SABNP - Structure et activité des biomolécules normales et pathologiques

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Structure-Activity of Normal and Pathological Biomolecules

SABNP

Under the supervision of the following institutions and research bodies:

Université d'Evry-Val-d'Essonne - UEVE

Institut National de la Santé et de la Recherche Médicale - INSERM

December 2013

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

Department for the evaluation of research units

On behalf of AERES, pursuant to the Decree of 3 november 2006[1],

- Mr. Didier HOUSSIN, president
- Mr. Pierre GLAUDES, head of the evaluation of research units department

On behalf of the expert committee,

- Mr. Franck PEREZ, chair of the committee

[1] The AERES President "signs [...], the evaluation reports, [...] countersigned for each department by the director concerned" (Article 9, paragraph 3 of the Decree n ° 2006-1334 of 3 November 2006, as amended).

Evaluation report

This report is the result of the evaluation by the expert committee, the composition of which is specified below. The assessments contained herein are the expression of independent and collegial deliberation of the committee.

Unit name:	Structure-Activity of Normal and Pathological Biomolecules
Unit acronym:	SABNP
Label requested:	UMR INSERM
Present no.:	U 829
Name of Director (2013-2014):	Mr Patrick CURMI
Name of Project Leader (2015-2019):	Mr Patrick CURMI

Expert committee members

Chair:

Mr Franck PEREZ, Institut Curie, Paris

Experts:

Mr Vincent CROQUETTE, École Normale Supérieure de Paris

Mr Sébastien FRIBOURG (representative of CSS INSERM)

Ms Agnès GIRARD-EGROT, Université Lyon 1 (representative of CNU)

Mr Andreas MERDES, Université de Toulouse

Scientific delegate representing the AERES:

Mr Pierre VIERLING

Representatives of the unit's supervising institutions and bodies:

Ms Florence GONNET (Doctoral School "des Génomes aux Organismes" ED n° 423)

Mr Philippe HOUDY, Université Evry-Val-d'Essonne

Ms Stéphanie POMMIER, INSERM

1 • Introduction

History and geographical location of the unit

The UMR INSERM/UEVE U 829 "Structure-Activity of Normal and Pathological Biomolecules" (SABNP) is a 780 m^2 laboratory located at Evry Val d'Essonne University's (UEVE) campus in Bâtiment Maupertuis. The laboratory is a single team organized around four main themes and around different facilities dedicated to molecular biology, recombinant protein production and purification, NMR solution spectroscopy, single molecule atomic force microscopy, biochemistry, eukaryote cell culture, optic imaging, neuron biology, and finally diamond particle's fabrication and modification.

The laboratory, formerly "Structure & Reconnaissance des Biomolécules", was created in 2007 as a "Single-Team Unit" under Mr Patrick CURMI's initiative, extending the NMR structural expertise of the unit to *in vitro* and *in cellulo* functional studies. Projects then evolved towards pluri-disciplinary approaches going from the atomic structure of biomolecules to their function in living cells.

Quite a lot of changes occurred in the unit during the period under evaluation. In September 2008, an assistant-professor joined the laboratory with the support of an ATIGE grant together with a INSERM CR, to study centriole. Both left the laboratory. A professor for research on molecular modelling and dynamics of biomolecules was recruited and left the laboratory on January 2012. An assistant-professor obtained a professor position in NMR spectroscopy at Université Paris 13. Finally, a CNRS CR working on diamond nanoparticles retired in 2012. Several people, including I) an INSERM-UEVE “Chaire d’excellence” to develop a group dedicated to neurobiology and cytoskeleton, II) a INSERM CR to develop molecular modelling and simulation projects (bioinformatics of GPCR and cytoskeleton), and III) two technical staff to support the unit for laboratory maintenance and technical aspects of molecular and cell biology and to fulfil molecular biology, protein expression and purification and modern cell biology arrived and are still part of the unit.

Management team

The unit is headed by Mr Patrick CURMI, research director at INSERM. He is responsible for various aspects of the life and future of the unit (strategy, collaboration, recruitment). He is also taking in charge a large part of the grant and fellowship applications, and of the needed representation of the unit in national and international committees and meetings. He is also discussing the scientific strategy of the unit on a regular basis, without particular timing or frequency, with the theme leaders.

AERES nomenclature

SVE1_LS1 Biologie moléculaire et structurale, biochimie

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	5	4
N2: Permanent researchers from Institutions and similar positions	2	2
N3: Other permanent staff (without research duties)	7	7
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	1	1
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral students, visitors, etc.)	2	1
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	**18**	**17**

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	6	
Theses defended	6	
Postdoctoral fellow having spent at least 12 months in the unit*	7	
Number of Research Supervisor Qualifications (HDR) taken	3	
Qualified research supervisors (with an HDR) or similar positions	6	6

2 • Assessment of the unit

Strengths and opportunities related to the context

One of the strength of the unit is its multi-disciplinary aspect associated to the clear incentive to converge towards a common question, which is and will be the dynamics and function of the cytoskeleton and particularly of microtubules. Aiming at these goals, various projects have been developed in this unit over the years. This diversity is both a strength and a challenge. One federative theme proposed by the unit is the understanding of the relationship existing between the atomic and molecular behaviour of biomolecules that participate in critical cell systems and functions. A federative aspect is to consider each project in the context of human pathologies. Above all, there is clearly an effort done by the unit to converge, at least partly, towards the study of the cytoskeleton and in particular, microtubule dynamics and function. For example, atomic models are achieved to design *in silico* drug candidates that

would target tubulin. The role of polyamines in the control of microtubule and +TIPs (+end Tracking Proteins) dynamics is also studied as well as the connection between stress granules and microtubules. This is a very important point since a lot of subjects are being currently studied by the unit considering the number of people and theme leaders.

In addition to its expertise on microtubules and tubulin, the unit is also recognized for its leadership in original fields like the biology of stress granules, the impact of polyamines on cell physiology and cell communication. The presence of the NMR, structural biology and bioinformatics platforms is important to preserve the unit's identity. The development of diamond-based nanoparticles is also recognized as an original aspect of the unit.

A very positive aspect is also the arrival of novel members. This is bringing new ideas, new expertise and creates novel links.

The laboratory is an important local member both for science and teaching animation. This has been highlighted by the representative of INSERM, UEVE and GENOPOLE. The platform dedicated to structural biology is actually recognized by GENEPOLE. INSERM, UEVE and GENOPOLE are actively supporting the unit by the creation of CR and ITA positions, Chaire d'excellence, ATIGE and grants.

The unit has also created and belongs to international networks.

The unit is also looking to apply its research and technologies. 'Biotech' development is an active part of the laboratory and it is supported locally. Close contacts are kept with the two spin-offs created: I) one to be launched beginning of 2014 (supported by OSEO) dedicated to biotechnological development of fluorescent diamond nanoparticles for biological applications, and II) one that was launched at the end of 2013 dedicated to *in silico* drug design to develop drug candidates targeting molecules of interest in the biomedical field.

Through one of these spin-offs, the unit will be implicated in a common project "DiamSciTech" (consortium of 17 team partners) that would be a part of the future Material Institute harboured by the Université Paris-Saclay in the next 3 years, and it will benefit from the clinical expertise MDs from novel Evry hospital for a medical perspective.

Weaknesses and threats related to the context

Sharing of R&D between the laboratory and both spin-off should be looked at to avoid duplicating the effort. This is particularly true for the diamond nanoparticle project. There is indeed a risk linked to the retirement of the former theme responsible, who has been the expert and one of the patent co-authors on diamond nanoparticles. It is unclear how much of this activity should be kept inside the unit and how much should be transferred to the spin-off.

Despite the clear convergence effort, the diversity of the themes may be a problem owing to the necessary critical mass necessary to achieve high-level work.

There is a clear need for people to take care of the NMR facility. However, the unit could not yet attract a good candidate. This is a strong emergency.

There is a relative scientific isolation at the level of the university. This is a problem for scientific development and young researcher training.

The main threat is probably linked to the organization of the unit. It depends too strongly on the investment and vision of its director. Although it is expected that the director of the unit contributes with his vision and energy, the unit is organized in four mostly independent axes. Each of the theme leaders should play a stronger role in the life of the unit. It is extremely important because, at the end of the next 5 years, the current director will step-out and it is worrisome that no leadership would have appeared to take over.

Recommendations

The unit may benefit from clarifying its relationship with their founded start-up for the next 5 years. This is particularly true for the nanoparticle project, which is in a transitory phase. If everything goes right, the critical mass may be found in the start-up rather than in the academic project. Owing to the very limited human resources, the unit may need to make clear choices.

A call for new projects should be organized to attract a small group around the NMR facility. Since this priority is recognized by the university and by GENOPOLE, it may be possible to create an attractive package. Without this, it is unlikely that the unit will quickly find the key person to take over the NMR responsibility.

The theme leaders should take their share in animating and supporting the unit. This is simply the expected behaviour of people who want to play an active role. In parallel, the unit director should try to delegate more both his role in representing and directing the unit.

As quite a few novel aspects of research are being developed (like real-time cell imaging), the unit should seek collaboration with expert laboratories to import the necessary expertise. The recent arrival of the INSERM-UEVE "Chaire d'excellence" will be positive to some extend to foster these aspects.

Because of the relative isolation of the university, it is important that the post-doctoral fellows and PhD students participate more to French and international meetings, and organize more trans-unit contacts at the university level, for example in the form of regular joint meetings and journal clubs.

3 • Detailed assessments

Assessment of scientific quality and outputs

This is a well-recognized unit for its work I) on cytoskeleton and microtubule dynamics and function, II) on fluorescent diamond nanoparticles, and III) in original fields like the biology of stress granules, the impact of polyamines on cell physiology and cell communication.

Its productivity with 36 articles, 4 reviews or book chapters, and 5 patents published during the evaluation period is relatively good quantitatively (a mean of 1.5 publications/year/FTE) and qualitatively (mean impact factor of 4.5). Among the most important publications signed as first or corresponding author by a member of the unit, one can mention 1 ACS Nano (IF = 12), 2 Small (IF=7.82), 1 FASEB J (IF=5.7), 1 Plos Comput Biol (IF=4.87), 1 Mol Biol Cell (IF= 4.8), 1 Biochem J (IF=4.65), and 5 J Biol Chem (IF=4.65).

Assessment of the unit's academic reputation and appeal

The academic reputation of the unit is good. The unit has a correct participation (35) to national and international meeting (12 invitations to international conferences), very biased toward the unit director.

The unit has established collaborations with expert laboratories. Several solid international contacts have been established to coordinate both research and educational activities. The unit participates in international networks ("réseau GDRI FMCEHP" and "réseau Franco-Sibérien"APILIFE" gathering 34 and 11 laboratories, respectively), some of which it has been initiated from scratch. A positive sign of the good reputation of the unit is its successful fund raising of one EU grant, two OSEO and two ANR grants (one as coordinator). It attracted also 7 post-docs and established long-term links with Algerian and Egyptian student networks.

Assessment of the unit's interaction with the social, economic and cultural environment

There is a very good involvement of the unit in the social and cultural environment. The unit director is also the vice-president of the UEVE scientific council. The unit participated to general public education (e.g. Fête de la Science, Université du Temps Libre).

The unit director has a clear intellectual property policy by ensuring evaluation of potential patenting prior to the initiation of projects. The unit created 2 start-up companies and grabbed large industrial contracts (worth 350 k€ in total). Five patents were filed during the evaluation period, which shows a strong commitment for the unit to apply their R&D.

Assessment of the unit's organisation and life

The organization is good and the atmosphere is very positive between theme leaders. The « lab council » is taking place twice a year in the presence of every member of the unit. Budget issues, recruitment policy and general organization of the laboratory are discussed in details and important decisions are taken there through a voting process. The unit appears well managed with weekly scientific meetings. Risks and hazards are taken into account.

However, as stated above, the unit's organisation and life depends strongly on its director. The other theme leaders should be more active and the unit director should delegate more (in particular owing to his additional, university level responsibilities).

Although two-yearly unit meetings are organized, more scientific life should exist (joined meeting, journal club).

Assessment of the unit's involvement in training through research

The involvement of the unit in training through research is good. A strong connection to university teaching in the frame of the Doctoral Schools "Sciences et ingéniérie" (ED n°511) and "des Génomes aux Organismes" (ED n°423) is to be noted. The unit trained more than 60 French and foreign students from high school to PhD and post-doc level, including technicians, engineers, bachelor's degree and master students. During the 2008-13 period, 6 students defended their PhD and 6 more started their training between 2010 and 2013.

These students are/were mainly affiliated to the Doctoral School "des Génomes aux Organismes" ED n°423. In addition, 7 post-doc fellows, 3 ATER, 41 trainees and pupils from France and 7 teacher-researchers from Algeria and Egypt for practical training in molecular biology have joined the unit. A lot of the trainees were officially under the direction of the unit director.

The PhD students are probably a bit too passive and should be more pro-active. Some seem to need more direction and the problem of the 4th year support should be clarified and discussed more clearly. Similarly, the PhD students and post-docs should clarify their professional project with their respective project leader.

Assessment of the strategy and the five-year plan

The strategy and 5-year plan has been evaluated as good. There is a clear intention that aims at reinforcing the convergence between the different projects and themes of the unit. The installation of a novel theme is an advantage for the future of the unit and many promising subjects are being pushed ahead like *in silico* docking to identify potent molecules, biology of stress granules or use and function of polyamines. Of course, classical projects of the unit related to tubulin and microtubule dynamics are still very promising.

The unit may however take even more in consideration the risk link to the lack of critical mass and expertise around the NMR. A call for project should be organized.

The relative isolation of the unit should be worked on in the next 5-year period.

The multiplicity of research projects may also be a problem considering the relative small size of the unit. A stronger focus on studies at the cellular level may be beneficial.

Above all, a stronger participation from the other theme leaders in directing and supporting the unit will be essential both to assist the unit director in his duties and to prepare the future.

4 ● Theme-by-theme analysis

Theme 1: Cytoskeleton dynamics

Manager's name: Mr Patrick CURMI

Workforce

Theme workforce in Full Time Equivalents	As at 30/06/2013	As at 01/01/2015
FTE for permanent professors	0.7	0.7
FTE for permanent EPST or EPIC researchers	0.5	0.5
FTE of other permanent staff without research duties (IR, IE, PRAG, etc.)	2	2
FTE for other professors (PREM, ECC, etc.)		
FTE for postdoctoral fellow having spent at least 12 months in the unit	2	
FTE for other EPST or EPIC researchers (DREM, etc.) excluding postdoctoral students		
FTE for other contractual staff without research duties		
FTE for doctoral students	4	
TOTAL	**9.2**	**3.2**

• Detailed assessments

Assessment of scientific quality and outputs

On this research theme, the unit has published a high number of articles (18) in peer-reviewed journals since 2008. These articles are generally published in international journals with a well-established reputation (e.g. J Biol Chem, Biophys J, Biochemistry, and others). The published work represents solid science at a very high technical level and can be considered as very good. Many of these articles are descriptive, providing an initial phenomenological characterization. It would be desirable that future research would be conducted to dissect more in depth cellular mechanisms and to investigate potential physiological relevance, such as the cellular role of STOP-dependent microtubule regulation in neurons, or the cellular mechanisms by which spastin causes axonal swellings.

Assessment of the theme's academic reputation and appeal

The unit has presented work on this research theme at numerous meetings. Most of these presentations were in the form of posters, in addition to plenary presentations as invited speakers in specialized conferences. The unit is very well networked and has initiated and maintained numerous international collaborations with partners in Italy, Ukraine, India, Algeria and France. Thanks to this high networking activity, the unit's appeal on this theme can be considered as excellent.

Assessment of the strategy and the five-year plan

The experts committee felt that the future project is good, but that there are weaknesses in the five-year strategy and in the experimental planning: there are certainly research activities that look very promising and that are expected to yield interesting results in the future (e.g. colchicin-carbendazim hybrid molecule, STOP, spastin). However, the experimental plans are relatively numerous and diverse, and there is not always a recognizable synergy between the subjects (for example, a recent project on actin aggregation may be diverting from the current focus on microtubules). It was also felt that the aims and potential milestones of future activities are not well defined. Moreover, the experimental planning lacks details, and the involvement of the different personnel of the research unit in the individual sub-projects is not well explained (*i.e.* who will do what?).

Conclusion

- **Overall opinion of the theme:**

The research in this theme aims to characterize the interactions between tubulin and several microtubule-binding proteins, such as CPAP and MAP6/STOP. Unexpected effects on microtubule dynamics by polyamines, by the gap junction protein connexin 43, and by the RNA-binding protein YB-1 have also been described. Moreover, work on microtubule drugs has led to two novel observations consisting into (I) the removal of axonal swellings by microtubule drugs, in neurons from spastin-knockout mice that serve as a model for 'Hereditary Spastic Paraplegia', and (II) an interesting synergy between the colchicine and benomyl microtubule drugs on microtubule stability and on the cell cycle. Each of these basic findings offers perspectives for future research, to explore in more depth structural aspects of tubulin binding, and cellular mechanisms affected by altered microtubule dynamics in diseases.

- **Strengths and opportunities:**

In the future, the group plans to continue several promising projects for which a basis was built over the past few years:

- I) The characterization of the CPAP-tubulin interaction, by studying the effects of point mutagenesis on the formation of the tubulin-CPAP complex, and on tubulin sequestration: this may be of interest both for understanding basic principles of tubulin polymerization, and for designing novel strategies for microtubule depolymerisation. The team may have a competitive advantage on this project, since currently no other group seems to analyse the CPAP-tubulin interaction at an atomic/structural level. However, if the goal was to develop a novel pharmacological inhibitor of microtubules, it should be kept in mind that a patent already protects any commercial use of CPAP as a destabilizer of microtubules.

- II) The work on MAP6/STOP may be given interesting new directions, by testing the effect of this protein on microtubules in neuronal cells (in-cell-NMR spectroscopy), and by evaluating the influence of intersectin on STOP/microtubule interaction and regulation of microtubule dynamics.

- III) A hybrid molecule of the microtubule inhibitors colchicin and the benomyl metabolite carbendazim will be synthesized and tested. Since the team has previously shown a synergy between these two types of molecules on microtubule stability, a hybrid molecule may potentially show improved properties as a microtubule inhibitor.

- IV) Promising earlier work on spastin and axonal swellings in model mice for Hereditary Spastic Paraplegia will be continued.

- **Weaknesses and threats:**

The aims of the sub-projects are relatively numerous and diverse. For a small research unit, there may be a risk of diversifying too much, and failing to investigating problems in depth. To mention an example, a new topic on actin-aggregating compounds has recently been explored, in addition to the team's ongoing research on microtubules.

Moreover, parts of the research proposal are not very profoundly developed: the future research plans on microtubule drugs in SPG4-knockout mice are only vaguely described. It remains unclear what will be done, and how the future research activities will extend already published knowledge.

- **Recommendations:**

The group has been using mainly biophysical and biochemical approaches, as well as computer-based simulation, to map protein-protein interactions and to characterize the binding properties of microtubule drugs. While this is probably due to the fact that this research theme has only recently been established around a nucleus of specialists in the field of biological structures and NMR, it may have raised a potential problem: over the last few years, much of the work published remained at the level of initial biophysical characterization of protein-protein interactions. As already mentioned in the previous AERES report (2009), it may be beneficial if the team focused on fewer topics, and explored them more in depth, for example by intensifying research activities on cellular mechanisms. Perhaps this can be achieved in collaborations outside this institute, or by recruiting future personnel with the appropriate scientific background.

Theme 2: Cellular and molecular biophysics

Manager's name: Mr David PASTRE

Workforce

Theme workforce in Full Time Equivalents	As at 30/06/2013	As at 01/01/2015
FTE for permanent professors	1	1
FTE for permanent EPST or EPIC researchers		
FTE of other permanent staff without research duties (IR, IE, PRAG, etc.)	1	1
FTE for other professors (PREM, ECC, etc.)		
FTE for postdoctoral students having spent at least 12 months in the unit	1	
FTE for other EPST or EPIC researchers (DREM, etc.) excluding postdoctoral students		
FTE for other contractual staff without research duties		
FTE for doctoral students	1	
TOTAL	**4**	**2**

• Detailed assessments

Assessment of scientific quality and outputs

Research in this theme focuses on the links between cell proliferation, the translational response to stress *via* stress granules, microtubule dynamics, the polyamine metabolism, and cell/cell gap junction communication. The originality of this theme is to bring together cellular approaches and molecular biophysics. By using AFM imaging and fluorescence videomicroscopy, global research of the theme highlights novel views on the dynamics of stress granules linked to cytoskeletal dynamics. The most important results concern polyamines. They favour microtubule assembly and are able to exchange *via* facilitated diffusion from cell to cell through gap junction. They actually promote formation of gap junctions between proliferating epithelial cells due to the extension of dynamic microtubule plus ends at the cell periphery. Through this exchange mechanism, polyamines act as signal transducer to stimulate the growth of adjacent cells and organize their response to stress by allowing the formation of stress granules. By this way, polyamines promote cell proliferation and mRNA stress granule assembly. Exchanges through gap junction are also involved in the adaptation of epithelial cells to chronic osmotic stress conditions.

During the past five years, the unit has published 17 articles in international peer reviewed journals of well-established reputation (e.g. Langmuir, J. Biol. Chem., Small) and one book chapter. The published work can be considered as very good with nine articles published in journals with IF > 4. The group is clearly a leader in protein/DNA interaction of single molecule by AFM imaging as attested by his international patent deposited in 2010.

Assessment of the theme's academic reputation and appeal

On this theme, the unit has a good participation in national and international meetings and it has been invited to four conferences. It is involved in the training of PhD and graduate students and has also established several national collaborations, and an international collaboration with Russia, on the RNA-binding protein YB-1.

Assessment of the theme's interaction with the social, economic and cultural environment

The unit has filed a patent for DNA chips based on mica adsorption and AFM detection. However, nothing concerning a technology transfer has been reported.

Assessment of the strategy and the five-year plan

In future studies, the unit plans to investigate *in vitro* the mechanisms of RNA granule assembly by AFM using purified RNA-binding proteins. By using recombinant forms of these proteins, they will investigate the role of protein factors (low complexity domains), electrostatics (polyamines) and macromolecular crowding (PEG) on mRNA granule assembly. The objective will be to approach the conditions of stress granule assembly that may exist *in vivo* in order to confront *in vitro* data with observations in cells. The study of microtubules/RNA granules may have potential applications for the translocation of neuronal RNA granules required for localized protein synthesis, in synapses for instance, and may have an impact for the comprehension of Alzheimer and other neurodegenerative diseases. Another topic to be pursued will be the investigation of links between the collective responses to stress, the regulation of the translation machinery through the exchange of small molecules (betaïne, polyamine, taurine…) and the rate of cell survival.

As a new perspective, the unit plans to analyse the interplay between tau (protein considered to stabilize microtubules and trigger the bundle formation in neurons), macromolecular crowding, and polyamines on microtubule bundling. I*n vitro* results will be confronted with those obtained in epithelial cells and neurons transfected with EB1 and/or recombinant tau, in order to observe microtubule dynamics and the impact of tau.

Finally, the group will take advantage of its recent discovery in order to explore the transition between quiescence and proliferation by analysing the changes in the microtubule orientation, microtubule dynamics and gap junction formation according the polyamine level in the cell.

Conclusion

- **Overall opinion of the theme:**

This work provides a good basis for promising future studies. It is expected to impact on research of cancer and neurodegenerative diseases.

AFM imaging skills of the unit allow them to pursue parallel studies on various aspects of nucleic-protein interaction. Another aspect of the project of this theme is to develop novel technology to rapidly detect minute amounts of complementary sequences from DNA adsorbed to mica, or to detect accessibility of site-specific proteins.

- **Strengths and opportunities:**

The unit has acquired a solid expertise in the analysis of microtubule dynamics by AFM or fluorescence studies as attested by the quality of the articles published in the past contract. This work is in strong connection with theme 1, in particular the studies on the effects of polyamines or RNA-binding protein YB-1 on microtubule dynamics, which procures a strong synergy.

- **Weaknesses and threats:**

The correlation between biophysical results and those obtained with culture cells is not fully explained. Nothing concerning the development of novel DNA-chips is proposed whereas it seems to be one of the objectives of the unit clearly announced in original and innovative aspects of research at U 829. The experts committee felt that the stress granule project remains too biophysical.

- **Recommendations:**

The program proposed is essentially based on biophysical approaches. Even though the results will be sound, the unit must pay attention to a strategy for transposing the results in a more relevant physiological/biological context. Notably, the planned research on gap junctions is really exciting, but the possibility to inhibit formation of gap junctions as anticancer strategy remains contradictory with the invasiveness of non-adherent cells in cancer. The unit has to be careful on the potential application of such possibility. The experts committee recommended to dissect more in depth the stress granule theme.

Theme 3: Structural Bioinformatics

Manager's name: Mr Charbel MAROUN

Workforce

Theme workforce in Full Time Equivalents	As at 30/06/2013	As at 01/01/2015
FTE for permanent professors	0.2	0.2
FTE for permanent EPST or EPIC researchers	1.25	1.25
FTE of other permanent staff without research duties (IR, IE, PRAG, etc.)	1.3	1.3
FTE for other professors (PREM, ECC, etc.)		
FTE for postdoctoral students having spent at least 12 months in the unit		
FTE for other EPST or EPIC researchers (DREM, etc.) excluding postdoctoral students		
FTE for other contractual staff without research duties		
FTE for doctoral students		
TOTAL	**2.75**	**2.75**

• Detailed assessments

Assessment of scientific quality and outputs

This theme consists into three lines of research, two of which are international collaborations with Mexico (Instituto Politechnico Nacional) on the 3D conformation and dynamics of certain GPCR, and with Qatar (Shafallah Medical Genetic Center, Doha) on the molecular mechanism and impact of pathogenic mutations (claudin-10) on some genetic disorders. The third line is directly connected to themes 1 and 2 and consists into I) the elaboration of a microtubule protofilament model to enlighten microtubule dynamics, II) the study of protein-nucleic acid recognition using a system made of a sub-domain of the YB-1 protein (cold shock domain) in complex with DNA or RNA fragments, III) in silico prediction of the toxicity of pharmacological compounds, and IV) the simulation of lipid monolayers in order to understand phospholipid dynamics in membranes. This third line has probably been reinforced by the recent arrival of its present manager at U 829 in september 2012.

The scientific output of this theme consisted in 2 articles in international peer reviewed journals and in the participation of nearly 6 other ones in the context of themes 1 and 2. As of today, it is also difficult to conclude about novel on-going projects since they have started less than one year ago.

Assessment of the theme's academic reputation and appeal

The expertise of the unit related to this theme is clearly recognized owing to the various international collaborations that recently started and were maintained.

Assessment of the theme's interaction with the social, economic and cultural environment

This theme is connected to the development of a structural bioinformatics platform that will also be another link to a spin off from the U 829.

Assessment of the strategy and the five-year plan

The arrival of the present theme's manager in September 2012 is reinforcing the interdisciplinary approach on MT studies developed in the unit. The proposed five-year research plan is quite large regarding the various projects tackled. Using bioinformatics approaches, the molecular mechanism of signal transduction by GPCRs, their interactions with the cytoskeleton/microtubule/actin, the molecular structure and dynamics of proteins and complexes studied in themes 1 and 2, and a group of various proteins/domains connected to pathological phenotypes will be investigated. The strategy includes recruitment of PhD and/or post-doctoral fellows.

Conclusion

- **Overall opinion of the theme:**

This theme provides an additional link between the unit themes 1 and 2 and is a supplementary connection, though independent, to a spin-off from the unit. The unique expertise of its manager will help understanding at the molecular level the processes studied at the cellular level by themes 1 and 2, hence providing a methodological bridge between in vitro and in cellulo experiments.

- **Strengths and opportunities:**

The strength probably comes from the international collaborations on the one hand, and the platform of structural biology and bioinformatics on the other. This theme benefits indeed from a privileged access to high computing systems and skills from a start-up company that should be launched by the end of 2013. Another strength comes from the proximity between the projects developed in themes 1 and 2 feeding the molecular modelling.

- **Weaknesses and threats:**

The recent arrival of the present theme's manager is expected to strengthen and benefit to the other themes in the unit. It is however not clear and not documented (short description of interaction) really how this will be practically managed. It is not clear whether there is a connection with the NMR structural biology platform.

The human workforce dedicated to this theme has to be reinforced since, as of today, it consists of only 1.25 FTE, which is not sufficient for investigating the numerous projects proposed for the next five years.

- **Recommendations:**

A refocusing (or a prioritization) of the projects is needed to concentrate the human workforce on the most challenging and promising questions. There is further a need to attract young scientists as well as to increase the number of PhD students and/or post-docs and increase the critical mass on the most promising projects through applications for external grants.

Theme 4: Diamond nanoparticles

Manager's name: Ms Marie-Odile DAVID

Workforce

Theme workforce in Full Time Equivalents	As at 30/06/2013	As at 01/01/2015
FTE for permanent professors	0.5	0.5
FTE for permanent EPST or EPIC researchers	0.25	0.25
FTE of other permanent staff without research duties (IR, IE, PRAG, etc.)		
FTE for other professors (PREM, ECC, etc.)	0.2	0.2
FTE for postdoctoral students having spent at least 12 months in the unit	1	
FTE for other EPST or EPIC researchers (DREM, etc.) excluding postdoctoral students		
FTE for other contractual staff without research duties		
FTE for doctoral students		
TOTAL	**1.95**	**0.95**

• Detailed assessments

Assessment of scientific quality and outputs

This theme concerns the development of innovative sensors based on doped diamond nanoparticles, which present the very interesting feature of having a bleach free fluorescence. This technological development should lead to promising applications. This field has received a renewed interest lately since these particles offer the very interesting property of having their fluorescence intensity sensitive to small magnetic fields, thus allowing very accurate magnetic field measurement at the nanoscale level. This feature is not especially of interest in this research unit who targets more biological applications, which can also highly benefit from this technology. This theme is an interesting challenge; the researchers have mainly focused on producing these nanoparticles with reproducible characteristics but also on functionalizing them to be able to bind them to specific targets. This is not an easy task and the group has come up with its own methodology, which is successful.

The number of publications (7) concerning this theme and its scientific quality (2 ACS Nano, 1 Small) is good. This work is known and appreciated by the community. The theme has led to 4 patents concerning the production of diamond nanoparticles, which is certainly a very good outcome.

Assessment of the theme's academic reputation and appeal

The expertise of the unit related to this theme is recognized owing to the local and national collaborations that have started and were maintained. However, its visibility on the international scene in the field of material sciences can be improved. The unit joined recently the project "DiamSciTech" that gathers the diamond specialists of the Université Paris-Saclay (17 partners). This consortium should thus boost the international reputation of the unit.

Assessment of the theme's interaction with the social, economic and cultural environment

The theme interaction with the social, economic and cultural environment is excellent; the laboratory is at the origin of a spin-off, which will produce the diamond nanoparticles. This spin-off seems to be promising as this project is supported by OSEO and Genopole and has won in 2012 and in 2013 the French Ministry Price of innovation, which is highly selective.

Assessment of the strategy and the five-year plan

This activity is original and promising; it is evolving in a very competitive field with strong forces not far in ENS-Cachan, École Polytechnique etc. Collaborations have already been initiated. This theme has been developed by different researchers some having left while its present leader has arrived recently in the field and has a very large teaching duty. The experts committee has thus the feeling that this theme may face the danger of not having enough personal strength to keep in the race. In that respect, the project presented was more or less the continuation of the present work. The researchers should develop collaborations with specialists of the fluorescence in biology to elaborate cutting edge scientific projects where their tools would be used to address fundamental biological questions.

Conclusion

- **Overall opinion of the theme:**

The main achievement of this theme is the patented industrial-scale fabrication method of fluorescent diamond nanoparticles, which can serve as a platform for biomolecule grafting, allowing for the development of various promising applications based on these innovative sensors in life sciences, material sciences and physics.

- **Strengths and opportunities:**

The development of a spin-off based on the laboratory "know-how" should provide improved fluorescent materials for the scientific community. The researchers have further developed a coupling methodology of these very interesting fluorescent nanodiamonds with antibodies. Through this theme, the unit is associated to the project "DiamSciTech" that would be a part of the future Material Institute harboured by the Université Paris-Saclay. This theme will also benefit from the clinical expertise of MDs from the novel Evry hospital for medical perspective.

- **Weaknesses and threats:**

It is a very competitive subject, which implies fabrication, characterization, cutting edge fluorescence equipment and strong biological questions. Unfortunately, efforts have only been dedicated on the two first items. The distribution of task and challenge between the laboratory and the emerging start-up is not clear.

There is a risk of being less competitive, which is linked to the retirement of the previous theme manager, who has been the expert on diamond nanoparticles (co-authors of patents on diamond nanoparticles).

- **Recommendations:**

There is a need to extend collaborations to stay in the upfront and more particularly with fluorescence specialists to address biological questions, for instance in the field of microtubule or in vivo cell tracing.

5 • Conduct of the visit

Visit date

Start	Wednesday, december 4th 2013 at 8.00 am
End	Wednesday, december 4th 2013 at 6.00 pm

Visit site

Institution	Université d'Evry-Val-d'Essonne, Bâtiment Maupertuis
Address	rue du Père Jarlan, 91025 Evry

Conduct or programme of visit:

08.30-08.45 am	Presentation of the AERES by the AERES Scientific Delegate (DS) to the experts committee (closed doors)
08.45-09.00 am	Presentation of the AERES by the DS to the unit
09.00-10.00 am	General presentation of the unit (results/project) by the unit director then discussion
10.20-10.50 am	Audition theme 1 "Cytoskeletton dynamics"
10.50-11.20 am	Audition theme 2 "Cellular and molecular biophysics"
11.20-11.40 am	Audition theme 3 "Structural bioinformatics"
11.40-12.00 pm	Audition theme 4 "Diamond Nanoparticles"
12.00-12.30 pm	Meeting with the representatives of the unit's supervising institutions and bodies *Auditoire : expert committee members and DS*
12.30-01.30 pm	Lunch (around posters)
01.30-01.50 pm	Meeting with permanent and contractual staff (without research duties) *Auditoire : expert committee members and DS*
01.50-02.10 pm	Meeting with the PhD students, post-docs and contractual researchers *Auditoire : expert committee members and DS*
02.10-02.30 pm	Meeting with the permanent professors, researchers from institutions and similar positions (without the unit direction) *Auditoire : expert committee members and DS*
02.30-02.45 pm	Meeting with the director of the "École doctorale" *Auditoire : expert committee members and DS*
02.45-03.00 pm	Debriefing *Presence : expert committee members and DS*
03.00-03.20 pm	Meeting with the unit director *Auditoire : expert committee members and DS*
03.20-05.30 pm	Meeting of the experts committee (closed doors) *Presence : expert committee members and DS*

Specific points to be mentioned:

Ms Jeanine TORTAJADA, UEVE vice-president, has participated to the meeting of the experts committee with the unit's supervising institutions.

Ms Marie-Pascale MARTEL, INSERM regional delegate, has participated to the meeting of the experts committee with the unit's supervising institutions and to all presentations.

Ms Florence LESECQ, representative of the elected C personals of the CSS 1 INSERM, has participated as an observer to all presentations and to the meeting of the experts committee with the permanent and contractual staff (without research duties).

6 • Supervising bodie's general comments

Evry, le 7 Mars 2014

Philippe HOUDY
Président de l'Université d'Evry Val d'Essonne

4, Boulevard François Mitterrand
91025 Evry Cedex

à :

Didier HOUSSIN
Président
Agence d'Evaluation de la Recherche
et de l'Enseignement Supérieur
20 rue Vivienne - 75002 PARIS

Direction de la Recherche, de la Valorisation et du Transfert

Objet : Réponse au rapport du comité de visite du laboratoire SABNP

Monsieur le Président,

Nous avons pris connaissance avec le plus grand intérêt de votre rapport concernant le projet SABNP porté par M. Patrick CURMI. Nous tenons à remercier l'AERES et le comité pour l'efficacité et la qualité du travail d'analyse qui a été conduit.

Ce rapport a été transmis au directeur du laboratoire qui nous a fait part en retour de ses commentaires que vous trouverez ci-joint.

Nous espérons que ces informations vous permettront de bien finaliser l'évaluation du laboratoire.

Restant à votre disposition pour de plus amples informations, je vous prie de croire, Monsieur le Président, à l'expression de mes salutations respectueuses.

Pour le Président de l'Université
et par délégation

Michel GUILLARD

UNIVERSITÉ D'ÉVRY VAL D'ESSONNE
Présidence

M. Philippe HOUDY

Bd François Mitterrand
91025 Evry Cedex
Tél. 01 69 47 70 00/78 00
Fax. 01 69 47 70 07

Laboratoire Structure et Activité des Biomolécules
Normales et Pathologiques
INSERM / UEVE U829
Docteur Patrick CURMI
Directeur

Evry, le 7 mars 2014

Response of the Director of UMR INSERM-UEVE U829 to the recommendations received from the AERES expert committee that appear in the evaluation report # S2PUR150008015 - Structure et Activité des Biomolécules Normales et Pathologiques - 0911975C.

The unit director and the members of UMR829 would first like to thank the AERES expert committee for the careful evaluation of our scientific production together with our involvement in formation, our attractiveness and our participation to the social and economic world.

General Observations

Weaknesses and threats related to the context

Expert committee: Sharing of R&D between the laboratory and both spin-off should be looked at to avoid duplicating the effort.

Comment from UMR829: There is a clear cut distribution of the tasks between the laboratory on one hand and the Synsight and DiamLite spin-offs on the other hand. Academic research will be performed within the laboratory whereas the enhanced value and marketing are the duty of these two spin offs.

Expert committee: Despite the clear convergence effort, the diversity of the themes may be a problem owing to the necessary critical mass necessary to achieve high-level work.

Comment from UMR829: UMR829 will increase its convergence effort. Regarding the critical mass, the objective of our research is to combine different approaches to provide an integrated view on biological processes. This necessitates maintaining the structuration of the unit in themes while keeping an efficient connection between the themes. Indeed, as pointed out by the committee, theme 2 develops

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its research in strong connection with theme 1 (see section theme 2 / Strengths and opportunities) and the proximity between theme 3 and themes 1 and 2 is also underlined by the committee (see section theme 3 / Strengths and opportunities). To increase the critical mass we, as all research units nowadays, are limited by the number of permanent position made available at the local and national levels. To overcome this difficulty we will attempt to attract such permanent position researcher or teacher-researcher by networking or dedicated calls. In addition, we always include salaries for hiring researchers or engineers in grant applications.

Expert committee: There is a clear need for people to take care of the NMR facility. However, the unit could not yet attract a good candidate. This is a strong emergency.

Comment from U829: We agree with the committee that this is an emergency. In line with this, a strategy to attract a permanent position NMR researcher has been launched at the international level. A potential foreign candidate has been identified and exchanges with him are ongoing.

Expert committee: There is a relative scientific isolation at the level of the university. This is a problem for scientific development and young researcher training.

Comment from U829: We agree with the committee that isolation of the unit within Evry University may be considered as a problem. To surmount this, we have developed within the unit a continuous animation effort through the invitation, at regular intervals, of speakers for invited conferences and of professors from abroad for short term stay in the laboratory (1 to 3 months). In addition, the Evry biology department has initiated recently a local Evry'Bio meeting initiative to foster collaborations between Evry University laboratories. This led us to start recently new collaboration with the I-Stem and IMBI-UMRS 951 laboratories (in addition to the long term collaboration that we have developed with the LAMBE). A proposal would also be to start a Biology Department cycle of conferences (including internal and external speakers). Finally, another aspect which will hopefully impact positively research and training is the forthcoming integration of Evry University in the Paris-Saclay University.

Expert committee: The main threat is probably linked to the organization of the unit. It depends too strongly on the investment and vision of its director. Although it is expected that the director of the unit contributes with his vision and energy, the unit is organized in four mostly independent axes. Each of the theme leaders should play a stronger role in the life of the unit. It is extremely important because, at the end of the next 5 years, the current director will step-out and it is worrisome that no leadership would have appeared to take over.

Comment from U829: Our unit was initially shaped as a single team structure. With time, novel themes have emerged thanks to the strong commitment of theme leaders. The objective is now for the theme leaders to more strongly influence the strategy of the unit and its future steering.

Recommendations

Expert committee: The unit may benefit from clarifying its relationship with their founded start-up for the next 5 years. This is particularly true for the nanoparticle project, which is in a transitory phase. If everything goes right, the critical mass may

be found in the start-up rather than in the academic project. Owing to the very limited human resources, the unit may need to make clear choices.

Comment from U829: The strategy to maintain research within the unit is dual: primarily through the hiring of post-doc fellows based on contracts with industry (it is worthy to note that the nanodiamond project contributes significantly to the financial resources of the unit). We will also try to attract a permanent position teacher-researcher or researcher to increase the permanent critical mass in the nanodiamond project.

Expert committee: The theme leaders should take their share in animating and supporting the unit. This is simply the expected behaviour of people who want to play an active role. In parallel, the unit director should try to delegate more both his role in representing and directing the unit.

Comment from U829: A particular attention will be given to reach this objective. Theme leaders actually are committed to foster such changes and will also increase their involvement in the representation of the unit at the national and international levels.

Expert committee: Because of the relative isolation of the university, it is important that the post-doctoral fellows and PhD students participate more to French and international meetings, and organize more trans-unit contacts at the university level, for example in the form of regular joint meetings and journal clubs.

Comment from U829: All PhD and Post-Doc fellows participate to French and international meetings. In addition, PhDs participate to the "Doctoriales" annual meeting organized by the GAO doctoral school. Finally, a journal club will be organized within the unit. As stated above the Evry'Bio meeting is also a place to exchange at the student level. Finally, we will contribute to organize joint meetings with other units in UEVE and Genopole for the members of this unit to present their work to other biology laboratories and laboratories from different areas of research to again foster interdisciplinary projects.

Expert committee: The PhD students are probably a bit too passive and should be more pro-active. Some seem to need more direction and the problem of the 4th year support should be clarified and discussed more clearly. Similarly, the PhD students and post-docs should clarify their professional project with their respective project leader.

Comment from U829: We are committed for the PhD work to complete within a 3 year period as recommended by the doctoral school. When this delay is exceeded (in average not more than a few months), we can obtain a support from university to cover the period between the end of the PhD grant and the PhD defence.

Expert committee: The multiplicity of research projects may also be a problem considering the relative small size of the unit. A stronger focus on studies at the cellular level may be beneficial.

Comment from U829: The strength of UMR829 is to be able to examine the structure-activity relationships of biomolecule of medical interest from the atomic structure to the function within living cells. This is not common but clearly we cannot concentrate our investigation on cell studies only. Our objective and hope is to open avenues on innovative aspects regarding the function of biomolecules at

different levels and with different approaches, such that data are then considered with other tools and methods. We consider that we have reached this objective when examining the citation index of the research papers that come out from our laboratory.

Theme 1: Cytoskeleton dynamics

Assessment of scientific quality and outputs

Expert committee: It would be desirable that future research would be conducted to dissect more in depth cellular mechanisms and to investigate potential physiological relevance, such as the cellular role of STOP-dependent microtubule regulation in neurons, or the cellular mechanisms by which spastin causes axonal swellings.

Comment from U829: These aspects are to be examined in depth thanks to collaboration with other specialists in these domains from France and abroad.

Assessment of the strategy and the five-year plan

Expert committee: The committee felt that the future project is good, but that there are weaknesses in the five-year strategy and in the experimental planning: there are certainly research activities that look very promising and that are expected to yield interesting results in the future (e.g. colchicin-carbendazim hybrid molecule, STOP, spastin). However, the experimental plans are relatively numerous and diverse, and there is not always a recognizable synergy between the subjects (for example, a recent project on actin aggregation may be diverting from the current focus on microtubules). It was also felt that the aims and potential milestones of future activities are not well defined. Moreover, the experimental planning lacks details, and the involvement of the different personnel of the research unit in the individual sub-projects is not well explained (*i.e.* who will do what?).

Comment from U829: The discovery that plant extracts from Algeria impact the actin cytoskeleton was a fortuitous discovery (serendipity) when looking for the impact of these extracts on the microtubule network. As the impact of these extracts on actin is dramatic and the molecular mechanism behind this effect not described, we decided to continue the exploration. Regarding the organization of future activity, AERES clearly recommended not to provide detailed work programs. Nevertheless, we attempt to complete the work on hybrid molecule through collaboration with industry. STOP investigation will develop in collaboration with another INSERM Unit and spastin research is under the responsibility of Dr Burgo (INSERM-UEVE Chaire d'excellence). Finally, research on natural products that target both microtubules and actin cytoskeletons are developed by two PhD students under the supervision of Dr Curmi and will benefit from a contract with industry (anti-microtubule compounds).

Expert committee: The characterization of the CPAP-tubulin interaction, by studying the effects of point mutagenesis on the formation of the tubulin-CPAP complex, and on tubulin sequestration: this may be of interest both for understanding basic principles of tubulin polymerization, and for designing novel strategies for microtubule depolymerisation. The team may have a competitive advantage on this project, since currently no other group seems to analyse the CPAP-tubulin interaction at an atomic/structural level. However, if the goal was to develop a novel

pharmacological inhibitor of microtubules, it should be kept in mind that a patent already protects any commercial use of CPAP as a destabilizer of microtubules.

Comment from U829: Here, the first objective is to provide the bound structure of a tubulin partner in condition closed to what occurs in solution. Regarding the possibility to patent future drugs that we would design from the structure that we expect to obtain (with the contribution of the Synsight company), to the best of our knowledge, we believe that it is not impeded by the patent cited by the expert committee. Indeed, the US7449563 B2 patent relates to the use of CPAP-derived polypeptides to destabilize microtubules (and to the encoding cDNAs) but not to drugs that may be based on the CPAP structure.

Theme 2: Cellular and molecular biophysics

Assessment of the theme's interaction with the social, economic and cultural environment

Expert committee: The unit has filed a patent for DNA chips based on mica adsorption and AFM detection. However, nothing concerning a technology transfer has been reported.

Comment from U829: Unfortunately, INSERM-Transfert has decided to discontinue its contribution to the fees to maintain this patent. This now renders difficult collaboration with industry to develop this technology.

Weaknesses and threats

Expert committee: The correlation between biophysical results and those obtained with culture cells is not fully explained. Nothing concerning the development of novel DNA-chips is proposed whereas it seems to be one of the objectives of the unit clearly announced in original and innovative aspects of research at U829. The committee felt that the stress granule project remains too biophysical.

Comment from U829: A significant effort is ongoing to correlate investigation on isolated molecules with cell research.

Recommendations

Expert committee: The program proposed is essentially based on biophysical approaches. Even though the results will be sound, the unit must pay attention to a strategy for transposing the results in a more relevant physiological/biological context. Notably, the planned research on gap junctions is really exciting, but the possibility to inhibit formation of gap junctions as anticancer strategy remains contradictory with the invasiveness of non-adherent cells in cancer. The unit has to be careful on the potential application of such possibility. The committee recommended to dissect more in depth the stress granule theme.

Comment from U829: This is clearly one of our objectives.

Theme 3: Structural Bioinformatics

Weaknesses and threats

Expert committee: The recent arrival of the present theme's manager is expected to strengthen and benefit to the other themes in the unit. It is however not clear and not documented (short description of interaction) really how this will be practically

managed. It is not clear whether there is a connection with the NMR structural biology platform.

Comment from U829: When appropriate, experimental structure results are discussed with the theme 3 leader to complete the view on 3D structure and explore the relevant dynamics aspects of the molecules under investigation.

Expert committee: The human workforce dedicated to this theme has to be reinforced since, as of today, it consists of only 1.25 FTE, which is not sufficient for investigating the numerous projects proposed for the next five years.

Comment from U829: The theme leader has applied for several grants since he joined us. We have just recruited a "Master 2" student and the project in the coming months is to present this student to the PhD program and to the scholarship committee. In addition, if funds are obtained, a collaboration might be established with the Synsight team on dedicated aspects. Among the grant applications to which we replied, a franco-lebanese program (CEDRE) was approved, allowing bi-lateral exchange and sojourns of students and main investigators in the following two years. A franco-mexican project submitted to CONACYT Mexico is awaiting response. We intend to welcome a post-doctoral fellow when the availability of funds from grants will allow it.

Recommendations

Expert committee: A refocusing (or a prioritization) of the projects is needed to concentrate the human workforce on the most challenging and promising questions. There is further a need to attract young scientists as well as to increase the number of PhD students and/or post-docs and increase the critical mass on the most promising projects through applications for external grants.

Comment from U829: As described above, the theme leader has applied for several grants since he joined us and succeeded for in establishing a collaboration with a Lebanese partner, and another collaboration with a Mexican partner.

Theme 4: Diamond nanoparticles

Assessment of the strategy and the five-year plan

Expert committee: This activity is original and promising; it is evolving in a very competitive field with strong forces not far in ENS-Cachan, Ecole Polytechnique etc. Collaborations have already been initiated. This theme has been developed by different researchers some having left while its present leader has arrived recently in the field and has a very large teaching duty. The committee has thus the feeling that this theme may face the danger of not having enough personal strength to keep in the race. In that respect, the project presented was more or less the continuation of the present work. The researchers should develop collaborations with specialists of the fluorescence in biology to elaborate cutting edge scientific projects where their tools would be used to address fundamental biological questions.

Comment from U829: We do collaborate with photophysicists as it appears in our publications. We also initiated collaborations with other biologists to enlarge the questions addressed on the use of the fluorescent nanodiamond possibilities. We finally are seeking for new collaborations on the other properties of nanodiamonds that may potentially be useful for biomedical applications.

Weaknesses and threats

Expert committee: It is a very competitive subject, which implies fabrication, characterization, cutting edge fluorescence equipment and strong biological questions. Unfortunately, efforts have only been dedicated on the two first items. The distribution of task and challenge between the laboratory and the emerging start-up is not clear.

Comment from U829: See response in section above.

Expert committee: There is a risk of being less competitive, which is linked to the retirement of the previous theme manager, who has been the expert on diamond nanoparticles (co-authors of patents on diamond nanoparticles).

Comment from U829: All the knowledge and skills linked to the retirement of the previous theme manager have been transmitted and are within the laboratory.

Expert committee: Through one of these spin-offs, the unit will be implicated in a common project "DiamSciTech" (consortium of 17 team partners) that would be a part of the future Material Institute harboured by the Paris-Saclay University in the next 3 years,

Comment from U829: Though the DiamSciTech project was not selected by the Paris-Saclay University in the present form (the response arrived after the AERES visit of the unit), we are in close contact with teams working on diamond within Paris-Saclay University and will participate to future call for tender from this institution.

Patrick CURMI