Grenoble institut des neurosciences

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Grenoble Institut des Neurosciences

From the

University of Grenoble 1

INSERM

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INSERM

Le Président
de l'AERES

Jean-François Dhainaut

Section des unités
de recherche

Le Directeur

Pierre Glorieux

May 2010

Research Unit

Name of the research unit: Grenoble Institut des Neurosciences (GIN)

Requested label: UMR_S INSERM

N° in the case of renewal: 834

Name of the director: M. Claude FEUERSTEIN

Members of the review committee

Committee Chairman:

M. Jacques GLOWINSKI, Collège de France, Paris

Other committee members:

M. Peter HOLZER, Medical University of Graz, Austria

M. Etienne AUDINAT, Université Paris-Descartes, Paris

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Committee members suggested by CNU, CoNRS, CSS INSERM, CSS INRA, INRIA, IRD

M. André NIEOULLON, CNU member

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M. Uwe SCHLATTNER, Université de Grenoble 1

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Report

1 • Introduction

- Date and execution of the visit:

The visit took place on January 27th and 28th January, 2010. After a brief closed-door gathering of the visiting committee, the laboratory director made a general presentation of the team's main achievements and its activities within the Grenoble research and clinical networks. Each group leader then presented its past results, and projects and future plans. The committee wishes to thank the Director of the GIN and his colleagues for the excellent organization of the meeting. Documents, oral presentations, visits of technical platforms and discussions with researchers, students and ITA were highly appreciated. A detailed analysis of the budget was also provided during the meeting. Finally, the committee had a long private discussion with the Director for complementary information on the organization, scientific strategy, governance and nominating procedure of the Director successor.

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

The « Grenoble Institut des Neurosciences » (GIN-U836) is a project of the Joseph Fourier University, INSERM and CEA, which was initiated when the GIN Director was President of the University.

Opened at the end of 2007, the GIN building (6000m2) and the neuroscience sector of the center of clinical investigations (CIC) provide excellent working conditions. The architectural (spatial organization, particularly) and technical quality of the GIN building, and the excellent organization of the neuroscience CIC sector should contribute to the visibility and attraction of the GIN. Well equipped and organized, several technical platforms are already operational.

Within the CHU, the GIN building is very close to the departments of neurosurgery, neurology and psychiatry and to the IRM and CIC services. This localization facilitates the continuous interactions of researchers and clinicians, particularly in neuro-oncology and neuro-degenerative diseases, two fields initially developed in Grenoble by the Professor Benabid whose contributions are highly recognized both nationally and internationally. The CHU is part of the dynamic campus of Grenoble, internationally known for its activities in physics, biology, engineering, micro- and nanotechnology but also for its large high quality scientific equipments and its close relationships with industry.

The main research fields of the GIN are neuronal plasticity and communication, oncology, high frequency neuro-stimulation in several neurological diseases, development of new technological tools thanks to micro and nanotechnology.

The Director of the GIN and his colleagues who participated to the realization of the GIN project must be congratulated. Scientific vision, tenacity, diplomacy and management capacities are required for the creation of such a large neuroscience research centre offering all these facilities and allowing multidisciplinary approaches as well as continuity between fundamental and clinical researches. The GIN is part of a more global strategy for the development of biological sciences in Grenoble. For many years, the Director of the GIN has played a determinant contribution role in this development.

- Management team:

It is foreseen that the present Director of the GIN will still act as Director for the next four years and that he will still benefit in this period from the competence of an administrative Director and from a motivated and dynamic administrative team. Although strongly suggested by the international scientific council (SAB), the Director was not able to nominate a Vice-Director. However, three team leaders were nominated to improve and coordinate the external relationships, the internal organization and the teaching policy. Regular meetings already take place and will

continue to take place in the future with all team leaders to discuss scientific matters. This group and representatives of young researchers and ITA (technical staff) will also regularly discuss all other aspects of the activities of the Unit.

- Research unit staff members:

The global population of the GIN will be around 220 persons (slightly higher than before). The numbers of teaching researchers and researchers will be closely similar as before (total 75) and the number of temporary teaching-researchers and post-doctoral fellows will be less than before (about 20). A large proportion of permanent teaching-researchers and researchers (total 57) are habilitated to act as research director for PhD students demonstrating the good environment of the 40 to 45 PhD students, which will be working in the institute. The total number of ITA (55 including 41 with a permanent position) is relatively small when compared to the overall population of teaching researchers and researchers but this is not particular to the GIN, several research centres being in the same situation.

	Past	Project
N1 : Number of researchers with teaching duties (Form 2.1 of the application file) :	38	36
N2 : Number of full time researchers from research organizations (Form 2.3 of the application file) :	40	40
N3 : Number of other researchers with or without teaching duties (Form 2.2 and 2.4 of the application file) :	17	19
N4 : Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file) :	43	41.3
N4 : Number engineers, technicians and administrative staff on short term contract (Form 2.5 of the application file) :	17	13
N5 : Number engineers, technicians and administrative staff with a tenured position (Form 2.6 of the application file) :	18	
N6 : Number of Ph.D. students (Form 2.7 of the application file) :	56	41
N7 : Number of staff members with a HDR or a similar grade :	56	57

2 • Overall appreciation of the research unit

- Summary of the overall appreciation:

As shown by the quality and efficacy of the GIN organization and the collective efforts made in two years, the GIN has already taken into consideration several recommendations of the SAB. Working conditions are excellent : spatial organization of the GIN building which facilitates interactions between the ten existing teams, quality of equipments, availability of four well organized technical platforms (including new MRI facilities for primate and human). Translational research (one original specificity of the GIN) is facilitated by the proximity of the neuroscience CIC sector and of the neuroscience clinical departments. In addition, CEA and CNRS biological or technical (including micro and nanotechnology) departments as well as connections with private companies (such as Clinatec) allow local collaborations.

Unfortunately, a Vice-Director was not nominated, but the governance has been reinforced by the presence of a competent administrative director and an administrative platform, and by the recent nomination of three team directors, which will be responsible for the coordination of various aspects of the functional organization of the Unit. Several appropriate dispositions have already been taken to improve the teaching and scientific training policies as well as the scientific animation. Young researchers or clinicians as well as post-docs benefit from an excellent scientific environment and they markedly enhance interactions between the various teams, but more postdoctoral fellows should be recruited. For historical reasons, important differences in size (number of persons) exist among the different teams. This is also the case for the repartition of ITA among the different teams. The presence of only one technician or their absence in some teams is indeed a limiting factor for the productivity of these teams.

The scientific strategy is largely based on historical specificities and capacities of the 10 teams at the origin of the GIN but also on the local (within Grenoble campus) potentialities of the three GIN institutional partners: University, Inserm and CEA. Four transversal and equilibrated research axis were chosen to reinforce the main scientific projects and to ensure appropriate collaboration and coordination within the GIN but also locally with other partners: 1) Cellular plasticity and pathologies of the nervous system, 2) Neuro-oncology, 3) Dynamic and pathophysiology of brain networks, 4) Innovative technology and methodology for Neurosciences.

Some internal mobility has already been achieved: several ITA were transferred to technological platforms, the team 5 Director was changed, team 11 was appropriately created by a redistribution of several researchers and clinicians, but the creation of team 12 may not be yet appropriate.

The global scientific production has slightly but significantly increased and combined publications of some teams reveal the synergistic effects of the new scientific strategy. This production is of good quality, but reaches excellence too rarely and should still be improved.

Indicating the good appreciation of the GIN and several of its teams by external scientific committees or Institutions, the GIN benefits from recurrent financial reports (Inserm, University, CEA) expected to be comparable to those previously obtained, financial support has been obtained for large equipments, most teams benefit from regional or national grants (substantial in several cases), but international financial support occurs only in a few cases. Efficient logistic for increased value of obtained data has been set up and several actions have already been taken in this direction.

For all these reasons, the GIN has several attractive scientific assets and a large diversity of facilities. Its international visibility should rapidly increase.

- Strengths and opportunities:

- Excellent scientific direction and animation by the GIN Director assisted by a competent and dynamic administrative director and administrative platform.

- Excellent working conditions and perfect localization within the CHU allowing close and permanent contacts between researchers and clinicians in neurosciences, particularly thanks to the well organized and equipped neuroscience sector of the CIC.

- Adapted transversal scientific strategy taking advantage of the historical specificities of the teams and of the local scientific environment allowing new collaborations between teams.

- Strong relationships between scientists involved in animal and human research in several teams. This continuity of fundamental and clinical research facilitating translational research and increased value is an important originality asset of the GIN.

- Diversity of competences of permanent teaching researchers, researchers and clinicians allowing multidisciplinary strategies.

- Efficient technological platforms with competent engineer and technician staffs and with sophisticated equipments (For example: bi-photon microscopes, MRI for primate, MRI 3 T imager, availability of a synchrotron of high energy on the campus).

- High diversity of animal models and techniques.

- Complementary expertise in the Grenoble campus with strong links with different institutions including the university, the CEA and the CNRS.

- Efficient organization of the scientific animation, the teaching and training of young scientists, the PhD student environment and the valorization development.

- Capacity to obtain local and national grants and strategies for new financial support (NeuroDis foundation, newly raised GIN foundation, Edmond J. Safra foundation)

- Policy for regional scientific collaboration (both national and international).

• Weaknesses and threats:

- Lack of a Vice-Director. Very soon, an important risk of internal tension will exist when the present GIN Director's successor will have to be nominated. However, according to the Director project, an international recruiting committee will be set up to recruit (in France or abroad) a Director with high scientific reputation who could eventually join the GIN with his/her own research team.

- Taking into consideration the number of permanent scientists and the facilities offered by the GIN, the global production and level of publications should be enhanced in several teams, the objective being to reach excellence.

- The number of projects in several teams is too high; this may impair the scientific production.

- In several cases, the international visibility should be increased by the presence of a larger number of postdoctoral fellows. This could largely significantly contribute to the further development of several projects and should also enhance the collaborations between teams

- Strong international collaborations are too limited taking into account the scientific history and maturity of several teams. This is also the case for international (European) financial support.

- There is little or even complete lack of engineers and/or technicians in some teams. This will particularly raise difficulties for the development of the last (number 4) transversal research axis and thus for increased value.

• Recommendations to the head of the research unit:

- Set up very rapidly and in priority his proposed strategy for nominating his successor, which could act as a Vice-Director in a transitory period. This will avoid internal difficulties and external pressure.

- Keep enough office and lab space for facilitating the Direction and choices of its successor.

- In order to improve the global scientific production (number and level of publications), ensure with exigency the chosen scientific strategy in the four transversal research axis to benefit as much as possible from the synergistic impact of efforts made by collaboration and coordination of teams. This will also require a reduction in the number of projects in several teams.

- Try to recruit researchers in some domains, which should be perhaps more represented in the centre: cellular electrophysiology, behaviour research or psychopharmacology for instance.

- Reinforce with priority the international policy to increase the GIN visibility. Thanks to the new financial support (foundations), this could be achieved by the development of a postdoctoral program, and by the organization of small international meetings in the specific research axis of the GIN

- Main recommendations of the GIN international scientific committee (SAB) made in 2007 just before the Unit opening should be recalled for a better appreciation of progresses achieved in two years

    - Proceed to the nomination of a Vice-Director and reinforce the scientific and administrative team of direction

    - The GIN should not be a place with a juxtaposition of independent teams but an integrated centre with some predominant research axis requiring intense collaborations between teams

    - For some teams, increase the number and level of publications and recruit more postdoctoral fellows

- Create a high level training program for students and young researchers, reinforce the financial strategy of the GIN and, finally, increase the participation to international programs (European particularly) as well as relationships with industry.

- Production results:

- Due to the brief existence of the GIN (two years only), such an appreciation is uncertain.

- It is surprising to see that the number of "publishers" among the persons included in the N3, N4 and N5 categories is relatively elevated when compared to the number of researchers belonging to the A1 category.

- No special comment can be made on the number of HDR. The number of prepared PhD thesis reveals that the GIN offers appropriate facilities and training for PhD students.

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

A1 : Number of lab members active in research among permanent researchers with or without teaching duties (recorded in N1 and N2)	69
A1 : Number of lab members active in research among permanent researchers with or without teaching duties (recorded in N3, N4 and N5)	34
A3 : Ratio of active members in the research unit [A1/(N1+N2)]	0.88
A4 : Number of HDR granted	12
A5 : Number of PhD granted	49

3 • Specific comments

- Appreciation on the scientific quality and the output:

In its appreciation, the committee has taken into consideration the brief life period of the GIN (opening at the end of 2007), the favourable factors linked to the general context, the scientific quality of the scientific environment and the numerous opportunities for positive evolutions of several teams and of progresses in the chosen four research axis.

The efficacy of the partnership of the University, INSERM and of the CEA in the creation and development of the GIN must be underlined. For several reasons, the CNRS should also be a partner of the GIN since several CNRS researchers are working in the GIN, the CNRS has several laboratories on the Grenoble Campus which collaborate or could collaborate with the GIN and, reciprocally, GIN facilities could be of interest for the CNRS. Finally, transversal researches of axis one particularly, are close to the CNRS interests. The new national policy of alliance of several institutions working in life sciences should facilitate this necessary evolution. A better harmonization of the different partners should simplify administrative procedures as well the management of human resources, which of course is a general comment and not the responsibility of the GIN.

In two years, globally, the GIN has successfully followed several important recommendations of the SAB. In particular, a coherent and adapted scientific strategy has been defined and the GIN is not any more a juxtaposition of independent teams. Collective efforts were made to ensure collaboration and coordination within the GIN, and also locally with other partners. For several reasons already mentioned, the choice of the four transversal axes of research is justified and, in a few years should have an impact on the global scientific production. Indeed, this scientific strategy should reinforce the main scientific projects and further enhance translational research, one of the original and pertinent characteristics of the GIN.

Briefly: 1) Teams one to four will particularly contribute to the first axis on "cellular plasticity and pathologies of the nervous system", which involves researches on the cytoskeleton, endosomes and exosomes, calcium channels in brain and muscles. 2) Teams 5, 6 and 7 are actively involved in the "Neuro-oncology" research axis; a convincing coordinated program including additional researchers of other teams has been shown. 3) Several teams (8, 9, 10 and 11) contribute to the third research axis on "dynamics and pathophysiology of brain networks". This important topic corresponds to a detailed analysis of cellular and network mechanisms of the deep brain high frequency stimulation method and of its new therapeutic applications; 4) Teams 5, 6, 7 and 11 but also several researchers and clinicians of other teams participate to the last research axis "Innovative technology and methodology for Neurosciences". They will highly benefit from the expertise and facilities of the Grenoble campus.

There is little doubt that the GIN already contributes to the development of Neurosciences in Grenoble and its neighbourghood. Several teams participate to local or national research networks. However, contributions to international research networks are more limited. There is no doubt that the resource centres (cerebral tissue banks) provide additional possibilities for these research networks and for national and international collaborations. Large financial efforts have been made for the equipment of technical platforms, which also benefit of qualified staffs. However, taking into account the expenses made, a higher utilization of these platforms should occur in some cases. For instance, very few centres have primate housing facilities and in general, such facilities require extensive and complementary scientific programs on primates, which presently does not seem to be the case in the Unit. Similarly, although the occurrence of "a clinical transcriptomics and proteomics platform in the GIN" is of particular interest, its requirement for the development of the overall scientific strategy of the Unit could be more extensively justified.

In two years, the scientific production (number of publications) has slightly but significantly increased and combined publications of some teams have been made revealing that the new scientific strategy will lead to synergistic effects. In several cases, the number of publications in journals with high impact factor seems to be higher for clinical publications than for other types of publications. As already indicated and noted in team reports, although the global production (number and level of publications) is of good quality, it reaches excellence too rarely. This production should be improved if one takes into account the historical scientific background and competence of several teams and, particularly, the total number of permanent researchers and teaching researchers in the GIN, the quality of the scientific environment and of facilities offered by the Unit. This could be achieved by reducing the too high number of projects in several teams, by more intense collaborations and by the recruitment of additional post-doctoral fellows. Although original by its thematic and clinical orientation, but estimated weaker than other teams by the SAB, team 8 which has much less permanent researchers and financial facilities, seems to have taken some advantage of the global dynamic of the GIN and should still be encouraged.

The number of PhD thesis is satisfactory and demonstrates the efficacy of the training policy and attractiveness of the GIN for PhD students from Grenoble but also from other cities, which is particularly encouraging.

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

Several criteria are generally used to evaluate the attractiveness and the impact of a research unit. Some of them can be enumerated: number of prices and honorific distinctions of the members of the Unit, invitations to present honorific lectures in important international meetings, invitations to write reviews in journals with high reputation, frequent publications in excellent journals, ability to obtain European grants, long term collaborations with well known foreign laboratories, temporary reception of high level scientists in the unit or attractiveness of foreign post doctoral fellows.

Time is required to reach some of these objectives and definitive appreciation cannot thus be made if one takes into account that the Unit was only opened at the end of 2007. Some of the criteria mentioned above are not yet fulfilled as indicated by the appreciation on the global scientific quality and production or comments made on the international policy (post-doctoral fellows, European grants). Nevertheless, numerous researchers who are part of the Institute have a high scientific level and several of them are well recognized in their research field at an international level. The past history of some teams, in particular, their appreciated successes in clinical research such as Parkinson treatment by neuro-stimulation, or neuro-oncology, contribute also to the impact of the Institute.

The Institute's attractiveness and its impact is expected to rapidly increased due to: 1) the excellent working conditions including the possibility to use entirely new technological platforms (including e.g. new MRI facilities for

primates and humans); 2) translational research, one original characteristic of the GIN is facilitated by the proximity of the neuroscience CIC sector and of the neuroscience departments from the university hospital known for its high standard of clinical research; 3) the Grenoble aera biocluster, with special reference to engineering (imaging, micro and nanotechnology, synchrotron) and connections with private companies (such as Clinatec), which favours collaborations of several teams.

Most teams benefit from regional or national grants, which are very substantial in several cases, and important financial support has been obtained for large equipments. There are also several favourable factors for the development of added value including the presence of researchers who have been working in pharmaceutical companies. The quality of the scientific environment, the number of trained PhD students and the recent recruitment of very qualified researchers also reveal the national impact of the GIN.

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

The governance has been reinforced by the presence of an efficient administrative director who is in charge of a well organized administrative platform, and by the recent nomination of three team directors in the administrative board, which will be responsible for the coordination of the external and internal communication, the teaching policy and the scientific animation.

The nomination of a Vice Director and thus of a potential successor of the present Director is presently the main problem of the Unit. As already indicated by the SAB, the designation of a Vice-Director who should have the capacities in four years (which is a relatively short period) to succeed to the Director is a priority. To succeed to the present Director, whose scientific and management competences as well as human qualities are evident, is a difficult task.

For reasons which should be further explored, the team leaders prefer to be in direct contact with the Director and the scientific governance seems to be ensured in the weekly meetings of the Director with the team leaders. This is likely also why no scientific coordinator was nominated for each of the four transversal research orientations. One could understand that the team leaders try to avoid a too hierarchical organization, but another interpretation is that there is no consensus on an internal scientific personality who could take in charge the responsibility of Vice-Director. Nevertheless, the committee still believes that the presence of a Vice-Director is necessary in a large Unit and that situations which require rapid decisions may occur in the absence of the Director. In addition, the position of Vice-Director during a transitory period provides the appropriate learning period for global management and for recognition by a large majority of the persons working in the Unit. To overcome this situation, and in agreement with the team leaders, the Director has proposed to nominate a recruiting committee (with external personalities) to help him to recruit a national or international scientific personality who could take in charge the Unit Direction in four years. According to his view, this personality could even develop his own team in the Unit. An honorific chair (E.Safra) and special financial support will be obtained for this project. According to the committee, this project should be undertaken in the near future to avoid anxious situations and internal tensions and (other) counter-productive situations that, which could slow down the dynamics of the Unit and be inappropriate for its visibility. A transitory period of Vice-Director would help the future Director to familiarize him/herself with the environment and all the local and national administrative structures.

Several successful decisions have already been taken for the development of several policies including: communication, scientific animation, young researcher formation and training, student teaching in neurosciences and added value. Team leaders and experienced researchers are involved in these important duties. Thus, the Unit appears to be particularly well organized but, as requested by the ITA, the global communication could be still improved by more frequent information meetings on the general orientations of the GIN.

The young researchers or clinicians as well as post-docs benefit from an excellent scientific environment. This appreciation is based on the high level of initial training of several teaching-researchers or researchers and clinicians in foreign laboratories or clinical departments, the high diversity of the competences of the team leaders and the number of teaching researchers and researchers who have the capacity to act as research director for PhD students. The recent recruitment of few new researchers is an additional proof of the quality and attractiveness of this scientific environment.

Very well organized, the PhD students markedly enhance the interactions between teams. The recruitment of a larger number of postdoctoral fellows will not only contribute to the scientific production, help to develop new techniques or conceptual approaches, but will also facilitate interactions between research teams as observed with PhD students.

As already indicated, depending on the historical background of the teams, differences exist in the total number of persons and the repartition of ITA among the different teams. The presence of only one technician or their complete absence in some teams is indeed a limiting factor for their productivity of these teams. The redistribution of some researchers leading to the creation of a new team (as observed for team 11) or the transfer of some technicians or engineers in technical platforms seems to be one strategy of the Unit to progressively reduce these differences. Nevertheless, an effort should still be made for teams completely devoid of technicians. As revealed by the visits of technical platforms or the meeting with the ITA, the engineer and technical staff seems well experimented and motivated. In general, the ITA's are pleased with their interactions with researchers and their working conditions. However, some of them who do not benefit from a permanent position are anxious for their future (which unfortunately is a general problem, not only for ITA but for young researchers as well).

Main lines of the scientific strategy have already been extensively discussed. In addition, the Committee agrees with the policy of internal mobility, which has led to the change of the team 5 Director or the emergence of team 11. The actual team 5 Director will retire during the next four-year term and is thus not allowed to lead a team during the next full-year term. The proposal of the new Director is a natural process of succession. This new Director is expected to have all the qualities required for this important responsibility. Due to a difference of views on the management of the Animal MRI Facility between the past coordinator of the platform and the GIN Director, this coordinator resigned from his role as pilot of the platform, and a new coordinator (team 5 researcher) was appointed in october 2009. Team 11, which is constituted by competent researchers and clinicians and has an original and interesting project, will reinforce the third transversal research axis.

The committee has also appreciated the Director decision to keep enough laboratory space for the recruitment of one or two external research teams. These teams should be outstanding to significantly enhance the Unit visibility. Therefore, the Unit should avoid a too rapid growth and keep enough space available for the development of the strategy of the future Director.

In this context, the recruitment of the young team13 on the basis of its selection (ATP/avenir grant) and original project, which should closely collaborate with team 1, should not have too much incidence impact on the laboratory space. However, for the reasons mentioned above, the creation of another emerging team on a distinct new project (proposed team 12) is questionable (or at least seems to be too premature). It can be understood that the teaching policy of the University will benefit of the presence of a new teaching researcher (proposed leader of team 12, who has interesting publications), but his integration in one of the teams of the first transversal axis 1 (according to modalities which have to be defined) appears highly preferable.

- Appreciation on the project:

Altogether, due to the competence and past contributions of several teams and to the new developed scientific strategy, the interesting and stimulating overall project of the GIN is convincing and should be encouraged and supported.

There are some cutting edge projects due for instance to the availability of several original animal models, to the efforts made to apply the neuro-stimulation method in epilepsy, or neuro-degenerative disorders other than Parkinson's disease or even psychiatric disorders, and to the existing capacities to develop new methodologies for clinical applications. However, the originality of the projects depends on the national and international competition. In this context, the projects of several teams could have also been presented in perspective with the main research lines of the most important competitive national or international teams.

Two factors should contribute to the feasibility of the project in four years: ensure strong and coordinated collaborations between the teams in the transversal axis and reduce the too high number of projects in several teams.

In addition to the diversified qualifications of the researchers and clinicians and the high motivation of students, the working facilities, the technological environment, the financial resources and the dynamics of the Unit, will undoubtedly contribute to the project feasibility.

4 • Appreciation team by team

Team 1: Pathophysiology of the cytoskeleton

Team leader: Mrs. Annie ANDRIEUX

- 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)	11	11
N3: Number of other researchers (Form 2.2 and 2.4 of the application file)	0	0
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	6	6
N5: Number 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 2.7 of the application file) Temporary researcher	4 1	5
N7: Number of staff members with a HDR or a similar grade	7	6

- Appreciation on the results

The team has developed two main axes, respectively on tubulin tyrosination (a reversible modification of the C-terminal end of alpha tubulin), and on the neuronal MAP STOP protein. In the first thematic, they have demonstrated a critical role of tyrosination in protein interaction and microtubule stability. Abolition of tubulin tyrosyination leads to post-natal lethality together with significant alterations of neuronal development (proliferation, morphogenesis). In 2002, this team has demonstrated that STOP gene inactivation induces brain functions and behavioural deficits, which can be reversed by antipsychotic treatments. They now show a similar effect of the tubulin-stabilizing agent Epothilone D in STOP null mice, suggesting its new and original application for the treatment of psychosis. Thanks to numerous collaborations, they have further characterized the neurological alterations of STOP null mice both at the functional and anatomical level, and have initiated a detailed cellular and molecular analysis of STOP functions, including the role of post-translational modifications and the identification of molecular partners.

The overall level and number of publications are good, sometimes in high impact journals, but the productivity might be further improved in regard to the size of the team. One can note that the recent publications signed in first or last position by a team member mostly relate on the tubulin tyrosination axis.

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

The team has acquired a clear international visibility, illustrated by various fruitful collaborations with national and international laboratories. In addition, because of the setting in which the research is performed, with all the

facilities and the possibility for close collaborations with other teams within the GIN or in Grenoble area (iRTSV), this team should be an attractive workplace for PhD students. A specific effort has to be made for the recruitment of Post-doc students, which is presently unusually low.

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

In accordance with the large size of the team, the internal management is well developed, both for the scientific organization and for human resources. Due to the close proximity of their research projects, it is expected that this team will have a predominant role in the integration of the new Team n°13 within the GIN, which will benefit from the ongoing collaborations between the two teams.

- Appreciation on the project

The project, in continuity with the previous work, will be structured according to the same two axes, STOP proteins and Tubulin tyrosination. For the first one, most of the tasks will be dedicated to the molecular and cellular dissection of STOP functions in the nervous system revealed by the pleïotropic phenotype of STOP null mice. The relevance of the latter mouse strain as an animal model for psychiatric disorders will be further explored through collaborations within the GIN. The general function of tubulin tyrosination in microtubule dynamics and intracellular transport will mainly rely on the use of yeast models.

- Conclusion :

This team, possessing a unique expertise in cell biology, has developed during the last years an original line of research centred on the role of the microtubule network in brain function and brain development. Its insertion within the GIN is thus fully justified and together with the proximity of the CHU, this will help the team in its desire to develop a more clinical research. The strategy extending from powerful yeast unicellular model to live animals is convincing. From this point of view, the study of tubulin tyrosination in brain development would deserve more attention in the project, even at the expanse of the too diverse projects on STOP proteins. The team will occupy a pivotal position for the integration of the original in vitro approach of the microtubule network within the GIN.

Team 2: Neurodegeneration and plasticity

Team leader: M. Remy SADOUL

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	4	3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	3	3
N3: Number of other researchers (Form 2.2 and 2.4 of the application file)	0	0
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	3	3
N5: Number 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 2.7 of the application file)	3	3
N7: Number of staff members with a HDR or a similar grade	4	4

- Appreciation on the results

The originality of the research program is high, with a particular interest for the molecular mechanisms which control the endocytosis and how cytosolic proteins could interfer with endosomal sorting, focusing on the function of CHMP2B, an endosomal sorting complex required for transport (ESCRT) and Alix, an adaptor protein which binds with ESCRT (discovered by this group), involved in the control of the apoptotic cascade and finally in the mechanisms through which exosomes could influence synaptic activity/remodeling.

45 publications, 6 reviews and 4 book chapters

H index 29, average citation 82, 4432 citations with 12 papers cited up to 100x. Publications are of high impact factors including 2 Nature Cell Biology 2005, 1 J. Neuroscience 2006 and 2 J. Biol Chem 2005-2008. However, most of these publications, 2 NCB, 1CDD, 1 HMG with only one author from this team neither as first nor senior author. The team leader is senior author in paper published in Biochem Soc trans 2009, Autophagy 2009, J. Biol Chem 2008, BBRC 2008, MCNe 2006, JN 2006,

Collaborations with national as well as several international groups.

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

790 KE of grants obtained during the last 4 years period, including those from ARC, AFM, ARECA, FRM ..; No European grant. ANR co-PI 106 KE ESCRT budding (2009)

- Appreciation on the project

In line with the previous orientiation of the team, the project has 3 complementary objectives.The first aim is to analyze the molecular mechanisms linking endosome intermediates, Alix protein and neuronal apoptosis, This might bring interesting openings in the field of neurodegeneration, and the recent recruitment of a young CR2 will ease the development of this part of the project. In the second part of the project, the influence of endosomal transport proteins on dendritic spine and synaptic plasticity will be analyzed using electrophysiology and videomicroscopy, and the interactions between the different components of endosomal complexes will be deciphered by taking advantage of C Elegans genetics. The third part of the project is centered on exosomes, and their role in normal and diseased nervous system. Although exosomes is a very active field at the moment, the project, which will check the possibility that miRNAs and RNAs might be released through exosomes, then characterize these RNAs through a transcriptomic approach will be of interest. The project development will benefit from the expertise revently acquired by two team members, on C Elegans model (researcher who just comes back from a two years training period in Oxford). and synaptic receptor trafficking (researcher who is currently doing a sabattical stay in Bristol, where he acquires this expertise).

The project is solid, original but not risky, and its feasibility is good.

- Conclusion :

The project is well organized, based on important data obtained some years ago by the team. It deals with important aspects of cellular biology and might open to pathophysiological mechanisms involved in neurodegeneration, through collaboration with team # 9.

Strategy and team direction are solid, and the recent expertise acquired by two team members will help the development of the project, as well as the recent CR2 recruitment

The level of publications is relatively modest for a rather big team, and this is certainly a weakness of the team.

Lack of post-doctoral students is a concern.

Team 3: Calcium channels, functions and pathologies

Team leader: M. Michel DE WAARD

- 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)	5	3
N3: Number of other researchers (Form 2.2 and 2.4 of the application file)	0	0
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	0
N5: Number 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 2.7 of the application file) Temporary researchers	5 1	2
N7: Number of staff members with a HDR or a similar grade	4	2

- Appreciation on the results

The main research line of team 3 is the study of voltage-gated calcium channels, their functions and associated pathologies. Its leader has carried out seminal works in calcium channel regulation by auxiliary subunits and G-proteins and he has a world reputation in this field.

During the past four years, team 3 has pursued many original objectives related to sperm ion channels, excitation-contraction coupling in muscle cells and excitation-transcription coupling in neurons, as well as structure-function of calcium channels and cell penetrating toxins.

The track record is excellent with more than 53 publications and reviews. 26 of them have been signed by a team member as first or last author in very good (J Neurosci, J Cell Sci, JBC, BBA, Dev Biol) to excellent (TIPS, JCI in press) journals.

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

Some results have a strong potential for valorization as testified by two patents and the creation of a business unit on toxin synthesis.

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

The team is being reorganized. The researcher who is coordinating the project on sperm ion channels will start its own independent group, and the subproject on excitation-contraction coupling will stop soon. The team will be composed of 3 full-time researchers with permanent position (2DR/1 CR), 2 PhD students and a post-doc.

- Appreciation on the project

The research project is focused on three aspects with high potential: G-protein regulation of calcium channels, gene regulation by calcium channel beta subunits and cell penetrating maurocalcine as a novel vector for innovative therapeutics. For each objective, a number of promising data have already been gathered.

- Conclusion :

In summary, this is a strong group. Its focusing on a limited set of research lines should help it to answer less, but specific and high-impact questions. For its future development, this group should aim to reinforce its workforce. The Institute should also consider the necessity to provide this group with a technical help.

Team 4: MUSCLES AND PATHOLOGIES

Team leader: Mme Isabelle MARTY

- Staff members

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

- Appreciation on the results

This new team, created in 2007, has emerged from the former laboratory of partner 3. It is composed of 2.5 permanent researchers, 1 MCU-PH, one PU-PH (part time), one ITA and 5 PhD students including two MDs. The thematic of the team, centred on the study of the muscle and its pathologies, might appear in some respects divergent from the dominant Neuroscience thematic of the GIN, but clearly fits in the cell biology approach shared with teams 1, 2 and 3. Although dedicated to different pathologies, the team is conducting a multidisciplinary approach gathering basic and clinical research, which is one of the main strength of the GIN.

The thematic is subdivided in two axes that correlate with the basic and clinical research approaches respectively. The first axis has focussed on the study of triadin, a family of proteins belonging to the multiproteic complex responsible for the excitation-contraction process. Following the characterization of the Triadin gene family and the production of their K.O. mice, the team has demonstrated the involvement of these proteins in the function and the ultrastructure of the skeletal muscle. This same multiproteic complex is also the target of several rare genetic myopathies. In the framework of a large French consortium headed by the team leader, the phenotypic

analysis of the mutations responsible for these diseases have been initiated, starting with the setting up of myoblast purification and culture from patient biopsies.

In the context of a young team, the level of publication is good but may be improved in the next years: Since 2005, twelve articles have been published with a member of the team signing in first or last position (Human Mol Gen; J Biol Chem, J Gen Physiol for the best ones); more than thirty other collaborative papers have been published. It is worth noting though that the publication of the triadin K.O. mice by a concurrent laboratory has significantly impacted on the publication of this work.

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

In two years, this team has acquired a clear visibility in its field of expertise, illustrated by the coordination of an ANR program “Maladies Rares” by the team leader and by regular invitated conferences in international meetings.

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

The global management is good but the provisional budget for 2010 emphasizes the need of raising new funds.

- Appreciation on the project

The project mainly consists in the continuation of the 2 main axes. The function of triadin will be further explored, either in cellular models by gain or loss of function strategies with a specific interest for its role in the organisation of the triad complex, or by the functional analysis of skeletal and cardiac muscles in triadin null mice. The phenotypic analysis of the pathological mutations will include physiological studies on human myoblasts and expression analysis. As a first therapeutic attempt, exon skipping strategy will be applied to a subset of myopathies that result from aberrant splicing. A new collaborative project that consists in the design of devices promoting in vitro muscle differentiation will be initiated, in order to analyse this process in pathological situations. Although each task of these projects is attractive, the significant diversification of the projects has to fit with the overall manpower and might necessitate establishing some priorities among them.

- Conclusion :

Following a successful emergence, this team has obtained a good reputation in France and at an international level. This is the only team in France able to ensure a genetic screening aimed at the Ryanodin receptor and the team director plays a piloting role in the related ANR network and has participated to high standard meetings such as Gordon conference or Biophysical Society. Nevertheless, in priority, the level of publication could be improved. This might require focussing on fewer projects, unless additional confirmed researchers or post-docs are recruited and more grants obtained. Due to the specificity of the thematic among the GIN, the promotion of internal collaborations whenever possible would further improve the integration of this promising team within the institute.

Team 5: Neuroimaging and Brain Perfusion

Team leader: M. Emmanuel BARBIER

- Staff members

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

- Appreciation on the results

After a 40 minutes presentation by the candidate team leader, including a short exchange with the committee, some members visited the MRI facilities. On the afternoon, the Evaluation Committee, in a closed door session, briefly discussed its impressions about the center and identified strengths and weaknesses of each of the research teams.

The proposed team 5 is in line with the group founded by A.L. Benabid and M. Decorps, later run and developed by the latter and then by C. Segebarth. It moved a few years ago from its remote location to the actual building hosting the GIN. The researches of this renowned group have been mostly oriented towards the development and the applications of in vivo magnetic resonance spectroscopy and imaging focusing on brain, initially in small animals (rats and mice) then later in humans. Its activities heavily rely on the MRI and animal facilities.

Important remark: The "mother" research unit and its surroundings have been recently reorganized (i.e. 1) relocation, 2) splitting of the research team and the animal MRI platform, and 3) newly appointed director).

The scientific production reported in the documents is good but the list provided seems to contradict the foreword stating that the past activity reported is the one of the team candidate but does not cover the activity of the current team 5.

- Appreciation on the attractivity

The results produced so far are of excellent quality and have led the original team to an international recognition.

- Appreciation on the project

The scientific quality of the team members is excellent, its research program is (maybe too) ambitious and manifold.

- Conclusions

  - Strengths and opportunities

The evaluators have appreciated and confirmed the SWOT analysis provided by the team. In summary: the integration of the team to the GIN is a real opportunity to integrate excellent and complementary competences in the field of neurosciences. The vicinity of the MRI platform with its existing and future (2 human 3T MRI) up-to-date instrumentations is another “plus”.

  - Weaknesses and threats

Similarly, the evaluators confirm the threats arising from the forthcoming retirements of the senior leaders of the team and of the animal MRI platform. They also want to stress that the number of projects might be too large with respect to the size of the group. On the other hand, the level of international contracts should be increased since it is favorable, both from a scientific point of view and from a financial one.

  - Recommendations to the head of the research unit

So far, the group has been efficient and productive with innovative research topics. For the next project, the group is likely to work with a staff reduced as compared to what it was in the previous period, while its aims are still ambitious. A strong component of research carried on humans is expected. The quality insurance of some processes, as initiated by the previous directorship should be pursued.

The period to come will be a challenge for this group which will have to keep its international visibility so far largely guaranteed by its previous director.

Team 6: Synchrotron Radiation and Medical Facility

Team leader: M. François ESTEVE

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	5	5
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	5	2
N3: Number of other researchers (Form 2.2 and 2.4 of the application file)	0	1
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	6 *	5
N7: Number of staff members with a HDR or a similar grade	7	7

6* stands for 6 students obtained their PhD in the last 4 years

- Appreciation on the results

By definition this team is built around the purpose of the utilisation of this big scientific instrument, which is the ESRF. This team has thus the unique opportunity of having a dedicated medical line sitting 15 minutes from the GIN building. Team 6 then stands at the interface between physics, biology and medicine in order to take benefit of this very bright source of X Rays, potentially very selective, between 10 and 100keV. The field of activity of the group is Imaging, Radiotherapy and Cerebral Tumours. It has obtained original results and methodological developments in fundamental radiation biology, in preclinical studies on rodent models of tumours with heavy elements coupled to radiotherapy. Interesting methods in nanochemical imaging of metals in the context of cerebral diseases have been developed.

The scientific production includes 75 papers in the best international journals of the field, which is very good for a small group. It is worth noting that half papers are leaded by the group itself, the second half showing the high degree of collaboration in which the members are involved. About 30 papers issued in collaboration with other teams from GIN complets this count.

As an effect of “big instrument community”, strong and stable partnerships are conducted with other equivalent centres in Europe, North America or Australia.

We can also felicitate the team for its ability to set up clinical trials regardless of the difficulty of setting up the regulatory and administrative files.

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

Senior members of the group have an international audience in their field and are regularly invited in conferences and international committees or expertise. One of the members has obtained the Peyre prize from the National Academy of Science. One of the team member has been requested to participate to the development of the Etoile Center in Lyon.

In the context of international network of synchrotron facility, one could expect a more important flux of foreign students, post doc and visiting professors. This should be a point to reinforce. As the whole GIN, the group benefits from a good regional support. An ANR funding is mentioned. The socio economic impact is reduced, it can be seen through a CIFRE industrial funding of a thesis in the field of dosimetry. Regarding direct impact on health care, it is clear that the synchrotron facility has to be used to make proof of concept and small clinical validation. Then, the next step has to be taken by technological companies to set up hospital compatible devices.

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

Obviously the team has two feet, one in the university environment, the other in the ESRF but this does not seem to raise any difficulty. This was very easily seen during the ESRF visit, as well as the very good integration of team members and their high level of support into this structure. The group is one of the founding units of the GIN in 2007 from a pre-existing structure. Its size does not justify special communication policy. The senior members are strongly involved and often conducting teaching actions at master level in the local university and engineering schools in Grenoble while also giving regular talks in other education centres in France. Their contribution to the local organisation of research at the physics medicine interface plays a significant role.

- Appreciation on the project

Considering the project, one of the key issues is the departure of 3 full time scientists. According to the team, this will not have a large impact due to the subjects and the incoming local collaborations. However, these departures must be analysed deeper since there is a risk of a decreased initiative potential in research programs.

The proposed program is in the continuity of the existing experience and will take full profit of the high degree of existing “know how”. It is focused first on the important issue of radiation cerebral therapy with many aspects being considered: BBB, high Z metals dose enhancement, micro beams for micro surgery of epilepsia. The second main track is nano-chemical imaging with different sub-projects. The themes are really relevant and there are not many such groups in Europe who can address them. Many of these projects being in collaboration, it is uneasy to state about the capacity of the reduced team to hold this in parallel. A special effort in funding for recruitments will be probably be a good guideline.

- Conclusion :

Team 6 has proved to be able to conduct under the coordination of its chief a very good level of scientific achievement and internationaly recognised skill in using the synchrotron radiation X ray source. Their neurology orientated research is well integrated in the GIN context with other teams especially along the axe 2 of neuro-oncology and at a lesser extent with team 9 in technological innovation for epilepsy. The group has a very large experimental background from cell to patient irradiation and radiobiology and a significant competitive advantage compare to other groups that just take advantage of synchrotron facilities for short campaign experiments.

Aside these strengths and opportunities, the departure of full time researchers may weaken the team. This, with the number of engaged projects in a highly competitive domain raises the question of its capacity to be reinforced shortly. International exhanges should be reinforced as well as funding for post doc preparing recruitments Being engaged in a too large number of collaborative tasks may alter the team identity.

The activity of this team unique in France is worth being strongly supported.

Team 7: Nano medicine and brain

Team leader: M. François BERGER

- 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)	3	5
N3: Number of other researchers (Form 2.2 and 2.4 of the application file)	7	5
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2	2
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	3	2
N6: Number of Ph.D. students (Form 2.7 of the application file) Temporary people	11	16
N7: Number of staff members with a HDR or a similar grade	8	9

- Appreciation on the results

This is a very active, creative team that focuses on neuro-oncology but develops within this area a relatively wide range of activities. A particularly strong point is the (further) development and application of cutting-edge technology (e.g. 'microNanoHarvesting strategies'). The team leader appears to function at the forefront of 'nano-medicine' in France. The team has close collaborations with several other teams within in the GIN and with other (local) organizations/institutions. The research performed by this team has a strong translational character. The team is eager to bring their preclinical findings to the clinic. Several findings of this team were patented, and negotiations with industrial partners are ongoing to commercialize (some of) these findings.

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

This team provides an exciting environment for those interested in neuroscience (esp. neuro-oncological) research. The team has strong links with local and national partners, but the international links seem to be less well developed. The research performed is very promising, but the exact clinical impact remains to be seen.

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

The team has developed a range of research projects, mainly within the area of neurooncology, with a good amount of funding. The team thus seems to be flourishing. Potential threats are a lack of focus (too many diverse activities for the number of people), problems with finding adequate (industrial) partners for further development and implementation of their findings, and the occurrence of negative side-effects when introducing their novel approaches in the clinical setting.

- Appreciation on the project

This research performed by this team is of very high quality, focusses on clinically highly relevant topics, and provides an exciting environment for (PhD) students and post-docs. One could argue that the research projects of this team are too diverse and that a more focussed approach would help to translate their findings into the clinic in an earlier phase.

- Conclusion :

  - Summary:

This is an excellent, productive team with a lot of creativity, a strong translational character. The expectation is that this team will succeed in bringing at least some of their findings into the clinic soon.

  - Strengths and opportunities:

Strong translational character; well embedded within GIN; good partnerships with (local/national) organizations/institutions outside GIN; high potential to 'industrialize' their findings and thereby provide funding for future research

  - Weaknesses and threats :

Delay in bringing findings to bedside because of problems with industrial partners, negative/toxic side effects, ethical considerations etc.;Lack of focus/too many projects/activities/ideas for the number of people in this team.

  - Recommendations :

May be try to focus a little bit more.

Team 8: Stress and neuro-digestive interactions

Team leader: M. Bruno BONAZ

- 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)	0	0
N3: Number of other researchers (Form 2.2 and 2.4 of the application file)	3	3
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	1
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	2
N7: Number of staff members with a HDR or a similar grade	6	5

- Appreciation on the results

Relative to the output of other teams of GIN, the output of original papers by research team 8 in the past period (2007 – 2010) has been rather low. However, this fact needs to be judged against the small size of the team, the lack of full-time researchers and the very small financial contribution from the GIN budget. Clinical and teaching duties appear to significantly curtail the contribution of the team members to research. A strength of the research work is its translational nature, the project being informed by clinical observations and feeding back on clinical practice.

- 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 an internationally well respected researcher, as evidenced from invitations to speak at international conferences and to write a review in Gastroenterology, the first journal in his field of research. This indicates that the team's research projects are at the forefront of contemporary neuro-gastroenterological research. The team has attracted several Ph.D. students and a number of relatively small local and national grants. The research performed by the team has the potential to be further integrated in GIN's research community, e.g., by interacting with teams using functional brain imaging and with the team using vagal nerve stimulation for epilepsy management.

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

Despite its small size and limited resources, the team is well structured and very ambitious in performing a relevant contribution to GIN's overall translational research strategy. The research projects of the team are focussed, and their overall impact is very likely to grow substantially if the support by GIN is enforced. It is important to note that all members of the team are clinicians with time-consuming hospital and teaching duties, which reduce their research disponibility.

- Appreciation on the project

The research projects (anti-inflammatory vagal reflex, role of corticotropin-releasing factor in the impact of stress on the gastrointestinal epithelium, brain-gut interactions involving the autonomic nervous system and the hypothalamic-pituitary-adrenal axis) are well developed and focussed and address cutting-edge research questions of contemporary neurogastroenterology.

- Conclusion :

  - Summary:

This is an ambitious team with a focussed project of strong translational character.

  - Strengths:

The team pursues a translational project with important and clinical implications.

  - Weak points:

The full impact of the team is curtailed by its small size, the lack of full-time researchers and the limited external funding.

  - Recommendations:

The team should be encouraged to seek increased support by GIN (full-time researchers) and national research agencies, to expand its collaboration with other GIN teams and, by these measures, to increase their scientific output and impact.

Team 9: Dynamics of synchronous epileptic networks

Team leader: M. Antoine DEPAULIS

- 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)	2	2
N3: Number of other researchers (Form 2.2 and 2.4 of the application file)	1	1
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	6	6
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)	1	1
N6: Number of Ph.D. students (Form 2.7 of the application file) Temporary researcher	5 2	6
N7: Number of staff members with a HDR or a similar grade	5	5

- Appreciation on the results

The general objective of the team is to understand the processes through which neurons generating epileptic seizures get synchronized just before a seizure and how these processes developed during epileptogenesis.

During the last four years, using mostly EEG recordings and fMRI, this team has identified the neuronal networks generating and propagating seizure in animal models of absence epilepsy (GAERS) and of mesiotemporal lobe epilepsy. In this latter form of epilepsy, their clinical data indicate the presence of several types of generators and have led to the description of a new form of the disease involving neighboring regions of the temporal lobe. In the two animal models, the team has also shown that circuits of the basal ganglia modulate the activity of the seizure generators and their most recent results suggest a modification of the dopaminergic tone in the model of absence epilepsy.

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

These results have led to the publication of more than 20 original articles, signed by a team member as a first or a last author, in good to excellent revues (PloS in Biology, Brain, Journal of Neuroscience, Neuroimage…). In addition, a large number of other original articles have been published in collaboration with other teams of the institute and with other laboratories. This excellent production had an important impact in the field of epilepsy and the team has recently acquired a good international visibility as evidenced by a large number of invited conferences during the last 3 years. This visibility and the ability of the team to raise regional, national (ANR, FFRE) and international (FP6) funds should allow them to attrack and recruit more young scientists, in particular from abroad.

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

The strategy and management of the team are very good. The coordinated activities of experimental physiologists and clinicians within the team are particularly relevant in the general organization of the research institute which aims at increasing the impact of its clinical and basic research activities. The communication of the team is good, with several team members involved in education and communication activities.

- Appreciation on the project

The current project of the team is focused on the role of astrocytes in regions of seizure generation, on that of basal ganglia in modulating seizure generators and the influence of cognitive and sensory processes in favoring the development of seizures. These ambitious projects will rely on the use of new techniques available in the unit (Two photon microscopy and calcium imaging) and on several collaborations within and outside the unit and bears great potential for even more significant contributions in the coming years in the field of epilepsy.

- Conclusion

This is a strong and mature team. Its visibility in the field of epilepsy, in both clinical and basic research domains, is very good. In light of the originality of the project, there is no doubt that the high level of publication will be maintained in the near future. Yet, recruiting more postdocs may lead to an even greater production and impact of the team.

Team 10: Dynamic and physiopathology of basal ganglia

Team leader: M. Marc SAVASTA

- Staff members

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)		3
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)		2
N3: Number of other researchers (Form 2.2 and 2.4 of the application file)		2
N4: Number engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)		3
N5: Number engineers, technicians and administrative staff without a tenured position (Form 2.6 of the application file)		7
N6: Number of Ph.D. students (Form 2.7 of the application file)		5
N7: Number of staff members with a HDR or a similar grade		

- Appreciation on the results

The team leader was in 2003 founder and director of a University Young Research team (CJF RNT 2414) and founder in 2005 of the Inserm Unit 704 “dynamic of neuronal network” to become now a group leader of team 10 “Dynamic of neuronal Network and Movement” of the GIN.

During his career that started in 1986, he has published 61 articles in peer review journals and 16 book chapters. His H factor is of 27.

The team works on four projects, namely:

Project 1: Motor aspects of Parkinson's disease related to STN-HFS

Project 2: Role of neuron-glia interactions in the basal ganglia output network

Project 3: On motor aspects of Parkinson's disease, Apathy and dopamine dysregulation syndrome.

Project 4: The role of the subthalamic nucleus within the basal ganglia network

Publications are of good to very good level including a number of papers in top journals in the general field of Neurosciences field such as J. Neuroscience (2009, 2008, 2006, 2005), 2(1*) in Brain (2007-2010), 2 in Ann. Neurol*, 1 in Lancet*, 5 in Lancet neurol* and 1 in NEJM*. The latest being mainly clinical papers (*). No patent so far.

The committee is confident, and hopeful, that the ongoing strategies of research should significantly improve the publication record of this team to reach more generalized journals in the next few years.

The team has directed 5 PhD students from 2006 to 2009. It was financed by several grants these last four years: ANR, private research contracts for a total of around 1.9 millions euros during the least 4 years.

Grants for the provisional budget 2010 are from: Michael Fox foundation 83 KE; Association France Parkinson: 30 KE, regional council, Neurodis 120 KE etc….

Thus, the team can gather grants efficiently, even at the international level, to allow for the projects to be fulfilled.

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

The team seems to be well recognized at the international level and attracted several young researchers recently including two INSERM full time researchers and potentially an assistant professor in the near future.

Members of the team were invited to dozen of seminars and conferences per year, but mainly for clinicians.

They have a large number of national and international collaborations validated by co authorships

The team manager has always been a member of a number of national and international committees, including INSERM CSS5, French Parkinson Foundation, and more recently of CSS1 Inserm (Neurosciences).

In 2004, he received the Foundation NRJ-Institut de France national award and in

2004 and 2009, awards from the France Parkinson Foundation.

The team has participated in a number of ANR grants, national grants and PHRC (over 10 the last 4 years) for a total of around 1900 KE from 2005 – 2010. However, the team has few contracts with drug companies

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

The team manager is the director of the doctoral School of chemistry and life sciences at Joseph Fournier University. Number of members of team 10 are involved in students training, with 7 PhD students during the last 5 years and 2 post doc. Five members of the team are involved in different training, masters to graduate school.

- Appreciation on the project

The project if well focused, relevant with knowledge in the field and the actual clinical situation. All methods, tools are available in the team to address most of the points of the proposed program.

The research program is well presented, and more focused when compared to the number of projects developed during the last 4 years, with transversal approaches from molecular biology to behavioral and clinical studies. A particular interest is set on the pathophysiology of Parkinson Disease and how high frequency stimulation could influence outcome of PD patients. It is interesting to note that this team is planning not only to validate the use of HFS for PD but also to combine integrative approaches to further understand how HFS may influence brain functions including NMDA receptors signaling, crosstalk between neurons and glial cells, dopamine-dependent pathways. Part of the program will be open to general functions of the STN, including interactions between motor, cognitive and emotional functions.

The interest of this research program is how questions will be addressed from molecular to functional events, from bench to bed by a group with a long lasting and internationally recognized expertise in the field. Among the questions that will be addressed: How does DBS affect individual neurons? What are the neuronal elements to mediate the effects of DBS? How does DBS affect neuronal networks? Results should provide not only basic knowledge of the pathophysiology of the basal ganglia but also knowledge to improve the use of HFS for clinical use, including for example, how intensity, frequency of DBS could be modulated with time to improve functional recovery.

New axis of research will be also developed including research to understand how dopamine-dependent pathways may influence neuronal network controlling apathy, depression or anxiety. In summary, the team leader has all the scientific knowledge and know how to perform this project. The project, after fullfillment will surely yield interesting and exciting new concepts in the field of Parkinson's disease.

- Conclusion :

It is important to note that the team proposes an interesting project. They have made key findings the last 4 years. This is a well established team with a strong potential in the field.

– Weaknesses and threats:

This team is working with a group of clinicians considered as leaders in the field. However, it did not appear clear to us how basic scientists and clinicians are collaborating to publish common papers. This point should be improved in the next few years with the help of two recently recruited INSERM researchers (CR), post-doctoral fellows and the expected recruitment of an assistant professor.

– Recommendations:

To take more risk in innovative projects. Consolidate the interactions with the clinical part of the team.

Team 11: Brain function and neuromodulation

Team leader: M. Olivier DAVID

- Staff members

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

- Appreciation on the results

This is one of the emerging teams of the unit which brings together members of the former teams 5, 7 and 10 and of the Psychiatry department of the Grenoble University Hospital. The team will be composed of 6 permanent researchers, assistant professors, professors and clinicians and 4 PhD students. The previous activities of the team members were centered on the functional characterization and the modulation of neuronal cerebral networks in different pathologies such as epilepsy, motor disorders and psychiatric diseases. Since 2005, 20 original articles have been published with at least one of the team member as first or last authors in high to low impact journals (PloS biology, Brain, Neuroimage for the best ones). Eight of these articles have been published by the team leader and altogether, considering articles in collaboration, more than 60 articles have been signed by the team members during the last 5 years. This is a solid production which relies on a very good knowledge of the studied models and the dynamism of the team leader, who has received an excellent training in both physics and biology, and occupies a central position in many collaborative projects developed by different teams of the institute.

- Appreciation on the project

The objective of the new team is oriented toward methodological developments in translational research aiming at improving the use and efficacy of brain stimulations in different brain disorders. The approach will rely on the use of invasive and non-invasive electrophysiological recordings, anatomical and functional MRI, modelling of dynamic systems, electrical deep brain stimulations and transcranial magnetic stimulations. The idea is to characterize precisely brain activities in different human neuropathologies and in animal models (mostly monkeys) and then to develop adaptive protocols of stimulation in order to modulate efficiently these activities. On the long term, the objective is to integrate these protocols in future neural implants. This is a very interesting and ambitious project which should be supported. The visiting committee, however, felt that it would have been more appropriate for this new and relatively small team to focus on a more limited number of models and diseases. The many collaborations of the team within the institute should also call for actions to transfer rapidly the new tools developed by the team to the other users. On this matter, the recruitment of an engineer would help this team which hosts only one technician, with no permanent position, in charge of the monkey colony.

- Conclusion :

On the basis of the previous activities and on the expertise of the team members, there is no doubt that this new team will be productive in the near future. Moreover, the ambitious objective to develop methodological approaches to modulate brain activity is particularly relevant in the overall strategy of the institute. A more precise roadmap on a limited number of projects may help this new team to achieve more rapidly this objective.

Team 12: Neuropathology and synaptic dysfunction

Team leader: M. Alain BUISSON

- Staff members

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

- Appreciation of the results

The research expertise of the team leader is towards the implication of exitoxicity, mainly glutamatergic) in neurodegenerative disorders. He concentrated his efforts in understanding and characterizing the roles of NMDA receptors both at the synaptic and extrasynaptic levels.

The publication record of the team leader, when settled in Caen, is of very good quality, and the journals where he publishes are of high impact factor (J Neurosci, JBC, FASEB, FEBS, J Neurochem…).

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

Not relevant, as the team leader is just moving to Grenoble

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

This team is a new team that was created following the recruitment of the team leader at the Grenoble University in September 2009. It is currently composed of the team leader, a post-doc and a PhD student. The team leader still shares his time between Caen, where he is based, and Grenoble for this academic year 2009-2010.

Among his duties in Grenoble, he is expected to set up the Neurosciences teaching and for this he will be helped by the future recruitment of an assistant professor shortly.

- Appreciation of the project

The project that was presented to the committee in written and during the presentation, did not appear to be mature enough and the main aims are not very clear. Among the aims presented, it was proposed to study the influence of actin in the synaptotoxicity induced by A¤, and by analyzing the different conformations of A¤. The study will use fluorescent proteins expression following transfection and calcium imaging techniques. A second aim is directed towards the role of endosomes in the penetration of A¤ proteins in neurons in collaboration with team 2. Moreover, the influence of the Tau protein in the cytosqueleton modifications will also be investigated using videomicroscope and the FRET technique in collaboration with team 1.The effects of molecules acting on the polymerization of actin, which are potential therapeutic candidates, will also be investigated. The originality of the project is questioned especially in light of major competition with international teams.

- Conclusion

We estimate that the whole project is not well centered especially given the size of the team and the fact that it needs time to grow and settle in Grenoble. Moreover, the team leader will be expected to have significant teaching duties and responsibilities. The feasibility of these projects by an independent team appears hazardous at best, despite the numerous and appropriate local collaborations.

Furthermore, the originality of the project is questioned especially in light of major competition with international teams.

In conclusion, the committee is well aware that this is a starting team that should be encouraged to settle down in Grenoble and grow into a full team. However, it seems to us that creating an independent team immediately is a risky move and we encourage instead the team leader to explore the possibility of joining team 2 or 1 at least until the team is mature enough and of sufficient size to become independent. Given the publication record of the team leader, the commitee confident that this will eventually occur in a short term.

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

Nom de l'équipe : Pathophysiology of the Cytoskeleton

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

Nom de l'équipe :Neurodegeneration and plasticity

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

Nom de l'équipe : Calcium channels, functions and pathologies

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

Nom de l'équipe : Muscle and pathologies

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

Nom de l'équipe : Functional neuroimaging and brain perfusion

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

Nom de l'équipe : Synchrotron radiation and medical research

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

Nom de l'équipe : Nano medicine and brain

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

Nom de l'équipe : Stress and neurodigestive interactions

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

Nom de l'équipe : Dynamics of epileptic synchronous networks

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

Nom de l'équipe : Dynamics and physiopathology of basal ganglia

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

Nom de l'équipe : Brain function and neuromodulation

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

Nom de l'équipe : Neuropathology and synaptic dysfunction

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

Nom de l'équipe : Molecular mechanisms of microtubule regulation by neuronal maps

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

PRESIDENCE

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UNIVERSITE JOSEPH FOURIER
SCIENCES.TECHNOLOGIE.SANTÉ
GRENOBLE 1

Grenoble, March 30th 2010,

AERES
Mr. Jean François Dhainaut

Subject : Comments of University Joseph Fourier Grenoble 1 on AERES preliminary report
Grenoble Institute of Neurosciences » (GIN) – UMR_S 836 – Head : Claude Feuerstein

Mr. Chairman of the visiting committee, Dear Colleague,

We have examined the preliminary assessment report dated March 17th 2010 for research unit :
Grenoble Institute of Neurosciences » (GIN) – UMR_S 836

On behalf of the University and all members of this laboratory, we would like to express our thanks for this thorough assessment.

We thank the committee for the quality of the reviewing procedure that has been conducted despite the restricted time given to the reviewing process, particularly along the on site visit. The quality of the reviewing process raised under the President authority was much appreciated. Although all the topics developed in the GIN could not be covered in their entirety by the various designed reviewers most analyses and recommendations were sound and built with a constructive and serious spirit.

Hence, only few punctual comments and corrections need to be taken into consideration. These are the following:

Overall appreciation of the unit:

- p.7 weaknesses and threats: the committee is anxious about the absence of a Vice-Director who should become the following director of the GIN after the actual director will end his duty, i.e. after the next quadrennial period will close. The evoked strategy, as correctly mentioned in the report, is first to raise a search committee to attract an external candidate of high level, who will become Vice-Director about 2 years before the end of the next quadrennial period. Although much effort will be placed in this task, in case this strategy fails after two years from now, the candidate future Director will be chosen among the PIs of the GIN, some of them being open to this possibility. The next two years period, in parallel with the action of the search committee towards an external candidate, will be appropriately used to help maturing the raise of a future candidate. In any case, a Vice-Director will be in place, whether external or internal to the GIN, 2 years before the end of the next quadrennial period.

The other weaknesses and threats detailed in the report with their respective constructive recommendations by the review committee are viewed as relevant and will be taken into consideration to help improve the quality of research developed in the GIN. Already, the claim by the committee that it considers the GIN as being of very good quality with excellent progression after 2 years from the creation of the GIN, appears most encouraging in the evolution of the GIN towards the highest international standard

- p.8 chapter “production results”: some mistakes having been incidentally introduced in the tables of researchers and clinicians numbers, correct numbers are listed in a separate factual set of tables. Considering the correct numbers, the ratio of active members in the research unit is close to 0.9, which is quite better than the 0.78 value presented in the report. Hence the remarks concerning the “publishers” and the appreciations about the global production of publications should be revisited in a more positive view.

- p.9 chapter ”Appreciation on the scientific quality and the output”, 2nd § of p.9: the 2nd research axis about “Neuro-oncology” not only concerns the two mentioned teams 5 and 6, but also team 7, the latter having its core research activity involved in neuro-oncology: team 7 has been omitted in the text of the preliminary report; also, in the same §, it should be noticed that the 4th research axis, namely “Innovative technology and methodology”, is not only developed in its technology aspect by team 7 and other researchers, but also by team 5, whose activity massively involves methodology developments around NMR technology, acquisition and analysis. Team 5 should be added in the report about the 4th research axis in relation with the methodology component of this axis on MRI. Hence the following corrections should be made: instead of “2) Teams 5 and 6 will be involved in the “Neuro-oncology” research axis”, one has to read: “2) Teams 5, 6 and 7 are actively involved in the “Neuro-oncology” research axis”;
also 4 lines after: instead of “4) Team 7 but also several researchers and clinicians of other teams participate to the last research axis “Innovative technology and methodology for Neurosciences””, one should read: “4) Team 5, 6, 7 and 11 but also several researchers and clinicians of other teams participate to the last research axis “Innovative technology and methodology for Neurosciences””.

- p. 11 chapter “Appreciation on the strategy, management and life of the research unit”, 4th § of p.11, the explanations about the change of team 5 director into a new one for the project period need to be clarified, such a clarification also being necessary to the actual team 5 director, who remains still on duty as team 5 leader until the end of 2010: obviously a confusion between platform and team 5 was incidentally introduced in the report. It has to be noticed that:

- the actual Director of Team 5 (Christoph Segebarth) will retire during the next four-year term. He is thus not allowed to lead a team during the next full four-year term. Christoph Segebarth remains director of team 5 until the end of 2010, i.e. during the running quadrennial full period. Emmanuel Barbier is the candidate director of Team 5 for the next quadrennial period starting in 2011, along a natural process of succession.
- A new coordinator for the Animal MRI Facility was appointed in October 2009. This change is due to a difference of views on the management of the Animal MRI Facility between the past coordinator of the platform (Christoph Segebarth) and the director of the GIN, thus leading Christoph Segebarth to resign from his role as pilot of the platform. The new platform coordinator (Chantal Rémy), was designed consecutively to the resignation of Christoph Segebarth. She is a researcher who belongs to team 5, along both the actual running quadrennial period and the next one.

The other general comments are related to the report specifically addressed to each team.

Appreciation team by team:

- Team 1: The team leader thanks the visiting committee for its positive appreciation of the efforts made in developing an original line of research centered on the role of the microtubule network in brain development and function. Team 1 is also glad to read that the team insertion at GIN is viewed as good.

A comment is needed about the assertion that "The overall level and number of publications are good, sometimes in high impact journals, but the productivity might be further improved with regard to the size of the team". It has to be noticed that the team has reached its present size only 3 years ago, when 3 full time researchers (1CR CNRS, 2 CR Inserm) and one teacher (UJF) joined the team whereas one researcher (CR CEA) came back from long leave in Canada. All of them had to catch up with the ongoing research in the team and had to develop their own project before obtaining new results and publications. Furthermore two full time researchers were absent for pregnancy leave (9 months for one and twice 9 months for another) during the last 3 years. Of course, all team members including the team leader are fully concerned by maintaining a high publication level and will put much effort to increase productivity in the years to come.

- Team 2: No specific reply to the report has been raised

- Team 3: No specific reply to the report has been raised

- Team 4: Since the review committee was devoid of a dedicated referee involved in genetics and/or myopathies - rare diseases, it is important to emphasize on the good reputation of this team, since it ensures a direct continuity between clinical-genetics studies and basic research. It is a prominent team involved in the Reference Centre for rare neuromuscular diseases. It is the only one team (in France and only one among the 3-4 others in the world) able to ensure a genetic screening aimed at the Ryanodin Receptor (RyR). Team 4 is a well known and internationally recognized group, which is able to study the structural myopathies with cores, as illustrated by the piloting role of the team leader in the related ANR network, as well as by the invitations by high standard meetings, such as Gordon Conference, Biophysical Society, etc. In the same way, team 4 just identified the first mutation present in the human gene of triadin.

- Team 5: The exact name of team 5 along the project for the next quadrennial period has been changed: it is "Neuroimaging and Brain Perfusion". Also, the numbers in the Table need to be corrected: N1 = 4; N2 = 4; N3= 4; N4 = 1; N5 = 0.
Regarding the list of publications, two files have been provided to the committee:
- One file that includes all publications issued from the whole GIN: Publications are ordered team by team and also listed as Interteams. In this file, the publications of all the current members of team 5 have been pooled (including those by O. David, the candidate Director for Team 11, H. Lahrech, a member of the project team 7), J. Coles (a recently retired member of Team 5))
- One file that presents the 'past activity' and the 'project' of team 5. The list of publications provided in this file contains only publications from the members of the project team 5. It might be this difference between the two files that should have been confusing.
Regarding the relationship between the candidate team 5 of the project report file and the Animal MRI facility, the point has been clarified: The coordinator of the Animal MRI Facility, Chantal Rémy, is a member of team 5 (both in the current and the candidate team 5). The candidate team 5 keeps a scientific piloting role to the Animal MRI Facility for the next four-year term, the staff members of the Animal MRI Facility (Engineers and technicians) being affiliated to the common services (the so-called team 0). Team 5 and the Animal MRI Facility will keep individualized separate budgets.

- Team 6: in the chapter "Appreciation of the project", it is mentioned in the report that "Considering the project, one of the key issues is the departure of 3 full time scientists. According to the team, this will not have a large impact due to the subjects and the incoming local collaborations. However, these departures must be analyzed deeper since there is a risk of a decreased initiative potential in research programs". Comments about this aspect are the following: One should notice that only one scientist (Nicolas Foray) will effectively leave the GIN to attend a team in Lyon. Charles Thomas (CR1 Inserm)

was hosted in the team 6 for convenience issues discussed with the Inserm RH. Boudewijn Van der Sanden shifts, in light of his research projects, from team 6 to team 7. Eventually, a junior scientist radiation biologist (Raphael Serduc) will attend the CR Inserm competitive recruitment step to enter team 6 as full-time researcher (with some realistic possibility of success after two well-ranked attempts).

Team 7: The information concerning the relevant suggestion for moving quickly to toxicology analysis and clinical proof of concept has been effectively been taken into consideration, since this aspect was the priority of the team in 2009, in relation with the accepted support of an "INCA translational grant" concerning the proof of concept of brain molecular fingerprint silicon-chip device. Toxicological analysis was thus completed and the clinical trial will start in 2010.
Also an error was introduced in the table on line N6: "past" column number should be read as 11, whereas project column should be read as 16 (instead of 1!)

Team 8: The weak points and recommendations are fully acknowledged and they can be considered in light with the fact that this team, which was not considered as an Inserm recognized team for the past quadrennial period, made considerable efforts and progress along this past period with the help of the GIN actions and encouragements, thus leading to appropriate research improvement and adequate focussing. With the hope that this team will benefit of a positive evaluation and recognition by Inserm for the next quadrennial period, the need to attract full-time researchers, as recommended by the committee, will become feasible and will contribute to lead this meriting young team in emergence to be raised to highest research standard in its specific field of expertise. Note that the team leader became an "internationally respected researcher", as specified in the report.

Team 9: No specific reply to the report has been raised, except about values in the tables, which need corrections to be made (see the separate file about factual corrections).

Team 10: The team leader thanks the visiting committee for its very positive appreciation of the research work conducted by the team. He is also glad to read that the team is well recognized at the international level, thus allowing to attract young researchers for both clinical and/or experimental studies.
One comment concerning the assertion that "*the topic could be considered as not highly original*": the team 10 leader wants to stress out that neuron-glia interactions in the basal glia, as potential or even key factors for intercellular play, represent quite an original issue carried out by the team along pathophysiological mechanisms involved in Parkinson disease models. The role of glia and intercellular plays also represent important elements to take into consideration by which deep brain stimulation might have a role and this role can be exerted via glia intercellular influence onto the concerned functional networks.
It seems also important to emphasize that synergic interactions between the clinical part of the team and the biological experimental one are more effective than what the review committee did perceive. Indeed the project on apathy, with the development of new models of apathy in the rodent, is directly issued from close interactions and discussions with the clinicians of the team and are the results of clinical problems found in patients at bed-side. Also, via the support of the foundation "NeuroDis" (the so-called RTRS in Neuroscience centred within Rhône-Alps), a young promising researcher was just recruited, who will help reinforcing the behavioural component of the GIN, in line with the general recommendations of the review committee.
Tables also need few corrections, which have been listed in the separate joint file.

Team 11: No specific reply to the report has been raised, except about values in the tables, which need to be made (cf. the second file).

It remains noticeable that this individualized team, with the added value of its remarkable expertise in methodology and technology, will not act as a platform but rather as a core methodological and technological pivotal team in the conceptualization approaches which take place both within the 3rd transverse research axis “Dynamics and pathophysiology of brain networks” and the 4th one “Innovative technology and methodology for Neurosciences”.

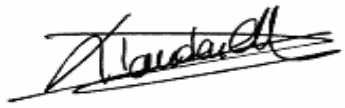
Team 12: No additional comments to the recommendations of the committee seem necessary. It indeed makes sense, at this actual step, to postpone the national-based individualization of this new team *per se*, when considering the quite limited size of the project new putative team 12 due to a most recent (few months) transfer of the team leader (a researcher-teacher, who will be only half time involved in effective research) from Caen to Grenoble. To date, such a new team effectively appears to evaluation at a too early stage and is still fragile, even though much promising. The relations with teams 1 and 2 look scientifically coherent, and such interactions with these specific teams already work.
In addition, in parallel with the situation of the newly selected Avenir position to the GIN (i.e. Isabelle Arnal), project team 12 has been awarded a 3 year-based young team program by NeuroDis Foundation-RTRS. This will bring comparable advantages as those of an Avenir Inserm program. It will place the project Team 12 of Alain Buisson into a symmetric situation as that of Isabelle Arnal with her Avenir Inserm position and dedicated individualized financial support as emerging team.

Besides, you will find enclosed in a separate document, some additional comments related to technical inaccuracies.

Yours faithfully.

P/ Le Président de
l’Université Joseph Fourier Grenoble I
Farid OUABDESSELAM

P/O Le Vice-président
du Conseil Scientifique de
l’Université Joseph Fourier Grenoble I
Laurent DAUDEVILLE



Enclosed : Some additional comments related to technical inaccuracies.

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