INM - Institut des neurosciences de montpellier : déficits sensoriels et moteurs

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on unit:

Institute for Neuroscience of Montpellier

INM

Under the supervision of the following institutions and research bodies:

Universite Montpellier 1 - UM1

Universite Montpellier 2 - Sciences et Techniques - UM2

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

January 2014

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

Department for the evaluation of research units

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

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

On behalf of the expert committee,

- Mr. Jonathan ASHMORE, chair of the committee

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

Evaluation report

This report is the result of the evaluation by the experts committee,the composition of which is specified below.

The assessment contained herein are the expression of independent and collegial deliberation of the committee.

Unit name:	Institute for Neuroscience of Montpellier
Unit acronym:	INM
Label requested:	INSERM
Present no.:	UMR 1051
Name of Director (2013-2014):	Mr Jean-Luc PUEL
Name of Project Leader (2015-2019):	Mr Jean-Luc PUEL

Expert committee members

Chair:

Mr Jonathan ASHMORE, University College London, United Kingdom

Experts:

Mr Gilles GHEUSI (representative of CNU)

Ms Marlies KNIPPER, HNO-Universitätsklinik Tübingen, Germany

Mr Gwendal LE MASSON, Neurocentre Magendie, Université Bordeaux 2

Mr Peter MCNAUGHTON, King's College London, United Kingdom

Mr Brahim NAIT OUMESMAR, Institut du Cerveau et de la Moelle Epinière - ICM, Paris

Mr Stéphane OLIET (representative of CSS INSERM)

Mr Serge PICAUD (representative of CoNRS)

Mr Bernd WISSINGER, Center for ophthalmology, University Clinics Tübingen, Germany

Scientific delegate representing the AERES:

Mr Yves TROTTER

Representatives of the unit's supervising institutions and bodies:

Mr Bernard GODELLE, Université Montpellier 2 - Sciences et Techniques

Mr Christian JORGENSEN (representative of Doctoral School CBS2 N°168)

Ms Marie-Lou KEMEL, INSERM

Mr Jacques MERCIER, Université Montpellier 1

1 • Introduction

History and geographical location of the unit

The Institute for Neurosciences of Montpellier (INM) will celebrate its 10th anniversary in february 2014. The institute is located in the Neuroscience (Head and Neck) hospital, closed to the university campus. It concentrates basic researches on transduction, integration and sensory and motor disorders. The INM houses several teams working on vision, hearing, somatosensory wiring, and myelination. Molecular to systems level investigations are carried-out through core technical facilities, which are opened to academic and private users outside the INM. Research outputs favor the development of new treatments for sensory and motor deficits, with a strong interest in inherited retinal and optic blindness, auditory neuropathies, neurodegenerative diseases (amyotrophic lateral sclerosis, giant axonal neuropathy), somatosensation disorders (touch and pain) and glial pathologies (gliomas and Charcot Marie Tooth disease).

Management team

The project is based on 5 certified-Inserm teams (Mr Christian HAMEL, Mr Jean-Luc PUEL, Mr Patrick CARROLL, Mr Hugues DUFFAU and Mr Cédric RAOUL). Since the Atip/Avenir grant of Mr Nicolas TRICAUD expires 1st of January 2015, this team will be part of the evaluation process to constitute an Inserm team. In contrast, the Atip/Avenir team of Ms Pascale BOMONT does not need to be evaluated since the grant continues up to 2016.

AERES nomenclature

SVE1_LS1_LS3_LS4_LS5

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	34	34
N2: Permanent researchers from Institutions and similar positions	29	29
N3: Other permanent staff : without research duties	11	11
with research duties	16	16
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)		
N5: Other researchers from Institutions (Postdoctoral students)	16	21
N6: Other contractual staff : engineers and technicians	16	19
TOTAL N1 to N6	**122**	**130**

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	22	
Theses defended	33	
Postdoctoral students having spent at least 12 months in the unit*	34	
Number of Research Supervisor Qualifications (HDR) taken	6	
Qualified research supervisors (with an HDR) or similar positions	31	31

2 • Assessment of the unit

Strengths and opportunities related to the context

The Institute of Neuroscience in Montpellier (INM), opened in 2004, successfully combines basic research on neurosensory diseases and basic mechanisms in six independent but collaborative research entities. The focus of research, on a combination of sensory-motor deficits linked through from the bench to the clinic, is unique in Europe and arguably worldwide.

The research in neuroscience carried out in the institute spans molecular to system level analysis of various neuronal disease forms and provides a mechanism that drives constant interdisciplinary exchange. The institute is organized well ensuring physical mixing of the teams on a day-to-day basis. There is close geographic proximity to those hospital centers which include ophthalmology, ENT, neurology, neurosurgery and neuroradiology. The net result is an extensive scientific sharing of skills and knowledge.

The organization of the institute into teams that are linked by the use of core technical facilities is of considerable merit. These core facilities are open not only to all INM team members but also to other academic and private users, a feature that can inspire constant and new cooperative activities and produce effective and (financially) profitable exchanges between the Institute and biotechnology and biopharmaceutical companies. This basic organization principle maximizes utilization of infrastructure and ensures quality. The efficient organization of these resources under the directorship of Mr Jean-Luc PUEL is a model of its kind.

The institute also has the potential of being an excellent training platform for students and postdoctoral fellows for it encompasses a wide range of research fields (engineering, physical, biological and clinical). Skills can easily be transferred from the research environment to the clinics, and equally importantly, can ensure that clinically qualified individuals can learn by immersion is a basic science environment. The university embedding ensures that the Master's programme and the doctoral school as well European Marie Curie training platforms can take full advantage of the institute as a multi-disciplinary platform for training. The proposed merger of UM2 and UM1 in January 2015 will cement further the key position occupied by the institute in neuroscience research and in training.

Weaknesses and threats related to the context

The limited number of PhD students in the institute remains a severe weakness from the point of view of research training excellence and the institute's future impact. It is also clear that there is an approaching threat of a space problem, particularly with respect to animal facilities. This problem needs to be addressed. There is also a threat, due to the new EU directive on animal welfare, of an increased administrative load for animal facilities, impacting on core committees, scientists and veterinary staff.

Recommendations

The experts committee recommends that the problem of limited numbers of PhD students, and the difficulty of recruiting students must be addressed at all levels. One is the easing of the stringent requirements around the registration of PhD students at the doctoral school of the university. The numbers supported by the university are limited. Indeed, the center could not be rated Excellent on the item "training through research" for this very reason. One obvious cause is that there are very restrictive conditions to register students (only 1 student per HDR, a 2nd is allowed if the first is in his/her final year). As young scientists need to have supervised a PhD student to pass the HDR, an experienced PI needs to take the administrative responsibility for young colleagues supervising PhD students so that they can obtain their HDR. However, the limit on 1-2 students prevents many experienced PIs from taking this administrative responsibility for they would then lose the possibility of registering their own PhD students. This vicious circle is hampering the unit's dynamism and the emergence of young scientists.

The experts committee recommends the easing of the apparent rule that students can only be taken on provided that the supervisor has at least 3 years of funding in place. This rule is stunting the emergence of talented and enthusiastic younger researchers and future team leaders. So the experts committee might suggest that the director of the unit should be allowed to guarantee a 3rd year of funding if a scientist can already demonstrate access to 2 years funding for the PhD student.

The experts committee recommends that the institute takes steps to facilitate the emergence of independent small teams from the existing very large teams. It was found that there are limitations on the use of grants being held by Researchers on short term contracts (for example, as above, the inability to recruit students). The experts committee considers that this may be very important for scientists were they to seek promotion to the DR level. The requirement that there should be two permanent positions in the creation of independent teams clearly limits the possibility of such teams emerging as independent in their own right.

The experts committee recommends that the institute identifies and cross cutting scientific questions and themes explicitly. Cross-cutting subject themes organized around platforms are very productive and interesting; such common themes emerged in discussion during the team presentations. However, no real cross-cutting topics were initially identified explicitly and presented as a specific objective of the center. For example, "Mitochondrial function and dysfunction" is clearly an identified research theme common to all teams. Therefore, the experts committee suggests that organizing a specific taskforce around this theme could be beneficial to the institute as a whole and could potentially produce considerable added value, raising all teams towards an outstanding level.

The experts committee recommends that the pressure for space on the animal facilities be reviewed and eased so that critical animal models can be maintained for the benefit of overall research of the institute. The experts committee suggests that as many options are explored as possible – including using external companies – to mitigate the rising costs of support, the pressure on space and consequent limitations on the animal usage for each team.

The experts committee recommends that thought be given to advertising the institute as being 'family friendly'; that is, to ensure that critical events and working arrangements are being organised so that staff with childcare and children at school are not disadvantaged. This means that the institute could advertise that official functions, including seminars are being held at times which favours researchers with family commitments. Such a policy is now widely advertised in many institutions around the EU; it can only act as a recruitment asset for the institute.

3 • Detailed assessments

Assessment of scientific quality and outputs

Overall the institute exhibits excellent scientific quality. It has an excellent publication record shown by all the teams being assessed. In addition to the overall quality and volume of original publications, INM members have deposited 9 patents since 2008.

Assessment of the unit's academic reputation and appeal

The unit is quite unique and has an outstanding reputation nationally and internationally in terms in terms of its breadth and focus on sensory-motor expertise. INM scientists are frequently invited to give lectures at national and international institutes and conferences. They have also been involved in the organization of various national and international meetings. The INM teams participate in a Laboratory of Excellence (Labex) project, entitled Epigenmed, and as well as in EuroBiomed, a center of excellence dedicated to rare diseases.

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

The unit has an exceptional and outstanding profile with industry, stimulating spinoff companies and holding nine patents as mentioned above. There are well-established collaborations with pharmaceutical and biotechnology concerns appropriate to translational research. It is also clear that the institute integrates seamlessly with the university. The development of a valorization/patent office within the institute will certainly be of a great benefit to all teams.

Assessment of the unit's organisation and life

The unit exhibits an outstanding combination of uniqueness, confidence and high visibility. The institute is transparently managed with clear governance appropriate to the multiple aspects of the institute. The axes developed by each team offer opportunities for multiple collaborative interactions amongst the INM researchers. The INM is organized in such a way that shared scientific equipment is located in common facilities accessible to all groups. Such equipment sharing ensures that there are quality, informal day-to-day exchanges between personnel including researchers, technicians, engineers, administrative staff and students.

Assessment of the unit's involvement in training through research

The unit is effective in training PhD students belonging to the “École Doctorale” CBS2 N°168, with an excellent record of thesis completion given the constraints on recruiting such individuals. It is supportive of staff at all levels and has been very effective at encouraging medically trained personnel to acquire basic science skills in a fully integrated environment.

Assessment of the strategy and the five-year plan

There is a clear five year strategy to develop enabling infrastructure, to recruit new talented groups and to ensure continued excellence of the unit. The plans include installing critical equipment for state-of-the-art electron microscopy and maintaining the productivity of the existing high-performing platforms. There are explicit plans to further promote clinical transfer and to reinforce the visibility of the institute nationally and internationally. It also takes into account the coming reorganization of the university environment. The experts committee considers that the forward planning for the institute is excellent in its scope and logic.

4 • Team-by-team analysis

Team 1: Genetics and therapy of retinal and optic nerve blindness

Name of team leader: Mr Christian HAMEL

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions (PU + DR)	4	4
N2: Permanent EPST or EPIC researchers and similar positions (CR + MCU)	5	6
N3: Other permanent staff (without research duties) (PH)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.) (Post doctorants)	5	5
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**16**	**17**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	5	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	6	7

• Detailed assessments

Assessment of scientific quality and outputs

This is high quality, internationally visible research in the field of inherited retinal dystrophies and inherited optic neuropathies including work on the genetic causes, genotype-phenotype correlation, pathophysiology of the disease (applying animal models and cellular models) and work towards the development and application of gene-based and pharmacological therapeutic intervention. There are a considerable number of highly-ranked

publications (7 with IF>7 and 8 with IF>10) (Ann Neurol, brain, Mol Ther, Am j Human Genet, J Neurosc, Hum Mol Genet, etc). There are 59 grants which include several EU grants.

Assessment of the unit's academic reputation and appeal

This is a team with a high international reputation and visibility in the principal fields of research. The team has partnerships in leading international research consortia (EU FP6 and FP7 projects, ERDC, E-Rare). There is clear evidence of the appeal of the team, as for documented by being able to attract a new PI to join the team as a group leader on retinal gene therapy with two other recently appointed researchers (1 MCU and 1 CR1 Inserm).

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

The team has decent economic environment interactions and as well as exploitation activities. It has cooperation with several companies, joint patents (together with Sanofi), and plans for the founding of a biotech company on retinal gene therapy. The team is involved with academic teaching and training activities, academic diploma for “inherited retinal and optic nerve degenerations”. In addition, the team has organised two local meetings, and demonstrates intensive networking and exchange with patient organizations (e.g. scientific boards). The team has developed specifc public domain software (TASE).

Assessment of the unit's organisation and life

The team is organized into three research groups (*inherited retinal dystrophies; *inherited optic neuropathies; *retinal gene therapy) and an additional structure for biological resources. The research topics and objectives of the research groups are well integrated. The groups apply and share overlapping technical and methodological approaches (genetics, animal models, retina/visual function, therapeutic routes). A novel “retinal gene therapy” group fits well (i.e complements prior competence and professionalizes gene therapy and iPSC approaches), and thus develops further prospects for therapeutical approaches.

Assessment of the unit's involvement in training through research

The team has organised participation in an EU-funded integrated training network. There is currently, however, only one PhD student in the combined groups of two PIs despite 5 professors/researchers. Only 5 PhDs have been trained during the previous period although both groups should be attractive to students because of the nature and opportunities of the topic and the quality of this team’s research. There has been prior success in training/promoting young scientists, but the main stumbling blocks are external and severe organisational constraints to further recruitment.

Assessment of the strategy and the five-year plan

The plan has three main areas of eye disease research: (1) genetic causes, (2) pathophysiology of disease and (3) development of therapies. This plan includes continuation of current strong areas of research (e.g in IRD and ION) by 1) implementing advanced, state-of-the-art approaches (e.g. extensive exome/genome sequencing), and by 2) characterizing the physiopathology of diseases on relevant animal models. The strategy reinforces the development of therapies (gene therapy and pharmacological therapies).

Conclusion

- ***Strengths and opportunities:***

Team 1 is well integrated with other research groups with many opportunites to share technologies, methods, approaches, knowledge, etc.

There are possibilities of integrating clinical phenotyping, genetic analysis, pathophysiology and prospects into therapies.

There is, and continues to be, close cooperation with clinical ophthalmology including strong links with the population of medical residents. This therefore is an opportunity for rapid translation of basic science into the clinic.

The interest in mitochondrial neurodegeneration is a remarkable opportunity to interlink with other research groups within INM.

- ***Weaknesses and threats:***

The experts committee considers that there no significant weakness in the team as proposed.

One group still needs to show proof of research productivity in this new setting.

Some of the work could benefit by access to large scale technical platforms (genomics, proteomics, pharmacological screens) at a national level.

There is always the possibility that funding opportunities for the translation of therapeutical approaches into clinical studies could be missed.

- ***Recommendations:***

The experts committee should like to see additonal consideration given to strengthening work on iPSCs (induced pluripotent stem cells) as model systems for pathophysiology and for therapy development in this team's work;

The experts committee should like to see the team consider ways of encouraging more PhD students to train in the area, e.g. by using further opportunities for industrial/ biotech sponsorship.

Team 2: Deafness, Tinnitus and Therapies

Name of team leader: Mr Jean-Luc PUEL

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions	8	10
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	4	5
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**15**	**18**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	9	
Theses defended	9	
Postdoctoral students having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken	6	
Qualified research supervisors (with an HDR) or similar positions	7	12

- ## Detailed assessments

Assessment of scientific quality and outputs

The team has an impressive list of publications, citations, patents, and book chapters so that over 5 years the scientific output has been excellent and in some places groundbreaking (PNAS, Hum Mo Genet, Antioxi redox Signal,

J Biol Chem, Am J Hum Genet, J Neurosc). The profile of the team leader and group members has been very high. The broad experimental approaches used for answering questions to the choosen topic of unraveling the mechanism of deafness and tinnitus are considerable, making this a single laboratory which is relatively unique and self-sufficient in its range of techniques. The laboratory has excellence in molecular approaches (two-hybrid, proteomics), anatomical (confocal, EM) as well as in functional studies (patch-clamp, single and compound action potentials and behavioral studies). The laboratory also has branched into translational research, including diagnostic tests and clinical trials. It this offers a wide spectrum of cellular, computational and translational expertise.

Assessment of the unit's academic reputation and appeal

The research covers within the hearing scene very competitive fields, including neuropathies, tinnitus, age-dependent hearing loss. As a result the team manages an enormous spectrum of excellent competitive research and training of many PhD students and postdocs. Topics of sound coding, synaptic machinery, neuropathies, Diaph, Rescue, ERpathies and age dependent hearing loss are all competitive and timely. The group has a tradition of addressing important issues in auditory neuroscience, particularly with respect to pharmacological interventions in hearing disorders, and has a high standing in the academic field.

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

There is a high level of communication at all levels, specialist and public engagement. The team is subdivided into five subteams headed by experienced researchers each of whom supervises postdocs and at least one PhD student (in total about 30 people). It is a large powerful and productive group with a strong national and international visibility. Of particular significance are publications, since 2008, of articles in newspapers and journals aimed at a wide public audience. There has thus been wide dissemination of the team's ideas and information about the field to a large readership.

Assessment of the unit's organisation and life

The majority of the projects require integration of multiple techniques, from auditory screening to imaging to cellular biophysics to molecular genetics. The laboratories are set up to ensure a good pipeline and is efficiently organized and equipped for the purpose.

Assessment of the unit's involvement in training through research

The team has been very effective in recruiting students with support from a wide range of fields and disciplines, with support coming from institutional as well as industry sources. Over the last period there has been an excellent recruitment of students with 9 doctoral dissertations defended.

Assessment of the strategy and the five-year plan

Each of the sub-teams has a clear vision of where they wish to be. In particular there are logical and well thought out plans to collaborate with other teams in INM and internationally (in particular with Mr Tobias MOSER's group in Goettingen and with Dr Marci LESPERANCE's group in the Ann Arbor, USA). There are also plans to consolidate sensory expertise by consideration of the recruitment of groups specialising in olfaction and taste. Of necessity these would be independent teams but the synergy with team 2 in terms of outlook and concentration on molecular, cellular and behavioural neuroscience would be considerable.

The importance of therapeutic translation is much to be recommended, with development of diagnostic tests for hearing function based on teams work in the past 5 years on computational models of hearing.

Conclusion

- ***Strengths and opportunities:***

This is an internationally high profile group that has been effectively and fully involved in training PhD students. The development of links with computational approaches to auditory function has been a new development over the past 5 years; this presents a major opportunity to capitalise on the computational and software expertise available at the university. The topics of sound coding, synaptic machinery, neuropathies, the genetics of diaph,

ERpathies and age-dependent hearing loss are all competitive and timely. The same applies to the team's new developments and approaches in single fibre recording.

- ***Weaknesses and threats:***

There has been a possible loss of direction in the specific skills in traditional auditory nerve recording that are required for detecting pathologies (such as synaptopathies associated with tinnitus) as for example in the loss in the last period of one senior investigator to Marseille; this may be critical for the team's avowed interest in the tinnitus field. Although team researchers have moved into the responsibilities which open up, it remains important to ensure that younger researchers are being trained up in the skills necessary for integrative and systems neuroscience. The large number of animals required for genetic studies places strains on the animal resources of the institute.

- ***Recommendations:***

The considerable electrophysiological experience in the team, which includes single fiber recording and CAP, should be encouraged in order to integrate these studies into tinnitus-research. There are clearly tinnitus animal behavior models still being developed in the laboratory and, if there is a plan to extend and combine these with electrophysiological experience in the periphery of the cochlea for tinnitus research, the team would be a commanding position.

There is a good scientific case not to separate the topicalities of IHCs hair cell presynaptic machinery (possibly including the plans to work on ER-pathies) and postsynaptic neuropathies, critical for developing tinnitus expertise.

The options for developing different ways to meet demands on animal provision should be continuously reviewed.

Team 3 : Somatosensory system development and pathology

Name of team leader: Mr Patrick CARROLL

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	6	7
N2: Permanent EPST or EPIC researchers and similar positions	6	6
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	2	3
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**14**	**16**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	1	
Postdoctoral students having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	3	3

- # Detailed assessments

Assessment of scientific quality and outputs

The team has an excellent publication record with the 5 well-cited papers including one EMBO J. paper entirely from the team, one Neuron paper mainly authored by the team, and one Science paper with two last authors from another group but in which the past work of the group has evidently played a key role. In addition there have been 4 book chapters and 6 reviews published.

The area of work of the team – somatosensory neuron specification and control of phenotype – is highly topical. There is a strong focus on the genetics of touch sensation, emphasizing specific molecule (e.g MafA, Ret, Zeb1,2) and their relation to clinical situations (e.g. hereditary diseases) and these interests are being studied in a broad range of systems including rodents and human. The basic work in this area seems certain to lead to translational opportunities in the near future. The group is already actively exploiting drug development opportunities in the area

of FL/Flt3 of interactions where there is a strong possibility of realising treatments for neuropathic pain, an intractable, disabling and widespread condition.

Assessment of the unit's academic reputation and appeal

The group has significantly advanced our understanding of neuronal specification at the level of basic science. A new pain pathway has been discovered on the basis of which a new therapeutic approach to pain silencing has been developed based on a TRPV1- Flt3 mediated aberrant pathway. The techniques being employed to develop FL/Flt3 antagonists are state of the art and show strong interactions with the team of Mr Jean-Philippe PIN in the Institute of Functional Genomics, another Montpellier INSERM unit. The potential for translation of this knowledge into treatments for neuropathic pain will significanly enhance both the reputation and appeal of the group, if successful.

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

As noted above, the team is developing a possible new treatment for neuropathic pain in collaboration with external industrial partners. The translation of this basic science discovery into potentially new treatments, together with the pharma-academic liaison, is very promising, and the team holds a patent related to the technology.

Assessment of the unit's organisation and life

The team is focussed on basic science and as such has a valid and important objective of understanding specification and modulation of sensory neuronal phenotype. There is evidence of a healthy spread of interests in the team with some members more focussed on basic science objectives and others more interested in the development of translational research.

Assessment of the unit's involvement in training through research

As with the general comment above, the number of PhD students in the INM as a whole is small by international standards where it would be usual for a successful PI to supervise 3-6 PhD students at any one time. With this reservation it appears that the PhD students in the team are well supervised and moreover have access to an excellent range of facilities in research.

Assessment of the strategy and the five-year plan

The five year plan is very strong with clear goals in each of the research projects proposed. There are proposals to identify Zeb1 in the peripheral nervous system and to link this work in to clinical group working on genetic diseases of the eye. There are appropriate plans to identify a transcriptional programme initiated by cMaf, a well as identifying the properties of Meis2 as a survival factor for DRG neurons. The 5 year plan also proposes to further the important study of the role FL/Flt3 in neuropathic pain and to develop the multidisciplinary project to identify extracellular pharmacological inhibitors as part of translational effort, for which the group has already deposited a patent.

Conclusion

- ***Strengths and opportunities:***

This is an excellent group close to the forefront of their area internationally. They have made some seminal discoveries and have collaborated well with other leading groups to produce significant publications in leading journals. Strong interactions with other groups internationally (e.g. group of Mr Gary R. LEWIN at Max-Delbrück-Centrum (MDC) Berlin) and locally (e.g. group of Mr Jean-Philippe PIN at Institute of Functional Genomics (IGF)) adds to the considerable strength of this group and opens up new dimensions that the group could achieve only with difficulty by themselves.

The experts committee sees the translational work underway in this group as a considerable strength. The group should continue with a combined basic science and translational approach – top basic science often leads to translational opportunities.

- ***Weaknesses and threats:***

The experts committee considers that there are no significant weakness in the team. In comparison with other leading groups in this area (Mr Quifu MA, Mr Gary R. LEWIN, Mr Patrick ERNFORS) it would perhaps be fair to recognise that they are not absolutely at the very front of the field but in this "hot" competitive and fast-moving field they are not far behind the international leaders.

Along with other groups at INM the experts committee is concerned at the low numbers of PhD students – this is particularly a problem for this group and leads to concerns that future scientists are not being trained in adequate numbers. A leading group such as this should be training many more than the "replacement numbers" of PhD students and one would expect graduates of this group to be populating many other leading labs and academic institutes with their graduates.

- ***Recommendations:***

Continue top-level basic science and continue to explore translational opportunities as these arise. The experts committee should like to see the team consider ways of encouraging more PhD students to train in the area, e.g. by using further opportunities for industrial/biotech sponsorship and by encouraging international students (who can sometimes be funded by home studentships) to join the team.

Team 4: Brain plasticity, neural stem cells, glial tumors

Name of team leader: Mr Hugues DUFFAU

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	10	11
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**12**	**13**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	7	5
Theses defended	4	5
Postdoctoral students having spent at least 12 months in the unit	4	2
Number of Research Supervisor Qualifications (HDR) taken	3	3
Qualified research supervisors (with an HDR) or similar positions	7	8

• Detailed assessments

Assessment of scientific quality and outputs

The team of Mr Hugues DUFFAU is composed of 21 researchers: 3 permanent clinicians and 6 permanent basic research scientists organized in 3 independent groups focused on clinical and fundamental neuro-oncology. The overall objective of the team is to provide better insights into clinical and experimental therapies of high and adult diffuse low grade gliomas. Experimental approaches are complementary and rely on the development of a large glioma biobank collection. One group in the team has made important contribution to the field of neuro-oncology by developing innovative “awake” neurosurgical technics of gliomas, combined with electrical stimulations for mapping brain connectivity. A second group has also shown that forced expression of several bHLH transcription factors can repress glioblastoma cell growth and provided proof-of concept that oxysterols (7¤-hydroxy-cholesterol) and phostine 3.1a could be promizing pharmacological compounds for GBM. The scientific productivity is excellent, 140 publications

(J Clin Oncol, J. Med Chem, Cortex, Hum Brain Mapp, Biochem Pharmacol, J Med Chem, Glia, etc) 2 books, 5 chapters. The team has owned 5 patents over the last five years.

Assessment of the unit's academic reputation and appeal

The team has a world reputation in "awake" neurosurgery of glioblastoma and develops one of the largest collection of GBM biobank. The team has a strong link with the department of neurosurgery and the université Montpellier. Eleven team members (among 21 in total) are MCU, MCU-PH or PU-PH, and have therefore teaching duties at the Medical School, Université Montpellier and School of Chemistry. The team is nicely integrated in the Montpellier campus and has attracted PhD students, post-docs and clinicians. The team leader is member of the national committee for universities and one senior investigator is member of the board of the Canceropole grand sud ouest.

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

Over the past 5 years, the team has obtained funding from public sources, charities and industries. The team has also developed strong collaborations with pharmaceutical companies. Team members have been actively involved in the organisation of international and national meetings. PIs have been regularly invited to give seminars at research centers, universities and foundations.

Assessment of the unit's organisation and life

The team is organized around 3 PIs with complementary expertises in clinical neuro-oncology, glial cells and stem cells biology and pharmacology. The program is focused on applied and basic research on glioma. However, most of the permanent members in the team have teaching duties, which might impair the progression of each project.

Assessment of the unit's involvement in training through research

The team has trained several PhD students and post-docs (the number is not precisely stated in the documents). 4 post-docs and 6 PhD students are currently part of the team. The training through research is excellent and the 3 PIs are actively involved in teaching and training activities in Master, PhD and MD programs.

Assessment of the strategy and the five-year plan

The five plan research plan is a nice follow-up of previous projects. The research plan focuses on three main topics:

1) functional brain mapping and their reorganisation induces by low grade gliomas;

2) cellular and molecular mechanisms regulating low and high grade glioma cells and stem cells;

3) at the INM the research program will mainly consist in the study of cellular and molecular mechanisms induced by the glycomimetic phostine, affecting GBM stem cells glycosylation and inhibiting their proliferation, migration and invasion in vitro and in vivo.

This research program relies on the complementary expertise of the 3 PIs, in clinical neuro-oncology and neurosurgery, glial/stem cells and biochemistry. The investigation of the brain connectome in glioma affected patients is innovative and relies on the internationally recognized expertise of the clinical group. The regulation of glioma cell fate and pharmacological projects should provide proof-of-concept indicating that transcriptional, metabolic and glysosylation pathways could be interesting targets against glioma.

Conclusion

- ***Strengths and opportunities:***

The interaction between clinicians and scientists within the team provides an excellent environment to translate basic discoveries into clinical applications and to attract bio-pharmaceutical companies.

- ***Weaknesses and threats:***

The heavy clinical and teaching duties of the PIs need to be managed to ensure proper development of each program. The team has only 2 CR1 researchers, and the recruitment of a full time researcher is important. Interactions between the groups could be strengthened to ensure efficient development of the projects.

- ***Recommendations:***

The basic science projects are strongly based on in vitro studies (Gliobank). The development of relevant animal models of GBM could be a nice addition to these projects. Collaborations with other INM teams should be considered to ensure the appropriate integration of the team within the institute.

Team 5: Motoneuron disease: Neuroinflammation and therapy

Name of team leader: Mr Cédric RAOUL

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	3
N2: Permanent EPST or EPIC researchers and similar positions	5	7
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	7	7
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**15**	**17**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken	6	
Qualified research supervisors (with an HDR) or similar positions	6	

- ## Detailed assessments

Assessment of scientific quality and outputs

The team focuses on the adult-onset neurodegenerative disease amyotrophic lateral sclerosis (ALS). ALS is a progressive motor neuron disease that is invariably fatal within years. It has been previously demonstrated that although death of motoneurons causes ALS symptoms, astrocytes and microglial cells accelerate motoneurons degeneration and ALS progression. Thus the degenerative process is triggerred by both cell-autonomous and non-cell-autonomous factors. The team focuses on the molecular pathways involved in the inflammatory response from microglial cells and astrocytes and the ways in which motoneuron death occurs.

This team has a very good expertise and a robust background in primary culture of motoneurons, molecular and cellular biology, biochemistry, electrophysiology and clinics. Since the team leader moved only recently (2012) from

Marseille to the institute, the team is a relatively 'young' group. Therefore, it might be too early to judge its performance in the INM. It is indeed hard to really differentiate the work that was done at Marseille and the work more clearly carried out at IMN. Nevertheless, the group is headed by a young researcher with a very solid expertise in this competitive field and well-connected with diverse collaborations. The group has already identified different key players and pathways implicated in motoneuron death. They have identified a new non cell autonomous pathways involving IFN and a lIGHT dependent motoneuron selective pathways with direct preclinical applications. The team holds a patent on IFN inhibitors.

The team is composed of researchers with high competence in their field, with complementary expertise and capable of conducting real translational projects focused on neuroinflammation. This group presents translational projects that are in line with the previous work of the team leader. Cellular and molecular projects have a real potential to initiate clinical relevant studies in the future. The project is in accordance with the competence of the team members. The studies should contribute to improve the diagnostic tools and treatment in ALS.

In total the team has published 152 papers, 25 IF 5 to 7, 30 IF 7 to 10, 5 IF > 10 (Nat Genet, Lancet Neurol, Ann Neurol, PNAS, Cell Death Diff, Neurology, Human Mol Genet), 4 books chapters, 12 educational publications.

Assessment of the unit's academic reputation and appeal

The team leader was competitively awarded an Avenir program in 2007 at the Mediterranean Institute of Neurobiology (Inserm UMR901 – Marseille) and received the Inserm Scientific Excellence Award in 2010. He has recently joined the INM whereupon he is now leading the 'Motoneuron Disease: Neurinflammation and Therapy' team. Each member has a high visibility at the national and international levels. The team is very productive, not only with respect to the number of publications but also in terms of their quality and impact on the field, also most of the very high impact factor journal were not published by the team leader at a senior position The group has been highly successful in raising funds from public agencies (ANR, FP7 Europe, Regional Council, Hospital, Inserm) and non-governmental associations (AFM, ARSLA, Thierry Latran Association, FAR, French and Spanish patient associations).

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

The team leader is a consultant for two different pharmaceutical companies ANIDA Pharam, USA and LASCCO SA, Switzerland.

Assessment of the unit's organisation and life

Because the team leader moved recently from Marseille to the institute, the team is a relatively 'young' group, thus it is difficult at this stage to analyze its organization's life as a whole. There is excellent technical support with two EI INSERM in the team.

Assessment of the unit's involvement in training through research

During the past 5 years, members of the team contributed to the dissertation of 11 Ph.D students. They participated to the juries of 28 Ph.D/M.D theses. Six team members have teaching duty in medical school, pharmacy and academic graduate courses. Five of them (PU-PH and MCU-PH) have clinical activities. Two of them are co-coordinators of teaching programs (Montpellier University Hospital and Nîmes Medical School). Overall, team members are involved in 36 teaching units.

Assessment of the strategy and the five-year plan

The team project for the 5 next years includes 5 tasks:

Examine the contribution of a proinflammatory cytokine TWEAK to non-cell autonomous mechanisms of motoneuron degeneration and evaluate the therapeutic potential of a TWEAK immunotherapy in ALS mice.

Evaluate the cytotoxic population of CD8+ T and NK cells that invade the CNS soon after the onset of the ALS disease and the therapeutic potential of the immunodepletion of these cells.

Investigate the molecular crosstalk between motoneurons and microglial cells in an ALS context.

Study the Fas- and INFg-induced hyperexcitability of motoneurons through an electophysiological approach in order to identify the chloride channels and cation-chloride co-transporters involved in mutant SOD1 mice.

Conduct a translational study focused on the genetic and clinical relevance of neuroinflammation in ALS patients.

This new team includes scientists with complementary competences and experiences necessary for the project. The project is in accordance with the competence of the team members. The research plan is very much in line with the earlier work of the team leader and other members of the group. It consequently follows up previous interesting results and leads on to both basic and clinical approaches. The project is of a very good quality overall and composed of different integrated axes. The association between INM and an ALS clinic could also be considerable asset for experimental procedure (iPSCs from the patient's skin fibroblasts) and for translational studies.

Conclusion

- ***Strengths and opportunities:***

The research theme is very relevant to fundamental and medical sciences. Molecular biology, pathophysiology and experimental/clinical neuroscience are planned concomitantly for a better understanding of the underlying causes and consequences of neuroinflammation in ALS. The project is a logical follow-up of previous research activities of the team members. There is a possibility to establish close collaborations with team 4 to initiate stem-cell therapies, e.g. cells that could differentiate into neurons and glia, allowing questions such as: could stem cells slow ALS progression, improve functions or speed recovery ? The team has an excellent record in the field and it is very likely that the projects will be mastered from the technical point of view.

- ***Weaknesses and threats:***

The number of PhD students is limited and more post-doctoral researchers would be advantageous for the further development and visibility of the team. As stated in the research report, the groups is focused on a single disease (ALS). Behavioral changes could provide interesting readouts for establishing the progression of ALS and the testing of tehrapeutic strategies, so there is a need for further development of functional assays (mouse behavioural tests).

- ***Recommendations:***

This group should be encouraged to develop his translational project on neuroinflammation in ALS which may have a positive clinical impact for exploring new therapeutic strategies. The opportunity to exploit the excellent research environment at the INM should also be encouraged. iPSCs from the skin of human patients should be considered as an alternative model of ALS. It is likely that this model will be of paramount importance in the field.

Team 6: Molecular Mechanism of myelination/demyelination and gene therapy in peripheral nerve

Name of team leader: Mr Nicolas TRICAUD

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions		
N2: Permanent EPST or EPIC researchers and similar positions	2	
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral students, visitors, etc.)	7	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**9**	

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended		
Postdoctoral students having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions		

• Detailed assessments

Assessment of scientific quality and outputs

Team 6 is a relatively new team in the institute since it arrived in 2011 as an Avenir/Atip team. The research activity is devoted to improving our understanding of the mechanisms involved in peripheral nervous system myelination, demyelination and related diseases (Charcot-Marie Tooth disease). The major output from this team came from the work carried out at the Swiss Federal Institute of Technology in Zürich where the PI was heading a research team. This work focused on the epithelial-like polarization of Schwann cells and its role in myelination. In particular, the team studied two key polarity proteins, Pals1 and Dlg1, and their roles in myelin thickness and length as well as in the demyelination associated with diseases. This work was published in high impact journal such as Science and the Journal of Neuroscience in 2010. This represents the basis on which the Avenir grant was awarded to the group leader to setup a new team in 2011 in Montpellier.

One assest of the team is its expertise in viral vector technology and its use as putative strategy for gene therapy in peripheral neuropathies. The group found that lentivirus injected in the sciatic nerve were only infected Schwann cells and not neurons in very young mice.

The overall quality of the team is reflected by the different prestigious grant that were obtained at the National (ATIP/Avenir in France; ETH Zurich grant and SNF funds while in Switzerland) and European (ERC starting grant consolidator) levels. The quality and quantity of publications is excellent with publications in high impact factor journals (Science, Neuron, PlosBiology, Nature neuroscience, PNAS, J. Neuroscience).

Assessment of the unit's academic reputation and appeal

Although young, the team reputation appears to be very good with the recruitment of several foreigns postdoctorate fellows in the last few years, including a Marie-Curie laureate. This is also reflected in a fairly good number of invitation at conferences (14) and active collaborations with groups in UK, Switzerland and France. The PI was invited as a speaker in several major meetings (Gordon conference, American society for Neurochemistry, ISN...). He was also chair of a symposium on peripheral neuropathies and is currently head of the imaging plateform of the institute. One member of the team is involved in teaching at the Université Montpellier 2.

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

The team is part of a Labex (EpiGenLed in Montpellier). The group leader organized two symposia at the ETH Zurich in 2007 and 2009. He is now heading the imaging plateform of the institute, a board member of the Montpellier RIO imaging network and a member of the science committtee of the Pôle Biologie-Santé Rabelais. He is also member of the scientific board of the Association Française contre les Neuropathies Périphériques and participates to initiation courses about peripheral nerve biology and biological science in different schools. Another member of the team has a important load of teaching duties at the university and has developped a website that provides valuable information on Schwann cell biology.

Assessment of the unit's organisation and life

The team wants to keep a limited number of persons (up to 8) and projects (max 3) to keep everything under control and to ensure feasibility of the ongoing work. The team is made up of permanent staff (2), postdoctoral fellows, students and research engineer. Master students are usually recruited for a short perod corresponding to their internship.

Assessment of the unit's involvement in training through research

As mentioned above, the team is composed of several students (PhD and Master) and a postdoctoral fellows. The two permanent staff are involved in teaching activities as well. The team trained 1 PhD student and 3 masters. Although, this item is diffcult to assess since the team was recently created (2011).

Assessment of the strategy and the five-year plan

The ERC-funded program represents the most important part (70%) among the 3 projects that the team will develop in the next 5 years. This award somehow caused the termination of all research activity on the polarization of the epithelium, which is unfortunate. The ERC project is very interesting since it focused on mitochondria in peripheral neyuropathy. The aim is to investigate mitochondria function in myelinating Schwann cell and myelinated axons in vivo. Experimental deficit in mitochondrial function will be generated using viral tools and the impact on myelinating process will be studied. Viruses encoding for fluorescent proteins will also be generated to monitor mitochodrial activity. The putative croostalk between glial and neuronal mitochondria will then be explored.

The two other parts of the project (15% each) are in the line of the previous work of the team. They deal with:

I) the molecular mechanism of demyelination and more specifically the role of the transcription factor Sox2 and

II) gene therapy apparoaches for peripheral neuropathies consisting of investigating the ability and selectivity of different viruses to infect Schwann cells.

Conclusion

- ***Strengths and opportunities:***

This is an excellent and small young team with very prestigious funding and excellent indicators of past activity. The projects are innovative and the tools developed should serve the local community. Attractivness is clearly an asset as reflected by the numerous postdoctoral fellows from abroad that have joined the team since it was setup in Montpellier. The team is on a rising phase and should gain in visibility, national and international, if it continues to deliver high profile publications and exciting novel results.

- ***Weaknesses and threats:***

The group has planned to focus most of its efforts, energy and resources on the ERC project that deals with role of mitochondria in healthy and diseased peripheral nerve myelination. This is clearly a threat since the main hypothesis, that axons produces toxic ROS, is still to be tested. There is a risk that the objectives associated with this new line of research might be more difficult to reach compared to the other ongoing projects. It is also unfortunate that the team has to stop the project on polarity genes because of the ERC funding. However, the tools allowing mitochondria activity have been developped and they will definitively be very useful for the team and probably for promoting collaborations within the institute. Another possible threat is that the research carried out by this team becomes technically-rather than hypothesis-driven.

- ***Recommendations:***

This group has a very considerable potential. The foundations of this new team should be consolidated to provide a strong ground for developing new research activities. This implies capitalizing on the present expertise and ongoing projects that have yielded high-impact publications, as well as strengthening collaborations within the INM with teams that could very much benefit from the new tools being developed. The development of transgenic and KO mice could be considered to complement and to implement the adenoviral strategies. The translation of basic science findings could be enhanced through external collaborations with clinicians.

The team should try to recruit a permanent scientist. The best strategy would be to identify a person that would complement the team in terms of expertise.

5 • Conduct of the visit

Visit dates:

Start: 23rd January 2014 at 01.00 pm

End: 24th January 2014 at 04.30 pm

Visit site: Institut des Neuroscience de Montpellier (INM)

Institution: INM, Hôpital St-Éloi, Université Montpellier 2

Address: Hôpital St-Éloi – Bâtiment INM

80 rue Augustin Fliche – BP 74103

34091 Montpellier cedex – France

Specific premises visited:

All ground floor and basement level laboratories of the institute; all platforms of the institute including Imaging, Tissue Culture, Molecular Biology and Histology. Animal facilities were explained and discussed although for obvious reasons it was not practicable to visit the facility.

Program of site visit

Agenda of the site visit
From 23th to 24th January 2014

Unit: INM, UMR 1051 (Renewal)
Present director : Mr Jean-Luc PUEL
Proposed director : Mr Jean-Luc PUEL

Experts committee, composed by:

AERES scientific delegate (DS):

- Mr Yves TROTTER

Experts committee:

- Chair: Mr Jonathan ASHMORE (United Kingdom);

- Members: Ms Marlies KNIPPER (Germany), Mr Peter MCNAUGHTON (United Kingdom), Mr Brahim NAIT OUMESMAR (France), Mr Gwendal LE MASSON (France), Mr Bernd WISSINGER (Germany).

Representatives of the institutions :

- Mr Stéphane OLIET INSERM (CSS6), Mr Serge PICAUD (CNRS 25), Mr Gilles GHEUSI (CNU 69).

Representative ITA:

- Ms Cathia GIRAUX PETRICONI (INSERM).

Day one – Date: Thursday January 23th 2014	
01.00 pm	Welcome of the experts committee by the INM director and the team leaders
01.20 pm	(closed-door) Experts committee organization and review task issues:
01.45 pm	Mr Yves TROTTER: the role and procedures of AERES
02.00 pm	Mr Jean-Luc PUEL: Presentation of the past and future scientific strategy of INM
	Team presentations:
02.45 pm	Team 1: *Genetics and therapy of retinal and optic nerve blindness*, Mr Christian HAMEL
03.15 pm	Team 2: *Deafness, tinnitus and therapies*, Mr Jean-Luc PUEL
03.45 pm	Team 3: *Somatosensory system development and pathology*, Mr Patrick CARROLL
04.15 pm	Break
04.30 pm	Team 4: *Neural plasticity, stem cells and glial tumors*, Mr Hugues DUFFAU
05.00 pm	Team 5: *Motoneurons disorders: neuroinflammation and therapies*, Mr Cédric RAOUL
05.30 pm	Team 6: *Molecular mechanisms of myelination and gene therapy in peripheral nerves*, Mr Nicolas TRICAUD
06.00 pm	Site visit
Day two – Date: Friday January 24th 2014	
09.00 am	Welcome coffee
09.15 am	ATIP Avenir: Ubiquitin Proteasome System in neurodegeneration and cytoskeleton architecture, Ms Pascale BOMONT
09.30 am	(closed door) Debriefing on the team presentations Internal meeting of the experts committee with the DS
10.30 am	Coffee break
10.45 am	Meeting with permanent and non permanent staff • Meeting with the technical staff *Audience: members of the experts committee and DS* and ITA representatives of the institutions • Meeting with PhD students and Post-docs and/or fixed-term contract researcher, engineers. *Audience: members of the experts committee and DS* • Meeting with researchers, professors and assistant-professors *Audience: members of the experts committee and DS*
11.45 am	Meeting with the director of the "École Doctorale" CBS2 N°168 *Audience: members of the experts committee and DS*
12.00 pm	Lunch
01.00 pm	Discussion with the official representatives of the institutions *Audience: members of the experts committee and DS* Ms Marie-Lou KEMEL (INSERM); Mr Jacques MERCIER (UM1); Mr Bernard GODELLE (UM2)
01.45 pm	Discussion with the head of the unit *Audience: members of the experts committee and DS*
02.15 pm	Closed Door synthesis meeting *Audience: members of the experts committee and DS*
04.30 pm	End of the visit

Specific points to be mentioned:

There were several recurrent themes in the discussion with the staff. These were:

- the limited number of PhD studentships;

- the mechanisms allowing the emergence of independent small groups;

- the request (from the postdoctoral researchers especially) that they be given the opportunity to teach (for example as a teaching assistant) as part of their career progression.

The technical staff of the INM raised some issues during their meeting with the experts committee.

a) There was concern about the health and safety regulations (« Hygiene et sécurité »). This task is ensured presently by a single person who is clearly insufficient to implement H&S regulations within the entire institute. It would be appropriate that at least another person is appointed to this very important duty.

b) There was concern about the follow-up of non-permanent technicians in terms of their career and missions/objectives. An annual meeting with this category of staff together with the leader of the team involved (or the institute director for the platforms) could be appropriate.

c) There was also concern on the effect of new regulations limiting the duration of recruitments to 3 years of non-permanent personnel (technicians, administrative staff and researchers). This was a major concern, since specialised, valuable knowledge and expertise will be lost.

The experts committee recommends that the first two points (a & b) should be addressed by the director through the organisation of at least an annual meeting with the non-permanent technical staff. The experts committee also shares the concern on the third point (c).

6 • Supervising bodies general comments

Université Montpellier 1

AES Droit, Sc. politique Économie IPAG ISEM Médecine Odontologie Pharmacie STAPS

nouvelle université de Montpellier
un projet, une ambition

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

Montpellier, le 25 mars 2014

Référence : JL.PUEL : S2PUR150008475-INM-Institut des Neurosciences de Montpellier-04342321N

Messieurs,

Je tiens à remercier le comité de visite AERES pour la qualité de son rapport d'évaluation concernant l'Institut des Neurosciences de Montpellier dirigé par le Professeur Jean Luc PUEL.

J'ai bien noté les remarques formulées par le comité de visite et je veillerai à ce que celles-ci soient prises en compte par le directeur de cette structure de recherche.

Vous trouverez ci-joint les commentaires généraux et spécifiques concernant l'unité de recherche ainsi que les commentaires de chacune des équipes de recherche.

En tant que tutelle Universitaire de cette structure de recherche, je n'ai pas de remarques supplémentaires.

Je vous prie d'agréer, Messieurs, l'expression de mes salutations les plus respectueuses.

Philippe Augé
Président
Université Montpellier 1

Assessment of the unit

General comment for the research unit

We are grateful to the AERES committee for the unit evaluation. We trust this will strengthen our research program, improve our day-to-day work and fix the weakness points identified by the committee. We acknowledge that the AERES committee recognizes the excellent scientific quality of the institute as well as the outstanding combination of uniqueness, confidence and high visibility. AERES committee also highlights the clear governance and considers that the efficient organization of the INM is a model of its kind.

Specific comments

"Mitochondrial function and dysfunction" is clearly a common theme research.

We totally agree that "Mitochondrial function and dysfunction" is a specific taskforce for the institute. Indeed, most genes responsible for optic neuropathies, frequently associated with deafness, peripheral neuropathies and myopathies, encode mitochondrial proteins. Also, the maintenance of the myelin sheath in peripheral nerve seems under close control of the mitochondrial physiology, a research topic developed in the ERC grant. Finally, ageing processes are partly dependent on mitochondrial pathophysiology and its DNA instability, as we showed in animal models of presbycusis and optic neuropathies. Therefore, we need to enhance our capacity to explore the mitochondrial physiology over its different aspects (respiration, mitochondrial network dynamics, mtDNA maintenance, control of apoptosis). To achieve this task, we therefore acquired new equipment for measuring mitochondrial respiration and promote inter-team interactions as well as external collaborations. We will also extend the call for new team to the basic mechanisms of the mitochondria functioning.

The number of PhD students in the institute is too limited

As mentioned by the committee, "The unit is effective in training PhD students belonging to the "École Doctorale" CBS2 N°168, with an excellent record of thesis completion given the constraints on recruiting such individuals". Looking carefully, the staff list of the unit shows that the number of HDR (29) and the number of PhD students (26) are quietly equivalent, which is in completely in ad equation with the doctoral school policy. As mentioned by the committee, the Doctoral School imposes very restrictive conditions to supervise students (only 1 student per HDR, a 2nd is allowed if the first is in his/her final year). In addition, Inserm accepts to hire a PhD only if the researcher guarantees access to 2 first years funding. A simple calculation demonstrates that the director of the unit cannot guarantee ~1 M€ for a 3rd year of funding [26 PhD x 36 k€ (one year salary)]. This is just an administrative problem. To increase the number of student, the rules of the doctoral School has to be change to allow the researchers to hire more than 1.5 students, and Inserm should accept to hire PhD student, even if the budget is only cover for 2 years.

The internal unit rule to create an independent team.

This rule to create independent team has been established at the creation of the Institute in 2004, following the recommendation of the Scientific Advisor Board. This rule imposes 2 permanent researchers (full research or associated professor) to promote the creation of competitive and attractive team. Note that this rule only concerns the teams that compete to be labeled by Inserm, and not ATIPE-AVENIR teams. Nevertheless, when new team only composed by a single researcher has been approved by the Steering Committee, we strongly support the development of this team by providing additional researcher. For example, we strengthen the Cédric Raoul's team by inciting Frédérique Scamps (CR1 Inserm) to join him and Sylvain Bartolami joined the Nicolas Tricaud's group to be labeled Inserm team. This collective process is a good way i) to select excellent outstanding researchers and ii) to promote and to strength independent team to be labeled by Inserm.

Space problem with respect to animal facilities.

To solve the problem of space for animal facilities, there are 2 options, i) to expend surface of our animal facility, or ii) to re-organize the animal care network of Montpellier (RAM). The later solution requires the limitation of our activities to functional sensory-motor investigation, whereas the growth and the maintenance of different strains would be insured in a central structure. Whatever the strategies, Inserm and the others academic institutions (Cnrs, Universities) have to contribute through financial (renovation: 1st solution and/or salaries for the 2nd solution). Within the other options the use of external companies to mitigate the rising costs and consequent limitations on the animal usage for each team.

Health and safety regulations (« Hygiene et sécurité »).

The committee underlies that a single person (Audrey Sénéchal) is in charge of health and safety regulations (« Hygiene et sécurité »). We agree that a single person is clearly insufficient because of the large size of the institute. We are therefore planning a new organization. A scientific advisor (Philippe Brabet, CR1 Inserm) agrees to help Audrey Senechal. In addition, we will nominate one people in charge of H&S in each team. Together with the Director and the General secretary, these people (the Engineer in charge of H&S regulations, the scientific

advisor and the 6 team representatives) will constitute the H&S committee that will meet every month to discuss, follow and address H&S problem and the research quality.

Follow-up of non-permanent technicians

The director is very careful of the future of the non-permanent technician. Therefore, he just starts to organize personnel meeting (with or without the team leader as the convenience of the non-permanent) one a year as he already does with the permanent technicians and administrative staff.

Regulations limiting the non-permanent period to 3 years

The European policy that plan to limit precarious jobs over 3 years (including Postdoc, Engineer and technicians) in state of 6 years as it is today. The direction of the Unit does not agree with this European rule, but has no control on this rule.

The institute as being 'family friendly'

This recommendation is very surprising as the director of the Institute is very aware of this problem. Since 2011, scientific and administrative meetings are organized at times which favor researchers with family commitments. For example, the internal and external seminars are program at noon, the Unit Council at 9 AM and the steering committee between 4 and 6 PM.

Team 01: Genetics and therapy of retinal and optic nerve blindness

Name of team leader: Mr Christian HAMEL

Assessment of the unit's involvement in training through research

In this paragraph, the committee mentions that "*only 5 PhDs have been trained during the previous period*". We would like to stress that this number corresponds to PhD students currently present in the team as at 30/06/2013, as indicated in the table p.7. In fact, from 2008 to 2013, 7 PhD students have been trained and have defended their thesis successfully, and 5 other PhD students are currently in training.

Weaknesses and threats

It is said that "*there is always the possibility that funding opportunities for the translation of therapeutical approaches into clinical studies could be missed*". For that reason, two patents have been filed in 2013 and one is in preparation, to help in finding funds, and private crowd funding for clinical trials have been engaged through internet. The recent creation of a biotech company for gene therapy will also be very supportive, hopefully with a capital of 4 million euro at the end of 2014, to facilitate the clinical transfer of our pre-clinical studies.

Recommendations

It is said that "*the committee should like to see additional consideration given to strengthening work on iPSCs as model systems for pathophysiology and for therapy development in this team's work*". We wish to indicate that not only do we generate and use iPSCs for retinal disease, but that we also started to produce iPSCs for the Wolfram disease optic atrophy in collaboration with the national platform iSTEM, to obtain retinal ganglion cells from patients to be used in pathophysiology studies and pharmacotherapeutic approaches. This was not mentioned in the audit presentation because of time constraints.

Team 02: Deafness, Tinnitus and Therapies

Name of team leader: Mr Jean-Luc PUEL

General comment for the research team

We are really grateful to the AERES committee for their Team evaluation that will strengthen our research project. The AERES referees stress in their comments that the team has an enormous spectrum of excellent competitive research. Moreover, the AERES committee acknowledges that the profile of the group members has been very high with an impressive list of publications so that the scientific output has been excellent and in some places groundbreaking. Finally, AERES reviewers underline that the laboratory has excellence in molecular approaches, anatomical as well as in functional studies.

Specific comments

Possible loss of direction in the specific skills

A concern raised by the committee is a possible loss in traditional auditory nerve recording because of the departure of one senior investigator to Marseille. Although this might have been the case, it turns out to be in fact the opposite. Indeed, with the help of Régis Nouvian (who carried-out single-unit recordings during his PhD thesis) and Gilles Desmadryl (who carried-out single-unit recordings in vestibular nerve), were able to recover this technical approach as we used to do in guinea pig. Moreover, the expertise of Jérôme Bourien enabled us to develop novel stimulation paradigms such as pair pulse protocols or ecological sounds in contrast to the single tone burst used over the last decades. Finally, the single-unit recordings is no more restricted to the guinea-pig species but also extended to other species such as gerbil. Therefore, we did not lose this technical skill but in contrary upgraded this competence. Next challenge will consist to extend this approach to the mouse species.

To ensure younger researcher training in the skills for integrative and systems neuroscience.

We definitively agree with the AERES comment. Therefore, we already take care that younger researchers are trained up for system level investigation. Under the supervision of Jérôme Bourien and Gilles Desmadryl, two PhD students are daily doing single-unit recordings (Antoine Huet in Guinea-Pig and Charlène Batrel in Gerbil). Because of their high success in this approach, we are confident that we can achieve another technical jump with single-unit recordings in mouse.

Large number of animals required for genetic studies

The space in the animal care facility is a real problem for all the teams of the Institute. Therefore, we carefully examine the relevance of the mice for our research program. However, the direction of the institute looks for the possibility to extend animal facility, or to export the maintenance of the different strains in a different structure. This problem should be solved in the beginning of the five-year plan.

To combine single fiber recording and CAP with behavioral tasks in tinnitus models.

Again, we definitively agree with the AERES recommendation. Indeed, our animal models of tinnitus and others auditory deficits are screened using the combination of the techniques we master. In addition, we aimed at investigating the auditory deficit with simultaneous recordings of CAP/Round-window neural noise/single unit recordings or CAP/Behavioral task.

To separate the IHCs hair cell presynaptic machinery and postsynaptic neuropathies.

Because any partition may be detrimental to our research, each animal model of auditory deficits and therefore tinnitus models is screened by all the experts of the teams. The efficiency of such interactions is reflected in many previous publications (see for example: Molina et al., 2013; Menardo et al., 2011; Ruel et al., 2008)

Team 03: Somatosensory system development and therary

Name of team leader: Mr Patrick CARROLL

Factual error

We do not use the zebrafish model, contrary to the statement in "Assessment of scientific quality and outputs"

General comment for the research team

We thank the committee for their positive appreciation of our team and future projects as well as for their helpful comments and suggestions. We agree that we need to increase the number of Ph.D. students in the team. Following the committee's suggestions, we will make a major effort to try and remedy this problem by recruiting foreign students through international fellowships in addition to the normal recruitment channels in the French system.

Detailed assessments

Assessment of scientific quality and outputs

The team has an excellent publication record with the 5 well-cited papers including one EMBO J. paper entirely from the team, one Neuron paper mainly authored by the team, and one Science paper with two last authors from another group but in which the past work of the group has evidently played a key role. In addition there have been 4 book chapters and 6 reviews published.

The area of work of the team – somatosensory neuron specification and control of phenotype – is highly topical. There is a strong focus on the genetics of touch sensation, emphasizing specific molecule (e.g MafA, Ret, Zeb1,2) and their relation to clinical situations (e.g. hereditary diseases) and these interests are being studied in a broad range of systems including zebrafish, rodents and human. The basic work in this area seems certain to lead to translational opportunities in the near future. The group is already actively exploiting drug development opportunities in the area of FL/Flt3 of interactions where there is a strong possibility of realising treatments for neuropathic pain, an intractable, disabling and widespread condition.

Assessment of the unit's academic reputation and appeal

The group has significantly advanced our understanding of neuronal specification at the level of basic science. A new pain pathway has been discovered on the basis of which a new therapeutic approach to pain silencing has been developed based on a TRPV1- Flt3 mediated aberrant pathway. The techniques being employed to develop FL/Flt3 antagonists are state of the art and show strong interactions with the team of Mr Jean-Philippe PIN in the Institute of Functional Genomics, another Montpellier INSERM unit. The potential for translation of this knowledge into treatments for neuropathic pain will significanly enhance both the reputation and appeal of the group, if successful.

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

As noted above, the team is developing a possible new treatment for neuropathic pain in collaboration with external industrial partners. The translation of this basic science discovery into potentially new treatments, together with the pharma-academic liaison, is very promising, and the team holds a patent related to the technology

Assessment of the unit's organisation and life

The team is focussed on basic science and as such has a valid and important objective of understanding specification and modulation of sensory neuronal phenotype. There is evidence of a healthy spread of interests in the team with some members more focussed on basic science objectives and others more interested in the development of translational research.

Assessment of the unit's involvement in training through research

As with the general comment above, the number of PhD students in the INM as a whole is small by international standards where it would be usual for a successful PI to supervise 3-6 PhD students at any one time. With this reservation it appears that the PhD students in the team are well supervised and moreover have access to an excellent range of facilities in research.

Assessment of the strategy and the five-year plan

The five year plan is very strong with clear goals in each of the research projects proposed. There are proposals to identify Zeb1 in the peripheral nervous system and to link this work in to clinical group working on genetic

diseases of the eye. There are appropriate plans to identify a transcriptional programme initiated by cMaf, a well as identifying the properties of Meis2 as a survival factor for DRG neurons. The 5 year plan also proposes to further the important study of the role FL/Flt3 in neuropathic pain and to develop the multidisciplinary project to identify extracellular pharmacological inhibitors as part of translational effort, for which the group has already deposited a patent.

Strengths and opportunities

This is an excellent group close to the forefront of their area internationally. They have made some seminal discoveries and have collaborated well with other leading groups to produce significant publications in leading journals. Strong interactions with other groups internationally (e.g. group of Mr Gary R. LEWIN at Max-Delbrück-Centrum (MDC) Berlin) and locally (e.g. group of Mr Jean-Philippe PIN at Institute of Functional Genomics (IGF)) adds to the considerable strength of this group and opens up new dimensions that the group could achieve only withdifficulty by themselves. The committee sees the translational work underway in this group as a considerable strength. The group should continue with a combined basic science and translational approach – top basic science often leads to translational opportunities.

Weaknesses and threats

The committee considers that there are no significant weakness in the team. In comparison with other leading groups in this area (Mr Quifu MA, Mr Gary R. LEWIN, Mr Patrick ERNFORS) it would perhaps be fair to recognise that they are not absolutely at the very front of the field but in this “hot” competitive and fast-moving field they are not far behind the international leaders. Along with other groups at INM the committee is concerned at the low numbers of PhD students – this is particularly a problem for this group and leads to concerns that future scientists are not being trained in adequate numbers. A leading group such as this should be training many more than the “replacement numbers” of PhD students and one would expect graduates of this group to be populating many other leading labs and academic institutes with their graduates

Recommendations

Continue top-level basic science and continue to explore translational opportunities as these arise. The committee should like to see the team consider ways of encouraging more PhD students to train in the area, e.g. by using further opportunities for industrial/biotech sponsorship and by encouraging international students (who can sometimes be funded by home studentships) to join the team.

Team 04: Neural plasticity, stem cells and glial tumors

Name of team leader: Mr Hugues DUFFAU

General comment for the research team

First, we would like to thank the reviewers for their positive and detailed analyses of our team and our projects. These comments will be helpful to improve our research strategy. Here are some replies to minor mistakes and some points raised in the AERES report

Mistakes in the report

It is said:

"*The five plan research plan is a nice follow-up of previous projects.*

The research plan focuses on three main topics:

1. *Functional brain mapping and their reorganisation induces by GBM".*
2. *Cellular and molecular mechanisms regulating low and high grade glioma cells and stem cells;*
3. *Development of pre-clinical and clinical applications of the glycomimetic phostine in GBM and other cancers"*

The project #1 on glioma-induced brain plasticity is performed by Pr H Duffau during awake-surgery. The patients are affected by low grade gliomas and not glioblastoma (GBM). The project #3 will be performed through a start-up creation for which a CEO and a R&D director and two engineers have been recruited. At the INM the research program will mainly consist in the study of cellular and molecular mechanisms induced by the glycomimetic phostine, affecting GBM stem cells glycosylation and inhibiting their proliferation, migration and invasion in vitro and in vivo.

Points raised by the reviewers

The heavy clinical and teaching duties of the PIs need to be managed to ensure proper development of each program.

1. We are aware of these duties but so far this has not been a major obstacle for the progress of our projects including writing of original publications, reviews, book chapters together with grant applications.
2. JP Hugnot teaching duties are carried out over a 3 month period (Sept-Oct-Nov) so there is almost 9 months fully dedicated to research. Reduction of his teaching duties will be sought in the future (possibly by obtaining a University of Montpellier-INSERM mixed chair).
3. Norbert Bakalara will obtain from his institution (ENSCM) a 30% reduction of his teaching duties.
4. Hugues Duffau performs a major part of his research in the operating theater to study brain plasticity and connectomic as well as the collection of glial tumors for the team's gliomabank.

The team has only 2 CR1 researchers, and the recruitment of a full time researcher is important.

In order to face this problem, we have taken several actions:

1. We are calling for recruitment of permanent researchers from other INSERM units by frequent advertising on the INSERM mobility portal and weekly letter (last call posted on INSERM letter, week 11 March 2014).
2. We are in contact with potential good candidates for INSERM and/or CNRS
3. Romane Auvergne who is currently in S Goldman's lab in Rochester has just published a nice paper on low grade/ high grade gliomas in Cell reports (Cell Rep. 2013 Jun 27;3(6):2127-41.). She is due to participate to INSERM/CNRS recruitment sessions (CR1) in 2015.
4. Two post docs working on gliomas (PO Guichet and Z Hassani) are also due to try to be recruited at INSERM or CNRS.

Interactions between the groups could be strengthened to ensure efficient development of the projects.

We fully agree with this comment but strong links are already in place between the groups. Notably:

1. JP Hugnot uses resections from patients operated by Pr H Duffau each week to derive low grade glioma primary cultures.
2. N Bakalara uses glioblastoma stem cell cultures for exploring the effects of phostines on migration and proliferation. These cells have been isolated and are cultured in JP Hugnot's group. N Bakalara will use low grade glioma cultures derived from patient's resection to test new anti-migratory compounds as well as for the identification of proteins and specific glycosylation patterns involved in low grade glioma dissemination.

The basic science projects are strongly based on in vitro studies (Gliobank).

We have developed a glioma-bank for several years, especially a unique bank comprising one hundred of low-grade glioma tumors including RNA and proteins. This bank has used to identify a patented prognosis signature for low grade gliomas (Reme et al, Plos One 2013). We will continue incrementing and sharing this precious bank with the scientific community.

The development of relevant animal models of GBM could be a nice addition to these projects.

Animal models for GBM are currently in use in the lab and were used in two recent publications by JP Hugnot's group (Glia 2013 + Stem cells, 2014, in revision). One of our main objective for the years to come is to develop an animal model for low grade glioma based on patient's derived cells. This will definitely be a major step in the field to find new innovative therapies. Different strategies are currently explored by JP Hugnot's group with the help of SIRIC Montpellier (sites de recherche intégrée sur le cancer)

Collaborations with other INM teams should be considered to ensure the appropriate integration of the team within the institute.

We confirm that such collaborations are already in progress, notably:

1. Study of neural basis of interactions between audition and language (collaboration with team 2, JL Puel)
2. N Bakalara is developing a new project in collaboration with Guy Lenaers (team 1) on the effect of the 7β-hydroxysterol and mitochondrial respiration of glioma cells.
3. Our expertise in drug design and development is shared with other teams, notably with Jean-Luc Puel (team 2) on glutamate analogs synthesis and with Pascale Bomont (avenir team) for the development of an in vivo screen for compounds in the zebrafish model for Giant Axonal Neuropathy.
4. -JP Hugnot collaborated with P Carroll's team (team 3) on the role of Zeb1 transcription factor in stem cells (published in Stem cells, 2010). Low grade gliomas are derived from myelinating cells which fail to differentiate. N Tricaud's team is currently exploring several genes involved in the regulation of adult myelination and collaborations will certainly emerge between the groups. In addition, the possibility of using hearing or vision loss models (team 1& 2) to explore the role of the pool of endogenous adult neural stem cells in brain plasticity will be considered.

Team 05: Motoneuron disorders: neuroinflammation and therapies

Name of team leader: Mr Cédric RAOUL

General comment for the research team

We would like to thank the AERES committee members for their positive evaluation and the constructive feedback received for our team project "Motoneuron disease: Neuroinflammation and Therapy". We were very pleased to see that committee members found our research theme to be very relevant to fundamental and medical sciences and that team members have high competence in their field with complementary expertises.

Specific comments

The committee raised three points regarding our weaknesses and threats.

Limited number of Ph.D student and post-doctoral fellow.

We fully concur with the committee members. As mentioned in the team assessment, we are a relatively "young" team, since the team was implanted at the institute in Jan 2012. Despite we grew up rapidly, factually from 1 to 15 over a two-year-period, we are still consolidating our task forces. Emmanuelle Coque has recently received a Ph.D fellowship and starts her Ph.D thesis in April 2014. We have already applied to European (E-RARE) FP7 program and to an American association for ALS (first step passed) for a post-doctoral fellowship. One Master student will apply for a doctoral school fellowship in June to pursue his thesis within the team. We are presently applying for a Ph.D fellowship in the Montpellier Université-CHU call for proposal.

The group is focussed on a single model.

We understand the committee members comment. However, it is noteworthy that to complete our analysis of neuroinflammation in motoneuron disease, we have recently received an animal model of ALS-frontotemporal dementia (TDP-43 mutant strain). We have also applied to the EU FP7 program E-RARE and to the FightSMA American foundation to investigate neuroinflammation in a mouse model of spinal muscular atrophy (SMNΔ7 strain of mice). We are currently investigating, regarding chloride homeostasis in motoneurons; a mouse model of Anderman syndrome (KCC3-deficient mice) as well as a un-yet described Anoctamin-6 deficient mice (in collaboration with Jan, L, UCLA, CA, USA).

There's a need for functional assays (mouse behavioural test)

We apologize to not having clearly stated this point. Indeed, we routinely do a close-follow up of mice with motor deficits. Indeed, to functionally describe motor impairment in mice, we use 1) The Cat-Walk system that allows an automated and complete analysis of motor skills, 2) The grid-test, which is an highly sensitive assays to accurately determined the first signs of motor impairment and 3) Electromyography that allows a quantitative assessment of motor functions. Moreover, a video tracking system for mouse spontaneous activity has been recently acquired. This test will be included in the battery of functional tests that we currently perform.

Regarding the scientific productivity

We would like to mention that our work, in collaboration with the team 3 of the institute, has been recently accepted for publication in EMBO Rep.

Otsmane, B., Moumen, A., Aebischer, J., Coque, E., Sar, C., Sunyach, C., Salsac, C., Valmier, J., Salinas, S., Bowerman, M. and Raoul, C*. Somatic and axonal LIGHT signaling elicit degenerative and regenerative responses in motoneurons, respectively. EMBO Rep, in press. *corresponding author.

Recommendation of the AERES committee

We will consider the recommendation of the AERES committee regarding the opportunity of iPSCs cells. This is indeed a judicious comment, especially with the ALS center led by William Camu in the team, which manages an important active file of patients and represents an important source of human tissues. We aim at, with the CHU of Montpellier and Nîmes (Pr. W Camu and Pr. S Lumbroso), integrating clinical phenotyping to genetic analysis. Although therapeutic approaches for ALS using stem cells are already under evaluation in several stem cell-oriented laboratories (for review please see Sreedharan, J et al., Ann neurol, 2013), we could take our clinical opportunity to pertinently address the relevance of our identified cellular and molecular mechanisms in human motoneurons.

Team 06: Myelination and gene therapy in the peripheral nerve

Name of team leader: Mr Nicolas TRICAUD

Team force

In the first table presenting the team workforce, 2 permanents positions and 3 “Other EPST or EPIC researchers” positions (ERC postdoctoral positions funded until 2018) should be added in the 2015 column.

Team workforce

In the second table presenting the team workforce one should be added to “Number of Research Supervisor Qualifications (HDR) taken” (HDR N. Tricaud) and one should be added to “Qualified research supervisors (with an HDR) or similar positions” both in the first column and the second.