillou Hospital. UMR6026 and UMR6061/IGDR participate in the Federative Institute of Research IFR140 "Functional Genetics, Agronomy and Health". These units also host several facilities, including two facilities that are part of the national scientific consortium GIS-IBiSA: the MRic platform (Micoscopy - Rennes Imaging Center) dedicated to Advanced Light Microscopy, Multi-Photonic Microscopy, NanoSIMS and Transmission Electron Microscopy; the Biogenouest® Genomic Platform of Rennes providing access to microarray production (transcriptome, genome and methylome) and statistical analysis of microarray data.

All teams are dedicated to fundamental research in the domain of cell biology and developmental biology (cell division, intracellular transport, cytoskeleton...), and genetics with implications in human diseases, such as cancers and genetic - mainly orphan - diseases and an emphasis on interdisciplinary approaches (especially physics and bioinformatics).

- Management team

The research Unit will be managed by the current director of UMR6061, assisted by a team leader as the deputy director.

- 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)	42	42
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	29	28
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 of the application file)	38	17
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	60,3	50,7
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	3,2	1,5
N6: Number of other researchers including postdoctoral fellows (Form 2.8 of the application file)	23	32
N7: Number of staff members with a HDR or a similar grade	43	41

2 • Overall appreciation on the research unit

- Summary

The Institute of Biology of Rennes will be composed of about 160 people in nineteen teams: fourteen teams from UMR6061 and five teams from UMR6026. There is a mixture of new, young teams, some promoted from within and some recruited outside from very good institutes in France or in Europe, and already established groups covering a wide-range of topics related to cell-biology, genetics and development with a strong emphasis on inter-disciplinary approaches. The unit will be headed by the former director of Institute of Genetics and Development of Rennes, assisted by a Deputy Director, who was already involved in organizing the fusion between the two UMRs. At the date of creation, the unit will be located in three different buildings of the Health Campus (Villejean) on the West side of Rennes, and one building of the Science Campus (Beaulieu), on the East side of Rennes. The new Institute of Biology of Rennes is clearly moving towards excellence. The Institute successfully recruited excellent young and promising teams, some already at a productive stage. The national recognition of several platforms within the GIS IBiSa consortium offering access to state-of-the-art advanced microscopy, genomics, proteomics and bioinformatics is also clearly remarkable. Finally, the Institute of Biology of Rennes is partially located and thus well-connected to the Pontchaillou hospital – providing unique opportunities for transfers from the bench to the bedside.

- Strengths and opportunities

- The institute appears well organized and is well guided by the current director.

- Attractiveness for promising young French group leaders coming back from abroad or from very good institutes in France attested by several INSERM-AVENIR and CNRS-ATIP groups.

- Active policy to financially support new teams that get extra money on the Unit's budget.

- Attractiveness for young researchers at CR or MCU level (12 new researchers during the 2006-2010 period and 6 new researchers corresponding to transfer of CNRS/INSERM CRs including 2 new team leaders).

- Some strong research axes including new thematics (membrane traffic & polarity, asymmetric division, epigenetics...), and inter-disciplinary research (biophysics, image analysis, bioinformatics...) with strong interface between biologists, physicists, clinicians and engineers.

- State-of-the-art facilities operating on the unit's (and IFR140's) budget including 3 platforms, which are part of the IBiSA consortium (MRic advanced microcopy, Microarray) with strong implication of several PIs, researchers and engineers of the Unit. Subsidized animal facility allows animal models to be developed.

- Links to the hospital provide the opportunity for medically relevant and translational research.

- Strong implication in teaching activity on the Health and Sciences campuses of University Rennes 1.

- Weaknesses and threats

- Attractiveness on the international level of non-French group leaders and young researchers is limited. This is a general problem in France, but an effort must be made to improve the recruitment of young researchers from abroad and to increase the turnover.

- The ratio of permanent vs. non-permanent researchers (e-g postdocs) is unbalanced and too high. The turnover at researcher level is also low.

- The size of some of the teams is suboptimal, and an effort should be made to increase size in order to achieve the proposed goals and reach and maintain visibility on the international level.

- In several teams, the ratio between researchers with teaching duties and those without is too high.

- Funding visibility of some of the teams is low. The teams should be encouraged to secure reasonable funding and raise more external funding on the national and international level (HSFP, ERC,...). A more active funding policy will also make teams more competitive in recruiting post-docs.

- Overall production of the unit is good and impact factors have improved, however the level of publications of some of the teams is rather average. Clinicians and biologists should collaborate efficiently and publish in journals with a higher impact factor.

- The participation of team leaders and researchers in international meetings as invited speakers is limited and there is clearly space for improvement here as well.

- Recommendations to the head of the research unit

- One of the main problems of the institute concerns the shortage of laboratory space. The institute foresees a major reorganization and thus, the number of participating groups will increase. Unfortunately, it is planned to split the institute in several places in Rennes. It would be better to centralize the Unit in one place as the distance between groups may impinge on vision to set-up strong communication between laboratories. University Rennes 1 envisages the possibility of regrouping the teams on the Health Campus in the future. However it is essential that this be acted upon at once to avoid delayed integration and destabilization of these teams.

- The different categories of personnel of the unit are very positive about and are willing to accompany the fusion project. However, some concerns were raised by ITA and IATOS regarding a number of customs within one or the other Units they wish to see generalized in the future unit. These issues should be clarified by discussion with the Direction of the future Unit.

- Given the idea to reinforce an interdisciplinary research environment for the future, further efforts are required to provide the basis for this very exciting idea (e.g. planning an early retreat for the entire Unit).

- Recruitment policy of non-permanent young researchers from abroad should be reinforced through active fund raising both on national and international (European Community,...) levels. Local possibilities of fellowships also exist from University Rennes 1 and the Région, which should be further explored and more actively exploited. The presence of a too high number of permanent researchers in the teams should be avoided as it reduces the turnover, and thus dynamism of the team.

- The Unit has formulated unique policies to support new research teams. However, a starting package of Eur 10,000 for new teams is somewhat limited. Possibly, the starting budget could be increased to allow the acquisition of special equipment, which may occasionally be necessary to perform world-class leading science. This package should also include a budget to hire non-permanent young researchers, favoring recruitment of foreigners whenever possible.

- The Unit should consider reinforcing its policy regarding the training of the Master and PhD students and postdocs through the organization of workshops (theoretical and practical) involving researchers of the Unit or outside. A small budget may be allocated to organize one-day classes by first-class scientists from France or abroad. English should be generalized for seminars.

- The institute is partially located at the Pontchaillou hospital in Rennes. Therefore, the great opportunity to bring results from the bench to the bedside (translational programs) should be taken into consideration. This aspect needs being reinforced in the future.

- Several groups have two co-leaders. This does not correspond to the general world-wide accepted group organization. In most of the cases, co-leadership is not justified and may even be detrimental for the running of the team and its visibility. These issues should be dealt with and leadership should be redefined through discussion between the director and the research teams.

- The evaluation committee raised concerns regarding one new team made of only one researcher (Team 4). The quality of this young researcher also is unquestionable. The proposed questions are novel and the project integrates nicely into the Unit's policy to reinforce inter-disciplinarity. However, this team comprises only a team leader and is entirely dependent on the implementation of imaging techniques that make the project risky, with unpredictable outcome. At the present stage, developing a team on this project and in this context is premature. The committee therefore recommend to integrate the expertise of this young researcher into a more established team (possibly team 14).

- Production results

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

A1: Number of permanent researchers with teaching duties (recorded in N1) who are active in research	42
A2: Number of permanent researchers without teaching duties (recorded in N2) who are active in research	28
A3: Ratio of members who are active in research among staff members [(A1 + A2)/(N1 + N2)]	1
A4: Number of HDR granted during the past 4 years	14
A5: Number of PhD granted during the past 4 years	42
A6: Other relevant item in the field *(i.e. number of first and/or last authors original publications in peer review journals)*	254

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

Team 1:"KIDNEY CANCER: MOLECULAR BASIS OF TUMOROGENESIS"

Leaders: Yannick ARLOT-BONNEMAINS & Cécile VIGNEAU

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	6	4
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 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)	2	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		0
N6: Number of Ph.D. students (Form 2.8 of the application file)	1	2
N7: Number of staff members with a HDR or a similar grade	6	6

- Appreciation on the results

This team includes 7 permanent scientists (3PU-PH, 1 MCU and 3 CNRS), 3 PhD students and two ITA. Originally, the team was created by a clinician, who co-directed it with another clinician in order to study renal carcinoma. The announced objectives were attained as assessed by a huge number of publications signed essentially by the clinician who initiated the team. Now the team has been completely reorganized, subsequently to the departure of the team's founder and of two other PU-PH. Three CNRS researchers and also a MCU coming from other teams of the Institute will join the group to develop the fundamental aspect of the research project in close relationship with the clinicians. This will provide expertise in genetics, cell biology and post-translational modifications. This was necessary for the development of the molecular and biological aspects of project, which was originally managed only by clinicians.

Subsequently to clinical data, the group's objectives focus on the role of pVHL deregulation in the development of Clear Cell Renal cell carcinoma (CCRCC). pVHL is a well known E3 ligase involved in the degradation of several proteins such as HIFa (Hypoxia-inducible factor) and mutations have been observed in CCRCC. The team will analyze pVHL mutations, phosphorylation state, E3 ligase activity and interaction with the microtubule network in different CCRCC cell lines, an *in vivo* model (mice) is currently being "developed".

The group developed several cultured cells systems and has access to a renal tissue bank. They also have expertise in renal pathologies. The researchers who joined the team with expertise in biology, have to invest a lot in the subject, which necessitates novel biological and molecular approaches. However, how they will organize for the realization of the work is not very clear.

There is a very impressive long list of publications from this team. However it is essentially papers in medical and specialized journals. In fact, only the scientists who recently joined the team have a reasonable publication record in the field of biology and biochemistry. This point should be improved in the future.

A clinical database and a renal tumor tissue bank have been created in Rennes, making the strength of the team. It also represents a good example of connection from the patient's bed to bench. However the credibility and

visibility of the biochemical aspects of the project are based on the new members and new co-leader of the team. They should efficiently collaborate with the clinicians.

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

The past team leader was nationally and internationally recognized as a leader in the field of renal carcinoma. This is supported by a considerable number of invitations to give invited talks in national and international clinical meetings in the field of urology. The other team leader also participated to a substantial number of international meetings. Continuing in this way should help to improve the visibility of the group in the future. However there is a dramatic lack of contacts with national and international partners in the field of VHL at the biochemical point of view.

The team was able to secure reasonable funding during the last period. However the forthcoming biochemical research should make the group competitive in raising more external funding. It should also make the team more active in recruiting post-docs, more particularly from abroad.

- Appreciation on the strategy, management and life of the team

This is a solid, well-organized team, with senior members highly motivated who drive their team very well. Clinicians and biochemists are complementary for the realization of the project, which is a very good example of connection between the patient's bed to the bench.

- Appreciation on the project

Subsequently to clinical data, the group's objectives focus on the role of pVHL deregulations in the development of Clear Cell Renal cell carcinoma (CCRCC). The visibility and the feasibility of the project rely on the complementarities of the clinicians and biochemists.

- Conclusion :

  – Summary

This reorganized team is a promising operating team in a highly competitive field. As most of the team's members were involved in clinical activities, they set up very interesting databases which represent an inestimable power for the future and for moving to molecular and biological aspects of the field of renal cancer. There is a strong potential for further scientific development

  – Strengths and opportunities

Mixing clinic, molecular and cellular biology makes the strength and the originality of the team. The most important strength is the access to patients that opens for translational research. In addition, the connection between Aurora A and VHL seems to be rather exciting and original.

  – Weaknesses and threats

Unfortunately, there is no obvious demonstration of leadership for the two new group leaders who have been proposed. In addition the level of the past publications is rather average.

  – Recommendations

The clinicians and biologists should collaborate efficiently and publish in journals with a higher impact factor. They should also participate to international meetings and initiate collaborations with other laboratories in the field of VHL and ubiquitin ligases. Due to the important link between the patient's bed and the bench, this team should be strongly mentored by the director and deputy director. However, the team leaders have to prove themselves and thus the opportunity to pursue should be reevaluated in 2 years.

Team 2 : "CELL CYCLE"

Leader: Claude PRIGENT

- Staff members

	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)	9	6
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 of the application file)	5	2
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	6	2
N7: Number of staff members with a HDR or a similar grade	6	2

- Appreciation on the results

This team is and has been focused in understanding how protein kinases regulate cell cycle progression in mammals/vertebrates. This topic is of high interest and relevance since cell cycle regulating kinases are strong candidates for targeted chemotherapy in several human cancers and are currently in clinical trials. The basic understanding behind the role of protein kinases in the command of the cell cycle machinery is therefore of utmost importance and is also an extremely competitive field. Importantly, this group has made seminal contributions to this topic, in particular on the protein kinase Aurora A, which had a large impact in the field about 10 years ago. More recently, the group appears to have been more dispersed, with secondary contributions in very good journals, and touching other topics by new team members, such as protein neddylation and ubiquitination. To what concerns the role of phosphorylation, the group is now focusing on the role of protein kinases involved in late stages of mitosis. This new focus is a smart move because very little is known about late mitotic stages. In this subject, the publication output is still limited, with one paper in revision in Journal of cell science on the Mnk1 protein kinase and its role during cytokinesis.

The team has a strong track record both in number and quality of publications over the last years, with several important contributions as main or secondary authors. In the last 5 years, and in the particular case of the team leader, the output has diminished, with only one shared senior authorship, which may reflect a heavier administrative burden. However the new focus on mitotic exit and the availability of a cell line expressing a Shokat mutant Aurora A will very likely invert this less productive trajectory, with several manuscripts in preparation. The team leader is regularly invited as speaker in National meetings and the team has regular presence in International meetings presenting several communications in poster format.

The team has established important international (including leaders in the field), national and local partnerships, which resulted in several high-quality publications. In future terms, some collaborations is to be strengthened. Previous partnerships with other labs appear solid and turned out to be important for the scientific output, as reflected in a number of joint publications.

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

One CNRS award to a staff scientist. No relevant invitations to international conferences and symposia, but the team is well recognized internationally.

The team has recruited excellent scientists in the past, one is now an independent group leader at the same Institute. More recently, the team has recruited two young researchers who came from internationally recognized

laboratories and are expected to develop into independent groups in the short term. The team also recruited two foreign students.

The team has a strong track record in fund raising and obtaining financial support from grants (over 1 million euros since 2004), and has already granted about half a million euros that will run until the end of 2013. This is quite remarkable and revealing in terms of the team's competitiveness for funding. There is also some commercial licenses with several companies on monoclonal Aurora A antibodies. No particular scientific cluster identified.

No clear indication on the participation of international or national networks. There are however long-lasting collaborations with foreign partners that appear very solid and resulted already in joint publications.

License on the commercialization of monoclonal Aurora A antibodies.

- Appreciation on the strategy, management and life of the team

The team is well organized and prepared for the transition to new fused Institute. The current research program is well thought and suitable to the team's expertise and track record. There is also a good balance between experienced and young researchers, which favors mentorship. The team leader has also been involved in the organization of scientific meetings and the team can be reached externally through a website.

Two team members who have recently joined will be starting new promising research lines (protein neddylation and the relationship between Cohesion and DNA repair). The construction of (state-of-the-art) Shokat Aurora A mutant is a powerful and unique tool to reveal Aurora A functions throughout mitosis and will result in cutting edge projects.

There is no clear indication on teaching duties, but the team clearly represents an International reference for this research unit, with a clear role in the local development of research activities and promotion of junior PIs to full independence.

- Appreciation on the project

The team will maintain its main focus on the study of Aurora A and has been developing state-of-the-art tools to study Aurora A kinase function throughout mitosis with high temporal resolution. The potential implications on cytokinesis and the spindle checkpoint are of very high interest and relevance. Additionally, the strategy used to identify new Aurora A substrates is extremely powerful. The team is also collaborating to generate mouse models to study Aurora A function, which might turn into valuable mammalian models to investigate the clinical potential of Aurora A inhibition. In addition, the investigation of protein kinases involved in mitotic exit is a smart move, as there is plenty of opportunities and very little known.

Resources are accessible thought core facilities run by permanent staff. The team leader directs the Microscopy facility, which is the most relevant for the research program proposed.

Overall, the research plan is original and based on a solid track record. The potential for cutting edge projects is high, specially associated with the role of Aurora A throughout mitosis, the role of protein kinases in mitotic exit and the study of "less-conventional" protein modifications have high potential.

- Conclusion :

  - Summary

This is a team with solid contributions in the cell cycle field, which are internationally recognized. Their work and knowledge on Aurora A has been and will remain their most competitive advantage. The team has slowed down a bit their independent research program over the last 5 years, maybe due to increased administrative duties of the team leader, but the team has designed a competitive and feasible research program that will most certainly invert this less productive period.

  - Strengths and opportunities

The team has a solid track record and expertise with protein kinases. The research team is balanced with a number of senior members that can work independently.

The team has developped unique cellular and animal models to study Aurora A activity with high temporal resolution throughout mitosis with a focus on the poorly explored role of protein kinases during mitotic exit. The investigation of the role of protein neddylation and the role of cohesin in DNA repair represent two niches of opportunity in the medium/long term.

– Weaknesses and threats

Protein kinases are a highly competitive field and the administrative burden of directing the new Institute may compromise a timely and successful implementation of the research program.

Given the number of permanent researchers in the team, there is little space available to promote healthy turnover.

– Recommendations

Increase the turnover within the team with recruitment of foreign postdocs.

Increase the international visibility of the group leader

Team 3 : "CYTOSKELETON AND CELL PROLIFERATION"

Leader: Régis GIET

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	0	2
N7: Number of staff members with a HDR or a similar grade	0	1

- Appreciation on the results

The team leader was formerly part of the team 2 and they have published together over the years in what has been a clearly fruitful cooperation. However, it was not clear whether they followed completely independent research lines, with them sharing inclusively senior authorship in some project(s). Despite this fact, it should be highlighted that the contributions of the team leader, signed as senior author, are of high relevance and impact, including papers in reference journals in the field such as J. Cell Biol., which is clearly above the average in the context of this research unit and of international level. Among these contributions, the role of PRP4 in the spindle checkpoint had a high impact in the field, but we were surprised that there was no independent follow-up on this protein and its relationship with the spindle checkpoint. In general, we were a bit confused with the past strategy and research program of the lab, going from the role of motor proteins in anaphase and cytokinesis, the spindle checkpoint, centrosome maturation, bipolar spindle formation, and protein kinases such as Aurora A. This reflects plasticity of the team, but on the other hand imposes some need to focus to remain competitive in this field in the long term. This need to focus appears already to be reflected in the research program presented, with the goal of identifying and characterizing MAPs involved in cell division during the development of the central nervous system of

Drosophila. This topic has been poorly explored and represents a powerful and relevant research line, within the team's expertise.

The team leader publishes regularly in very good journals, some of which have a strong impact in the field. This is clearly exceptional record within this research unit and internationally very competitive. No record of invited seminars but regular poster presentations in international meetings. He is currently supervising two PhD students.

The team leader has long-term collaborations with team 2 and his former postdoc lab, both being his former supervisors. These are obviously helpful when one is starting an independent research program, but may limit the visibility of the junior PI. In addition, the team leader has granted local and external (Institut Jacques Monod, Paris) collaborations with internationally reputed labs, which are appropriate for his new research program.

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

The team leader has been awarded the Bronze medal from CNRS in 2008. He clearly enjoys from an excellent local and national reputation, but at the international level this is at least not reflected by invitations to conferences and symposia.

The team is relatively recent and has one permanent staff member, two PhD students and one technician, all apparently French.

The team leader has been awarded an ANR grant (150 Keuros) while formerly in part of another group. This grant ended in May 2010, however he currently participates in one grant from ARC together with a team in Paris and team 19.

No indication of international networks but participates in one national network, including local collaborations. Previous international collaborations were with former post-doc advisor, and more recently with a group in Germany.

- Appreciation on the strategy, management and life of the team

This is a new and young team, which appears balanced but needs to focus its research.

As a full time researcher the team leader is not directly involved in University teaching, however the team was able to attract two PhD students and seems quite dynamic and collaborative with other local labs.

- Appreciation on the project

The project of the new team will be based on the past work of the team leader, focusing on the isolation and identification of novel microtubule-associated proteins that play essential roles in cell division. The research approach proposed by the team is coherent, and also solidly based on the competences of the team leader. The basic idea is to identify microtubule associated or interacting proteins, which play a specific function in cell division. Starting with a proteomic approach (comparative isolation of microtubule-associated proteins during mitosis and interphase), the group wants to identify candidate genes with specific functions in mitosis. Subsequently, they will obtain Drosophila RNAi strains that suppress specifically (and efficiently) the expression of these genes in the central nervous system and perform functional studies. This approach is aimed to identify novel cell cycle regulators that are important in the context of the whole organisms where cells are dividing under physical constraints and in a polarised manner. This is in contrast to previous approaches (like MitoCheck) where immortalized cell lines have been used to study the regulators cell division.

The scientific project of this team is of good quality and well thought. The necessary collaborations at the local and National level have been assured, and there is sufficient funding for the next two years available

Resources are accessible through core facilities run by permanent staff. Fly stocks are also available through the Vienna RNAi Center. Funding sources of the team are good, and the team is involved in several collaborations.

The research covered in the proposed program deals with neural stem cell division, one of the hottest areas in the cell biology and biomedicine fields. The proposal overall is original and brings together a set of complementary expertise that are well designed and are likely to result in high impact publications.

- Conclusion :

– Summary

This is a promising team leader. The team leader has made significant contributions to the field, mostly in collaboration with former PhD and post-doctoral advisors. The research program for the next 4 years is original, relevant and realistic and will help the lab to focus on a highly competitive subject.

– Strengths and opportunities

Good track record in the field; Young and dynamic team; Exploration of an important niche related with stem-cell research; Scientific environment is adequate for the proposed project.

– Weaknesses and threats

The group leader made the choice to stay in the same unit. This may compromise his chances of raising competitive funds and his national and international visibility; poor record of international invitations to conferences ; No clear proof of future funding for the proposed research program.

– Recommendations

This is a highly promising research team that must be supported by all means. Clear recommendation to focus the present/future research and develop a truly independent research program that is not coincident with previous mentors. Internationalization by means of collaborations, organization and participation as invited speaker in international conferences should be encouraged to increase the visibility of the work, attract talented students and postdocs and be competitive for national and international funding. Should be encouraged to apply for ERC starting grant.

One recommendation is to accommodate Teams 3, 11 and 19 in very close vicinity in the new unit to allow daily interactions in addition to joint lab meetings and journal clubs, etc. in order to strive for the creation of a strong microtubule hot spot in the research landscape of the new institute.

Team 4 : "DYNAMICS OF CHROMATIN ARCHITECTURE"

Leader: Sébastien HUET

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	0	0
N7: Number of staff members with a HDR or a similar grade	0	0

- Appreciation on the results

This newly established research team proposes to study dynamics of the chromatin architecture. The proposed questions are of novelty and originality, with however limited resources. But this concerns the projects rather than the results. We don't think we can evaluate the results, as the team was not part of the unit before.

The PI has published 9 papers during the passed 4 years, with 2 (Biophysic Journal and J. Virol) first author paper, and 2 shared 1st author papers (one in EMBO J).

A collaboration will be established with a team of the IGDR for the use of FRET imaging at high acquisition rates to study chromatin condensation in prophase. The PI also has several national and international collaborations.

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

- Appreciation on the strategy, management and life of the team

There is currently no team, just a team leader.

The team leader is MCF but has a Chaire CNRS-UR1. It is unclear whether he is involved in teaching.

- Appreciation on the project

The scientific project of the team is at the interface of physics and biology. It addresses important questions related to the organization of chromatin in the nucleus. It is mostly based on innovative microscopic approaches and biophysics tools. There are 3 mains axes that will be developed. The first part focuses on the analysis of the chromatin in interphase. Two different approaches will be undertaken to be able to visualize in live cells the chromatin of a single chromosome. The second axis concerns the reorganization of the chromatin fiber during prophase and relies on one of the tools used in the first part. Descriptive analysis will be combined to functional approaches in order to explore the impact of candidate proteins on chromatin condensation. The third part aims at studying higher levels of folding of the chromatin fiber. This difficult task depends on a PALM microscope.

Unfortunately, it is not clear whether the team have already access to such a microscope due to unclear financing source. The feasibility of the project in a 4-years period is difficult to assess with limited previous basis. It largely depends on advanced imaging techniques, which can be risky.

The financing support of the team is not clear at this stage. So far the team leader is the only member of the team.

The project is innovative and relies on novel microscopic approaches. It addresses original questions related to the organization of the chromatin in the nucleus and the dynamics of the chromatin architecture during various biological phases of the cell (cell cycle, transcription). However, the project is very risky.

- Conclusion :

  - Summary

The approach heavily depends on implementation of imaging techniques that makes the project risky, and the outcome difficult to predict. Developing a team on this project and in this context is premature.

  - Strengths and opportunities

The main strengths of the project are its potential for cutting-edge technologies and its interdisciplinarity.

  - Weaknesses and threats

There is no research team and no financial support at place. The whole program relies on people and instruments that are not available yet and not guaranteed. The group leader has limited background in the chromatin field.

  - Recommendations

Developing a team on this project and in this context is premature. The recommendation is to integrate the expertise of the team leader in a more established team (such as team 14, possibly). The effort to develop a super-resolution microscopy system should be a concerted action of the imaging plateform together with the unit, which will also be beneficial to other teams.

Team 5 : "EPIGENETICS AND CANCER"

Leader: Christian JAULIN

- Staff members

	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	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 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)	0	0
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	0	1
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

The team was created in 2004 in Montpellier and moved to the IGDR in Rennes in January 2008. The main project of Team 5 is to explore the role of HDAC activity during mitosis and in particular during the establishment and maintenance of mitotic spindle assembly checkpoint (SAC), in order to better understand the anti-proliferative activity of such enzymes. The team has shown that indeed, HDAC activity is necessary for SAC function. In contrast to most models involving HDAC, this mechanism appears to be independent of transcription. These results have potential important consequences in anti-tumor strategies. The team has also obtained data on the role of HDAC3 in sister chromatid cohesion, providing a functional link between sister chromatid cohesion and the mitotic "histone code. They have also revealed an unexpected role for Aurora A in maintaining sister chromatid cohesion via phosphorylation of CENP-A.

The team has published five articles (one per year) in journals of impact factors from 3,2 (Chromosome Research) to 12,75 (Genes and Development). This is very good given the small size of the team. In addition to these, members of the team are associated with 7 publications.

The team leader has been invited to one international meeting, and has participated to three other meetings (with posters for 2 of them). It appears from the list provided that other members of the team have not been communicating at meetings. Participation to international conferences should improve.

There was only one PhD student who was in the lab until the end of 2008. This student is second author on two publications, but has no accepted publication as first author. It is mentioned in the project part that such a paper has been submitted. A new PhD student has joined the lab in Sept 2010.

The team has local (team 2), national and international collaborations. Several publications were obtained from the collaboration with the team in Orsay.

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

The team leader has been invited to one international meeting. The team leader has been promoted DR2 at the INSERM.

The attractiveness of the team seems rather limited so far and recruitment from abroad should be improved. There is only one post-doc currently in the lab, who is coming from Rennes. The previous post-doc has been recruited to the Team as CR2 at the CNRS, highlighting the high quality of this researcher, who is coming from Montpellier, where the Team comes from. This researcher is part of many of the lab publications, including one as 1st author position in Genes & Dev. The ability to attract scientist from abroad or from elsewhere in France is a general problem in the Institute, which should be improved.

The team leader has been very successful in raising funds at many local and national grant institutions, including the ANR.

There is no report of participation of the Team to national or international networks. However, the team collaborates with foreign partners (one in Japan, one in the US).

The results on the role of HDAC in mitotic spindle assembly checkpoint might have consequence in anti-tumor strategies. However, no socio-economic partnership has been established to exploit these results (patents etc).

- Appreciation on the strategy, management and life of the team

The team is rather small. It would be important to recruit at least few non permanent members.

The team's projects are very original and therefore contribute to cutting edge research in the institute.

The team leader has been appointed deputy director of the new unit, and he therefore plays an important part in the re-organization of the Institute and the structuration of the research at the local level.

- Appreciation on the project

The project of the team is to gain insights into the epigenetic control of centromeric function. To date, most of our understanding of histone modifications at centromeres comes from antibody-dependant approaches, which are limited by the existence and the quality of such antibodies.

The first part of the project consists in identifying systematically (by mass spectrometry) centromeric histone modification using a CENP-A Tap-tagged strategy and to study the role of such modifications in centromere function. This part relies on collaboration with the proteomic platform of the University of Laval. Profiles of interphase and mitotic chromosomes will be compared.

The second part of the project follows the recent identification, by the team, of a novel histone methyltransferase for H3K4 that is specific for H3K4 methylation at centromeres. To validate the hypothesis that H3K4 methylation at centromere is important for sister chromatid cohesion, the team plans to identify interacting factors through streptavidin-biotin affinity approach.

The last part of the project aims at unraveling the different functions of Aurora B kinase in mitosis through specific inhibition of its activity at different time-points during this process. To do so, and to avoid unspecific effects of inhibitors, the team will generate a mutant version of Aurora B, which responds specifically to a given inhibitor. This part will benefit from the expertise of the Team 2 which has used a similar approach for Aurora A.

These three main projects are very exciting. They might be a little bit too ambitious given the actual size of the team.

Overall this project should shed new lights onto the epigenetic control of centromere function.

The 3 axes, which are developed by the team aims at addressing related questions concerning the regulation and the function of histone modifications during mitosis, but in independent ways. This organization presents two main advantages: (i) problems encountered in one specific project will not hamper the progression of the others and (ii) results from one project can benefit the others.

The project is overall ambitious and appears well structured. Deciphering the “histone code”, or at least the catalogue of histone modifications that are present at centromeres is important as so far our knowledge on the subject is limited. The identification of a novel H3K4 HMT apparently specific for centromeres represents a real breakthrough.

- Conclusion :

  - Summary

The team has obtained very interesting results concerning the epigenetic regulation of centromere function and continues addressing very important questions. The proposed project is ambitious and the team has integrated well in the Unit.

  - Strengths and opportunities

The scientific questions are well defined and exciting. Important results in the field of epigenetic regulation of centromere function have already been obtained by the team. The team contributes to reinforce research in the epigenetic field of the Unit. The publication record is very good.

  - Weaknesses and threats

The project is ambitious and the team should increase its size to achieve the proposed goals.

There is not enough participation of the team to international meetings, especially for members other than the team leader.

The attractiveness appears limited.

– Recommendations

The team should improve attractiveness and visibility by recruiting post-docs from abroad (internationally) and through participation to international meetings. The size of the team should also increase a little (through the recruitment of short-term members such as post-docs or PhD students rather than with permanent researchers), especially since the team leader will be involved in the structuration of the Unit as a deputy director.

Team 6 : "GENE EXPRESSION AND ONCOGENESIS" (GEO)

Leader: Marie-Dominique GALIBERT

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	5	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 of the application file)	6	4
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	5	2
N7: Number of staff members with a HDR or a similar grade	5	2

- Appreciation on the results

The team includes 4 staff scientists, 2 post doctoral fellows, 2 pHD students and one technician. Unfortunately, the organisation of the team has been modified with one of the two co-leaders who left and is now at the head of another team. Consequently, the size of the team also decreased around half.

The team focuses on understanding the genetics and epigenetics mechanims involved in the transcriptional deregulations of cancer, with two models, melanoma and the TEL/AML1 positive childhood leukemia. They developped genomic screens and microarrays and selected factors involved in the progression of these cancers (TYRP1 in melanoma, UDF1 in UV-dependent skin cancers and RUNX1 in TEL/AML1 leukemia). The aims for the forthcoming years are to analyze the precise functions of these factors by combining invalidation strategies, examination of target gene expression profiles (ChIP seq), and the analysis of the transcriptional regulation of the corresponding genes (epigenetic modifications of the promoters). The team has a strong background in the field and developped the adequate tools.

The team leader is regularly invited to international meetings in France and abroad. Several PhD thesis have been defended during the last years. However, though very long, the list of publications is rather average.

This is a dynamic team which set up tumour sample collections and organized a network of international collaborations.

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

The team leader is recognized in the field and is invited in several international meetings. Moreover the group attracts PIs from abroad as visitors and regularly recruits new PhD students and post docs. However, due to the recent decrease in the size of the team, new students should be recruited during the forthcoming year.

The team also succeeded in raising substantial funding from diverse organisations (LNCC, ARC, Region Bretagne). However most of them end at the fall of 2010. Submitting new applications in the forthcoming months is absolutely required to continue the work.

Finally, the group has established effective and complementary collaborations with local (Rennes University and Hospital), national (in Strasbourg) and European (in Bruxelles) partners. In addition the project integrates the Cancéropôle Grand-Ouest Glioma network, and several clinical networks (Grand Ouest hémato-onco-pediatrie anf the french therapeutical group FRALLE).

- Appreciation on the strategy, management and life of the team

This is a dynamic team with a strong communication policy. Unfortunately, all team members contribute to teaching, decreasing the time devoted to research.

- Appreciation on the project

The team focuses on understanding the genetics and epigenetics mechanims involved in the transcriptional deregulations of melanoma and the TEL/AML1 positive childhood leukemia. This is a challenging and promising project but the strong background of the team in the field as well the network of collaborations makes it feasible, though funding appears to be limited for the forthcoming years.

- Conclusion :

  - Summary

The project is a good combination of clinical and biochemical approaches on 2 models, melanoma and leukemia.

  - Strengths and opportunities

The team is dynamic with efficient collaborations, a good network and good access to patients and approaches

  - Weaknesses and threats

Unfortunately the publications are rather average. Moreover funding visibility is limited.

  - Recommendations

The team should go deeply into the different points of the project, focusing mainly on the mechanistic issues. The team should be more active in raising funds.

Team 7 : "GENETIC EXPRESSION AND DEVELOPMENT"

Leaders: Serge HARDY & Luc PAILLARD

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	5	4
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 and 2.7 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)	2	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	2	2
N7: Number of staff members with a HDR or a similar grade	4	3

- Appreciation on the results

The research activity is focused on the biochemical characterization of RNA-binding proteins (RBPs) and their implications for development in vertebrates. Thereby, the team has focused on the frog Xenopus leavis (embryos) as a model to address the physiological relevance of RBPs. They integrate mechanistic studies and high-throughput screening e.g. for identification of targets for selected RBPs. Four major projects have been pursued:

i) Studies on tissue-specific splicing regulation by the polypyrimidine tracts binding proteins (PTB). They defined a regulatory cis-acting element that determines alternative splicing of alpha-tropomyosin mRNA-precursors in myotomal cells compared to other cells. They also established protocols to deplete splice-site recognition with antisense morpholino oligonucleotides and showed the physiologic relevance for this splicing event in muscle cells. They also implemented several proteomic approaches to identify other or novel RBPs that participate in splicing regulation.

ii) Function of Celf1/CUGBP1 in somite segmentation. Celf1 is a highly conserved RBPs that regulates somatic segmentation without impairing myotomal segmentation in X. laevis. In the last period, the researchers found an important mRNA target for Celf1, called Su(H), that could be associated with segmentation defects caused by Celf1 mis-regulation.

iii) Since other crucial targets for Celf1 may exist, the group has established procedures to globally identify targets for this RBP with cross-linking immunoprecipitation of Celf1 followed by sequencing of bound RNAs (so-called CLIP-Seq assay).A first analysis of CUGBP-1 targets in HeLa cancer cells defines almost 3,000 potential mRNA targets, most of them are bound in 3'-untranslated regions (UTRs).

iv) Chromatin dynamics and genome-wide controls of gene expression. In collaboration with teams at the UMR6026, the team performed a gene expression profiling of breast carcinoma cells treated or not with estradiol, defining a list of responsive genes. This project gave some promising results – whatsoever, it is not in strong line of the other research activities regarding the level of gene expression control (transcriptional control) and model system (human cell lines).

During the passed 4 years the group has achieved interesting results of good quality.

The research team has published 28 publications with average to good impact. They got two scientific invitations to international conferences (However, there are no invitations for the two current group leaders). The

data was orally presented at eleven meetings, nine of them located in France. They also presented more than 15 posters at meetings, mainly in France. Five Ph.D. completed their thesis, and one habilitation.

The team established 2 local, 2 national and 2 international collaborations. Most of these collaborations should be continued, and new ones will be encountered in the future.

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

Since the team uses latest genomics technologies (e.g. high-throughput sequencing), it will certainly remain attractive for many students and postdocs in the future. Moreover, their great expertise with frogs as a model system makes them attractive for other groups that even work in less-related fields of research. The group should persist on this unique expertise with this animal model.

The PIs and group members had been to numerous conferences.

The team was able to attract several PhD students (5) and postdocs (2). Since the postdocs left the lab, the team should try to attract new postdocs – if applicable they should come from another country.

The group has obtained substantial funding through the last years. This includes prestigious grants from the ANR, ARC, and the CNRS. No international grants were obtained.

- Appreciation on the strategy, management and life of the team

There is apparently a good atmosphere in the group. Two group leaders will share the lead of this team and did not report any problems by doing so. However, shared leadership may become problematic in certain circumstances and may cause difficulties to track responsibilities. Clear rules and responsibilities have to be defined – just in case some problematic event may arise.

The implementation of latest genomics expertise is state-of-the art. However, the group mainly works on two RBPs that are studied for years now. Although there are certainly many novelties that can be discovered in the future, the group may think to study/screen for other RBPs that play roles for important physiological processes in the frog. Embarking new lines of research may lead to more high-impact journal publications.

Four members of the team are involved in teaching. The team appears to have a heavy teaching load.

- Appreciation on the project

The proposed project will investigate the function of selected RNA-binding proteins in vertebrate development. It is planned to integrate high-throughput approaches to define targets and impact of RBPs on mRNA fates and then to perform more detailed cellular and biochemical analyses on particular mRNA targets that are physiological relevance. Therefore, the future research is mainly in line with previous activities and no major changes in the research direction are foreseen. The proposed project is divided into 4 work-packages:

i) The group wishes to dissect the molecular details for alternative splicing of tropomyosin in X. laevis. The group has apparently found several candidate RBPs by proteomics means that could also participate in the regulation of this message. However, the next steps for this analysis should be and what these proteins are is not greatly explained in the project synopsis.

ii) Phenotypic analysis of animals inactivated for RBPs. This is a descriptive study of RBPs and their effect upon depletion in X. laevis. For instance, PTB should be depleted and splicing substrates should be revealed with DNA microarrays/ deep sequencing. Likewise, the authors suggest to study Celf1 protein function in mouse models (collaboration with other groups with mice genetics expertise). We wish to note that similar studies have been previously performed with orthologous/related RBPs in other systems. Therefore, we propose think about embarking new studies on other, less-well characterized RBPs that show interesting phenotypes in this animal.

iii) Genome-wide identification of deregulated mRNAs in RBP knock-down animals and

iv) Global identification of targets for RBPs with CLIPseq (see above).

Both of these projects propose to use latest genomics technologies to unravel targets for PTB and Celf1 and possibly for other RBPs. At this point, such an analysis is becoming necessary to unravel the impact of these proteins

for gene expression control. The group has recently undertaken efforts to establish these techniques in the lab and preliminary results that were obtained and sound promising. Of note, the genome-scale analysis may need the implementation of bioinformatics and moreover, clear questions have to be addressed for analysis of genomics data. Likewise, difficulties may arise with the integration of data obtained from the genome-wide screen and the physiological relevance. This is a difficult task and how the data should be analyzed in this regard has only been vaguely described.

There is collaboration with diverse platforms run at the University of Rennes I. Furthermore, collaboration with sources for deep-sequencing have been established.

The project appears to be profound. The researchers will implement techniques that have been developed by other laboratories. The methologicaly advantage is mainly given by the implementation into the frog model. The morpholino-based antisense oligo approach could hold great promise in frogs and could be used to screen for factors that participate in important developmental processes (such as segmentation defects in early embryos).

- Conclusion :

  - Summary

The project basically follows previous lines of research focusing on PTB and Celf1 RNA-binding proteins to target their mechanistic and functional roles. Several tools are available now in the lab that gives the team advantage to other teams in an international and competing environment. These are mainly the establishment of the CLIP-Seq technology and profound expertise with the frog model system, which is rather unique in the field of post-transcriptional gene regulation. The group should take advantage of this unique opportunity. The project plan is less-well defined - a more detailed research plan may be beneficial to formulate a more clear vision for future. Finally, the group was able to attract substantial funding for their research and is generally well organized.

  - Strengths and opportunities

The team has unique opportunities because of the great expertise with X. laevis model system. This allows combining biochemical approaches, genetics and physiology. The team may even become very influential group in their field, if they could combine the frog model with latest functional genomics to screen for “novel” RBPs that play important roles for development.

  - Weaknesses and threats

The team should try to attract new Postdocs and PhD students – if possible at least half of them should come from abroad (non-French). The team has two group leaders, which is very different from the usual way. It is not clear to the committee how the teams functions in terms of defining the research focus, and attract external grants. In order for the team to produce more high quality papers, it is recommended that the team clearly defines one group leader who can take full responsibility for the research.

The research project mainly deals with two RBPs that have already been studied for years and thus, this appears less attractive. The team may think about the establishment of new lines of research to study important RBPs in frogs. Since there are so many uncharacterized RBPs in the frog and other eukaryotes, the team should think about to embark new lines of investigation to characterize these.

  - Recommendations

This is a promising research team. It is suggested to focus on the most promising part of the projects that will lead to good papers in the near future. The team should also start to think about new lines of research that makes them internationally unique (e.g. perform a systematic screen to find other RBPs that play a role during frog development). The team should try to publish in higher-impact journals, which will undoubtly improve the international visibility.

Team 8 : "GENETIC OF PATHOLOGIES RELATED TO DEVELOPMENT"

Leader: Véronique DAVID

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	7	6
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 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)	3	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	3	2
N7: Number of staff members with a HDR or a similar grade	5	5

- Appreciation on the results

The aim of the this team is the study of two developmental pathologies (holoproencepaly and MRKH syndrome). The first part of the work is genetic approaches on large human cohorts in the aim to identify new genes. This part of the study seems to be attempted by the discovery of candidates and the results are published in numerous papers. The second part of the work on the second pathology is also based on studying cohorts. For this pathology, the team has set up a national network of clinical research (PRAM). By studying a cohort of 57 patients, they show that MRKH syndrome could be due to an early embryonic insult affecting the mesoderm-derivating tissue. This work is of high quality is cleary clinical research. The team has an old collaboration with a lab at NIH, which has also a large cohort of HPE patients. Moreover the team has set up a network for both pathologies in France.

The team leader published numerous papers (19 directly from the team, 3 inter-team). In most of them, the team leader is not in first or last author. Some of the published papers have been signed by graduate students in first position. Four students have obtained their PhD during the last 4 years. One of them seems not to have signed papers as first author.

Several collaborations have been developed at the local, national and international level, some of them have given rise to publications.

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

By setting up a French network in developmental pathologies the team is recognised in the field and the team has been able to federate a large amount of clinicians. On the one hand, numerous students, both with medical and scientific background, are a demonstration of the attractiveness of the topic and of the team. On the other hand, the poor number of post-docs shows a moderate attractiveness for more experimented scientists and could be a problem for renewal in the future.

One award from a French society. No invitation in a French or international meeting is mentioned

Only one teacher joined the team for the next quadrienal.

The team has been able to raise mostly national fundings, in particular from the Brittany region.

The participation to international and national scientific network of this team is correct. Most of the communications are from permanent members.

- Appreciation on the strategy, management and life of the team

Most of the team members are clinicians with high amount of clinical duties.

No scientific animation is described

The team comprises a majority of teachers with important implication in teaching.

- Appreciation on the project

To go further with their study on developmental pathologies, the team has choosen to recrute more patients to increase the cohort size and also to develop an experimental model on chick embryos. The choice of this model is cleary exposed and will be developed by a scientist who has joined the team in the past few years. The strategy is to use inhibitors of known pathways. Clearly, even if two axes are mentioned in the report, the study on HPE seems to involve most of the people in the team.

The team is now composed of 9 permanent people (6 teachers and 2 full-time researchers), 2 graduate students and 2 technical/engineers. One teacher has joined the team for the project. It seems that the second axis is supported by only one full-time researcher.

The project of this team is to continue to address the mechanisms that are at the origin of the studied pathologies through the development of an experimental model recently imported in the laboratory.

- Conclusion :

– Summary

This team is performant in clinical research and tries to go deeper at the mechanistic of these developmental pathologies. This strategy must be encouraged, especially because of the constitution of the team (teachers and clinicians, that can not do research more than 50 %). To go further with experimental research is probably a good way to attract post-docs and to raise funding.

– Strengths and opportunities

The team has access to cohorts of patients and has access to a wider foreign cohort, which should allow to obtain robust results based analogy and comparison.

– Weaknesses and threats

Basic research should be reinforced. There is clearly a lack of anticipation for grants and for models. At the present stage, the number of full time researchers (including postdoc) is too low and the ratio between permanent and non-permanent researchers is unbalanced. Findings are potentially exciting but there is no functional proof that the mutation is actually causal to the disease.

– Recommendations

The team should profit of internal expertise (Notch signaling) and increase collaboration with others teams of the unit and with external groups.

The team should aim at publishing in higher profile journal. To increase the skill of team in basic research and mechanistic underlying the pathologies, the group leader should hire postdocs and reinforce collaborations.

Team 9: "CANINE GENETICS"

Leaders: Catherine ANDRÉ & Christophe HITTE

- Staff members

	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 and 2.7 of the application file)	11	5
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	9	2
N6: Number of Ph.D. students (Form 2.8 of the application file)	3	3
N7: Number of staff members with a HDR or a similar grade	3	3

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

The scientific activity of the group is extremely original and of high-quality. The impact of the results is internationally recognized.

Past research has been organized into three complementary axes:

i) Analysis of the genetic bases of dog disease as spontaneous models for human disease

The team uses the dog as a model to study the genetic disposition of monoallelic as well as mulitfactorial diseases. The findings obtained with dogs can occasionally be transferred to human to map novel markers/genetic elements for disease. The team has installed the Canine Bio bank CaniDNA and an French veterinarian network to collect dog samples. To date, thousands of DNA, RNA and preserved tissues samples are stored and available for projects in this Biobank.

At this stage, samples for genetic disposition have been collected for several diseases. Regarding cancer, thousands of samples have been collected for histiocytic sarcoma in the Bernese Mountain Dog. Three loci have been identified and/or are under further investigation. Likewise, loci have been identified for melanoma, genodermatoses, epilepsis and others. This data is of pivotal importance and will guide more targeted investigations in humans in form of collaborations (often the predisposition of diseases are conserved between human and dog).

ii) Genetics and function of olfaction

This team will close down since the project leader will retire. The group investigated the olfactory receptor in dogs and in particular their reactivity towards specific molecules. This was a very interesting and unique topic for research. The group seeks now for a candidate to continue these lines of investigations.

iii) Bioinformatics and statistics

This team is improves the annotation of the dog genome. The team has also developed several programs that are of value for the dog community. For example, the program AutoGRAPH automatically constructs comparative maps between a reference genome and two to three tested genomes.

The team has a very good publication record. One reason is certainly the strong collaborative efforts made by this group. There are almost 40 original publications - some of them have been published in very prestigious journals such as Nature (e.g. the dog genome), PNAS etc.

The established veterinarian network is unique in France. The network will be extended in future. There are plans to synergize with similar networks in other European countries.

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

The group leaders have been invited speakers at five conferences (one international). The members of the team gave oral presentations or presented posters at numerous national and international meetings.

This team is exceptional compared to other research groups of the Unit: The team was able to attract 10 Postdocs and even more Ph.D. students. Therefore, this is one of the few teams where the number of non-permanent researchers is higher than the number of permanent researchers/teachers. Because of its original and unique research, the team will certainly be able to attract national and international students/postdocs in the future.

The team is well funded with national and international grants. Of note, substantial funding has also been raised by a group leader who retired recently. The team has an ongoing collaboration with a biotech company and filed one patent. It further pursues this collaboration.

The team launched the veterinarian network and the CaninBioBank (see above). Diverse international connections exist.

One patent has been filled in collaboration with a small Biotech company. Further collaboration is planned.

- Appreciation on the strategy, management and life of the team

The team is well organized. Note that one previous group leader has retired and two former PIs take now the lead of the team. We propose that one team leader may be sufficient to effectively guide the group and to take all of the responsibility.

The project is unique and cutting-edge. The team is well connected to establish as a world-class leading team.

Both team leaders contribute to teaching. It appeared that mainly one team leader is actively organizing a dense network with other teams from the same/other research units.

- Appreciation on the project

The scientific activity of the team for the period 2012-2015 will continue on the same bases with strong collaborations and interdisciplinary research. The major research axis includes:

i) Analysis of the genetic basis of dog diseases a models for human diseases. Major focus is on continuation of cancer projects (osteosarcoma, glioma). In the past, many dog samples have been collected and can now be used to identify the predisposition of genes, to identify chromosomal regions of interest. In addition, new collaborative projects are planned on other types of cancer. A dermatology project, as well epilepsy and developmental disease projects are also planned for the future – however, no details are given on the plan for their execution in the project synopsis. To achieve these tasks, the team will use previously developed methods but they also intend to use novel implementations (e.g. sequencing of breed specific diseases).

ii) Development of bioinformatics and statistics tools is further provided by one leader of the team. This is certainly required to allow sophisticated analysis of data obtained from genetic linkage and other analysis.

iii) A new research projects is to analyze quantitative structural variations of the dog genome (part of a European consortium). Copy number variations (CNVs) have recently attended great interest as it was found to make a great difference between genomes of individuals in vertebrates and also in humans. Therefore, this is a very hot-topic with great potential.

iv) The identification of SNPs to identify patterns of genetic variation that indicate recent selection events of canine species. Also this project is of great interest and can be performed with sufficient numbers of samples in dog. The possibility in dogs to analyze in-breed and out-breed linkages generally enhances the reliability of the data.

Several great scientists have been hired to join the team. For instance, a new group leader has been recruited to perform genetic association studies. He will take a lead on the epilepsy and developmental disease project (possibly a reason why the goals for this project have not been outlined in sufficient detail).

- Originality and existence of cutting edge projects

As mentioned above, the project is very original and cutting-edge.

- Conclusion :

  - Summary

The team has acquired profound expertise to perform the task proposed in the project. It has several promising resources that allow to take an internationally recognized lead in the field of canine genetics. Moreover, the work may become of great medical interest for diagnostics and it may build the foundation to develop novel drugs to cure dog or human disease.

  - Strengths and opportunities

The Canine Bio bank, and several recently hired bioinformatics experts will be beneficial for the successful execution of the proposed research. The group established a god network of veterinarians and further developed expertise in dog genetics that is unique in France. This team has an extraordinary potential to analyze genetic diseases. Successful combination of genetic and bioinformatics.

  - Weaknesses and threats

No particular weakness and threats have being recognized.

  - Recommendations

This is certainly a group with great potential, which should be supported at all levels. Importantly, the committee feels that the team should be headed by one leader, and in this case one of the proposed group leader has the potential, the motivation and the energy to fulfill this function alone.

Team 10 : "INTEGRATED FUNCTIONAL GENOMICS & BIOMARKERS"

Leader: Jean MOSSER

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	5	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	0
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 of the application file)	6	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 engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	1
N6: Number of Ph.D. students (Form 2.8 of the application file)	5	2
N7: Number of staff members with a HDR or a similar grade	5	2

- Appreciation on the results

During the last quadriennal, the team was headed by two co-leaders. The team was composed of 29 persons. This team will be separated into two teams in the next quadriennal (Team 6 and Team 10). The following appreciation of the results therefore concerns both Team 6 and Team 10

The team used a combination of different approaches to understand the genetic and epigenetics basis of tumor development: CGH array, quantitative transcriptome analyses (including miRNA) and analysis of DNA methylation of cis-regulatory sequences. This type of project is very wide in addition of being highly competitive and a huge number of groups, both in France and abroad, are asking the same questions with similar approaches. The team has focused on different types of tumors.

The first is glioblastoma, a very aggressive tumor, for which the team has identified a transcriptome signature, which correlates with recurrent genetic abnormalities.

The second project focuses on melanomas. The team has investigated several pathways (i) the alternative splicing of Mitf, a gene involved in development of melanomas for which they found a correlative link between such splicing and metastasis; (ii) the role of TYRP-1 in melanoma progression and (iii) the link between skin cancer and UV response, which led us to identify USF-1 as a key sensor of the UV-response.

The third project concerns the TEL/AML1 leukemia, where specifically deregulated genes were identified. Among them, the team concentrated on CD9 both as a diagnostic tool and to understand the molecular mechanisms that lead to its down-regulation in leukemia.

The last project is on a metabolic disorder that eventually leads to liver cancer in some cases.

Several of these projects have required bioinformatics tools that the team has developed, for some of them in collaboration with the “laboratoire de mathématiques appliquées”.

Altogether, these projects are very diverse. Many results have been obtained but it seems that they could be of higher impact if the team was not as dispersed.

The team has published numerous papers (26 directly from the team, 7 inter-team and 31 with at least one member of the team). However, the overall impact factor is low.

Team leaders of the previous team have been invited speakers to several meetings, national and international. However the leader of team 10 has been invited mostly to local events. Other members of the team have also participated to meetings (oral presentation or posters). One patent has been obtained, which concerns leader of Team 6.

Six students appear to have obtained their thesis during the last 4 years. Given the size of the publication list, it is difficult to assess what was their scientific production.

Several collaborations have been developed at the local, national and international level, some of them have given rise to publications.

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

Leader of Team 10 has been invited mostly to local meetings. No award is described.

The team as it was during the current quadriennal is very big. It is composed of 7 permanent research scientists, 3 post-docs, 16 graduate students and 3 technical persons. Most if not all permanent researchers, post-docs and grad students appear to come from Rennes.

The team has been able to raise many regional and national funds, in particular from the ANR.

The participation to international and national scientific network of this team is limited, regarding of the possibilities, especially for the glioblastoma project that has been made the object of a recent call for tender.

One patent has been obtained, which concerns the leader of Team 6.

- Appreciation on the strategy, management and life of the team

The team is very big, headed by two team leaders who appear to be in charge of distinct projects, which are very diverse. Altogether, this organization raises important issues in terms of visibility. Some of these issues have been addressed by splitting the team in 2.

No scientific animation is described.

The team leader is heading the IBisA microarray facility. Major part of the team is composed of teachers (PU-PH or MCU-PH) who have lot of teaching at the medical school.

- Appreciation on the project

Among the 4 projects in which the previous team has been involved in the past years, two are continued by the "new" team 10. The projects are intimately linked to the microarray plateform that the team developed and which has been labeled by the GIS IBiSA in 2009.

One of the project focuses on hemochromatosis, a mulifactoriel disease with variable penetrance: whereas most of the patients are homozygous for a mutation within the HFE gene, the penetrance of such mutation is very low. The aim of the proposed project is to search for other loci involved in this disorder. Based on a candidate approach, the team has already identified a polymorphism 3' of BMP2 that correlates with ferritin level. The goal now is to extend this type of analysis to the entire genome, through 2 complementary approaches, one in human, the other in the mouse. The first one is a genotype/phenotype association study. This type of approach highly depends on (i) the size of the cohort, (ii) the genotyping procedure and (iii) the choice of the phenotype to which the genotype will be linked. This last part is not well described, so it is difficult to assess its feasibility on a large cohort of 500 patients. It is also important that these patients are very well characterized in term of overall phenotype and disease severity. Results will be verified on a distinct cohort, but nothing is said to the downstream research: the identification of the gene/locus involved, functional analysis to validate/confirm the data. From what is described, this part of the project will only identify some polymorphisms associated with phenotypes.

The second approach uses a mouse model (Hfe-/-) to identify eQTL. This is a collaborative project with a team in Toulouse. The genetic background of the mice appears to modulate iron accumulation in the liver and the project aims at searching for modifier genes. Intercrosses over two generations have identified 5 regions on different chromosomes. However the size of the candidate regions are not mentioned but this can greatly impact on the likeliness of identifying the modifiers. It is likely that a 2 generation intercross gives rise to a large candidate region.

However, this QTL approach is coupled to transcriptome analysis that should help identifying candidate genes. Four transcripts have been already identified. Other will probably follow. However, downstream analysis confirming or aiming at elucidating the underlying mechanism are not well described. In addition, there is no mention of a cross comparison between the data obtained in both human and mouse approaches.

The second project concerns the molecular characterization of glioblastoma, by combining genomic, epigenomic, transcriptomic and proteomic analysis. This will be done in 4 different tumor compartments. Importantly, the team also proposes to initiate similar analysis on tumor stem cells derived from GBM samples. Some details of the analysis are lacking: How will the proteomic be done? This type of approach usually requires large amount of material. Is it compatible with the analysis of different tumor compartments? Of tumor stem cells?

Finally the team proposes to develop transcriptome and methylation markers in GBM, which could eventually be used in diagnosis. All these projects rely on multiple collaborations, mostly national, especially depending on large cohorts, which are essential for generating high quality data.

The team is now composed of 9 people (3 permanent researchers, 3 research technicians/engineers and 2 PhD students. Four people (only permanent ones) are involved in the first project whereas 6 participate to the second. We do not know however whether any of the team member participates and to which extent to the microarray plateform. Strikingly, one of the two PhD students appears on none of the projects described.

The team‘s projects aim at identifying new loci involved in different cancers. This is clearly important for our understanding of the diseases and the search for downstream therapeutic tools. However, the field is highly competitive and other groups in France and abroad address similar questions with more powerful approaches. In addition, there is no project aiming at addressing scientifically relevant downstream questions. In addition, the team appears to focus on the identification of potentially involved loci but validation experiments as well as projects aiming at understanding the underlying mechanisms are missing.

- Conclusion :

  - Summary

The team refocused its projects and limited these to two, which seems reasonable, considering the new composition of the team. The significant number of projects was probably a handicap for a visibility outside.

  - Strengths and opportunities

The team as published many articles with some in good journals. It has developed the opportunity for integrated approaches to identify new loci “involved” in hemochromatosis and glioblastoma. The team has access to large cohorts of patients.

  - Weaknesses and threats

The proposed projects might help identifying new loci involved in hemochromatosis and glioblastoma but they are rather descriptive and ambitious downstream functional approaches are lacking. The team is not integrated into national and international network on these pathologies. Objectives are not well defined. There is no internal collaboration mentioned with groups working on animal models for glioblastoma. The team has limited competitivity in this “hot“ field.

  - Recommendations

The team leader should improve communication skills and should develop connection with existing national and international network. The team should better define scientific goals and spread their means of studies to be able to remain competitive in the announced projects.

Team 11 : "CELL DIVISION: A REVERSE ENGINEERING"

A SYSTEMS, PHYSICAL BIOLOGY APPROACH TO CELL DIVISION MECHANICS

Leader: Jacques PÉCRÉAUX

- Staff members

	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)	0	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	0	0
N7: Number of staff members with a HDR or a similar grade	0	0

- Appreciation on the results

This is a new group that will only join the research unit in January 2011. The PI has a modest track record as PhD student and post-doc, with one major publication as main author. This is acceptable because the PI represents a very important and qualified interface between two worlds (Physics and Biology) and has been trained in world reference labs in the field of Biophysics and Systems Biology. The PI's main interest has been on asymmetric cell division and proposes an interdisciplinary approach to this problem, starting with C. elegans as model system, but with predicted excursions to Drosophila and mice. This new program focus on three main goals: 1) regulation of spindle length; 2) spindle centering and orientation; and 3) targeting of force generators to the cortex. The PI proposes to model these processes in silico and then experimentally test predictions from these models. His expertise in quantitative imaging analysis will also be used on the evaluation of the experimental data. Alternatively, he proposes a set of experiments, which can after be reproduced in silico to determine the best theoretical fit. Overall, the research program is thoughtful and relevant, providing complementary expertise to more traditional approaches. It is likely that this program will have a very positive impact in other local labs.

Two papers in co-first authorship, one of them in a very good journal. Minor contribution in a top publication in Cell and other secondary contributions in biophysics journals. Communications in International Conference proceedings.

It is premature to evaluate this aspect, although it seems that the PI has already started collaborations in France and most likely will interact a lot with the local community working on cell division aspects.

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

This is a new team ATIP/AVENIR team that will only start in January 2011. There is no information on recruitment.

Only one collaboration at the National level disclosed. However, due to his unique expertise, the PI will be very attractive to participate in scientific networks at the local, national and international level.

The generated software will be made freely available to the research community as Image J plugins.

- Appreciation on the strategy, management and life of the team

The team leader has no teaching duties. This team, due to its interdisciplinary nature, will play an important role as a hub for scientific interactions at the local level.

- Appreciation on the project

The proposed project is well-structured, hypothesis-driven and is relevant not only at the experimental level, but also theoretically. It seems adequate to the previous experience and track record of the PI and focuses on a relevant biological problem, with implications to other systems. It seems a bit overambitious for a team, whose future composition is unclear and it is not sure whether the PI enjoys of sufficient international recognition to attract talented students. On the other hand the interface between Physics and Biology may be attractive to a different target population of students and very much necessary to increase the training in frontier science. All support should be given in order to obtain independent funding and access to all necessary resources.

This interdisciplinary project has very high potential for cutting edge research, especially in the context of larger scientific networks, for which specific international funding exists. This is a perfect candidate for the Human Frontier Science Program.

- Conclusion :

  - Summary

This new team will start only in January 2011. The track record of the PI is not impressive but the level of training of the PI in biophysics offers some guarantees for the future. The proposed project is well-structured and covers a wide-range of interdisciplinary approaches to a biologically relevant problem. High potential for cutting-edge research and participation in international networks.

  - Strengths and opportunities

Interdisciplinarity; potential for interactions with the local, national and international community; young PI with clear ideas ; excellent opportunity for international funding on interdisciplinary science.

  - Weaknesses and threats

Questionable international visibility; modest track record of publication; limited current funding.

  - Recommendations

This team should be supported and integrated in the research unit in a way that allows the promotion of local interactions (joint lab meetings; shared student supervision; joint grant applications, etc). The team should be encouraged to obtain independent funding and good opportunities exist at the International level. The international profile should be raised.

Team 12 : "REGULATION OF STRESS ADAPTATION" (MARS)

Leader: Carlos BLANCO

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	7	7
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 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)	3	3
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	2	2
N7: Number of staff members with a HDR or a similar grade	3	3

- Appreciation on the results

The aim of the project was the understanding of bacterial adaptation to stress. Researches were carried out to bring some elements of understanding in the response of bacteria to osmotic and oxidative stresses, especially in alpha and epsilon divisions of proteobacteria (Sinorhizobium meliloti and Campylobacter jejuni).

One part of the project concerned the role of the RNA-binding protein Hfq, which is involved in resistance to stess and in pathogenicity of numerous bacteria. Thereby, Hfq acts as a RNA chaperone that mediates the association of non-coding regulator RNAs and target messenger RNAs. Importantly, Hfq is essential for virulence for several bacterial groups, including Brucella; however, its role in S. meliloti has not been investigated. The team has undertaken efforts to study this protein in different bacterial strains. For instance, studies of the functions that are lost by an hfq mutant of S. meliloti have revealed that Hfq plays a key role in the establishment of the symbiosis between S. meliloti and its host Medicago sativa. The team has also performed a comparative proteomic analysis between wild-type and hfq mutant allowing the identification of 442 proteins, which synthesis was reduced and 75 proteins, which were overproduced. Most of these proteins are involved in cell metabolism or stress resistance. Further analysis of these proteins and the role of Hfq for their regulations is planned for the future. Likewise, several studies deciphered genes and proteins that mediate oxidative and osmotic stress in different bacterial strains. Interestingly, the team has preliminary data on the ability of C. jejuni to survive to cold aqueous stress and the implication of a post-transcriptional regulator CsrA (Carbon storage regulator) in this process.

The team published more than 30 papers mainly in low-impact journals.

Several local, national and international collaborations have been set-up. There is also a partnership with industry to develop novel tools for the detection of pathogenic bacteria (e.g. Campylobacter in the poultry product).

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

No notable achievement was raised regarding impact and attractiveness of the team.

- Appreciation on the strategy, management and life of the team

The team has a large number of teachers but only few researchers. Overall management may be suboptimal.

No cutting-edge and highly creative projects have emerged during the last period.

Apparently, there are heavy teaching duties in medicine and biology. Teaching is shared by several team members – the exact contribution of each member could not be not evaluated.

- Appreciation on the project

Project A: Analyses of ribosomal modulating factors will be studied from the phytopathogenic bacteria Erwinia chrysanthemi that belongs to the γ-proteobacteria group like E. coli. The plan is to knock-out the genes of the E. coli orthologs (RaiA(PY), RMF and HPF, RsgA) and to study the phenotype under various stress conditions. Furthermore, the ribosome profile, EM structure of ribosomes and aspects of transcriptional regulation will be considered. Mutants of Erwinia chrysanthemi are available through the "E. chrysanthemi network".

The considered factors have been studied intensively in E. coli over the last 10 years. To perform now an analogous study in an organism, about which much less is known than about the model bacteria E. coli will probably not lead to ground-breaking results and thus not yield papers in journals with a high impact factor.

Project B: The ribosomes of two bacterial strains, viz. the symbiotic Sinorhizobium meliloti and the pathogenic Campylobacter jejuni, will be screened under various stress conditions for associated factors, which might represent ribosomal modulating factors. The bacterial species have been selected because the lab has experience concerning their physiology and genetics. The associated factors will be identified by MALDI-TOF, then purified and their effect tested in vitro. Mutants concerning the corresponding factors will also be tested for their role in stress adaptation.

Again the argument holds why a fundamental systematic approach is suggested for two species, although similar experiments have been already made in other species, particularly in E. coli. The argument that the modulating factors mentioned under Project A are exclusively present in enterobacteria is true for some but not all factors. For example, the hibernation-promoting factor SaHPF in Staphylococcus aureus mentioned in the project description is an ortholog of the E. coli factor HPF. New factors probably exclusively present in the two species might be found.

Project C: In recent years it became clear that toxin-antitoxin (TA) systems play important roles in regulation networks including various regulatory systems. The authors identified a TA system (tox-DopR) in Sinorhizobium meliloti involved in adaptation of osmotic stress. The predicted structure of the toxin seems to be related to RelE, a well studied and highly specific RNase in many bacteria. The behavior of this TA system at various salt conditions will be studied as well as its structure (NMR) and its ribosome localization via EM, both in collaborations within the institute.

This is a project worth mentioning; elucidation of its relation to osmotic stress might lead to an improved and extended knowledge about the RelBE systems. The 70S•RelE X-ray structure has been published in Cell 2009. A well-done analysis has the potential to become published in a good journal.

- Conclusion :

  – Summary

The team suggested studying a couple of regulatory proteins in exotic bacterial strains. The factors have been already studied intensively in E. coli. Repeating experiments in one strain, which have already been performed in another strain, is not very attractive.

  – Strengths and opportunities

The team has profound expertise in microbiology techniques.

  – Weaknesses and threats

The team has a questionable international visibility and a modest track record of publication. See also comments above to the project.

  – Recommendations

It might be wise to integrate the members of the team in other more efficient groups, considering their expertise in microbiology.

Team 13 : "CELL POLARITY, MEMBRANE TRAFFICKING AND SIGNALING"

Leader: Roland LE BORGNE

- Staff members

	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	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 of the application file)	4	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	2	2
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

After 5 years of existence, the ATIP+ team now comprised of 2 staff scientists (McU and CR1), 2 postdoc, 2 Ph.D students and two research assistants, is at a very productive stage.

The team is interested in the contribution of membrane trafficking to the regulation of Notch-dependent cell-fate decision of Sensory Organ Precursor cells in the dorsal thorax neuroepithelium of Drosophila. Activation of Notch signalling by its ligand Delta requires Dl endocytosis for some yet unknown reason(s). One important contribution of the team was to demonstrate that the ubiquitin-ligase Neuralised can trigger the transcytosis of Dl from a basolateral to an apical plasma membrane localization, making Dl available to bind and activate Notch in MDCK cells. Another approach of the team was to apply a reverse genetic screen to identify proteins with membrane trafficking regulatory functions that could regulate Notch signalling. This screen has been very successful leading to the identification of several novel regulators of Notch. These include the clathrin adaptor complex AP-1, which was found to regulate Notch and Sanpodo (regulator of Notch signalling) delivery to a specific E-cadherin/F-actin-rich apical plasma membrane subdomain, which may represent a signalling plateform for Notch. In addition the Escrt machinery components, septins and septin interacting proteins have also been identified.

The team leader has also initiated some productive collaborations both within the institute and outside. These have led to the identification of a novel mechanism through which the cell cycle Aurora-A kinase can control Notch signalling by regulating the phosphorylation and activation state of Numb, a known regulator of Notch and Spdo endocytosis. This is interesting as so far Aurora-A had been shown to regulate Numb only indirectly via phosphorylation of the partitioning defective proteins. Another significant finding is the discovery that Dl is enriched on exosomes that are secreted by signal-emitting cells as a mean to controlling Notch signalling over long-range (several cell diameter) distances.

The research is highly relevant for our understanding of fundamental processes such as regulation of cell polarity, asymmetric cell division and cell fate determination. The research performed and proposed is a very good combination of original and risky approaches (for example the development of nanoparticles as modulators of signalling) with more conventional approaches.

The results implicating Nl in Dl transcytosis have been published in Mol Biol Cell in 2010. The team also contributed to two review articles in Current Opin Cell Biol (2006) and Traffic (2010). Two manuscripts describing the role of AP-1 in Notch signalling and the identification of Dl exosomes are being submitted. One article has just been

accepted in Current Biology. Collaborative projects also led to co-authorship in two articles published in EMBO J in 2007 and J Am Chem Soc in 2009.

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

The group leader has established an excellent national and international network. He is invited to international conferences (Notch Meeting, 2009, Drosophila Molecular & Developmental Meeting, 2010).

The group appears to be an attractive place for predoc and PhD students. Recruitment of postdocs is limited, however this is a general problem in the entire Institute.

The PI has been successful in raising external funds from local (Rennes Univ., Région Bretagne) and national agencies (INCa, ANR, ARC).

The team has collaboration with foreign groups and has established a very good network with national and international groups.

- Appreciation on the strategy, management and life of the team

The excellent young, energetic investigator has a strong leadership potential.

The team members all have clearly defined projects.

The research is really original and the projects are clearly cutting edge.

- Appreciation on the project
- Existence, relevance and feasability of a long term (4 years) scientific project

The research team focuses on two broad topics related to Notch signalling and cell fate decision. In addition to these projects, the team has technology development objective relevant to their own and other Unit teams' research regarding electron microscopy in drosophila mutants.

Project 1. Based on their previous genetic screen identifying AP-1's function in trafficking of Notch and Spdo to the basolateral membrane, they plan to characterize the underlying mechanism and address a potential role for AP-1 in Spdo and Notch endocytosis from the apical surface. A classical antibody capture assay will be developed using the imaginal disc, which allows access to the apical surface (not possible in the dorsal thorax). With this assay they will also look at the role of Numb in endocytosis (or Spdo) as mean of generating distinct plasma membrane domains during asymmetric division of SOP cells. In addition, novel genes have been identified, which, when depleted, phenocopy the defects in AP-1 mutants. One of these genes encode a large conserved protein of unknown function, which will be characterized regarding its interplay with Notch signaling and AP-1 function. On a collaborative basis with team 18 and another French group, the function of AP-1 during epithelial cell polarity establishment in the drosophila tracheal system and in apico-basolateral polarity will be characterized.

Project 2. DE-Cadherin has a role in the SOP lineage by controlling the orientation of pIIa cell division. The team already found that DE-Cadh, although required, is not sufficient to orient pIIa cell division. The contribution of other junctional and cytoskeletal components (Canoe, Disc lost, Crumbs, septins...) will be investigated. The dynamics of DE-CadhGFP at junctional domains will be analyzed in wild-type and mutants (AP-1, Numb...) to correlate defects in junction remodeling and alteration in Notch/Spdo localization and activity. Based on their work which has identified a population of Dl-enriched exosomes that are released in the extracellular midia of S2 cells, proteomic MS/MS analysis has been performed and has identified several proteins that may contribute to Dl-exosome formation. The role of these proteins will be addressed by gene silencing. Alternative mechanisms of signal transmission by filipodia formation or vesicle shedding rather than exosome release will also be tested. Similar approaches will be used to identify and study exosome's contribution to Wingless signalling through collaborations.

Finally, the team with two other groups (in the unit and outside) wants to develop and apply correlative light and EM microscopy based on high pressure freezing to combine state-of-the-art light microscopy data and immunoEM in mosaic mutant backgrounds.

The performed and proposed projects are clearly cutting edge and original.

- Conclusion :

  - Summary

A young, dynamic team exploiting a powerful genetic system to ask fundamental questions about membrane traffic and its role in cell fate decisions.

  - Strengths and opportunities

The leader has proven an excellent scientific leadership. He has a clear vision on how to run his research program, asks original questions and applies innovative approaches.

The project is exciting and ambitious. Feasible if the group can grow. The leader was able to establish a very good international network and to be in contact with the possible main competitors in his field.

  - Weaknesses and threats

The group might be too small to address all the questions raised and become really competitive with the strongest players in the Developmental Cell Biology field.

  - Recommendations

The recommendation of the committee is to continue in this excellent direction. As all the prerequisites are there (successful team, very good scientific environment, excellent facilities), the leader should be more active in attracting international postdocs.

TEAM 14 : "SP@TIO-TEMPORAL REGULATION OF TRANSCRIPTION IN EUKARYOTES" (SP@RTE)

Leader: Gilles SALBERT

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	3	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 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)	2	4
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	2	3
N7: Number of staff members with a HDR or a similar grade	1	2

- Appreciation on the results

The team includes 4 permanent research scientists, 1 post doctoral and 3 PhD students and 4 technicians. This is one of the 5 teams from the former UMR6026 that joined UMR 6061. The leader is the past head of UMR 6026. The objectives of the team are mainly to understand chromatin dynamics and plasticity associated with transcriptional activation. The team focuses essentially on the transcription of ER-target genes. On-chip methods, microarrays and 3C techniques are combined to analyze epigenetic signatures, the recruitment of specific enzymatic complexes and the formation of intra-chromosomal chromatin loops. Chromatin attributes allowing pioneer factors to be recruited are also investigated. Finally the team aims at developing an in silico project in order to identify new estrogen-dependent modules based on their DNA sequence and through genomic studies

The research carried out by the group is of top quality, and very competitive and will bring very important novel information in the field of transcription dynamics

The group has a very good and high level publication records with papers in Nature.

The permanent researchers and postdoctoral fellows cover competences either in molecular biology and biocomputing, thus making the project feasible and visible.

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

The productivity of the team relies essentially on one research scientist who is an expert in the field of ChIPs and transcription dynamics. He is the author of the Nature papers and it is him who is invited to the international meetings and who gets the awards (Médaille de bronze du CNRS et Médaille de la Ville de Rennes)

Funding is quite successful with grants from ANR, Equipe Labellisée LNCC and funding from the European community. However funding should be renewed for the next years.

- Appreciation on the strategy, management and life of the team

The competences of the permanent researchers and postdoctoral fellows are complementary in the fields of molecular biology and biocomputing, and thus adequate for realizing the project. The Sparte members are actively involved in LMD training.

- Appreciation on the project

The proposed project is ambitious and challenging. Due to the expertise of the team in the field, the research plans are well focused, realistic and quite feasible during the forthcoming years, provided that the team reinforces funding.

- Conclusion :

  – Summary

This team and collaborators have made breakthrough in the understanding of gene regulation dynamics and is pursuing on innovative aspects.

  – Strengths and opportunities

The group has a very good expertise for developing the project both in the molecular biology and biocomputing approaches. In addition, biological concepts are original and overall quality of science and publications is excellent.

  – Weaknesses and threats

Funding should be reinforced

  – Recommendations

The team should take the opportunity of the fusion to both enlarge and share their competences and interests.

Team 14 : "SIGNALLING IN MOUSE OOCYTES AND EARLY EMBRYOS"

Leader: Guillaume HALET

- Staff members

	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 and 2.7 of the application file)	1	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 engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	0	1
N7: Number of staff members with a HDR or a similar grade	0	0

- Appreciation on the results

The research team proposes to study signaling events during oocyte maturation, fertilization, and early embryonic development. The proposed questions are of novelty and originality, and of high quality. These questions are closely related possible improvement of assisted reproduction technologies (ART), and are of great clinical significances.

The group was recently created with the support of an ATIP grant from CNRS. The team leader had a very successful post-doctoral period that generated good profile papers in Development and Dev. Cell. Since establishing the group, the team leader has begun to exploit results he obtained as a post-doc on calcium signaling during fertilization and on phosphoinositide PIP3 production during oocyte meiosis. Some progress has been made concerning the polarized activation of Rac1 and Cdc42 in the mouse oocyte, depending on signals from meiotic chromosomes and the meiotic spindle approaching the oocyte cortex. The team also provided preliminary evidence that polarized activation of Cdc42 in the blastomere can drive the polarized recruitment and activation of the Par polarity complex and that this may be fundamental for establishment of an apico-basolateral polarity of the blastomere.

The research team is newly established in France. The young and energetic PI has an extremely impressive publication record with relatively high numbers of research papers, including papers in high impact journals, such as Developmental Cell, Development. The PI is also actively involved in international communications in his field with conference presentations.

The PI has a long and steady history of collaborating with world leading researchers,. These leading experts will provide very helpful and steady supports to the PI's new lab.

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

The team is clearly attractive: the team leader has rapidly recruited one PhD student and 2 postdoc researchers. The team leader was awarded an ATIP grant on a highly competitive basis. This can be extended for a further 2 years. The team has top international collaborators. Most collaborations are outside the institute.

The PI was awarded a ATIP fellowship by the CNRS for 3 years (2009-2011) to become a group leader. This is possibly to be extended to 5 years. This is very impressive. The PI was also invited to give talks in influential international and national conferences.

The PI seems to establish his team in France quickly. He has recruited 2 postdocs (one is from UCL, UK, apparently of high quality).

The PI has a impressive record of attracting funding, as listed in his report.

Stable networks and collaborations with international leading teams were established.

- Appreciation on the project
- Existence, relevance and feasability of a long term (4 years) scientific project

The objectives of the team, which are very clearly defined, aim at understanding mechanisms underlying (i) asymmetry during meiotic divisions, which is essential for the oocyte to retain maternally contributed components and (ii) polarity in preimplantated embryos at blastomere stage.

Project 1. Based on their preliminary observation that Rac/Cdc42 are activated in a polarized fashion in the oocyte and later in blastomeres, they will use a candidate-based approach to identify Rho GEF(s) that may act upstream to mediate polarized Rac/Cdc42 activation. Another very original aspect of this problematic will be to assess the contribution of RAN signaling to activatory Rac/Cdc42 signals from meiotic chromosomes and spindle.

Project 2. Understand the mechanism of meiotic arrest in Rac/Cdc42-deficient oocytes with respect to meiotic spindle assembly checkpoint and meiotic spindle integrity and/or Microtubule-kinetochore attachment.

Project 3. Identify Rac/Cdc42 downstream effectors in polarity establishment in the oocyte and early embryos largely based on the usual suspect list.

The project proposed target key questions that are closely related to clinical practice, and is believed to have impact in understanding female infertility and improving ART. Therefore, the project stand firmly as a clinical relative project, and the feasibility is high in the long term.

The project itself is at the cutting-edge of the field.

- Conclusion :

  - Summary

This is a young promising team tackling questions that are valuable to basic understanding of cell division and cell polarity and to the understanding of human reproductive failure, one of the most common health problems in men and women and a common cause of birth defects. The lab has been successfully established in France, and the basis of the projects seem very solid. Very well planned projects with solid basis. Well-organized team with qualified researchers. The report and proposal target key questions concerning important issues of oocyte maturation, fertilization, and early embryonic development. The human resources and financial supports are in their place, and the strategy of the research is steady. Collaborations with world leading experts in the field will greatly facilitate the success of this dynamic group.

  - Strengths and opportunities

The PI is at the cutting edge of his field with impressive and high level publications, and with excellent scientific leadership with a clear definition of the team's objectives. Innovative mechanisms and hypotheses. Based on previous experiences and solid trainings from UK, the PI has a great opportunity to become an international leader in this field.

  - Weaknesses and threats

As a new group leader the PI has successfully recruited postdoc researchers. To successfully perform the proposed projects, more well trained researchers and larger grants are needed.

– Recommendations

This is a very promising new team that was established in France. It is essential to recruit more postdoc researchers and Ph.D. students for the interesting project.

Team 16 : "STRUCTURE AND MOLECULAR INTERACTIONS"

Leader: Jean-François HUBERT

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	6	5
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 and 2.7 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)	5	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	2	4
N7: Number of staff members with a HDR or a similar grade	4	3

- Appreciation on the results

This fairly large team uses proton NMR to document protein-phospholipid interactions. The group also operates a technological platform comprising NMR spectrometers, fluoremeters and circular dichroism spectrometers.

The scientific activity of the group is threefold with a focus on peptide interactions with artificial membranes/micelles, the identification of the surface interfaces involved in dystrophin interaction with membrane lipids and the influence of different osmolytes on dihydrofolatereductase substrates binding using NMR spectroscopy.

2 researchers left the team, one joined, 2 ITA left the team; the number of graduate students is constant (4 on average).

The group scientific output in terms of publications is relatively poor to fair. Only 2 articles out of 20 were published in journals with impact factors comprised between 4 and 6 with the first and/or senior authorship being that of members of the team. 19 oral communications and 14 posters were given/presented by members of the team at local, national and international meetings.

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

The group has limited visibility and success at both national and international level. Collectively, they have been invited to give a single talk at international conferences. No award is highlighted.

Two PhD theses were defended over the evaluation period. One very productive post-doctoral fellow is now established with a permanent position at the University of Limoges. A limited number of collaborators, one of which is from the UK, are listed. The collaborations have led so far to a very limited number of publications.

The group has very limited success in raising funds. It has been supported by 4 small grants. It is unclear whether this is because the team members did not apply to larger funding agencies or to a lack of success.

- Appreciation on the strategy, management and life of the team

No indication on the team organization, management and animation is provided. The team leader will change after the evaluation and the former leader is staying in the team, which might reflect an original democratic organization.

With several Professors and MCU, the team is certainly involved in teaching activities. The team members seem to be fairly involved in student training activities (4 PhD and 2 M2 students on average per year). The number of students attracted by the team certainly reflects the quality of the teaching delivered by the team members.

- Appreciation on the project

Project A: Dystrophin is an important protein at least in muscle cells of vertebrates. Mutations of this protein are the cause of Duchenne muscle dystrophy (absence of dystrophin, usually frame-shift mutations) or the milder form of Becker-Kiener muscle dystrophy (BMD; short forms of dystrophin, usually in-frame deletions). Biophysical techniques will be applied to study mechanical properties of membrane models in the presence of dystrophin and plus/minus its main ligands actin and β-dystroglycan. Biochemical studies will complement the analyses studying folding, conformation, oligomeric state and conformational changes upon lipid binding (NMR, H/D exchange; collaboration with Grenoble). A backup with in vivo studies applying fluorophores and cross-linker (mass spectrometry) is mentioned. Truncated dystrophin forms known from BMD patients will be considered.

This is certainly the most interesting project of the proposal. Since the length of fragmented dystrophin is not related to the phenotype, some of the repeated units must be more important than others. The identification of the more important repeats in the frame of the suggested experiments would be an important achievement.

Project B: NMR and H/D exchange measurements devoted to document the influence of membrane curvature and model peptide structure on the interaction of peptides with small unilammellar vesicles (SUVs), also the influence of peptide structure on membrane curvature with the aim of designing membrane curvature generators will be performed. A program with peptides from marine organisms will be continued.

It is evident that groundbreaking results will not be obtained in this project.

Project C: The lipid environment of cytochrome C modulates/affects its activities. The corresponding conformers of cytochrome C will be analyzed by NMR.

The vague description of the planned experiments does not allow a detailed evaluation.

None of the three projects is at the cutting edge of what is done in the field. The project aiming at characterizing the interaction of polypeptides that may be used as membrane curvature sensors or generators and antimicrobial polypeptides interaction with phospholipids might lead to interesting findings. However, it is uneasy to assess the feasibility and potential outcomes of this project given the briefness of its description. Similarly, it is uneasy to assess the rationale and feasibility of the cytochrome C project. Nonetheless, these projects will benefit from the hardware available at the facility.

- Conclusion:

  - Summary

The proposed approaches are not particularly innovative. The activity of the team, its scattered points of interest and its international visibility will not allow this group to reach the top international level. No contingency plans are provided. The rationale of the « cytochrome C project » is unclear. Two of the projects are poorly described. The team members should seek for publications in high impact factor journals.

  - Strengths and opportunities

The committee sees in the project analysis of the dystrophin and its fragments the most important scientific potential. It is possible that interesting results may be achieved provided that the relatively large group is focusing on this subject. The connection with the clinic is an asset for the project.

The high proportion of young researchers is an asset of the team.

– Weaknesses and threats

The proposal is of varying quality and partially described in an unclear manner (cytochrome c project). The team is not well balanced between teachers and full-time researchers (including postdocs). Funding is limited; the scientific output is relatively poor.

– Recommendations

The scientific goals have to be better defined, and the group should try to present the results in higher profiled journals.

The group should take advantage from the fusions of both labs and should try to develop internal collaborations.

Team 17 : "TRANSLATION AND FOLDIND"

Leader: Reynald GILLET

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	4	4
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 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)	2	2
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	2	1
N7: Number of staff members with a HDR or a similar grade	3	3

- Appreciation on the results

This group originates from the fusion and a year later the split of two teams. The fused ensemble had an appealing objective: investigating the relationship between the structure and the dynamics of macomolecular assemblies. The team has documented the molecular chaperone Hsp90 dimerization and oligomerization, translation on the bacterial ribosome and the supramolecular organization of the yeast mitochondrial ATP-synthase using cryo-electron microscopy and image reconstruction. The team has also made an in silico incursion into the amyloid field through a database. The rationale at the origin of moving within this last topic as opposed to developing methodological aspects that would benefit the imaging approaches is not provided.

The productivity of the team in number of papers could be better (16 for 6 scientists). Two recent papers with first or last authorships from the team were published in journals with impact factors of about 5, one about 9 (EMBO-J 2010). The team members gave 6 talks at mainly national conferences. 13 poster presentations were given over the considered period. The number of scientists and ITA within the team is overall constant since 2007. 3 PhD students defended their thesis. A single PhD student is preparing its thesis at the moment.

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

No award apart from a local scientific “installation” award is highlighted.

Three team members appear to be involved in local/national organizational issues and in organizing scientific meetings.

The team appears fairly successful in raising national and local funding. It is unclear whether the team members are the coordinators of the ANR grants or participants.

The team appears to have a decent national collaborative network, however, this does not reflect the limited number of collaborative papers.

- Appreciation on the strategy, management and life of the team

No indication on the team organization, management and animation is provided in the evaluation document.

With 2 Professors and 2 MCU, the team appears significantly involved in biochemistry, molecular and structural biology and bioinformatics teaching activities. The team members appear also heavily involved in organizing a number of activities within the University of Rennes 1 (teaching, training, informatics and professor/MCU selection). 4 PhD and 7 M2 students were trained over the considered period.

- Appreciation on the project
- Existence, relevance and feasability of a long term (4 years) scientific project

Line A: Ribosome and translation

Work package 1: Ribosome biogenesis

The aim is to study the structure of the well-known intermediates of ribosomal biogenesis by cryoEM: 32 and 43S precursors of the 50S subunit and 21S precursor of the 30S subunit of E. coli ribosomes.

Some weeks ago the course of the 30S assembly in vitro applying the total reconstitution method by means of EM and mass spectrometry has been published in an excellent paper in Science by another group. Therefore, the plan of studying the in vivo precursors is timely and interesting. Cooperation with a group in Paris to isolate larger quantities of precursors is optimal; he is one of the leading figures concerning production of native ribosomal precursors. Not only strains with null mutants of either dnaK or dnaJ should be used as suggested, but also wild-type E. coli cells under heat stress, which also will yield larger amounts of precursors.

Work package 2: Structural aspects of the ribosome by cryoEM

The researcher in charge of this work package is an offspring of another group in Rennes well known for their work on trans-translation (tmRNA); he also worked for some time with a group in Cambridge (Noble prize 2009). He recently published the cryoEM structure of a tmRNA•ribosome complex in EMBO J. (not yet present in the publication list), which at the moment represents the state-of-the-art in the field of trans-translation. They plan to isolate various complexes illustrating how the monster tmRNA moves through the ribosome.

In summary, this is an excellent and internationally competing program concerning the analysis of structure and mechanisms trans-translation. The future program for the next four years is a logic extension of the interesting results so far obtained.

Line B: Protein folding

Work package 3: Co-translational folding

Two team members plan to study the structure of polysomes accumulated after overexpression of distinct mRNA fragments after isolation (in vitro) or in cells (in situ). The E. coli cells will contain an inactivated trans-translation system in order to increase the yield of polysomes. They want to study the folding of protein domain as they emerge form the ribosomal tunnel exit.

The plan is to develop cryoEM techniques similar to the “cell tomography” developed by a group in Munich. This is certainly an ambitious program of high scientific interest. They should also consider using E. coli mutants, which should contain in addition to an inactivated tmRNA system a partially inactivated arfA gene, since as shown recently in Mol. Microbiol. a knock-out of the genes tmRNA and ArfA produces a synthetic lethality. However, the goal to study co-translational folding with the techniques they intend to master and to develop is impossible with the current methods and probably will not be achieved within the next four years period. In contrast, polysome arrangements under various conditions can be studied as shown recently in a pilot paper.

Work package 4: Characterization of Hsp90 oligomers

Hsp90 is an almost universal chaperone present in bacteria, mitochondria and eukaryotes. Recently the group reported in an important paper in JBC (could be published even in a better journal) various types of Hsp90 oligomers and demonstrated that the hexamer (type II of the oligomers) forms a ring structure as shown by electron microscopy. Now they suggest extending this experimental line by analyzing the structure of Hsp90 together with co-chaperones, substrates and inhibitors. The latter ones have attracted interest in the last three years due to their anti-cancer potential. The feasibility of this work package is highly dependent on the choice that will be made for the yet unidentified Hsp90 client proteins.

They have established their standing and visibility in the Hsp90 community in the last three years. The experimental plan is a logic extension of their important achievements.

Work package 5: Misfolding and conformational disease

The “amyloidoses” are a heterogeneous group of severe diseases with the common feature that distinct proteins become misfolded, are deposited in the interstitium forming amyloid fibrils and causing the disease. A former member of the team has established a database containing « molecular signatures of amyloid precursors ». The team plans to exploit this database for the detection of both general patterns and rules within a collaboration. Another collaboration focuses on in vitro studies of peptides that play a role in kidney diseases, since this organ is a main target for amyloidoses. The corresponding peptides will be overexpressed in E. coli and the aggregation behavior studied. Protective mutations will be predicted and tested concerning fibril formation. In a set of in vitro experiments they intend specifically to document immunoglobulin light chain and fibrinogen A¤ aggregation as known from kidney degeneration diseases. This work package might benefit from competences within the team and Rennes University hospital.

This program has an important medical potential. The experimental program is not too complicated and therefore has a good success-probability.

All 5 work packages contain original design elements. Work packages 1, 2 and 4 are cutting edge projects. The goal of work package 3, namely to study co-translational folding, is out of reach at the moment, but the intended development of techniques for “cell tomography” is of utmost scientific interest. The part of work package 5 dealing with kidney degeneration is interesting and has the potential to develop to a cutting edge project.

- Conclusion :
  - Summary

The scientific program of the group is a good example of a collaborative program with three important and related experimental lines. The scientific visibility of the group is good and is capable of expansion.

  - Strengths and opportunities
  - Weaknesses and threats
  - Recommendations

Some experimental recommendations are given under “Appreciation on the project”. The program is very ambitious, and it might be wise to define and regularly re-define experimental priorities in order to improve the scientific output.

Team 18 : "MEMBRANE TRAFFIC AND POLARITY IN C. ELEGANS"

Leader: Grégoire MICHAUX

- Staff members

	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 and 2.7 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)	1	1
N5: Number of engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	1	1
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

Research in this team concerns the contribution of the adaptor complex AP-1 in the establishment and maintenance of epithelial cell polarity in C. elegans. It is split in three directions: i) The genetic identification of AP-1 interactors based on their capacity to enhance partial lethality of unc-101 mutation (AP-1 mu subunit). Four genes have been identified: Rab10, Dab-1, Vps32 and APM-1. Focus has been made on the function of Rab10 in basolateral localization of LET-32/EGF-R during vulval development. A parallel study in collaboration with the former group leader of the PI has shown that AP-1 and Rab10 are required for secretion of von Willebrand Factor (VWF) in HUVECs. ii) Mechanism of apical recycling of Par3/Par6 complex. The team found that AP-1 loss-of-function mutation results in defect in elongation of the embryos (3-fold stage arrest). At the cellular level, actin organization and most membrane traffic markers appear normal. However, the apical domain extends dramatically and a mislocalization of the polarity Par3/Par6 complex to the basolateral cortex is observed. Based on EM analysis, an accumulation of VPS-32 endosomes and a loss of Rab11 recycling early endosomes is observed in unc-101 mutant. Only Rab11 seems to be required for Par3/6 apical localization, indicative of a novel role for AP-1 in promoting recycling and maintenance of Par3/6 at the apical cortex together with RAB11 and VPS32. iii) The team has demonstrated that AP-1 and RAB10 interact to allow targeting of the EGF-R to the basolateral domain of vulval precursor cells for normal vulval development. The analysis of the role of AP-1 in cell polarity in several developmental processes by this group is diverse and original. With respect to the second part, the finding of AP-1/Rab11 interplay in controlling the apical recycling of the Par3/Par6 polarity complex is very original. The relevance of this research lies in polarity being studied in a whole developing organism rather than in cells in culture.

The research is highly original. The obtained results are exciting and have a potentially high impact on studies in other systems as well. The advantage of these studies is the use of an organisms rather than cell in culture.

One drawback is that the publication of the group is modest. However, the leader has changed subject after is postdoctoral studies and started the C. elegans system and epithelial polarity in his own laboratory.

As yet, there is no publication by the team leader as senior author. In the past 4 years the leader has 3 collaborative papers in Genetics, JCS and Reproductive Toxicology and a recent paper as first author in Journal of Thromobosis and Haemostasis (IF=6).

The team leader is also co-author of one review article in Med. Sci in 2009. The story describing the role of AP-1 in apical targeting of PAR proteins is about to be submitted to Nature Cell Biology (the journal has already been

contacted and the NCB editor is interested in reviewing the paper). A second collaborative paper describing the role of AP-1 in EGFR degradation will also be submitted soon.

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

The team is presently quite small (4 members). Additional fund raising will be important to consolidate the team. After being awarded an AVENIR grant on a highly selective basis, other funds have been mainly national. Success of grant applications will be critical for the future of the group.

The international visibility is still limited (this could be the result of changing the subject and not having publications yet) and should be improved.

The team has been successful in attracting both postdocs and students. At least one postdoc was from abroad.

The team has been successful in raising funds, at the local and national level. However, the future of the team heavily relies on the ability of the team leader to find funds for the future years as most grants are ending in 2010.

The group has local, national (Strasbourg) and international collaborations.

- Appreciation on the strategy, management and life of the team

The leader was able to attract both postdocs (at least one from abroad) and students.

The leader has found an exciting niche. The projects are cutting edge and are already revealing novel aspects that are relevant for the epithelial and membrane traffic fields.

- Appreciation on the project

The team has three defined projects related to the role of membrane traffic and protein degradation in regulation of cell polarity. The team uses two independent but complementary systems, the epithelium and the early embryo.

Project 1. The team showed that AP-1 & Rab11 are required for apical localization and recycling of the polarity Par3/6 complex at the apical plasma membrane. The goal is now to identify other components involved in Par3/6 apical targeting using both a candidate approach and an unbiased screening approach based on genes required for viability and embryo elongation in C. elegans (150 genes). The contribution of plasma membrane phosphoinositides (PIP2 and PIP3) will also be analyzed. This part of the project should be performed by a PhD student already in her third (last)-year of her thesis. To allow achievement of the proposed goals a postdctoral fellow should be hired.

Another aspect of this project deals with the identification of proteins involved in Par complex localization. RNAi-mediated loss-of-function of 2500 genes required for C. elegans embryo viability will be assessed for defects of GFP-Par6 localization in intestinal epithelial cells. Priority will be given to genes involved in membrane traffic as well as trans-membrane (junctional) proteins that will be further functionally characterized. This project will give an overview of factors required for Par complex localization in an epithelium in a whole organism.

Project 2. This part of the project deals with the localization of Par complex components and E-cadherin by immunoEM with respect to plasma membrane subdomains and intracellular compartments as these proteins appears to be trafficked for normal function. This type of approach provides some ideas about steady-state localization of the proteins and visualization within transport intermediates and/or intracellular compartments may turn to be difficult. This is not the most exciting part of the project and it is not clear what are the expected results and how it could help the rest of the project.

Project 3. This project investigates the role of cullin ubiqutin ligases CUL2 and CUL5 in the degradation of Par complex components and how degradation contributes to generate antero-posterior polarity during asymmetric division in the early C. elegans embryo. The project will also address whether Par6 ubiquitination and subsequent degradation depend on phosphorylation by candidate kinases (PKC-3, GSK-3 and MAPK).

The intended work is generally original and the results obtained are exciting and will likely lead to cutting edge projects. The discovery of AP-1 as responsible for apical targeting of PAR-6 is new and exciting. The potential is high.

- Conclusion :

  - Summary

Young group leader with very good potential and a very interesting on-going project that should now be concretized by publications.

  - Strengths and opportunities

Exciting results with impact on other systems. Good mixture of developmental biology, genetics and molecular (cell) biology.

Good complementarity of the team leader and associated young staff scientist and research assistant. This is a well-defined and ambitious project.

  - Weaknesses and threats

The future of the group is dependent on many ongoing grant applications and production of high impact publications (2 papers will be submitted very soon).

  - Recommendations

The leader should publish rapidly the exciting results he has obtained and apply for grants to be able to keep working on this interesting project. Because of the limited resources available at the moment, the team leader should focus.

Team 19 : "TUBULIN AND INTERACTING PROTEINS" (TIPS)

Leader: Denis CHRÉTIEN

- Staff members

	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	1
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 and 2.7 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 engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.8 of the application file)	2	1
N7: Number of staff members with a HDR or a similar grade	1	1

- Appreciation on the results

This team originates from a split of the team Structure & Dynamics of macromolecules in 2007. The team is an international reference in the microtubule field. The team leader is considered as one of the leading figures in the field of microtubule ultrastructure, and the group has recently also made some important contributions to the rapidly

growing field of microtubule plus end binding proteins, or +TIPs (one recent paper in Nature Cell Biology). Amongst other things, the team has described that microtubules possibly elongate by incorporation of tubulin molecules into flat sheets that straighten, for unknown reasons at one point, and close into the hollow tubes that are microtubules. The team has also shown that GDP and GTP-like tubulin molecules differ within the microtubular lattice by high-resolution cryo-EM and image averaging and analysis. The team has finally contributed to documenting the interaction of 4 microtubules associated proteins and has invested efforts in documenting at high resolution the structure of large macromolecular assemblies within the cells such as the centrosomes and the axonemes by cryo-EM and image averaging and analysis.

The team has contributed overall 14 papers over 4 years. Although of limited size during the last 3 years, the team, mainly as partners, has contributed papers in high impact journals (1 Curr. Biol., 1 EMBO J., 2 JBC). The team also contributed one paper in a high impact journal (Nature Cell Biology) in 2008 with senior authorship. The team contributed 3 invited talks at international conferences, 3 other talks at national/local conferences, and overall 23 poster presentations.

The team has a fairly strong national/local collaborative network. A long-lasting international collaboration with physicists has generated a published model for microtubule lattice mechanical properties.

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

The number of scientist within the team has dropped to the STRICT minimum over the last 3 years. The present size of the team (1 scientist, 1 ITA and 1 PhD student) is sub-threshold.

The international visibility of the team is witnessed by 3 invitations to give talks at international meetings. Two team members, a permanent scientist who left the team recently and a PhD student have been awarded prestigious distinctions, ATIP/Avenir grant and the Pierre Favard Prize, respectively. The collaborations of the team have generated so far 1 and 5 papers, respectively, and overall over 15 poster presentations.

In the past, the team leader had recruited one high-level staff scientist who became recently independent and several very good PhD students. At present, the team has no foreign scientists. This should be improved, but it depends also on the ability of the team to grow and on the ability of the institute to strengthen its international standing. A good start is the international postdoc program of the University Rennes 1 to which the institute belongs.

In the past he team has been able to obtain national (ANR, ARC, CNRS) and local (University of Rennes 1 and IFR 140) funding as long as it comprised 6 persons on average. A permanent scientist who left the team recently has been awarded a prestigious distinction/grant, ATIP/Avenir grant.

Upon increase in size, the team should have no major problems raising research funds.

The team has established numerous collaborations. One international collaboration with physicists has been productive (one publication for the period we are interested in). The national and local (mainly with physicists) collaborations generated so far 1 and 5 papers, respectively, and overall over 15 poster presentations.

- Appreciation on the strategy, management and life of the team

While scientifically the group has performed very well, they have encountered some organizational difficulties within the last 6 years. The team fused with another team in 2004, and split into two groups shortly after this fusion (in 2007).

The team members have been involved in the local/regional EM platform. They appear also obviously heavily involved in developing, in collaborations with physicists and experts in computer science, software development devoted to image analysis and 3D image reconstructions.

The team members appear involved in teaching activities as well as in the life of the Unit. They are involved in reviewing/expertise and training activities. 4 PhD, 3M1 and 3 M2 students were or are trained.

- Appreciation on the project

The future project of the team is based on the continuation of their successful lines of research, and underlines the importance of collaboration considering that the major strength of the team is their technological expertise in the field of microtubule electron microscopy. This approach is strongly appreciated since the team has a

unique expertise that can be applied in many different projects, however the team in its present size is not suited to develop a broad-range biological approach. The move of the team to the new institute will further strengthen the collaborative work since they have already established a joint project with the team 3.

Although appealing the proposed project is not likely to be fully feasible with the present size of the team. This remains true even with the first class competences of the team leader and the proposed collaborative network. The team leader is aware of these difficulties.

The proposed project is highly ambitious. The team plans to pursue its investigations on the molecular basis of microtubule structure and function and integrate the findings they will make at the molecular level within cellular structures and context. The team leader wishes to participate to a network (mainly constituted of cell and developmental biologists) which objective is to establish an integrated "molecule to organism" approach. Three structural projects, heavily relying on cryo-EM imaging and image analysis, are presented. The first deals with tubulin conformational changes upon GTP hydrolysis within the microtubules comprises a work package devoted to developing software that deal with image distortion that may ease microtubule 3D reconstruction. The second project tackles the interaction and its consequences of microtubules + end binding proteins. This collaborative project, with an international expert in the field, is funded till 2011. The third research tract aims to integrate information gathered at the molecular level within a cellular and organismal level. A tripartite collaboration with local and national partners has been established to this end.

- Conclusion :

  - Summary

The proposed project is very ambitious. It is important that the team increases in size since two group members recently left the lab.

  - Strengths and opportunities

International reference in the microtubule structure field.

Established unique techniques in electron tomography and image analysis tools.

Actively involved in local and national and international interdisciplinary collaborations.

  - Weaknesses and threats

Current size of the team that is sub-optimal.

The group leader should seek senior authorship when possible and for additional independent financial support.

The group leader is underselling his first-class contribution.

  - Recommendations

One recommendation is to accommodate Teams 19, 3 and 11 in very close vicinity in the new unit to allow daily interactions in addition to joint lab meetings and journal clubs, etc. in order to strive for the creation of a strong microtubule hot spot in the research landscape of the new institute.

We encourage the team leader to submit his work to journals with broader audience.

The team needs state-of-the-art specific equipment (high resolution and sensitivity cameras) for EM image acquisition and tomographic reconstruction. It is critical this request is granted.

Intitulé UR / équipe	C1	C2	C3	C4	Note globale
INSTITUT DE BIOLOGIE DE RENNES	**A**	**A**	**A+**	**A**	**A**
CANINE GENETICS [PRIGENT-ANDRE-HITTE]	A+	A+	Non noté	A+	A+
KIDNEY CANCER: MOLECULAR BASIS OF TUMOROGENESIS [PRIGENT-ARLOT BONNEMAINS-VIGNEAU]	B	A	Non noté	A	A
REGULATION OF STRESS ADAPTATION [PRIGENT-BLANCO]	B	B	Non noté	B	B
TUBULIN AND INTERACTING PROTEINS [PRIGENT-CHRETIEN]	A	A	Non noté	A	A
GENETIC OF PATHOLOGIES RELATED TO DEVELOPMENT [PRIGENT-DAVID]	B	B	Non noté	B	B
GENE EXPRESSION AND ONCOGENESIS [PRIGENT-GALIBERT]	B	A	Non noté	A	A
CYTOSKELETON AND CELL PROLIFERATION [PRIGENT-GIET]	Non noté	A	Non noté	A+	A
TRANSLATION AND FOLDING [PRIGENT-GILLET]	A	A	Non noté	A+	A
SIGNALLING IN MOUSE OOCYTES AND EARLY EMBRYOS [PRIGENT-HALET]	Non noté	A	Non noté	A+	A+
GENE EXPRESSION AND DEVELOPMENT [PRIGENT-HARDY-PAILLARD]	A	B	Non noté	A	A
STRUCTURE AND MOLECULAR INTERACTIONS [PRIGENT-HUBERT]	Non noté	B	Non noté	B	B
DYNAMICS OF CHROMATIN ARCHITECTURE [PRIGENT-HUET]	Non noté	A	Non noté	B	B
EPIGENETIC AND CANCER [PRIGENT-JAULIN]	A	A	Non noté	A	A
CELL POLARITY, MEMBRANE TRAFFICKING AND SIGNALING [PRIGENT-LE BORGNE]	A	A+	Non noté	A+	A+
MEMBRANE TRAFFIC AND POLARITY IN C. ELEGANS [PRIGENT-MICHAUX]	A	B	Non noté	A	A
INTEGRATED FUNCTIONAL GENOMICS AND BIOMARKERS [PRIGENT-MOSSER]	B	A	Non noté	B	B
CELL DIVISION: A REVERSE ENGINEERING [PRIGENT-PECREAUX]	Non noté	A	Non noté	A+	A
CELL CYCLE [PRIGENT-PRIGENT]	A	A+	Non noté	A+	A+
SPATIOTEMPORAL REGULATION OF TRANSCRIPTION IN EUKARYOTES [PRIGENT-SALBERT]	A+	A+	Non noté	A+	A+

C1 Qualité scientifique et production

C2 Rayonnement et attractivité, intégration dans l'environnement

C3 Gouvernance et vie du laboratoire

C4 Stratégie et projet scientifique

Statistiques de notes globales par domaines scientifiques

(État au 06/05/2011)

Sciences du Vivant et Environnement

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

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

Intitulés des domaines scientifiques

Sciences du Vivant et Environnement

- **SVE1 Biologie, santé**
  - **SVE1_LS1 Biologie moléculaire, Biologie structurale, Biochimie**
  - **SVE1_LS2 Génétique, Génomique, Bioinformatique, Biologie des systèmes**
  - **SVE1_LS3 Biologie cellulaire, Biologie du développement animal**
  - **SVE1_LS4 Physiologie, Physiopathologie, Endocrinologie**
  - **SVE1_LS5 Neurosciences**
  - **SVE1_LS6 Immunologie, Infectiologie**
  - **SVE1_LS7 Recherche clinique, Santé publique**
- **SVE2 Ecologie, environnement**
  - **SVE2_LS8 Evolution, Ecologie, Biologie de l'environnement**
  - **SVE2_LS9 Sciences et technologies du vivant, Biotechnologie**
  - **SVE2_LS3 Biologie cellulaire, Biologie du développement végétal**

PRÉSIDENCE

Guy Cathelineau
Président

UNIVERSITÉ DE RENNES 1

Rennes, le 08 mars 2011

Vos réf. : S2UR120001333
Institut de Biologie de Rennes– 0350936C

Monsieur Pierre GLORIEUX
Directeur de la section des unités de recherche
Agence d'Evaluation de la recherche et de
l'Enseignement Supérieur (AERES)
20, rue Vivienne
75002 PARIS

Monsieur le Directeur,

Je vous adresse mes remerciements pour la qualité du rapport d'évaluation fourni à l'issue de la visite du comité d'expertise concernant la future unité mixte de recherche **« Institut de Biologie de Rennes »,** résultat du projet de fusion des UMR actuelles 6026 « Interactions cellulaires et moléculaires » et 6061 « Institut de Génétique de Rennes ».

L'université de Rennes 1 sera particulièrement attentive à ce que les recommandations formulées par le comité de visite soient prises en compte.

A la lecture de ce rapport, vous trouverez ci-joint, les réponses du directeur d'unité auxquelles nous souscrivons en totalité, en y ajoutant quelques précisions sur les deux éléments suivants :

La création de l'institut de Biologie de Rennes correspond à une volonté partagée entre les tutelles Université de Rennes 1 et CNRS-INSB, de fédérer et structurer la recherche en biologie sur le site universitaire rennais. Cette nouvelle unité sera donc une pièce maîtresse, à conforter et à soutenir, dans la stratégie de recherche de l'université de Rennes 1 pour le prochain contrat quinquennal et, comme le souhaite le comité, avec un lien renforcé avec le secteur santé et recherche clinique.

L'université de Rennes 1 a pris connaissance des recommandations du comité concernant l'activité de recherche autour de la thématique scientifique « microbiologie » ainsi que de la réponse solidement argumentée du directeur de l'équipe de recherche concernée. Sur cette base, et une fois le rapport définitif d'évaluation établi, l'université, avec ses partenaires, s'attachera à bâtir une solution d'intégration scientifique et structurelle la plus appropriée pour le développement de cette thématique de recherche qui est adossée à une activité de formation totalement reconnue et stratégique pour l'établissement.

Je vous prie d'agréer, Monsieur le Directeur, l'expression de ma considération distinguée.

Le Président de l'Université de Rennes 1

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Vague B (2012-2015)
Unité de recherche : dossier unique

ANSWER to the AERES' report

The Institute of Biology of Rennes

UMR fusion 6026 & 6061

Directeur : Claude PRIGENT

CNRS – Université de Rennes 1

Université de Rennes 1, Faculté de Médecine
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35043 Rennes Cedex
Tél. : 02 23 23 49 52

DIRECTION OF THE INSTITUTE

First I would like to thank the committee for their extensive and detailed evaluation of the institute, and for their constructive comments.

Strengths and opportunities

I appreciate the acknowledgement of my investment in the direction and the work that has been done over the last years in terms of attractiveness, recruitments, policy to support young group leaders, establishment of interdisciplinary research, the running of state-of-the-art facilities, the links build with the hospital and the implication in teaching.

Weaknesses and threats

- Non French Group leader
We are currently negotiating with an American Researcher from the Rockefeller University (USA) who will come with a group leader position in the institute. In the future, priority will be given to international recruitment of new group leaders.

- I agree the analysis of the ratio permanent vs non permanent (post-doc), we are working on increasing the number of post-docs. (*but this specific comment may have been grounded on inaccurate figures, see table corrections*).

- I agree the committee's concerns about the size of some teams, we are also working on it, for instance D Chretien will recruit a MCU this year.

- There are teams with too many researchers with teaching duties. I do agree that statement although this is a very difficult issue since each of them must teach 192h per year: far too many. As long as their teaching burden is so heavy, they cannot be in a favourable position to develop a competitive research project alone. The current solution found is to associate several of them on a single research project in order to achieve the scientific "critical mass" required to perform the project.

- Regarding funding, I do encourage scientists to apply to competitive international grants calls. Jacques Pecreaux is currently competing for an HSFP grant, Reynald Gillet is applying to an ERC grant and to the EMBO Young Investigator programme and, as suggested by the committee, Regis Giet will apply to the ERC. Moreover, a young group leader, currently located in the USA and applying for a position in the IGDR, is currently competing for an ERC grant.

- Regarding production, scientific strategy reflections with the group leaders will be initiated in order to improve publications impact factors.

- I agree the last comment regarding invitation in international meeting: this must be improved. Since this is closely related to publication impact, improving scientific production quality should also lead to increase invitation rate to international meetings.

Recommendations to the head of the research unit

- I fully agree the first sentence and the comments « *However it is essential that this be acted upon at once to avoid delayed integration and destabilization of these teams* », this is indeed essential and negotiations are ongoing with the University.

- Several meetings with ITA and IATOS will be organised in 2011. These meeting were deliberately programmed after the visit of the AERES committee in order to prioritize focusing on the institute's scientific project.

- A retreat will be organised in 2011 and will be held on a regular basis in the future.

- I agree that the "new team package" is not attractive enough. However, the committee must be aware that, in 2011, the CNRS funding contribution to the institute has significantly decreased (40 000 € less compared to 2010), and the University contribution has also decreased (10 000 € less). Although I would be ready and willing to give 50 000 € + a post-doc salary as a starting grant to newly recruited team leaders, the institute cannot provide alone the funding for such a package. We are working on finding a solution with our financial partners.

- As I said during my presentation, we do organise workshops for PhD and post-doc but mainly through the platforms. We are now thinking of a specific training program for PhDs in the institute.

- I agree that relationship with the hospital should be reinforced and I am working on it.

- Concerning shared team leaderships, only team#1 will be kept with two group leaders: Yannick Arlot (basic research) and Cecile Vigneau (clinical research) because, given the dual complementary nature of their research project, a co-leadership appears justified in this specific case. For the other two-headed groups, Luc Paillard will become the sole leader of team#7, and Catherine André will be the only team#9 leader.

- As suggested by the committee and in agreement with Gilles Salbert and Sébastien Huet, team#4 will not be created, and Sébastien Huet will join Gilles Salbert' Team.

- According to the committee's recommendation, team#12 will not be created in the institute. Carlos Blanco and his group have nevertheless chosen to remain together as a team. In accordance, they will not longer be part of our project and they will join another structure more suitable to their scientific interests, *i.e.* a structure dedicated to microbiology.

Team 1: Kidney cancer : molecular basis of tumorigeneisis
Group leaders: Yannick ARLOT-BONNEMAINS & Cécile VIGNEAU

We are grateful to the committee for the comments on the project.

Appreciation on the impact, the attractiveness of the team and of the quality of its links with international, national and local partner:
The group is new and begins to connect with the scientific world of VHL and will intensify its connections already existing in the field of ubiquitination and E3 ligase.

Note: The group regrets that there was no oncology clinician in the committee.

Team 2: Cell cycle
Group leader: Claude PRIGENT

First I would like to thank the committee for their constructive comments.
I fully agree with the evaluation of the team.

As mentioned in the evaluation report, administrative duties corresponding to the direction of the institute have been time consuming over the last years. Under those conditions, the presence of talented researchers in the team is very helpful and greatly appreciated.
I expect administrative duties will diminish in 2012 for two reasons (1) I will insure the direction of the new UMR with the help of a deputy director and (2) the restructuration of the team has clarified objectives.

My own project regarding Aurora-A (financed by an ARN Blanche) was quite long to set up, but data are now accumulating and work should be concretized in the next years with several good papers emanating exclusively from the Cell Cycle team. This should further increase the international visibility and attractiveness of the team thereby allowing recruitments of foreign post-doctoral fellows.

Team 3: Cytoskeleton and cell proliferation
Group leader: Régis GIET

First of all, we appreciate the very favourable comments about our emerging group in the AERES report.

The committee members have raised a few minor issues that we would like to clarify. The first one was about the research performed by the team leader when he was previously part of the team 2. We would like to point out that during the last few years, we have followed independent research lines in most of our projects, with a specific approach focussed on the drosophila model. As underlined by the committee, this autonomous work has led to the publication of several recent papers signed by the team leader as senior author. Moreover, the leader of team 2 does not appear as an author in two of these publications (J Cell Biol 2010, PLoS ONE 2011), which testifies of the complete autonomy of our team. According to the research program we presented to the committee, we will continue to perform a truly independant and original program, with the goal of

characterising new MAPS involved in spindle assembly and cell proliferation in the CNS of drosophila.

The second concern raised by the committee was about our future funding. In the past, the team leader has been awarded an ANR grant. We have recently secured a grant from ARC (subvention libre) for the next 3 years (about 28 KEuros/year for our team) together with team 19 and the team of Antoine Guichet (Institut Jacques Monod, Paris). As suggested by the committee, we will also apply for an ERC starting grant. We are thus confident that we will get funded in the next few years in order to carry out successfully our research program.

Team 4: Dynamics of the chromatin architecture
Group leader: Sébastien HUET

The team leader would first like to answer to one specific comment raised by the committee. Indeed, in his report, the committee mentioned, concerning the group leader, that *"it is unclear whether he is involved in teaching"*. In his "fiche individuelle d'activité", which was part of the documents transmitted to the AERES, the team leader explicitly mentioned that, as a Maitre de conférence chaire UR1/CNRS, his teaching activities correspond to 64 hours per year.

Despite acknowledging the quality of the interdisciplinary project presented by the team leader, the committee considered that it is premature to establish a group on this subject due to unsecured resources in terms of funding and men-power, and uncertainties concerning the feasibility of the setting up of a super-resolution microscope in the host institute. The team leader accepts these comments but would like to mention two points:

- Since the visit of the committee, the group leader has been informed by the CNRS that he will receive support from a research technician (arrival in May 2011). This technician, who is specialized in cellular and molecular biology will be of great help for the success of the project.

- The setting up of the super-resolution system is indeed risky. However, only one of the three tasks of the presented project relies on the successful development of such advanced imaging system. The two other tasks involve microscopes which are available on the MRic imaging facility and are thus completely independent from the establishment of the super-resolution setup.

Following the recommendations of the committee, the group leader will be integrated in the team 14, with which he is already collaborating. This will allow him to pursue his research project in the more secured environment of an established team.

Team 5: Epigenetics and cancer
Group leader: Christian JAULIN

We are grateful to the AERES committee for their very positive analysis of our scientific production and our projects. Their helpful and constructive comments are much appreciated.

The small size of the team is acknowledged. Yet, we would like to emphasize that the team has

arrived in Rennes in 2008 as a skeleton crew (2 staff scientists and a PhD student in her last year of PhD training) and thus is still in its growth stage. Efforts are made to attract international non-permanent students and post-docs, as testified by the recent recruitment (Sept 2010) by the team of a non-French PhD student who performed most of his undergraduate and post-graduate training abroad.

The fact that the team is not part of a formal network such as an FP7 program is also acknowledged. However, we would like to point out the quality of the collaborative network that the team has set up in the past years: tight collaborations with some of the most competitive international leaders in the field of chromosome dynamics (Jonathan Higgins, Harvard Medical School; Yoshinori Watanabe, University of Tokyo) and proteomics (Guy Poirier, University of Laval, Québec) have been established and secured. In addition, the Team leader is coordinator of two competitive grants (Cancéropôle Grand Ouest and ANR "Programme Blanc") that involve another CNRS team in Nantes (Christophe Thiriet, UMR 6204).

Low participation of the team (members other than the Team leader) to international meetings is accepted as true and all the team members will be strongly encouraged to present their results at international meetings.

Team 6: Gene expression and oncogenesis (GEO)
Group leader: Marie-Dominique GALIBERT

- Appreciation on the results:

During the last quadrennial, the team was headed by two group-leaders developing distinct projects. In order to increase the **visibility**, the group has split, **focusing** now on understanding the **specific gene expression program** that is turned on to drive and promote cancer development.

This choice led to a diminution of the existing driving forces, but this reorganization in place since Spring 2010 permitted also to **attract** one researcher (David GILOT) and one post-doctoral fellow (MB TROADEC) (September 2010).

- Appreciation on the impact, attractiveness of the team…

Knowing that PhD students are part of the driving forces required to execute the scientific project, we plan to attract and raise fund to permit the training of PhD students, as in the past years: **5 PhD students have been trained under my supervision**: 2 have fix positions and the 3 others are pursuing post-doc training.
In addition, we plan to **increase the number of staff member with a HDR** and do anticipate that David GILOT does have the adequate track records to undergo a HDR application.

Raising fund is definitely central in our work, and since 10 years it has been one of my duty, providing subside for consumables, for the development of animal models, to fund PhD and post-doctoral fellow and also to permit to each member of the team to attend to at least one international meeting per year. To reassure the committee, we have already submitted applications for international (France-US) and European (EORTC) grants and applied to an ANR call in addition to the more local grants.

- Appreciation on the strategy, management and life of the team

Teaching duty reduces the time devoted to research, however it is an efficient way to attract Masters and PhD students.

Also to balance these teaching duties, we favor post-doctoral applications (3 post-doc fellows), and to reinforce the team we are presently training post-doctoral fellows to apply for academic permanent position (CNRS, CNRS).

Team 7: Genetic expression and development
Group leader: Luc PAILLARD & Serge HARDY

We thank the AERES committee for acknowledging our strength and uniqueness that are to combine state-of-the-art genomic approaches and profond expertise with the frog model system, with opportunity to "become very influential group". Below are answers to the main points raised by the committee.

1. Weaknesses and threats: "The team should try to attract new Postdocs and PhD students – if possible at least half of them should come from abroad (non-French)". We will endeavour to always have at least 2 PhD students simultaneaously in the group, as has always been the case, and grant applications will be applied for to cover postdoc fellowships. Our successes with non-French recruitments, especially students or postdocs from developped countries, are growing, with a German postdoc (2008-2010) and an Italian long-term PhD internship (starting 2011, an information that was not given to the committee because it was not confirmed at the time of the visit).

2. Weaknesses and threats: "The team has two group leaders (...) it is recommended that the team clearly defines one group leader who can take full responsibility for the research". In accordance with this comment, the team will be headed by one group leader, Pr Luc Paillard.

3. Weaknesses and threats: "The team may think about the establishment of new lines of research to study important RBPs in frogs". Also Recommendations: "The team should also start to think about new lines of research that makes them internationally unique (e.g. perform a systematic screen to find other RBPs that play a role during frog development)". We have two main lines of projects, one dealing with RBPs (Celf1, Ptb) for which we have several tools, including internationally exclusive tools (floxed Celf1 mouse strain), and a more exploratory one aimed at characterizing the developmental functions of new RBPs in Xenopus. We have already characterized the expression patterns of 6 new RBPs and undertaken their knock-down in Xenopus. The preliminary results are promising and suggest a role for some of these RBPs in somite segmentation or immune system development. Clearly, the committee recommends that we add significantly more weigth on this line, and this recommendation will be taken into account.

4. Recommendations: "The team should try to publish in higher-impact journals, which will undoubtly improve the international visibility". We accept this comment. Currently, we have 3 manuscripts submitted or in preparation for submission in journals with IF>10.

Team 8 : Genetic of pathologies related to development
Group Leader: Véronique DAVID

I thank the evaluating committee for its constructive remarks.

The recommendation of the committee for the unit is to develop strong collaborations between clinicians and biologists and that is one of the strengths of our team, which provides a good access to patients and therefore opens to translational research. These collaborations allowed us to collect the most important sample collection in Europe and to set up a clinical and biological database, making the strength of the team. It also represents a good example of connection from the patient's bed to bench.

Here, we are going to answer to the committee remarks:

- In the scientific report, we omitted to describe the scientific animation of our team. We have set up weekly meeting for 2 years. In these meetings, results and strategies are deeply discussed with each member of the team.

- We would like to precise that the second axis of our research project (MRKH) is supported by one full-time researcher, two teachers and one technician.

- Our basic research has been reinforced on HPE by the recruitment of a full-time researcher who has joined the team and developed an animal model to study the signalling pathways involved in brain development. The international community recognized this approach as our first results were recently published in Human Molecular Genetics (IF 7.40). (Dupé V, Rochard L, Mercier S, Le Pétillon Y, Gicquel I, Bendavid C, Bourrouillou G, Kini U, Thauvin-Robinet C, Bohan TP, Odent S, Dubourg C, David V. NOTCH, a new signaling pathway implicated in Holoprosencephaly. Hum Mol Genet. 2011 Mar 15;20(6):1122-31. Epub 2010 Dec 31).

- Furthermore, important results dealing with genetic mechanisms triggering MRKH syndrome are about to be published in Orphanet Journal of Rare Diseases (IF 5.85). (Morcel K, Watrin T, Pasquier L, Rochard L, Le Caigne C, Dubourg C, Loget P, Paniel B-J, Odent S, David V, Pellerin I, Bendavid C, Guerrier D. Utero-vaginal aplasia (Mayer-Rokitansky-Küster-Hauser syndrome) associated with deletions in known DiGeorge or DiGeorge-like loci).(Under proofs correction at the time of writing)

- We are quite confident in obtaining new fundings, as we applied to numerous grants (two PHRC, ANR jeune chercheur, COREC and Agence de la Biomédecine). In these grants, we have notably asked for Post-doctoral fellowship fundings.

- We would like to emphasize that our recent findings are very exciting, as we have demonstrated that Notch pathway is implicated in early forebrain development. To go further in this direction, we have already established collaboration with the team of Roland Le Borgne.

Team 9: Canine genetics
Group leaders: Catherine ANDRÉ & Christophe HITTE

We are very pleased that the committee judged the scientific activity of the group of high quality and extremely original!

Indeed we developed complementary axes (F. Galibert, C. André and C. Hitte) and have complementary skills that gave us strength and efficiency with a quite good expertise in the field of dog genetics. We will keep the same line for the next 5 years! This is also appreciated by our international collaborations, which are often long term and efficient collaborations.

We attract Post Docs and PhD students and are able to obtain corresponding funding. The canine Bio-Bank and Vet network are indeed unique and well structured with a national Vet Net. However, we have a crucial need in a permanent staff for technical support and strongly hope this will be possible in a near future.

To answer the committee recommandations, while a two-head and shared direction of the team appeared positive to us, we accept the recommandations and propose that C. André is the group leader and Christophe Hitte is the deputy leader.

On behalf of the team, I thank the committee for their very positive analyses and enormous work for the whole analyse of our Institute.

Team 10: Integrated functional genomics & biomarkers
Group Leader: Jean MOSSER

I would like to thank the AERES committee for its constructive evaluation of our team and for giving us recommendations that we will follow for the next five years.
Nevertheless I would like to bring precisions in regards to some remarks made by the committee.

1-"no internal collaboration mentioned with groups working on animal models for glioblastoma".

We have an ongoing collaborative project with Team 9 "Canine Genetics" on a comparative functional genomic approach to decipher some of the molecular features of GBM that are conserved between the two species. Unfortunately, we have unsuccessfully applied to two grants. Nevertheless, I am confident with the fact that this collaborative project will be initiated this year, in the context of the Canceropole Grand-Ouest glioma network.

2- Team positioning:

"The team has limited competitivity in this "hot field"
"The team is not integrated into national and international network on these pathologies"

-For the hemochromatosis thematics, I would remind that we work under a national collaborative network supported by two national ANR grants and one national PHRC grant (two of which are coordinated by our team). The scientific production of this network has led to significant publications in the *Am J Hum Genet*, *Blood*, and *Genome Biology,* including authors from the different teams involved in this collaborative network. I would also like to mention that this national network also provide downstream functional approaches linked to the largest hemochromatosis French cohort and also to an unique French hemochromatosis mouse model pedigree.

-For the glioblastoma thematics, I would like to stress that this is a new project initiated less than four years ago. Nevertheless, our team coordinates a national grant "STIC" including 10 different French centres. Moreover, over the last two years, we have been selected for oral presentations in the two international and European meetings of reference in neuro-oncology: one time in the international meeting (WFNO, Japan, 2009) and twice in the European meeting (EANO, Maastricht, 2010). Last year, we were also invited for a plenary lecture in this later meeting (EANO, Maastricht, 2010). Finally, we got the "Takao Hoshino Award" in 2009 at the WFNO meeting (http://wfno2009.umin.ne.jp/hoshino/index.html).

Please also notice that our very recent data published in *Clin Cancer Res* (2011) and *BMC Genomics* (2010; "highly accessed") has led to a collaboration, this year, with the French group leader in glioma research (Inserm U 975) to develop a translational genetic approach at the national level.

We hope that our answer can help mitigate the weaknesses and threats identified for our team by the AERES committee.

Team 11: Cell Division: reverse engineering
Group leader: Jacques PÉCRÉAUX

First, I would like to thank the aeres committee for these encouraging comments and helpful suggestions. Prior to any other answer, I would like to highlight the fact that the propose modeling will use statistical physics and mechanics equation mainly and only in a second time simulations (*in silico*) as an illustration mean mainly. However, collaboration with *in silico* approach expert (F. Nedelec, EMBL, Heidelberg, Germany) is planned.

I agree that the limited number of publications hinder the attractivity of the team and consequently, I prioritize the submission of two manuscripts already written and directly related to my current research interest. Additionally, I aim to submit two other manuscripts related to my last postdoctoral training and more related to image processing by coming fall.

As suggested in the report, I pay a strong attention to the integration in the unit and already organized lab meeting together with team 18. To foster skills sharing, I already share equipment (the microscopy set-up is located on the platform e.g.), and knowledge through teaching in microscopy/image processing course organized in coming spring for example by IFR 140.

Aware of my responsibility in enabling a flow of external funding, I already applied to Brittany "starting team" grant, HFSP Career Development Award, and currently to FP7 / Marie Curie, Career Integration Grant. I was also involved in ARC, semi-heavy equipment grant application in collaboration with other teams of the unit.

Taking advantage of my multidisciplinary approach, during fall 2010, I already initiated collaboration with M. Delattre (ENS Lyon) on evolutive aspect, F. Jülicher and Nenad Pavin (MPI-PKS, Dresden, Germany) on broadening theoretical physics modeling of spindle positioning, F. Nedelec (EMBL, Heidelberg, Germany) on *in silico* modeling of the mitotic spindle, A. Schroder (BioZentrum, Technical University Dresden, Germany) on systems approach of candidate proteins involved in centering, J. Prost and J.-F. Joanny (Curie Institute, Paris) on deeper theoretical physics modeling of the spindle and J.-C. Olivo-Marin (Pasteur Institute, Paris) on image processing of microtubules through a engineer training. These collaborations seems to me to cover the range of my research goals and appear sufficient for the coming year to avoid loosing focus.
Eventually, I also made contacts with neighboring teams D. Chrétien on microtubules régulation (UMR6026 Rennes), R. Le Borgne on using fly SOP (UMR6061 Rennes), C. Kervran on image processing (INRIA Rennes), to enable knowledge exchange locally.

Team 12: Regulation of stress adaptation
Group leader: Carlos BLANCO

Firstly, we take observations regarding our past activities into consideration. We have published about 30 papers in journals appreciated as low impact factor. Nevertheless, it must be considered that in microbiology, the highest impact factors for regular papers are around 4. We published mainly in J. Bacteriol (IF 4.03), Applied Environ Microbiol (IF 4.5) and Environ Microbiol (IF 5.28) that are considered as good journals by the microbiologist community.

We agree that the team is composed only of teachers, few PhD students and post docs. The consequence is that part of our time is dedicated to support and promote training in microbiology. This was described in individual team member's forms. The corresponding master degree (MFA) has just been positively evaluated by AERES.

Considering the scientific evaluation of our project, we feel that expertise was done by experts without deepen knowledge and scope activities in microbiology. The following items detail our comments on the different points that have been noticed by experts.

The first item is relative to ribosome modulating proteins. Structures and ribosome interactions of RaiA, RMF and HPF have been well characterized in *E. coli*. Their important physiological roles were deduced from nutrient starvation experiments only. These proteins are conserved in enterobacteria only; no orthologs were detected in other bacteria genomes. Direct analysis of ribosomal proteins allowed isolation of SaHPF in *S. aureus*. SaHPF has a structure similar to *E. coli* HPF but not the same physiological role.

This questions the importance of ribosome modulating factors in bacterial stress response: i) Are their role conserved? ii) What are their places in regulatory network of stress response? iii) Since their roles seem crucial, it is important to identify the corresponding proteins in other bacterial phyla.

The two first questions may easily be solved in enterobacteria using different strains to test the robustness of the hypothesis. We choose *Dickeya dadantii*, an enterobacteria easy to manipulate and with dense data on gene regulation, stress and pathogenicity. Our aim is to determine the physiological role of ribosome modulating factors. Our preliminary data have shown that synthesis of ribosome modulating factors is induced during growth at high osmolarity; furthermore inactivation of the corresponding genes reduced osmo-resistance. These preliminary results suggest that these proteins are at least involved in ribosome preservation and also in molecular mechanism of stress adaptation. Thus, our aim is not to reproduce the experiments done in *E. coli*. We suggest that these proteins have the ability to modulate ribosome activity and could potentially induce ribosome selectivity to favor translation of stress genes.

It is important to analyse the exact role of these proteins before concluding like J. Monod (1965, Nobel price dissertation) that "what is true for *E. coli* is true for the elephant". Moreover, understanding of the role of a protein in cell needs also to consider its regulation and its place in global regulatory circuits. This was never done for these proteins in *E. coli*.

General schemes have been elaborated from data on *E. coli*, however they may not be applied *sensus-stricto* to other bacteria; including phylogenetic related ones. To validate the existence of similar proteins in other bacteria, we choose organisms that are not related to *E. coli* but that would never be considered as exotic.

Sinorhizobium meliloti is of crucial importance in earth for atmospheric nitrogen fixation. It is a plant symbiont that allows to analyse conditions never encountered by *E. coli* like intracellular life

in eukaryotic cells; a common experience for many human pathogenic bacteria. *Campylobacter jejuni* is one of the most important foodborne pathogen in the world. It faces many conditions in food processes; never encountered by *E. coli* lab cells. Regarding ribosome modulation factors, nothing is known in these bacteria.

Fortunately, experts understood importance of Toxin-antitoxin systems in stress adaptation. This part is studied in *S. meliloti* because the corresponding genes are not present in *E. coli*. While this TA system is related to RelE, it has a different role. Thus, knowledge of structures in *E. coli* is not enough to explain cellular regulatory circuits. Structurally related proteins could have different roles in different organisms. This illustrates the potentiality of studies in "exotic" strains. In conclusion, we believe that expertise was done by experts without deepen knowledge and expertise in microbiology.

In conclusion we agree that our team is not well located in this laboratory. We believe that the dispersion of team members will lead to the loss of microbiology expertise and will be detrimental for microbiology master at the University of Rennes I. Thus, we wish to reach another structure having microbiology as a central preoccupation.

Team 13: Cell polarity, membrane trafficking and signaling
Group Leader: Roland LE BORGNE

We would like to thank the members of the committee for their careful evaluation of our work and projects and for their thoughtful comments. We are gratified that the committee found that 'the research is really original and the projects are clearly cutting edge'. While the project was judged 'exciting and ambitious", we are very conscious that the feasibility of the project relies on hiring post-doctoral researchers. Thanks to the recent publications of the team and the participation of meetings (specific adds will be made at the EMBO workshop on Septins, The american Flymeeting, The cell cycle cancer and development meeting…), we are expecting to become more visible and attractive for international post-docs.

Team 14: Sp@tio-temporal regulation of transcription in eukaryotes
Group leader: Gilles SALBERT

We agree with most comments and recommendations of the evaluation committee but would like to reaffirm that our productivity relies on the joint competences of all the members of the group rather than of a single person.

Team 15: Signalling in mouse oocytes and early embryos
Group leader: Guillaume HALET

The team **Signalling in mouse oocytes and early embryos** wishes to thank the AERES committee of experts for a constructive discussion, positive comments and suggestions, and an overall very encouraging review. We are aware that the team needs to grow further in order for the scientific

objectives to be reached. Our main goal is now to secure larger grants and to attract more experienced scientists to join the group.

Team 16: Structure and molecular interactions
Group leader: Jean-François HUBERT

Coherence and complementarity of the projects:
- Project A concerning dystrophin has been presented as the main project and will be pursued.
- The evaluators mentioned than project B and C have to be better explained. These projects had not been fully developed in the written presentation, according to the recommendation made to the team leaders to present a main project. Anyway, the general aim of our research is to bring understanding of protein/membrane interactions. Project A aims to bring molecular information about dystrophin function in muscle cells, allowing to understand the link between dystrophin mutation and patient phenotype. Some answers will be directly helped by project B development, which aims to analyse peptide-liposomes at the molecular level. The work on peptides generator or sensor of curvatures, will provide molecular data to better understand their function. We started this work under the request international leaders in the field (B. Antony and G. Drin) and will lead to fundamental findings. We will then be able to directly apply the general concepts and methodology deriving from the above studies for the analysis of the parts of dystrophin bearing such membrane binding amino acid sequences.
- Project C is currently in progress for a thesis. In the field of protein-lipid interaction analysis, cytochrome c represents a highly valuable model of peripheral membrane protein. Especially, the structural modifications induced by interactions with cardiolipin are involved in the initiation of apoptosis. From this model, general concepts and specific methods can be developed. It has to be mentioned that the team has a strong background expertise in paramagnetic proteins analysis; this guaranties reaching objectives.

Therefore our projects are very complementary.
Lipid/protein interactions analysis constitutes our strong federative scientific goal.

Molecular modelling expertise:
The presence of young researchers has been evaluated as an asset of the team. I strongly agree with that and I want to highlight that among them, a specialist in molecular modelling and dynamics has been recently recruited by the group. O. Delalande comes from a worldly recognised theoretician team. Nowadays, modern structural biology absolutely requires such expertise and first projects implying modelling together with experimental approaches are already moving on in the group (two papers submitted in March 2011). The growing potency of powerful molecular modelling approaches, in addition to the existing expertises in the team therefore strongly reinforces the group and allows ambitious projects. Modelling of larger and larger protein-membrane systems will be carried out until 2012.

International audience:
A network of national and international collaborations about dystrophin and muscular dystrophies with structural biologists, physicians as well as geneticists and clinicians already exists (three papers submitted in March 2011) and will be reinforced. Muscular dystrophy clinicians from an American hospital recently contacted us as experts in the field of structure of dystrophin with the aim of understanding at a molecular level some particular patient phenotypes.
We welcomed two post-docs from Argentina (4 months) and Brasil (one year) in the past two years. One of our PhD students is from Liban, another from Algeria; we are expecting one from Tunisia.

Internal collaborations:
The evaluators recommend developing internal collaborations in the future lab. In the past 3 years, we published 4 papers in collaboration with members of the future lab (S Hardy, G Salbert). Our aim is of course to maintain and establish all collaborative links that will reinforce our publication potency....

Scientific animation and management:
- Weekly internal results presentation or lecture club will be running.
- Even if mentioned as "original" by the evaluators, I think that managing a team can be done with a democratic organisation.

Team 17: Translation and folding
Group leader: Reynald GILLET

We thank the committee for insightful comments on our project. Please find below the specific answers to the remarks and an addendum to the missing points:

1) Appreciation of the project

With regard to the main concern of the committee on work package 3 we decided to modify it. The 3D analysis of polysome arrangements *in situ* will be studied as part of work package 2 (structural aspects of the ribosome by cryo-EM) while the folding of protein domains as they emerge from the ribosomal exit tunnel will be delayed for at least two years and evaluated again after setting up the cell tomography methods in the laboratory.

2) Team organization, management and animation

I insist here on the fact that the different work packages are part of a unique project in which all the **permanent researchers** will step in:

Reynald GILLET (PU UR1) as group leader and ribosomologist (WP1, 2, 4, 5) (WP3 has been removed)

Christian DELAMARCHE (PU UR1) as a bioinformatician (WP4, 5)
Cyrille GARNIER (MCU UR1) as a biochemist (WP 4, 5)
Emmanuel GIUDICE (MCU UR1) for image analysis and computational simulations (WP1, 2, 4)
Jean-Paul ROLLAND (IR UR1) as a microscopist (WP1, 2, 4)
Daniel THOMAS (DR1 CNRS) as a structural biologist and microscopist (WP1, 2, 4)

We all work into the same place. Internal seminars are held every Monday and alternate between scientific seminars and meetings on the every day functioning of the team.

3) Regarding the scientific production, seminars and conferences

Productivity of the team in number of papers is 19 and not 16.
Moreover, since the visit of the committee:

Two new articles have been accepted and one international meeting invitation as a speaker has been proposed to R Gillet to a J Monod conference on "The translating ribosome: towards mature proteins"

⇨ B Felden, **R Gillet**. SmpB as the handyman of tmRNA during *trans*-translation. RNA Biology 2011, in press

⇨ Tarabout C, Roux S, Gobeaux F, Fay N, Pouget E, Meriadec C, Ligeti M, **Thomas D**, Ijsselstijn M, Besselievre F, Buisson Da, Verbavatz Jm, Petitjean M, Valéry C, Perrin L, Rousseau B, Franck Artzner F, Paternostre M, Cintrat Jc. Chemical control of peptide nanotube diameter: a strategy based on the structure of the nanotube. Proc Natl Acad Sci U S A 2011, in press

4) Regarding the coordination/participation to the grants

Ongoing grants (one new*)
ANR JCJC 2009-2013 R Gillet (250 k€) COORDINATOR
ANR MIE R Gillet 2010-2014 (40 k€) PARTICIPANT
ANR JCJC 2011-2015 C Garnier (200 k€) COORDINATOR
Ligue contre le cancer C Garnier (35k€/2008) COORDINATOR
Ligue contre le cancer C Garnier (35k€/2011) COORDINATOR
Ligue contre le Cancer R Gillet (2 years post-doc funding) COORDINATOR*
Sanofi AVENTIS (private contract for expertises) D Thomas COORDINATOR
Britanny Region: PhD grant L Moullintraffort (2010)
French Gvt: PhD grant F Weis (2008)
CNRS; University (~10k€/year)

Ongoing applications:
European Research Council Starting Grant (1.5M€) R Gillet COORDINATOR
Institut Universitaire de France 2011 R Gillet COORDINATOR
EMBO Young Investigator Program 2011 R Gillet COORDINATOR
Britanny region: PhD grant C Delamarche COORDINATOR
CRITT Santé C Delamarche COORDINATOR
Labex "Biomarkers" C Delamarche PARTICIPANT

6) Involvement in the local environment

Reynald Gillet has been elected as the coordinator of the scientific department "Biology and Expression of the Genomes" of the future Unit

Daniel Thomas heads the Electron microscopy platform from the Mric (Microscopy Rennes Imaging Centre)

Jean-Paul Rolland is in charge of the technical monitoring of the Electron Microscopes from the platform

Annie Cavalier is in charge of the cryo-methods into the platform.

7) Neither strengths nor weaknesses were emphasized by the committee for our team. A word here would have been welcome.

Team 18: Membrane traffic and polarity in *C. Elegans*
Group leader: Grégoire MICHAUX

We are currently addressing the most pressant recommandation of the commitee with one paper submitted and the preparation of two more articles. We wish to precise that both post-docs were from abroad (UK and Lebanon) and that funds have been secured for 2011. Further grant applications will be submitted during the year and we are actively seeking new post-docs.

The commitee was not entirely convinced by the EM project. However we believe that it is a key component of our research project; it was absolutely essential for the submitted article and will certainly be critical again in the future. Knowing precisely where polarity determinants and junction proteins are localised is essential. For instance we found that E-cadherin can be basolateraly localised in epidermal cells in AP-1 depleted embryos. However the confocal resolution limit prevents a detailed analysis of this phenotype and only imuno-EM can answer this kind of questions. Further developments including correlative light microscopy and EM will be established in collaboration with the group of Roland Le Borgne (team 13)

Team 19: Tubulin and interacting proteins
Group leader: Denis CHRETIEN

We appreciated the comments of the jury. Yet, we would like to point out that, in collaboration with theoretical physicists, we have developed a model that explains how the longitudinally outwardly curved (not flat) tubulin sheets close into microtubules as a consequence of an increase in sheet width and lateral inward curvature (see Jànosi et al., Eur Biophys J, 1998; Chrétien et al.; Cell Struct Funct, 1999; Hunyadi et al., Biol Cell, 2007; see also Mahadevan and Mitchison "Powerfull curves", Nature, 2005).

We fully agree that the size of our team is sub-optimal. Hopefully, we will be reinforced this year with a lecturer position. We will also try to attract new researchers, either at the post-doctoral and/or permanent scientist levels. The structure of the team, focusing on a single thematic, will allow the principal investigator to invest more time in research, and hopefully sign more papers with senior authorship.

Grouping the 3 teams involved in cytoskeleton research is certainly a wise advice. Yet, it is also essential that our team remains in close vicinity to the cryo-electron microscope, which is our daily research instrument. Along this line, we acknowledge the fact that we need new equipment to acquire data at higher resolution, this is essential to develop further our projects and remain competitive at the international level.