IGH - Institut de génétique humaine

Rapport Hcéres

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

Department for the evaluation of research units

AERES report on research unit

Institute of Human Genetics

IGH

Under the supervision of the following institutions and research bodies:

Nouvelle Université de Montpellier

Centre National de la Recherche Scientifique - CNRS

February 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,

- Ms Catherine DARGEMONT, 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 assessments contained herein are the expression of an independent and collegial deliberation of the committee.

Unit name:	Institute of Human Genetics
Unit acronym:	IGH
Label requested:	UPR or UMR
Present no.:	UPR 1142
Name of Director (2013-2014):	Mr Giacomo CAVALLI
Name of Project Leader (2015-2019):	Mr Monsef BENKIRANE

Expert committee members

Chair:	Ms Catherine DARGEMONT, Institut Jacques Monod, Paris
Experts:	Mr Ian ADAMS, Institute of Genetics and Molecular Medicine, Edinburgh, United Kingdom
	Ms Asifa AKHTAR, Max-Planck-Institut fur Immunbiology und Epigenetic Freiburg im Breisgau, Germany
	Mr José ALCAMI, Unidad de inmunopatologia del sida, Madrid, Spain
	Mr Christophe ANTONIEWSKI, Laboratoire de Biologie du Développement, Paris
	Ms Valérie BORDE, Institut Curie, Paris (representative of CoNRS)
	Ms Bénédicte CHAZAUD, Institut Cochin, Paris
	Ms Michelle DEBATISSE, Institut Curie, Paris
	Mr Luciano DI CROCE, Center for Genomic Regulation, Barcelona, Spain
	Mr John DIFFLEY, London Research Institute, London, United Kingdom
	Mr Marco FOIANI, European Institute of Oncology, Milano, Italy
	Mr Bob LAHUE, Center for Chromosome Biology, Galway, Ireland
	Mr Helder MAIATO, Instituto de Biologia Molecular e Celular, Porto, Portugal
	Mr Christian MUCHARDT, Institut Pasteur, Paris
	Mr Didier TRONO, Laboratoire de Virologie et Génétique, Lausanne, Switzerland
	Ms Claire VOURC'H, Institut Albert Bonniot, Grenoble (representative of CNU)

Scientific delegate representing the AERES:

Mr Pierre COUBLE

Representatives of the unit's supervising institutions and bodies:

Mr Philippe AUGE, Université Montpellier 1

Mr Michel DESARMENIEN (representative of Doctoral School CBS2 n°168)

Mr Bernard GODELLE, Université Montpellier 2

Mr Thierry GRANGE, INSB, CNRS

Mr Jacques MERCIER, Université Montpellier 1

Mr Michel ROBERT, Université Montpellier 2

1 • Introduction

History and geographical location of the unit

The visit of IGH took place on from 05th to 07th February 2014. IGH is a CNRS unit founded in 1998 by Mr Jacques DEMAILLE and located within the Arnaud de Villeneuve Biomedical Campus in Montpellier, at close vicinity of other CNRS and INSERM laboratories. It has been directed by Mr Marcel MÉCHALI from 2003 to 2006, then by Mr Alain BUCHETON till 2010 and Mr Giacomo CAVALLI since 2011. From its onset, the main scientific interests of IGH concerned the organization, dynamics and expression of the genome from the molecular to the organism levels as well as the pathological consequences of dysregulation of these processes. IGH is composed of 21 teams organized in three departments, "Genome dynamics", "Genetics and Development" and "Molecular bases of human diseases".

Management team

The director, Mr Giacomo CAVALLI, is assisted by a deputy director, Mr Philippe PASERO, and a general administrator forming the Directorship board and a steering committee (director, deputy director, including heads of the departments Mr Monsef BENKIRANE, Mr Bernard DE MASSY, Ms Martine SIMONELIG and the director of Genopolys, Mr Marcel MÉCHALI). The group leader's board and the Scientific Advisory Board are consulted to define the scientific policy of the Institute such as the selection of new research groups.

The Institute Council as well as ad-hoc committees participate to more general (organization, budget..) or technical aspects (equipment imaging, animal facilities, cell culture, health and safety) aspects of the Institute activities. A health and safety committee has been held according to the CNRS rules. Mr Monsef BENKIRANE is proposed to become director of the IGH for the next 5 years and Mr Dominique GIORGI as the deputy director.

CNRS is so far the unique stakeholder of IGH but this Institute now negotiate the possibility of being associated with the Université de Montpellier.

AERES nomenclature

SVE1 Biologie Santé

Unit workforce

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	8	5
N2: Permanent researchers from Institutions and similar positions	47	50
N3: Other permanent staff (without research duties)	38 (37,4)	37 (36,3)
N4: Other professors (Emeritus Professor, on-contract Professor, etc.)	1	2
N5: Other researchers from Institutions (Emeritus Research Director, Postdoctoral fellows, visitors, etc.)	34	32
N6: Other contractual staff (without research duties)	26	23 (22,8)
TOTAL N1 to N6	**154 (153,4)**	**149 (148,1)**

Unit workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	26	
Theses defended	38	
Postdoctoral fellows having spent at least 12 months in the unit*	26	
Number of Research Supervisor Qualifications (HDR) taken	14	
Qualified research supervisors (with an HDR) or similar positions	35	38

2 • Overall assessment of the interdisciplinary unit

The Institute for Human Genetics (IGH) in Montpellier became a flagship for life sciences in France during the past 10 years. A majority of the teams perform outstanding and highly innovative research, some of them being world-leaders in their field. A major effort has been made over the past 5 years to set up an official status for junior groups and attract international scientists (PhD students, postdocs and PI). The intellectual atmosphere of IGH is very intense and scientific life well organized. Most scientific projects proposed for the next 5 years are simply superb and the experts committee has no doubt that the future director, will be able to pursue this quest of excellence. Although involvement of IGH scientists in teaching activities was rather modest over the past years, they have recently accepted to reorganize and develop the Genetic, Epigenetic and Bioinfomatic Master programs that will contribute to disseminate their unique expertise and knowledge in these domains in the Montpellier area.

The Institute has been able to develop close links and mutualisation with Institutes on the same campus, and in particular IGF (Institut de Génomique Fonctionnelle). The experts committee feels that an association between IGH, as an UMR, and the novel unified Nouvelle Université de Montpellier would be of mutual benefit for both partners (if well thought out and balanced) particularly in light of the expanding de Villeneuve Biomedical campus.

In summary, this is a world-class institute which represents an essential pillar of Life Sciences in France.

Strengths and opportunities related to the context

- world-class institute as judged by outputs and fundings;
- great balance of excellent and very promising junior group leaders and outstanding senior Pis;
- ambitious scientific projects organized around synergistic axes;
- intense internal and external collaborations;
- very active scientific life creating an exciting environment for students and postdocs alike;
- exemplary leadership and governance bringing the institute to the forefront of the scientific community;
- highly attractive institute for national and international scientists;
- provide state-of the art infrastructures for a large number of technologies.

Weaknesses and threats related to the context

- suffers from insufficient transgenic mouse facilities;
- suffers from insufficient office space for young PIs and researchers;
- insufficient administrative support for international fundraising and partnership with industry;
- insufficient number of PhD studentships.

Recommendations

- continue the quest for excellence;

- association with the future Montpellier University was deemed a highly beneficial initiative which would provide an opportunity to participate in life science policy and education;

- continue to strengthen the mentoring program for young group leaders;

- improve involvement in master programs to disseminate institute expertise and attract PhD students;

- develop strategy to interact and integrate with the coming faculty of medicine and university hospital;

- this outstanding institute deserves a strong support, including administrative support for fundraising and management of human resources (in particular regarding assistance to international students/postdocs), science communication, and time-limited contracts by the stakeholders, as well as an increase in the number of PhD fellowships;

- explore all avenues to maintain the former director of IGH and current director of Genopolys in activity (not as an emeritus).

3 • Detailed assessments

Assessment of scientific quality and outputs

The scientific production of IGH has been outstanding with 302 publications between 2008 and 2012, including 50 % with the first and the last authors from IGH. 20 % of these research papers have been published in high profile journals with an IF>10 (2 Nature, 9 in other Nature series, 6 Cell, 2 Science, 7 Genes & Dev, 6 Mol Cell, 7 EMBO J, 5 PNAS, etc) and the mean of the IF over the period is 7,6 for all papers, and 8.8 when considering papers with IGH members as first and last authors.

Ongoing research is highly innovative and has led to several seminal papers on the identification of PRDM9 as a major determinant of meiotic recombination hotspots (Baudat et al., Science 2010), the role of piRNAs in maternal mRNA deadenylation and decay (Rouget et al., Nature 2010), the organization of chromosomal domains (Bantagnies et al., Cell 2011; Sexton et al., Cell 2012), identification of SAMHD1 as the dendritic and myeloid-cell-specific HIV1 restriction factor (Laguette et al., Nature 2011) the role for the microprocessor and transcription terminator components to induce premature termination of PolII RNA (Wagschal et al., Cell 2012), the role of MCM9 in the assembly of pre-replication complexes and proper homologous recombination (Lutzmann et al., Mol Cell 2008 and 2012), the Fanconi Anemia protein FANCD2 and DNA replication (Lossaint et al., Mol Cell 2013), new insights in the replication stress response (Crabbé et al., NSMB 2010; Tuduri et al., NCB 2009) and the cross-talk between TGFb signaling and orphan nuclear receptors to control neuronal remodeling during fly metamorphosis (Boulanger et al. Nature Neuroscience 2011).

Since 2008, a total of 39 IGH PhD students have defended their thesis with only 5 without published papers yet.

Assessment of the unit's academic reputation and appeal

The outstanding academic reputation of IGH is attested by the award both of national and international competitive funding. Of note, 6 ERC grants (4 advanced, 1 consolidated, 1 junior), 4 ATIP/Avenir, 22 grants from ANR have been attributed to IGH scientists. Other grants were obtained through collaborative work, in particular 5 groups belong to the European network of Excellence Epigenesys, another EU-FP7 HIT-HIDDENHIV is coordinated by an IGH member, and the Labex EpigenMed has been initiated by the IGH director and is now directed by an IGH group leader.

Both senior and junior members of IGH have received prestigious honors, such as memberships of EMBO (3 new members), CNRS “Médaille d’Argent” (2), “CNRS Médaille de Bronze” (1), awards from the French Academy of Science (6) and from foundations or charities (FRM, Ligue Nationale contre le Cancer) among others. The strong reputation of the groups of this unit is also attested by the numerous invitations to national and international meetings and talks in various universities and prestigious institutes.

Many PIs of the unit participate in expert committees (ERC Starting Grant Committee Life Science, FP7-HEALTH committee, ANR and ANRS committees, INSERM and CNRS recruitment committees, ARC/Ligue Nationale contre le Cancer/Sidaction scientific committees), or editorial committees (Invited editors or members of editorial boards for PLoS Genetics, PLos One, Cell Reports, Epigenetics and Chromatin, Retrovirology, etc) and participate actively as referees in scientific reviewing.

PIs of the unit have been regularly involved or are currently participating in the organization of national or international meetings (EMBO Conference Series on Nuclear Structure and dynamics, the EMBO Conference Series on Meiosis, Academy of Sciences International Conference “Epigenetics, Reprogramming and Development”, EMBO YIP Genome Integrity, AFRAVIH 2014 meeting, AIDS vaccine international meeting, IBC’s Annual International Conference, etc).

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

Technological transfer activities are rather modest at IGH. Only 10 patents and 2 IDNN have been accepted over the past 5 years and few groups only develop collaborative projects or consulting activities with industry. However, IGH members mentioned during the visit that some contracts with companies have been delayed or even worse, are seriously in danger because of a serious lack of support from the juridical CNRS services.

Translational activities of IGH are still fair. According to the outstanding quality of groups working on HIV or mechanisms involved in carcinogenesis, this modest interest for applications of research is surprising and a major

effort is expected to be done over the next years. The experts committee has however noticed the proposed association between an IGH team and members of an INSERM unit that aims at developing novel therapeutic strategies to target replication forks in cancer cells, notably in Multiple Myeloma.

One can note that some PIs are members of scientific councils of French scientific charities, or deeply involved in governmental structures or agencies dedicated to pathologies (ANRS, SIRIC, Canceropoles, etc).

IGH strongly participated to the initiation and elaboration of Genopolys (led by one of the IGH group leader and former director), a structure created by CNRS, INSERM, UM1 and UM2 but also supported by the city, the department and the region as well as by the Sanofi company. Genopolys, a structure inaugurated in 2013, is dedicated to training, scientific exchanges and scientific dissemination in life sciences and medicine in order to foster debates between scientists and industry, scientists and medical doctors, scientists and society.

In addition to this initiative several group leaders participate to public events such as “Fête de la Science”.

Assessment of the unit's organisation and life

The director of IGH is assisted by a deputy director, and a general administrator forming the Directorship board and a steering committee (director, deputy director, heads of the departments and the director of Genopolys). According to the recommendations of the previous evaluation committee, a Scientific Advisory Board has been created that assists IGH in its scientific policy, in particular in the selection of new research groups. Based on discussions with staff scientists during the visit, the experts committee recommends to the IGH direction to better communicate on decisions and internal rules in order to keep the spirit of IGH membership. The experts committee appreciated the very positive opinion of technicians, engineers and administrative staff on the IGH governance and atmosphere. However, the quite brutal management of personnel employed on temporary contracts bythe local administration has been underlined. In addition, it was also mentioned that the deficit in personnel for management will be aggravated by the new ERCs and by the future association of the IGH with the university.

A major effort has been made over the past 5 years to introduce the status of junior group leader (5 years contract, lab space of 50 m^2, access to institute facilities, financial support when necessary) and to implement their mentorships, including lab management course, designation of an internal and an external mentor with at least two contacts per year, two evaluations, the last one being performed by AERES or the SAB. The experts committee was deeply impressed by the scientific quality of the junior groups.

The unit is composed of autonomous groups, each under the direction of one, or in some cases two PIs, which are responsible for the financial and scientific direction of their group. The Institute Council as well as ad-hoc committees participate to more general (organization, budget, etc) or technical aspects (imaging, fly and mouse facilities, conventional animal facilities, L3 labs, health and safety, IGH store, informatics and biocomputing, washing and media preparation, building maintenance, administration) aspects of the Institute activities. All groups have access to these institute facilities. However, despite this appropriate organization, a strong recommendation of the experts committee is to be aware on the space for offices, in particular those dedicated to the staff scientists. Two groups were proposed to be co-led by two PIs but the experts committee feels that, in these cases, there is no added value for teams of this size to be co-managed by team leaders with similar skills and expertise.

Although the total budget (excluding salaries of staff members) has increased by over 250 % within the past 5 years, the IGH resources are mainly based on the ability of PI to be successful in competitive national and international calls. Indeed the proportion of the CNRS subsidy, which serves to maintain infrastructures, displays a regular decrease. On the same line, it is more and more difficult for IGH (as all CNRS labs) to get staff positions for technicians and engineers. This situation can become problematic to run or develop technical facilities. This critical situation likely constitutes the main reason why IGH is searching for new stakeholders, namely universities.

The experts committee feels that an association between IGH (as an UMR) and the novel unified Nouvelle Université de Montpellier would be a good opportunity for both partners. The university could then take advantage of the outstanding scientific expertise and resources to renovate the educational program in Life Sciences. On the other side, IGH could fully integrate in the Campus (notably with the new Faculty of Medicine). IGH could profit from new support sources, in particular administrative support, that could be mutualized between the Life Sciences Institutes on this Campus, regarding fundraising, science communication and international meeting organization, human resources management, assistance to international scientists.

The scientific life of IGH is very intense and well organized. It is divided in internal and external events. There is a weekly lab seminar during which all researchers, postdocs and PhD students present the results of their studies. Once per year, a day is devoted to the new comers. Scientific retreats are organized in each department every 2 years

and the Journées de l'IGH bring together the complete institute every 2 years. On the other side, external seminars are organized every week. The recent opening of Genopolys facilitates the participation to seminars organized by other labs from the close environment. In addition, each department organizes seminar series with leading scientists of a field. One can note that the high density of labs devoted to life science in Montpellier is very favourable to foster a very dynamic scientific environment.

Assessment of the unit's involvement in training through research

The IGH staff members contribute to teaching at different levels of LMD (Licence, Master and Doctorat) some being responsible or co-responsible of Licence and Master courses particularly in genetics, epigenetics and bioinformatics, as well as cancer biology. It is somehow surprising that only 22 scientists (for 56 staff scientists in total) are involved in teaching activities, mainly to a low extent (less than 6 hrs per year). An increased involvement in teaching duties that is planned in the next 5 years may improve the attractiveness of the institute for students.

IGH is affiliated to the Doctoral School CBS2 “Chemical and biological sciences for health” and is deeply involved in the organization of this school. 38 PhDs have been defended during the past five years, which is a low number compared to that of staff scientists in the IGH (56 including 29 with an HDR), that could be improved. More precisely the supervision rate (number of PhD students/HDR) is good but more researchers should be stimulated to get their HDR. In addition IGH participates to an international PhD program organized and financed by the Labex EpiGenMed. Group leaders of IGH unanimously complained on the low number of PhD fellowships, and in particular those granted by the Region Languedoc Roussillon that have been cancelled. Obviously, the number of fellowships is not adapted to the number and quality of Institutes devoted to Life Sciences in Montpellier.

The mean duration of the PhD is 48 months (+/-8.5 months), which is on the high side compared to French standard, even in life sciences. Each PhD student benefits from a customized thesis committee and a mentorship program, in addition to the excellent scientific environment of the IGH (notably in terms of seminars, conferences and other international scientific events). A common request from PhD students and postdocs is that IGH could set up a travel support fund to help send students/postdocs to conferences. This could be competitive, with applicants writing a short proposal. In addition, IGH may provide more/better career development; specifically, courses or in-lab training in manuscript writing, grant writing and manuscript review. Finally, IGH should be aware to provide internal communication both in French and English to not exclude international students and postdocs (along the same line, nearly all formation courses provided by the ED are in French only!).

Assessment of the strategy and the five-year plan

Beside keeping, or even better improving the exceptional scientific level, the proposed project of IGH for the next five years follows different axes:

- to create more bridges between IGH and clinicians. This task should be facilitated by the new medical school next door and the hosting of a Professor of Medicine in human genetics. Interaction with Hospital on the campus should be strongly encouraged;

- to develop bridges between IGH and industry: IGH proposes to include an R&D director in the SAB, to use Genopolys as a hub in particular to organize a dedicated meeting in 2015;

- to develop Bioinfomatics: for this purpose, their last call for PI selected a bioinformatician. In addition, a Professor position has been created to replace one of the group leaders responsible for the development of an important dabase. Finally, ongoing discussions are taking place to create a bioinformatic facility in the Pole Rabelais;

- to improve attractiveness for PhD students and postdocs. For this purpose, scientists from IGH are aware that it will require a deeper involvement in teaching. The experts committee proposes to mainly focus on Master’s program, and particularly on Master 1. In addition the experts committee recommends to better facilitate the integration of international scientists (internal communication both in French and English, courses in English, assistance for administration, for finding apartments, etc);

- to improve fundraising: IGH proposes to join forces of IGH, IGF and CBS to establish a grant office (EU, International funding agencies, foundations). Such an initiative should be encouraged and supported.

4 • Team-by-team analysis

Team 1: Chromatin and Cell Biology

Name of team leader: Mr Giacomo CAVALLI

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions	4	4
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	4	2
N6: Other contractual staff (without research duties)	3	3 (2,8)
TOTAL N1 to N6	**13**	**11 (10,8)**

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

• Detailed assessments

Assessment of scientific quality and outputs

The PI is an internationally renowned leader in the field of chromatin biology. His laboratory is known for outstanding work on polycomb group (PcG) and trithorax group (trxG) proteins and their role in cellular memory and dynamic gene regulation. Since PcG misexpression has been associated with cancer, the work performed in this team group is highly relevant and potentially has profound impact on biomedical research. Using Drosophila as the major (but not exclusive) experimental system, the team made seminal discoveries in four areas. First, they provided

paradigm shifting insights into how PcG and trxG are targeted to DNA. The group published a landmark paper in 2009 providing the first genome-wide binding profiles of PcG and TrxG proteins. Ongoing research in different Drosophila species revealed among, other findings, an unexpected stability of PcG binding at sites that are bound in different species. The new data, which will be submitted soon, suggest that H3K27me3 domains are of critical importance for PcG binding. Second, the group aims at understanding how PcG proteins regulate cell proliferation, differentiation and polarity in specific tissues during development. They were able to show that one PcG gene called ph acts as a tumor suppressor. This establishes a new area of research with potentially great impact for cancer biology. In addition, this group studies eye tissue and the ovary, breaking new ground in deciphering the tissue-specific roles of PcG genes. A third breakthrough was made in the area of nuclear organization, a field that has become extremely fruitful die to major technological developments, some of which were driven by this group. For instance, they used chromosome conformation capture technology to show that two Hox gene loci colocalize with PcG bodies in cell nuclei. Interestingly, they showed that many genomic loci colocalize with PcG bodies, suggesting the existence of a previously unknown network of PcG-mediated gene contacts in the 3D space of the nucleus. Ongoing work revealed exciting new principles of genome partitioning and chromosome folding. Finally, they identified new regulatory components of PcG proteins using genome-wide screening approaches. In a fruitful collaboration with the Drosophila RNAi Screening Center at Harvard, the group identified hundreds of new PcG target genes, only two of which have been analyzed so far. In summary, this group has been extremely productive and established new principles of PcG-mediated gene regulation and genome function. Although this might seems an unfocused approach, all these aspects are intimately linked, and investigating all facets of Polycomb functions is indeed necessary to properly characterize the role of Polycomb complexes. The lab is one of the few in the world that implements this simultaneous approach strategy, while likewise being one of the few that routinely publish solid results in top-impact journals. The group has indeed published 25 papers in top-tier journals such as Cell, Nature Genetis and Plos Biology, many of which are reviews.

Assessment of the unit's academic reputation and appeal

The team leader has established national and international collaborations with prestigious laboratories. Moreover, he is directly involved in the FP7 EpiGeneSys NoE as board member, and he is Editor of several journals, including PloS Genetics. He has been awarded numerous awards, most notably the silver medal of the CNRS and an EMBO membership. The team is supported from both national and international agencies (including an EC ERC Advanced Investigator Grant). Multiple members of the lab are foreigners and are supported by competitive fellowships. The PI serves as editor of several top-tier journals. He is a reviewer for many scientific journals and grant agencies both in Europe and in the US. He organized conferences including EMBO, Gordon and Keystone conferences.

Finally, the PI has been the director of the IGH for the past 5 years.

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

The PI has been the vice-president of an ARC committee and served in various other leadership functions. He gave various TV interviews and participated in a movie communicating science with the general public. He was also the steering leader of the Labex EpiGenMed further highlighting his outstanding role and involvements in policy development and governance. The team has published several collaborative papers, showing his ability to successfully manage multiple strategic alliances with other groups. The group has developed and applied highly innovative methods to study various aspects of developmental gene regulation and memory. The te stays at the forefront of technological developments, which in combination with its creativity, makes this group highly competitive.

Assessment of the unit's involvement in training through research

The team provides an exciting research environment and excellent training opportunities. Five PhD students have been hired since 2010, all of whom (except one) have been co-authors on multiple papers, showing the high quality of training. In addition, a member of the lab is now responsible for organizing genetics teaching at the Université Montpellier 2. In particular, they re-organized the future Genetics, Epigenics Master.

Assessment of the strategy and the five-year plan

The future research is well defined and will focus on the detailed characterization of the PRC1 and PRC2 complex using mass spectrometry and well-established genomics methods. These studies also include the analysis of the biological role of PcG targeting, the investigation of the role of nuclear organization and chromosome folding in gene regulation. The latter will be expanded into new areas such as pluripotent and senescent cell states.

The proposed experiment builds on the expertise already existing in the lab, but also attempt to enter new areas such as cell reprogramming. Success of these new areas, which involve ES cells and move away from the core PcG questions, will depend on strong and persistent infrastructure and strategic alliances with experts in these areas. Since the PI has a strong track record in establishing fruitful collaborations, the likelihood of continued success is very high.

Conclusion

- **Strengths and opportunities:**

The PI is a highly accomplished PI with a strong track record in identifying and successfully pursuing fundamental questions in genome biology.

The team has successfully trained five PhD students and participated in teaching and thus played an important role in training of young scientists.

The team has enlisted high-profile collaborators in key areas supporting research in his group.

- **Weaknesses and threats:**

Due to the highly diverse research activities, the lab will increasingly depend on collaborators and core facilities. This bears the risk of diluting efforts and slowing progress.

The analysis of new targets that were identified in the screen bears the risk of further diversifying the research program, making it more difficult to keep momentum in all areas and thus potentially decreasing the training potential of individual (and less experienced) lab members.

While the proposed research in the area of ES cell biology and senescence are very well defined and interesting, moving into these areas without necessary expertise might weaken the competitive advantage of the group that is clearly existent in the fly work. The financial support from external grants will significantly be lower starting from September 2015.

- **Recommendations:**

Establish new collaborations in the area of ES cell biology and enlist advisors in areas that are not part of the lab core competence (such as mass spectrometry). This will ensure the high quality training of PhD students and post-doctoral fellows. The lab should make a concerted effort to secure additional funds to continue at the same top-level as in the last 5 years.

Team 2: RNA Silencing and Control of Transposition

Name of team leader: Ms Sévérine CHAMBEYRON

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	2
N3: Other permanent staff (without research duties)	2 (1,8)	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**5 (4,8)**	**4**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended	1	
Postdoctoral fellows having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

This team was created mid-2010. They study the genetic as well as epigenetic mechanisms involved in transposable element (TE) repression by piRNAs in the germ and somatic cells of the *Drosophila* ovary. A seminal work published in Genome Research established piRNAs as epigenetic, intergenerational initiators of the "ping-pong" cycle involved in I-element repression in the germ-line. In a collaborative work, the team also showed that maternally transmitted piRNAs are involved in the silencing of the Tirant TE in ovarian somatic cells. Using a Dominant-negative Drosha construct, the team identified mir14, among other potential miRNAs, as an indirect regulator of primary piRNA biogenesis in these somatic cells, likely through the repression of piRNA biogenesis genes. During the evaluation period, the team acquired the bioinformatic skills required to mine small RNA sequencing datasets. This is an important achievement as these skills are mandatory to stay at the forefront in the field. In a context of intense competition in the field, the group is making steady progress. The group has set up a national collaboration and has

published independently in EMBO reports, Genome Research and a paper is in press in Methods, which are all well respectable journals. Before its creation, two members of the team published an article in PNAS.

It is clear that the demonstration of chromatin-independent epigenetic functions for small RNAs in animals is a very timely topic and therefore continued focus research by the group is bound to constitute a breakthrough in the field.

Assessment of the unit's academic reputation and appeal

The team leader has given presentations in prestigious meetings (Cambridge, Keystone, Jacques Monod conference) and was involved in the organization of a national meeting on TEs. A member of the team who is long recognized in the RNA silencing community was invited for a talk in an international workshop at Les Treilles. The team is highly respected in the piRNA biology field. The coming years will therefore be important for the group to become a prominent researcher at the international front. The PI is highly encouraged to attend international meetings to increase exposure to the mainstream field.

The team leader reviewed manuscripts for various journals (RNA, PLoS ONE, etc.) and was invited editor for PLoS genetics. The PI is also working as expert for the ANR French agency to evaluate grant applications. The PI was sitting in the evaluation committee for the recruitment of an Assistant Professor in Université Lyon 1.

Assessment of the unit's organisation and life

The team is relatively small but well balanced with 2 senior scientists, including a very experienced researcher, 2 engineers and 1 assistant engineer and 1 post-doc and 1 PhD student. The scientific production fits with the task force, and the projects are ambitious but rationally planned. This is indicative of an efficient working group. Attention will be required to maintain the bioinformatics skills in the group.

Assessment of the unit's involvement in training through research

The team leader participates in the teaching in different Masters in France, in M2 at the Curie and M1 in Montpellier. One PhD student has graduated since the creation of the unit in 2010, which is a good achievement. 4 Master students had internship in the unit, including 2 Master-1, 1 Master-2, 1 BTS and 1 IUT student. Further participation in teaching is highly encouraged to gain more experience and also increase exposure to prospective PhD students.

Assessment of the strategy and the five-year plan

The future project involves studying the contribution of aging in piRNA production by comparison of young and old ovaries. The lab has obtained interesting preliminary results which suggest that the age-induced piRNA accumulation occurs when the egg chamber is formed. This data points to an aging effect on piRNA production in the GSCs or in the cystoblasts. The group plans to explore these interesting observations further by performing a variety of assays including in situ hybridization, qRT-PCR and RNA seq analyses to study the deregulation of the I and/or F-elements in the ovary. The team wishes also to study how the pool of maternally deposited piRNA is maintained and/or renewed in the germ line during larval, pupal and adult life. Finally, the role of miRNAs in piRNA biogenesis will be further addressed using a simplified OSC cultured cells system and expression of Dominant-negative Drosha protein in these cells. These projects have very high potential to bring important insights into the frontline of piRNA field. Maintenance of bioinformatics skills in the team, through collaboration if needed, will be critical in these plans.

It was clear during the site visit that the group has made several interesting observations, which need to be strengthened using a variety of approaches. The PI appears to know the task ahead of her and as long as the group focuses on indicated project, they are bound to make tremendous progress in the coming year or two.

The five year plan is ambitious but very feasible, provided the team maintains or even gains further momentum by increasing laboratory personnel and bioinformatics support.

Conclusion

- **Strengths and opportunities:**

This group is working on a very interesting and competitive topic. The team has visibility in the field and is in a strong position with two experienced senior scientists and a solid permanent technical staff. The experimental models are powerful and give a clear advantage in the competition. The bioinformatics skill required for the analyses have been well introduced in the unit. Local access to advanced microscopy and NGS technologies will be highly beneficial to the projects of the team

- **Weaknesses and threats:**

The team has yet to gain momentum in terms of personnel recruitment and breakthrough publications. It is critical that the bioinformatics skills are maintained in the team and young researchers are hired at PhD or Post-Doctoral positions. The competition for ideas in the field is intense; this must be frequently assessed and the strategies must be adapted accordingly.

- **Recommendations:**

Good bioinformatics skills are scattered in the IGH. The difficulty to hire an expert in computational biology could be compensated through local, close collaborations. Increased visibility through teaching in French Masters may help to recruit PhD students. The PI is encouraged to continue to seek advice from the mentorship program set up at IGH, this will help the group to streamline their research and also to gain confidence and experience in strategic planning.

Team 3: Meiosis and Recombination

Name of team leader: Mr Bernard DE MASSY

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	5	5
N3: Other permanent staff (without research duties)		1 (0,8)
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)		2
N6: Other contractual staff (without research duties)	2	2
TOTAL N1 to N6	**7**	**10 (9,8)**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended	1	
Postdoctoral fellows having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

This group has published 24 scientific publications between 2008-2013. This includes several primary papers in top quality journals where members of the team are corresponding/co-corresponding authors (Science, 2 x PLoS Biology, Genes & Development, EMBO J, Cell Reports). Notably, the *Science* paper published by the group reporting the identification of PRDM9 as a determinant of meiotic recombination hotspot choice is an outstanding and seminal finding in the field. The group output also includes reviews/commentaries in top quality journals (Annu Rev Genet, Nature Rev Genet, Cell, Mol Cell, Curr Op Genet Dev). The quality and quantity of the scientific output of this team is therefore excellent, and the standard of journals that the team is publishing in is excellent.

The research over the last five years has focused on identifying and characterizing factors involved in regulating the initiation of meiotic recombination in mice. The group has elegantly used mouse genetics to make a major breakthrough in the field by identifying PRDM9 as a major determinant of recombination sites in mice. A parallel strand of investigation in the team has been identifying mouse orthologs of meiotic recombination proteins present in budding yeast. Again, the team has made significant advance in this line of investigation and has identified two mouse meiotic recombination genes in this way. The group has used mouse genetics and cytology showing that these genes are required for meiotic recombination. Following the key finding on the role of PRDM9 in determining meiotic recombination hot spots, the group is now continuing in the characterization of the factors that influence the specificity of DSB formation in meiosis. The PI is a world leader in this field.

Assessment of the unit's academic reputation and appeal

The PI is routinely invited at conferences on meiosis and on recombination. He has been awarded a number of prizes, including the CNRS silver medal. He is an EMBO member since 2011 and has been awarded an advanced ERC grant. He provides ad hoc reviews for top journals (Nature, Science, Cell, etc.). The PI's high standing in the field is illustrated by his organization of EMBO and GDRE conference series on meiosis. His excellent national reputation is illustrated by his membership of ANR, INSERM and Laboratory of Excellence committees. The PI's reputation and the high quality scientific output of this team make them an attractive destination for PhD and post-doc candidates.

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

Very good, the team has contributed articles, press reports, and press conferences to communicate their research. The team leader contributes approx 9 hours per year to university teaching.

Assessment of the unit's organisation and life

The composition of the group (4 research scientists, 3 PhD students) is appropriate for the research being undertaken. The expertise covers mouse genetics, meiosis and recombination.

Assessment of the unit's involvement in training through research

The team has very good involvement in training through research and has trained 9 Masters and 1 PhD student between 2008 and 2013. The team currently has 3 PhD students training with them.

Assessment of the strategy and the five-year plan

The research questions being addressed in the five-year plan are important and timely. More mechanistic insight into early meiotic recombination is needed to extend the genetic findings in this field. They propose to dissect the mechanism of PRDM9 function further by investigating its *in vivo* binding sites, the importance of its methyltransferase activity, its possible role in regulation of gene expression, and identifyng and characterizing protein interactors. The team is well placed to generate significant advance in this area, and the lines of investigation proposed make a coherent program of work that is likely to generate high quality research outputs.

They also propose to investigate the link between meiotic double strand break sites and chromosomal axes. This line of investigation has significant scope as, despite its presumed importance in the early stages of meiotic recombination, very little is known about this process, particularly in mammals. The team's characterization of MEI4 and REC114 provides a potential route into dissecting this problem, and gives the team with a competitive advantage in this area. The proposed development of an *in vitro* assay for SPO11 activity has the potential to be very powerful as the bulk of the research in the mammalian meiosis field relies primarily on immunocytological analyses. Reconstituting aspects of the early meiotic recombination *in vitro*, if successful, would be a major breakthrough in the field.

Conclusion

Excellent group and excellent PI. The research activity is cutting edge.

- **Strengths and opportunities:**

Seminal findings over the last five years, and the scientific reputation of the team leader, quality of technical expertise in the team, excellent publication record, and track record in addressing important scientific questions are all major strengths of this team. The future research plans are aimed at extending previous advances that have been made by this team to try to understand major events in meiosis that are of significant interest but still very poorly understood. Thus, there is considerable scope for this team to continue generating high quality research and maintaining their excellent level of scientific output.

- **Recommendations:**

Expansion of the Institute's mouse facilities and bioinformatics support would help allow the group to make the most of the opportunity to exploit the recent advances that they have made in the field.

Team 4: Biology of Repetitive Sequences

Name of team leader: Mr Jérôme DEJARDIN

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	1	1
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	4	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**5**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral fellows having spent at least 12 months in the unit	4	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The group is still young (created in 2009). During his postdoc, the PI has developed the PICh (Proteomics of Isolated chromatin) method to study the composition of chromatin-associated proteins on particular loci. The group is now going further with the development of a quantitative version of the "Proteomics of isolated Chromatin segment approach" (qPICh) technique for the analysis of mouse heterochromatin. The challenge has been taken up with the identification of 130 factors identified at pericentric heterochromatin. In addition to protein components, they are also studying the importance of chromatin-associated modifications. The possibility to combine PICh with mass spec analysis to identify histone marks reinforces the power of the PICh approach, a tool to analyse the role of chromatin modifiers. This has a great potential to identify new pathways or reveal novel functions of already existing factors.

The lab's main direction of research can be subdivided into four main themes: role of epigenetic regulators at pericentromeres and telomeres, importance of ALT pathway in human cancers, dissecting the function of new heterochromatin associated protein Smchd1 and identification of novel factors important for heterochromatin regulation.

The PI has published quite well with his postdoc mentor, but major publications from his own lab are yet to come. Several publications appear to be in preparation way, as indicated in the proposal.

The lab is also involved in several international and national collaborations, which are bound to give interesting insights and bring the PI forward in the international front.

Assessment of the unit's academic reputation and appeal

The PI has obtained several prestigious funding including an ERC starting grant (dec 2010-dec 2014) and a Inserm Avenir label in 2010. He is also a member of the epigenesys network of excellence 2012-14. During the last period, the PI has been regularly going to international meetings and being selected for talks, which again is a sign for his recognition in the international community. The lab has been successful in hiring a number of international postdocs from leading labs in the epigenetics field, which is a very good sign for the PI's ability as a group leader and attractiveness for his lab's research focus. Several international collaborations are also undergoing. The PI is reviewing for a number of respectable journals. Since 2013 he is also an editor for Epigenetics and Chromatin.

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

The PI was involved in a couple of interviews with local newspaper/radio.

Assessment of the unit's organisation and life

The PI is the only researcher with a permanent position. 3 post-docs have joined the group as well as one engineer and one PhD student. These positions have been obtained through an ERC funding and through the obtaining of a Marie-Curie post-doctoral fellowship. The lab currently contains 10 members. This is a good size for a lab. Like many others, the lab is in need of bioinformatics expertise.

Assessment of the unit's involvement in training through research

The PI has been involved in a couple of workshops and training initiatives. However, it appears to be moderate at this stage. The group leader is leading a team of 10 people, which requires extensive training and supervision.

Assessment of the strategy and the five-year plan

The projects proposed for the next 5 years concern different aspects related to heterochromatin structure and function in normal and tumour cells. This includes analysis of pericentric and telomeric heterochromatic regions. The group will combine the analysis of specific factors and general approaches such as PICh to understand the status of these regions in different physio-pathological contexts. A specific focus on a small number of factors such as SMCHD1 will also be performed.

Conclusion

- **Strengths and opportunities:**

A very promising young group with novel methodologies at hand to study heterochromatin.

The data that have been obtained constitute the basis for further comparative analysis of heterochromatin partners in different physio-pathological situations. Good scientific visibility of this young PI.

- **Weaknesses and threats:**

For the current team size, the productivity is still modest. The research plan is very broad so the group may need to focus in the coming years. A good balance will have to be found between large scale approaches and the necessity to focus on a few factors, so as to avoid the risk of dispersion.

- **Recommendations:**

Group with a strong and unique expertise in the field of heterochromatin. This young group should be strongly supported by IGH. The PI is encouraged to continue to seek advice from the mentorship program set up at IGH, this will help the group to streamline their research and also to gain confidence and experience in strategic planning. The assessment clearly arrives too early in this case. It will be important to complete the various projects into a publication in 2014.

Team 5: Epigenetics and Splicing

Name of team leader: Ms Reini Fernandez DE LUCO

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	1	1
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	1	3
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**2**	**4**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended		
Postdoctoral fellows 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		1

• Detailed assessments

Assessment of scientific quality and outputs

During a post-doc, the PI made a very nice contribution to the field connecting regulation of alternative splicing to chromatin by showing that methylation of histone H3 at lysine 36 (H3K36) inside the coding region of the FGFR2 gene affected inclusion of an alternative exon in the mature FGFR2 message. The modification allows for recruitment of the MRG15 protein that in turn favours the recruitment of the PTB RNA binding protein. This observation published in Science in 2010 was one of the first to connect a specific histone modification to regulation of alternative splicing. This study was followed up with observation of a long non coding RNA recruiting Polycomb, inducing H3K27 methylation, and inhibiting MRG15 recruitment, that is currently being submitted for publication.

The lab in Montpellier, established in 2013, intends to explore novel mechanisms defining and maintaining cell-type specific splicing programs with a long term goal of predicting and possibly correcting these programs. The team being established for less than a year, the local output was not evaluated.

Assessment of the unit's academic reputation and appeal

The PI was invited to write several reviews (Cell, Current Opinion in Genetics and Development) in the wake of the post-doctoral work, illustrating the reputation in the field.

The PI was further awarded membership at the European Epigenesys network that structures the scientific community working on epigenetics and systems biology, further documenting her integration in the community.

The PI was also invited to speak at several international meetings over the last four years.

The PI has been very successful in gathering funding from several sources including the very competitive Atip-Avenir grant, a grant for newly established teams by the FRM, and a grant from Plan Cancer.

Finally, the PI has already put together a team with several postdoctoral researchers.

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

Not evaluated - the group is too recently established.

Assessment of the unit's involvement in training through research

The PI obtained an HDR (habilitation) in 2013 and plans to hire students as soon as possible. The PI also wishes to be enrolled in a teaching program.

Assessment of the strategy and the five-year plan

The project aims at extending the postdoctoral findings, and proposes to use in vitro epithelial to mesenchymal transition of tissue culture cells associated with genome-wide approaches to identify histone modifications and lncRNA influencing the outcome of splicing reactions during cell lineage reprogramming. The group also whishes to explore an inverse impact of splicing on chromatin structures.

The long term goal is to be able to predict and eventually to correct pathological disorder linked to splicing. Thus, the project is relevant to human health since some cancer-specific splicing isolforms have been involved in tumorigenicity.

This project is timely and ambitious. Yet, the outcome is uncertain and in particular it is not clear whether the chosen approaches will allow to uncover chromatin signatures that modulate splicing beyond those already known.

The composition of the team (3 post-docs including a bioinformatician) is very coherent with the project, although contacts with clinicians or labs directly dedicated to cancer research could be improved.

Conclusion

- **Strengths and opportunities:**

• Original and attractive projects;

• Expertise in this field;

• Strong links with the international community;

• Good funding;

• A potential for ground-breaking discoveries.

- **Weaknesses and threats:**

- Expected results are relatively poorly defined;
- An *in vitro* working model that may rapidly be limiting.

- **Recommendations:**

- Eventually parallel the search for new epigenetic patterns with an in depth study of the mechanisms allowing already identified histone modifications to affect alternative splicing;
- Establish more contacts/collaborations with groups involved in cancer research/therapy;
- Seek internal mentoring support throughout the establishment of the lab.

Team 6: Gene Regulation

Name of team leader: Ms Rosemary KIERNAN

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	3
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	2	3
N6: Other contractual staff (without research duties)	2	1
TOTAL N1 to N6	**6**	**7**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended	2	
Postdoctoral fellows 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	1	2

• Detailed assessments

Assessment of scientific quality and outputs

The team leader has recently started her own group in 2009. The topic of investigation has been centered on the study of transcriptional mechanisms that govern the human immunodeficiency virus type 1 (HIV-1). This topic was previously investigated by the PI. The lab has three main research lines:

1) **the Role of the Ubiquitin/Proteasome System (UPS) in Transcriptional Regulation.** The main effort here is to investigate the function of the proteasome-associated protein, PAAF1. Results suggest that Spt6 is targeted by the proteasome in the absence of PAAF1. PAAF1 interacts with the N-terminus of Spt6, suggesting that PAAF1 protects Spt6 from proteolysis. Under experimental conditions of low levels of PAAF1 or Spt6, the expression of many genes is deregulated, including several oncogenes and tumour suppressors.

2) **transcriptional Regulation Mediated by Microprocessor, Setx, Xrn2 and Rrp6**. The goal here is to understand mechanisms that contribute to RNAPII pausing at the HIV-1 promoter. Results indicate that RNAPII pausing and premature termination is mediated by the co-operative activity of ribonucleases, Drosha/Dgcr8, Xrn2, and Rrp6. This extremely important work was published in Cell in 2012.

3) **characterization of H3.2 Histone Deposition Complexes.** The aim is to identify the deposition complex for the histone variant H3.2. A novel set of proteins, including the Chromatin Assembly Factor 1 (CAF-1) subunits and a subcomplex of MiniChromosome Maintenance (MCM) helicases, together with AntiSilencing Factor 1 (Asf1) seem to mediate the deposition of H3.2 both in vivo and in vitro. These results were published in 2014 in NAR.

As a whole, the team has been extremely productive both in quantity and in quality which is an excellent output for a recently established lab.

Assessment of the unit's academic reputation and appeal

The lab has an increasing reputation and has secured funding from competitive calls including the European Research Council recently awarded to the PI.

The PI is regularly invited to international conferences. She participates to several networks including one between France and China. She is a member of the editorial board of Retrovirology.

She has attracted several international postdocs in her team.

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

PI is a member of the Women in Life Science Database.

Assessment of the unit's involvement in training through research

The team leader is actively involved in training master and PhD students. Two PhD students have defended their thesis. One of them published as a first author.

Assessment of the strategy and the five-year plan

The team has presented a very interesting research plan for the next 5 years. The proposed projects are the right balance between continuity and innovation, and between originality and risk-taking. In particular, they plan to characterize the Rrp6 complex and its targets using proteomic and genome wide approaches. They have also obtained convincing preliminary results on the study of the proteins that associate on the HIV-1 promoter by the “PICh” approach. This is done in collaboration with the PI of another group of the unit, who designed this technique. Finally, a more therapeutic-oriented aim is to interfere with the small TAR RNA function in order to reverse viral latency and make cells more susceptible to therapy.

Moreover, the team is establishing new collaborations within IGH and outside. The goals proposed are all reachable in the 5-years time-frame.

Conclusion

- **Strengths and opportunities:**

The team’s investigation is centred on a group of related projects that aim to characterize the basic principle of gene regulation. Their model system and approach will allow them to compete in a highly competitive field. The connection with human disease will be of interest for potential translational medicine research and will likely increase the chances for additional funding in the next years, especially from the EC H2020.

- **Weaknesses and threats:**

The major weakness is the limited critical mass within this lab. Although the team has established multiple collaborations with other groups at IGH, it is suggested to increase the lab size. The team leader should also put more effort gaining visibility at international level (by giving talks at international conferences, for instance, or hosting international conferences).

- **Recommendations:**

This group has a very good prospective: the results generated in the past years are very exciting and the future research lines are well-planned. Increasing the size of the group will allow it to be competitive at the international level.

Team 7: Replication and Genome Dynamics

Name of team leader: Mr Marcel MECHALI

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	5	6
N3: Other permanent staff (without research duties)	2	2
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	4	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**11**	**10**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	2	
Postdoctoral fellows having spent at least 12 months in the unit	3	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The PI is a world leader in the field of DNA replication, who has made numerous important contributions over the years. The team produced 21 papers during the review period, including 10 original research articles in top journals with the team leader as last author (2 Mol Cell, 2 Genes & Dev, 1 Genome Res, 1 Chromosome Res, 1 PNAS, 1 Nature Com, 1 Mol Cell Biol, 1 Cell Cycle). Since the PI is senior author on almost all of his listed publications, this publication list really reflects the output of the team. The high quality and impact of these papers is illustrated by recommendation by the Faculty of 1000 of 4 of them, and 2 have been highlighted by News and Views or full comments. In addition, six reviews have been written, some in very high impact journals such as Nature Rev Mol Cell Biol or Current Op Genet Dev. Finally, 6 patents have been produced, making the achievement really impressive. Together, this is an outstanding level of output.

Assessment of the unit's academic reputation and appeal

This group is widely recognised for ground-breaking work in the field of DNA replication. The PI is a member of the Academy of Sciences. The work of the team is highly cited and the PI is regularly invited to speak at international conferences. The PI is also the director of the Labex EpiGenMed, the GDR Eukaryotic Chromosome Replication and its Checkpoints, and the GDRI France-Japan. The PI was also awarded the Prix René and André Duquesne from Ligue contre le Cancer, 2011. Thus, the academic reputation and appeal of the PI and the team are world class.

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

The PI is the director of GENOPOLYS, an interface between basic research, clinical science, industry and the citizenry which has the objective of diffusing scientific culture in life science. He is also Member of the Board of Management of the Montpellier “Pole Rabelais” for Biohealth.

Assessment of the unit's involvement in training through research

The PI has been exceptionally effective at training PhD students and postdocs to become independent group leaders. Significantly, 5 junior scientists from the team were recruited at the CNRS during the review period.

Assessment of the strategy and the five-year plan

Main objectives of future research:

1. study of replication origin usage in cell differentiation and cancer: the team proposes to determine whether and how the positioning of DNA replication origins influences cell fate during differentiation (using mouse ES cells relatively easy to differentiate into neural progenitors) or cancer progression (using human models of cancer development).

2. OGRE elements as mammalian replicators. The team proposes to place OGRE elements (wild-type or mutated) at ectopic positions to evaluate the role of OGRE and G quadruplex structures in origin specification. Another goal is to determine whether the position of replication origins influences cell identity.

3. characterization of novel regulators of DNA replication identified by TAP-tag. Recent results from the team suggest that MCM9/MCM8 complex might be the eukaryotic MMR helicase. They now propose to check biochemically that the MCM8-MCM9 complex has DNA helicase activity. They will then dissect the interactions of MCM8-MCM9 with replication complexes and their impact on genome stability via the MMR pathway. In addition, the team has shown an interaction of ORC with a new protein they called Obi1. Their working hypothesis is that Obi1 stimulates origin licensing and is involved in the licensing checkpoint control (see point 4).

4. Pre-RC checkpoint and cancer. Recently, the concept of a licensing checkpoint has emerged from the fact that perturbing the licensing reaction stops normal cells from growing but kills cancer cells as they enter in an abortive S phase. The team obtained results showing that expression of a non-degradable Geminin leads to cell death in cancer cell lines while non-transformed cells stop proliferating in G1. The team proposes to use a Human model of cancer development to investigate the integrity of the licensing checkpoint at different steps during progression towards transformation, and to determine the role of geminin in this process.

The five-year plan is an excellent mixture of ‘bread and butter’ analysis, which follows nicely from past work, and some very promising and exciting preliminary findings that are ambitious, but should lead to significant contributions and further significant publications. The PI has established himself as a world expert in the methodology required to analyse DNA replication origins and replication patterns genome wide. The desire to extend the work into cell differentiation systems and cell transformation systems should be encouraged.

Overall, this is an exciting proposal, with real potential to generate major findings in the next five years.

Conclusion

- **Strengths and opportunities:**

- world leader team in DNA replication;

- strong, international team.

- **Weaknesses and threats:**

Uncertainty regarding whether the CNRS and university will keep the laboratory going as the PI approaches normal retirement age may erode the ability to recruit world class researchers, which would be unfortunate for the unit.

- **Recommendations:**

Make a commitment to maintain the lab at its current full strength while the PI is successful in attracting external funding.

Team 8: Molecular Virology

Name of team leader: Mr Monsef BENKIRANE

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	3	3
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	5	7
N6: Other contractual staff (without research duties)	3	3
TOTAL N1 to N6	**12**	**14**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	3	
Postdoctoral fellows 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	1	3

• Detailed assessments

Assessment of scientific quality and outputs

The review committee saluted the PI's accomplishments in the field of HIV molecular biology, which has translated into important and internationally lauded discoveries. A longstanding contributor to our understanding of HIV transcription, for instance through the work on the TAT transactivator and of the interplay between microRNAs and LTR activity, the team ventured successfully during the last few years into broader issues of high relevance for AIDS pathogenesis. This led them notably to discover SAMHD1, an important viral restriction factor countered by the lentiviral VPX protein and responsible for part of HIV's failure to replicate in non-dividing cells such as resting lymphocytes or monocytes, and to elucidate the role of VPR in minimizing IFN responses in HIV-infected cells.

Assessment of the unit's academic reputation and appeal

The team's work is recognized by the peers worldwide not only as very exciting but also as thorough and truly reliable. The PI was recently awarded several prizes (e.g. Retrovirology 2012, Liliane Bettencourt 2013), was elected to EMBO (2012), and is the recipient of an Advanced ERC grant. In addition to caring for his own research, the team leader has vigorously engaged into servicing the scientific community, whether by sitting on various committees at the national and international levels, by organizing conferences or by providing ad hoc reviews for top journals (Nature, Science, Cell, etc.).

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

Actively involved in outreach activities, as appropriate for a team involved in AIDS research.

Assessment of the unit's organisation and life

Team members appear to develop skills adequate to pursue scientific careers, which suggests productive interactions within the unit. Some inbreeding to be careful about (see below).

Assessment of the unit's involvement in training through research

Most of the people who left the laboratory are continuing their career in science. The Pi is also involved in PhD training and lecturing.

Assessment of the strategy and the five-year plan

The team will tackle an all-important issue, the mechanisms of HIV latency in vivo, and will seek approaches to overcome this barrier to viral eradication. They will capitalize on the development of inventive tools to identify latently infected cells in a non-human primate model of HIV infection, exploiting synergistic collaborations with another French team engaged in the development and study of these animal models. The technical challenges are not negligible, as the frequency of latently infected cells may be very low, hence complicating some or the proposed analyses. However, even partial success would bring extremely interesting information, qualifying this part of the project as belonging to the “high risk but very high potential” category.

Conclusion

A clear leader team of the field, with remarkable achievements and exciting future projects.

- **Strengths and opportunities:**

Very strong track record, exciting projects in important area. The PI has also proven to be an excellent mentor for young scientists, and a very productive and appreciated collaborator within the institute.

- **Weaknesses and threats:**

Internal emergence of pseudo-independent groups could be detrimental in the long term, both to the team as a whole and to the individuals steering these efforts instead of launching fully independent operations.

The PI should be careful not to be swamped by his new administrative responsibilities when he becomes IGH director next year.

- **Recommendations:**

Keep it up!

Team 9: Genetic Instability and Cancer

Name of team leader: Mr Angelos CONSTANTINOU

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	3
N3: Other permanent staff (without research duties)	1 (0,8)	1 (0,8)
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	4	2
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**8 (7,8)**	**6 (5,8)**

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

• Detailed assessments

Assessment of scientific quality and outputs

The group is fully operative since 2011. The research aims at characterizing the factors and pathways mediating the stability of replication forks in response to replication stress. The group has recently published an important observation on how FANCD2 controls replisome function following checkpoint activation (Mol Cell 2013). Additional high quality publications were in PNAS, EMBO J and J Cell Biol. The group is engaged in relevant scientific questions and, overall, the scientific productivity is very promising.

Assessment of the unit's academic reputation and appeal

The PI has been awarded several grants from Swiss and French agencies. The PI provides ad hoc reviews for very good journals (Mol Cell, NSMB, EMBO, etc.) and is review editor for Frontiers in Cancer Genetics.

Assessment of the unit's organisation and life

Each team member has a clearly defined project. There is good diversity of expertise. The IGH is an excellent location for this work.

Assessment of the unit's involvement in training through research

The Pi is involved in teaching activities aimed at Master students and in training PhD students.

Assessment of the strategy and the five-year plan

The project is articulated in different tasks:

I) studying the surveillance mechanisms controlling replisome/fork stability (investigating the role of FANC proteins and the checkpoint machinery);

II) studying the DNA-structure specific activation of the DDR;

III) investigating the connections between FANCD2 and the spliceosome;

IV) the connections between FANCM and pyrimidine degradation.

Overall the project is ambitious and the tasks well connected with each other. The spliceosome interaction might be separately fundable, perhaps via Horizon 2020. The PI has the right expertise to complete the tasks successfully. The expected results might definitely contribute to change our way of thinking about replication stress.

Conclusion

The group is clearly integrated in the new environment and very collaborative. The PI is the right person in the right place. The science is excellent.

- **Strengths and opportunities:**

A fantastic opportunity for the institute. Collaborative and integrated group with the right skills to produce original work. Excellent self-sense and intuition. Good opportunities through collaborations to link their biochemical findings to biological activities.

- **Weaknesses and threats:**

No major weaknesses. The experts committee is confident that the scientific productivity will continue to accelerate.

- **Recommendations:**

The group needs full support from the Institute. It might be useful to explore institutional synergies to facilitate interactions with scientists/facilities working in the protein structure field. There also seem to be opportunities for additional extramural support from French and European agencies.

Team 10: Homing, Immune Activation and Infection

Name of team leader: Mr Pierre CORBEAU

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	2
N2: Permanent EPST or EPIC researchers and similar positions	2	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)		
N6: Other contractual staff (without research duties)	1	
TOTAL N1 to N6	**7**	**5**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	2	
Postdoctoral fellows having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The group has developed several research projects aiming at the study of CCR5 and CXCR4 as HIV-1 receptors, the mechanisms leading to tropism switch and the characterization of new therapeutic targets against HIV. Technical approaches to these issues combine basic methodologies and the study of clinical samples from HIV-infected patients.

Major achievements in the last years are:

1. the description that transduction signals triggered by HIV-1 binding to CCR5 and CXCR4 increase the efficiency of reverse transcription and HIV infectivity;

2. the observation that global immune activation observed in HIV-infected patients is related to CCR5 expression and is reduced by treatment with CCR5 antagonists;

3. circulating CC-chemokines induce CCR5 down-regulation in vivo, thus increasing intracellular location of this receptor;

4. the characterization of new proteins belonging to the type 1 sphingosine 1-phosphate receptors family (S1PR1) that are able to dimerize with CCR5 and whose expression increases HIV infection through ligand-induced signal transduction and transcription activation;

5. to develop S1PR1 ligands to induce CCR5 down-regulation as a mean to inhibit HIV-1 infection;

6. the expression of different isoforms of CXCR4 and its impact on HIV-1 binding, chemokine-driven functions and the potential switch from R5- to X4-tropic variants.

The team has identified original approaches and provided new insights in the field of HIV-1 receptors and viral entry that remains a major area of research in the field of AIDS pathogenesis. Of note, these results are always considered in a clinical context in order to identify new targets for therapeutic intervention (GPCR agonists, gene therapy) to control HIV infection. Relevance and translation of research results represent added values of the team.

In the last 5 years 18 papers have been published in high and medium impact journals. Scientific production directly related with the different projects as main group and excluding reviews is limited to 8 articles (2 AIDS, 2 J AIDS, 3 Blood, 1 Immunology). The level of productivity is therefore good but not outstanding.

Assessment of the unit's academic reputation and appeal

The group and particularly the PI have good projection and visibility at French and international level in this particular area of HIV research with numerous invited conferences, mainly in France. However participation in international committees of scientific evaluation or major congresses is lacking.

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

Of note the interplay with clinical units and pharmaceutical companies which are very positive aspects of this type of research.

Assessment of the unit's organisation and life

The team is composed of 2 CNRS research scientists, 1 university lecturer, 1 hospital assistant, 1 PhD student, 1 technician and 1 scientific assistant.

Regarding laboratory structure the composition of the group is insufficient to address in a competitive manner the research objectives proposed. The fact that the team leader splits his time with other tasks as responsible of immunology units at CHU and teaching activities requires a solid laboratory structure that is not currently reached. Recruitment of post-doctoral and young researchers with high commitment towards this specialized research is particularly important and if the group is not able to attract and support post-docs it is a matter of concern because it may be a sign of the team's insufficient appeal

Assessment of the unit's involvement in training through research

A strong effort and investment of the group is related with training of young PhD students.

Assessment of the strategy and the five-year plan

Future projects of the laboratory are based on previous work of the group and the capacity to have access to patients material. Essentially, three different projects are proposed:

I) to study the interactions between S1PR1 and its ligands with CCR5;

II) the regulation of different CXCR4 isoforms;

III) a new approach aiming at the study of cell activation signalling that can elicit DNA damage in bystander cells.

Research proposed for the future is original but deserves some comments:

– expected results on the role of CXCR4 isoforms in R5→X4 switch can provide a correlation but not a cause-effect relationship and the proposed gene therapy strategy seems difficult to move to the clinical setting;

– the description of interactions between S1PR1 and CCR5 is probably the most interesting project currently running but its relevance depends on the role of these proteins in primary cells;

– finally the new project aiming at the identification of inflammatory molecules leading to bystander DNA damage is not clearly defined and discloses a high risk.

Conclusion

- **Strengths and opportunities**:

Major strengths of the team are the originality of their findings and approaches in a field of HIV research that is still important, good collaborations with pharmaceutical companies and clinical groups and the translational perspective of research. Finally, the generation of a new and interesting patent aiming at the development of drugs against a new target could be important not only for HIV infection but in other inflammatory diseases.

- **Weaknesses and threats:**

Weaknesses of the group are a reduced scientific output, the absence of post-doctoral researchers and a modest international projection. From a scientific perspective the global impression is that there is an over-dilution of the effort and that the team moves from one question to another very fast without completing previous work. Therefore, in many issues, the group provides superficial data without in depth analysis and strong development of the different findings. Collaboration with other groups in the field of chemokine receptors could help in this setting.

- **Recommendations:**

A major recommendation is to focus on one specific and ambitious project – probably the study of new GCPR molecules- and to perform in depth analysis of both basic and applied research on this issue in order to improve the level of publications and the strength of the findings provided by the group. Exploratory work in other fields can be considered provided it does not interfere with priority research. Collaborations with groups having developed complementary expertise in the field could help to address and get better insights in the different research projects proposed.

Team 12: IMGT®, the international ImMunoGeneTics information system®

Name of team leader: Ms Marie-Paule LEFRANC

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	1	1
N2: Permanent EPST or EPIC researchers and similar positions		
N3: Other permanent staff (without research duties)	4	4
N4: Other professors (PREM, ECC, etc.)	1	2
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	2	
N6: Other contractual staff (without research duties)	7	9
TOTAL N1 to N6	**15**	**16**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	3	
Postdoctoral fellows 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	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The team covers two different research avenues: On one hand the IMGT (International ImMunoGeneTics information System) and on the other hand a line of research on genetics of rare diseases, mainly in the study of immunodeficiency syndromes. The laboratory is composed of 2 senior emeritus scientists, 4 permanent staff (2 research engineers, 2 engineers), 9 CDD (one PhD student, one Post-doctoral student, 7 biocurators and engineers). Of note the high turnover of personnel in the last years and in particular the lack of junior and tenure researchers which represents a major limitation to pursue current investigations.

The IMGT is a reference platform created in 1989 that targets the genetic analysis of immune repertoire, preferentially Immunoglobulin (IG) and T cell receptor (TR) genes. Nowadays the platform comprises 7 databases, 17 online tools and integrates sequence analysis with genomics, proteomics, structure and functional genomics. It has

been developed an original notation and ontogenic classification system and major achievements are the generation of these new tools together with their application to antibody humanization, next generation sequencing technologies and clonotype determination.

Scientific production is very good with more than 50 articles published in the last 5 years, the majority in high and mid-impact journals with some outstanding papers in collaboration.

Regarding the second research avenue of the group led by another senior emeritus scientist, up to 25 publications have been generated in the last years mostly in collaboration with other teams. This publication profile is common when studies on genetic of rare diseases are generated but a position as senior authors would be expected in some articles thus reflecting a clear leadership in particular issues. Budget distribution is not clear in the report.

Assessment of the unit's academic reputation and appeal

IMGT is a high-quality integrated knowledge resource that provides a common access to standardized data from genome, proteome, genetics, 2D and 3D structures, for exploring immunogenetics and functional genomics. It is a global reference in immunogenetics and immunoinformatics through the building of a unique ontology relying on identification, description, classification, numeration, localization, orientation and obtention.

It is dedicated to the analysis of all molecular components related to the field of immunology including IG and TR genes, to major histocompatibility (MH) proteins, related proteins of the immune system of vertebrates and invertebrates, therapetic monoclonal antibodies, fusion proteins for immune application and composite proteins for clinical applications. IMGT has more than 150,000 users. It contains 7 databases and 17 online tools.

The platform benefits from strong collaborations with international organizations (NCBI, HGNC, EBI, UniProt, WHO-IUIS, WHO-INN) and with high quality teams in the field of immunology.

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

There are financial agreements between IMGT® (CNRS) and 15 pharmaceutical societies for IMGT® online access and/or IMGT/LIGM-DB downloading and financial agreements between IMGT® (CNRS) and Janssen for the internal use of IGMT databases and tools

Contribution in the Labex MabImprove awarded by the Ministry of Research and Education in the ‘Investments for the Future’ program in 2011.

Several patents were filed.

IMGT has received national and international labelisations and recognitions through labelisation and membership (member of International Medical Informatic Association (IMIA), certification ISO 9001:2008; Rio and IBiSA labelisation). IMGT has received fundings from multiple European, national and regional programs.

Assessment of the unit's organisation and life

The group is now composed of two Emeritus Professors (including the PI), of 2 research engineers and 2 engineers with permanent positions. Nine members are on CCD. The activity of the group is tightly linked to the platform itself. The number of CDD reveals the strong capacity to obtain money and to establish partnerships.

Assessment of the unit's involvement in training through research

The group greatly contributes to training activities through teaching, the organisation of tutorials (organisation and creation of Master 2 modules in bioinformatics) and the organisation of 8 educational workshops (France, USA, Greece, Italy, etc).

Assessment of the strategy and the five-year plan

The means to maintain this platform is certainly a central issue. In particular the creation of a position specifically dedicated to the platform appears as a key issue for its survival. A Professor should be hired to join and lead the platform this year.

Conclusion

- **Strengths and opportunities:**

Major strengths of the group are the excellence of the IMGT platform that is a global reference in the field, the continuous adaptation of bioinfomatic tools to the new platforms and data generated by Next Generation Sequencing Technologies. Of note the effort to run their own research projects in the field of hemato-oncology and immunodeficiency diseases and not become restricted to a high level "technical platform". Strong interactions with other platforms, groups and international organizations. The visibility, prestige and impact of the PI is excellent : invited to international conferences, reviewer of prestigious journals and scientific agencies and in the organization of international workshops.

Both the PI and senior scientist are committed to teaching activities, creation of new masters and supervision of PhD students. As an added value strong collaborations with clinical units and international networks allow the application of the genomic technologies to clinical diagnosis and pathogenetic studies in human diseases.

- **Weaknesses and threats:**

Some aspects are a matter of concern, mainly the necessity to maintain a small research team within the group which requires a clear leadership not only regarding the technical aspects of the platform but also the research projects. To this aim, the arrival of a Professor is very good news.

The income generated by the platform is only sufficient to cover the salaries of the engineers.

- **Recommendations:**

The future of the platform is clearly a central issue. Its existence and development are intimately associated with the charismatic group leader who has gained a strong international reputation in the field of immunoinformatics. The initial choice, made by the group leader to create an integrated information system based on high-quality standards, has made IMGT the global reference in immunogenetics and immunoinformatics, contributing to its international visibility. One can easily measure that the setting of this platform, its recognition by international instances, has not been an easy road. Judging from the number of users and industrial contracts established, the potential for economic development appears to be important. Moreover, the platform not only feeds academic and industrial research, but represents and important tool for the training and formation of researchers and students.

The creation of a position specifically dedicated to the platform appears as a key issue for its survival.

Team 13: Genome Surveillance and Stability

Name of team leader: Mr Domenico MAIORANO

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	1	1
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**2**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	2	
Theses defended	2	
Postdoctoral fellows having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	1	1

• Detailed assessments

Assessment of scientific quality and outputs

The team is interested in how cells maintain their genome integrity while they are permanently submitted to endogenous and exogenous stresses. Most important achievements are the following:

The team has reconsidered the current model proposing that the S-phase checkpoint is activated by excess of RPA-coated ss-DNA. They have shown that partial RPA depletion, allowing replication to proceed but not nucleation of RPA on ssDNA, still permits checkpoint activation. They have further shown that ssDNA and replication intermediates, not RPA, are essential to recruit the 9-1-1 clamp. In addition, through a very fruitful collaboration with a team in Toulouse, they have discovered that the accumulation of replication intermediates at stalled forks depends on the activity of DNA polymerase k¤ and that Pol k is required for checkpoint activation, through its interaction with Rad9.

The team has also undertaken to identify the mechanisms leading to checkpoint relaxation during early stages of embryogenesis. They have focused on:

1) G1 arrest failure after DNA damage in mouse ESCs that they have correlated with the presence of high level of CDC25A. Accumulation of CDC25A in these cells relies on high expression of Dub3, a deubiquitylase known to controls Cdc25A protein abundance in other models. Very interestingly, they have shown that Dub3 is a novel factor required for pluripotency maintenance in ES cells.

2) S-phase arrest, which is silent at earlier stages of embryogenesis. They have shown that Pol eta and monoubiquitinated PCNA are present at replication forks even in the absence of damage and that Pol eta is responsible for checkpoint silencing.

The team was started 6 years ago. During the period under evaluation, the team has produced 7 original publications in good to very good journals (1 Mol Cell, 1 EMBO J, 3 NAR and 1 BBRC) and 2 review articles.

Assessment of the unit's academic reputation and appeal

Good for a young group leader:

• selected oral presentations: EMBO workshops on "Cell Biology of early mouse development" (Cambridge, United Kingdom 2012) and "Exploring the logic of the Cell Cycle" (Montpellier, France 2011). Jacques Monod Conferences "Biological responses to DNA damage" (Roscoff, France 2008);

• the group has benefited of an ARC subvention libre from 21/12/2006 to 13/12/2008 – 200,000 €. FRM "Equipes" from 2007 to 2010 - 300,000 €, of INCa projets libres "checkpol" from 2007 to 2010 – 35 000 €, of an ANR (the PI was porteur de projet) checkdev from 1/1/2013 to 30/12/2015 – 298,000 €;

• scientific networks: member of GDR 2915 « Replication of eukaryotic chromosomes and its checkpoints »;

• membership: faculty of 1000 Biology, Trinity College (Oxford, United Kingdom);

• peer reviewer for Nature Cell Biol., EMBO Journal, EMBO Reports, Nucl Acids Res, Mol Cell Biol, Mol Biol Cell, J Cell Science, J Mol Biol, Exp Cell Res, Chromosoma;

• reviewing for grant agencies: Cancer Research Campaign (CRC-UK), Biotechnology and Biological Sciences Research Council (BBSRC, UK), Medical Research Council (MRC, UK), and Ligue Contre le Cancer, Cancéropôle Île-de-France, ANR.

Assessment of the strategy and the five-year plan

Taking into account the specific roles of TLS polymerases during embryogenesis as checkpoint sensors and/or normal components of the fork, the team proposes to determine the impact of TLS polymerase depletion or overexpression on the rate and the nature of mutation during embryogenesis and oncogenesis. In the latter case, they will also focus on Rad18, the ubiquitin ligase that initiates TLS by monoubiquitinating PCNA. In parallel, they will pursue the characterization of the physiological role of Ddx19, a putative RNA helicase substrate of Chk1 that they have previously identified in a screen for novel checkpoint proteins.

The question of checkpoint suppression in early embryos is interesting and has recently shed light on unsuspected functions of TLS DNA polymerases. Pursuing this study will provide the team with an original research niche. The project dealing with somatic/cancer cells is also very interesting but will be highly competitive. The search for new players involved in checkpoint regulation, notably those that maintain genome integrity, is promising.

The overall consistency of the project is good, and it is worth mentioning the adequacy between the expertise in the PI's and collaborator's teams.

The credibility of the strategy is good.

The quality of the SWOT analysis is good.

The five-year plan is probably too ambitious and dispersed relative to the size of the team.

Conclusion

- **Strengths and opportunities**:

Very original niche with the embryogenesis part of the proposal, adequate expertise and well-chosen collaborations. Very good technical competence in genetics and biochemistry.

- **Weaknesses and threats:**

Too small a group, with no permanent collaborator except de PI. There is a risk of dispersion despite good collaborations. In addition, very powerful teams start to be involved in the field (notably on the newly identified functions of TLS DNA polymerases in cancer development).

- **Recommendations:**

The team should be helped in its development or to better focus its projects. Indeed, in the present state, it is not clear that the team has reached the right balance between size and project diversity, and they should try to improve this.

Team 14: Maintenance of Genome Integrity during DNA replication

Name of team leader: Mr Philippe PASERO

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	4	7
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		1
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	1	2
N6: Other contractual staff (without research duties)	2	3
TOTAL N1 to N6	**8**	**14**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	4	
Theses defended	2	
Postdoctoral fellows having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	2	
Qualified research supervisors (with an HDR) or similar positions	3	5

- ## Detailed assessments

Assessment of scientific quality and outputs

The PI has emerged in the past five years as one of the most exciting young researchers in the genome stability field. The team uses a variety of cutting-edge techniques, including molecular combing and ChIP-Seq to address fundamentally important questions about the causes and consequences of DNA replication stress. The team is highly collaborative and consequently highly sought after by researchers wanting single molecule combing analysis. Whilst this has resulted in a significant number of collaborative papers, the team also has a very impressive list of senior author publications in some top journals including Nat Cell Biol, EMBO J, NSMB, Mol Cell and others. The experts committee would like to particularly highlight the work on the Sir2 and histone deacetylases in DNA replication as being genuinely paradigm-shifting (now in press at Molecular Cell). The work on chronic stress and dNTP pools was also very influential. Finally, the experts committee is also encouraged to see the team beginning to explore systems outside budding yeast.

Publication output during the review period has been very good: 32 publications including 10 reviews (Curr Opin Genet Dev, Current Genomics, Transcription, etc) and 23 original articles. The team has been leader in 6 of these original articles, all published in excellent journals: Nat Cell Biol, Molecular Cell, 2 x Nat Struct Mol Biol and 2 x EMBO J. In addition, highly productive collaborations have lead to 17 publications, many of them in high impact journal such as Molecular Cell, Nat Struct Mol Biol, J Cell Biol, J Mol Biol, PNAS, EMBO J and NAR among others.

Assessment of the unit's academic reputation and appeal

Responsibility for steering and level of scientific involvement in international and national projects.

1) invitation to 27 international conferences (3 as chairman) and 21 seminars since 2008. Organization of 8 national and 4 international meetings;

2) the PI is vice-president of the National Committee (CN2) of ARC (since 2009), member of the scientific committee of the Cancéropôle GSO (since 2010) and of the SIRIC Montpellier Cancer (since 2012), member of the Scientific Advisory Board of the CRCM, Marseille (since 2013), chairman of the AERES visiting committee of iRCM, CEA/INSERM (2013).

From 2008 to 2013, the team has initiated 10 international collaborations, leading to 11 articles. Two Professors from Sherbrooke (2008) and Stanford (2013) universities spent several months in the lab on sabbatical.

Prizes: Delahautemaison Prize - FRM (2010), Bronze Medal 2013 – CNRS.

The PI is deputy director of IGH since 2011,

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

The team leader is:

1) member of the scientific committee of the Canceropôle Grand Sud-Ouest (INCa) and coordinator of the 'Genome, Structure and Function' program since 2010;

2) member of the scientific committee of the SIRIC Montpellier Cancer (since 2012);

3) participant of the third Franco-Chinese Exchange Program of the Charles de Gaulle Foundation (2013);

4) participant of a translational research program with the Academia Sinica (Wen-Chin Yang, Taiwan) to isolate novel anticancer molecules from Chinese Herbal Medicine that target replication forks;

5) patent CP-1651-TW, 25/11/2011 (Yea-Lih Lin).

Assessment of the unit's involvement in training through research

The PI has participated to international Master and PhD courses as lecturer, organized the EMBO YIP PhD course (EMBL, Heidelberg) from 2008 to 2010, coordinated the Training Program of the SIRIC Montpellier Cancer (since 2013) and is now co-organizer of the Master Program on Cancer Biology of the University of Montpellier (starting in 2013).

Several of the PhD students have moved on to postdoc positions and several of the postdocs have assistant professor positions.

Assessment of the strategy and the five-year plan

Over the past five years, the team has shown that replication-associated genomic instability is prevented by the operation of a wide variety of mechanisms that remain largely uncharacterized. These mechanisms also have major implications for tumorigenesis and for drug resistance. In the next five years, they will continue to study the origin of spontaneous replication stress, to identify new proteins involved in the detection and rescue of stalled replication forks. The proposed project is original and ambitious, and remains realistic given the expertise of the team.

In addition, they propose new projects aiming to develop innovative strategies to overcome drug-resistance of some cancers. Notably, in collaboration with a Taiwanese group, they will look for new replication inhibitors derived from traditional Chinese herbal medicine. In parallel, they will explore the possibility to develop novel therapeutic

strategies to target replication forks in cancer cells, notably in Multiple Myeloma. MM is currently incurable due to emergence of resistant sub-clones, but the mechanism responsible for resistance to treatment is unknown. The team proposes to explore the DNA repair and genomic instability status of resistant cells to identify genes whose deregulation is linked with poor patient survival. A leader in the field of MM, will join the lab at IGH with eight collaborators. With this major reinforcement, the team proposes to identify MM biomarkers predictive for treatment sensitivity and to initiate phase I-II clinical trial to overcome resistance. These projects represent an important switch from basic research to clinical application, which will constitute a true challenge for the team.

This is an excellent and ambitious 5 year plan. Maintaining strength in budding yeast whilst moving into mammalian systems is a solid, sensible strategy. All of the budding yeast projects follow nicely from previously published research and some very nice unpublished data. Regarding work in mammalian cells, the proposals for working on the intersection of RNA processing and replication is highly topical, and will nicely complement his budding yeast work.

Conclusion

- **Strengths and opportunities:**

- expertise in highly technical and important technologies;

- excellent scientific reputation in the field;

- very strong team of researchers.

- **Weaknesses and threats:**

- no significant weaknesses;

- it will be difficult to maintain strengths in all areas proposed without diluting efforts;

- the individual projects could be more synergistic to gain added value from the individual projects.

- **Recommendations:**

Consider consolidating some areas of research to improve scientific synergies within the group.

Team 15: Development and Pathology of the Gonad

Name of team leader: Ms Brigitte BOIZET

Workforce

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
N1: Permanent professors and similar positions	3	1
N2: Permanent EPST or EPIC researchers and similar positions	2	3
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	1	
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**6**	**4**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	4	
Postdoctoral fellows having spent at least 12 months in the unit	1	
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	3

• Detailed assessments

Assessment of scientific quality and outputs

A major goal of this group is to understand the roles of the prostaglandins in the overall physiology and function of the embryonic and adult gonads. On one side the lab is exploring the role of SOX9 in the regulation of the L-Pgds gene in vivo, and on the other hand they are studying the involvement of L-Pgds in cryptorchidism, a testis migration defect. Using KO strategy they have shown that L-Pgds KO animals display unilateral and bi-lateral cryptorchidism and adult cryptorchid testes showed an increase in spermatogonia apoptosis. Using a variety of assays their recent data suggests that PGD2 controls the mitotic arrest in germ cells of the developing male gonads, making it among the first signalling molecules involved in this process early is development.

This team is a well-established group with a number of collaborations. They have published 20 scientific articles between 2008-2013. In addition to a number of senior author publications in more specialised journals (Fertility & Sterility; Journal of Urology; Sexual Development; Journal of Ovarian Research; Developmental Dynamics),

and a number of clinically oriented publications, the group's key publications are a research publication in Human Mutation, a research paper in Development, and a second research paper in revision in Development. In general the journals that the group has selected for their publications are appropriate. The scientific output is good, and comparable to other internationally recognized researchers in the mammalian gonad development/germ cell sex determination field. The team's publication in Human Mutation that PGDS mutations cause cryptorchidism in mice is an important finding that could potentially provide some mechanistic insight into this common clinical condition. There is good quality careful science in this publication, the cryptorchidism only occurs in a proportion of the PGDS mutant mice and it has been 'missed' by other groups working with these mice. The group's publication in Development, primarily uses mouse genetics to dissect out tightly interlinked and connected pathways (FGF9, SOX9, prostaglandin D2). The quality of the research here is again very good, and is an important advance in determining the epistatic relationship between these pathways. The manuscript in revision in Development reports finding that L-PGDS/H-PGDS double mutant embryos exhibit impaired masculinization of the germline and hyperproliferation of male germ cells, would place prostaglandin D2 as one of the signalling molecules communicating the somatic sex determining decision to the germline and would implicate this pathway as a risk factor for testicular cancer. This submitted work will represent a significant advance in the field, and investigating the roles and mechanisms of prostaglandin signalling in the developing gonad represents an important research question. The group is recognized as the leading group working on this signalling pathway in gonad development.

The group has also started an interesting local collaboration of studying Mus Minutoïdes wild mouse, as an example of “natural sex-reversal”. Here they are using a multidisciplinary approach to study the genetic basis of this novel sex determination in mammals. This is clearly a very interesting project that should provide interesting insights into the sex determination cascade.

The group has also been trying to determine SOX9 binding sites in the developing gonad. This line of research has been progressing slowly, but seemed to be close to submission for publication.

Assessment of the unit's academic reputation and appeal

The PI has international standing in the field, and is typically invited and represented at the major meetings in the field (International symposium on the biology of sex determination, European Testis Workshop). This is a well-respected lab that is collaborating at national and international fronts. The PI has excellent reputation nationally as evidenced by her co-organisation of the joint national meeting between the French Sociey for Developmental Biology and the French Society for Cell Biology in 2012. The excellent national reputation of the group is illustrated by successful grant funding (two ANR grants, one Cancéropôle grant).

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

The lab works at the interface of medical and basic research. The PI also appears to be actively involved in teaching and training, and the group contributes approx 15 hours teaching per year. The group makes a good contribution to the social and cultural environment by participating in the Fête de la Science disseminating research on sex determination to high school students.

Assessment of the unit's organisation and life

The research group is relatively small, and its modest expansion through external funding should be encouraged to capitalize on the advances being made. The strong link between the prostaglandin signalling project and testicular cancer could open up new potential funding streams for this group. The lab appears to be well funded, but is lacking highly ambitious personnel to be involved in high risk/high gain type of projects.

During the committee's visit, the team requested to become co-led by the current PI and another senior scientist of the group. This request was considered and discussed by the experts committee, and in this case the committee feels that there is no added value for a team of this size to be co-led by team leaders with similar skills and expertise. The experts committee feels that the current PI provides stronger scientific contribution, and should remain as sole leader of this team.

Assessment of the unit's involvement in training through research

The PI also appears to be actively involved in teaching and training as evidenced by lectures, courses leading a lab with master and PhD students and postdocs. The group has a very good record in training PhD students: two students from this group have defended their thesis between 2008-2013.

Assessment of the strategy and the five-year plan

The group plans to continue in the two areas they have been working on namely understanding the role of PGD2 in gonadal differentiation, and expanding on the study of the complex genetic network involving SOX9 in gonadal differentiation towards the Sertoli cells lineage. They plan to further expand their work in understanding the disorders leading to testicular carcinogenesis and infertility.

The team's strategy of continuing to investigate the germ cell phenotype in L-PGDS/H-PGDS double knock-out mice is very good. This part of the five-year plan is consistent with the strengths and expertise of the team, and raises an interesting and important question. The link between prostaglandin D2 signaling and testicular germ cell tumors has clinical relevance, and opens up the potential for funding through cancer-oriented funding streams. The proposed collaborative project between this lab and team 20 investigating translational regulation in the L-PGDS/H-PGDS double knock-out germ cells is strongly encouraged due to the likely synergistic interaction between groups working on similar systems but in different species. The team also proposes to investigate the effects of prostaglandin signalling on the epigenome of germ cells, and a similar collaboration with experts in epigenetics is encouraged to help maximize research progress in this area. Both parts of the L-PGDS/H-PGDS theme in the five-year plan are technically feasible, have a very good chance of success, and are likely to generate very good primary research publications.

The five-year plan also proposes to use genome-wide DNA methylation and eRNA profiles from fetal Sertoli cells to determine the kinetics of SOX9-dependent enhancer activity in this lineage. The topic studied is definitely of great biological significance and broad interest. However, this progress in this project has been slow over the last five years, and it was not easy to see in the proposal how the group is going to tackle the major challenges ahead of them using a cutting edge research program. The experts committee felt that the group would benefit from focusing its efforts and resources on the prostaglandin signalling component of their future proposal.

Conclusion

- **Strengths and opportunities:**

This is a well-established group working on a very interesting and important research theme of gonadal development that has also immediate implications for human health. The group has strength and expertise in both SOX9 and prostaglandin signalling in the testis, and the group is doing the right thing in continuing to investigate deeper in this area. The time that the group has invested in generating and characterizing L-PGDS/H-PGDS double knock-out mouse gives them a competitive advantage in the field that can be exploited by investigating the phenotype of these mice in more detail as proposed in the five-year plan. The relationship between prostaglandin signalling and testicular cancer opens up opportunities for using cancer-oriented funding streams to expand this area of the group's research.

- **Weaknesses and threats:**

The research program needs to integrate some of the modern methodologies to gain momentum into performing mainstream research. This could also help with overall attractiveness of the lab for PhD students that the group is reporting to have problems recruiting. The group ought to be wary of investing too much time and effort into less productive lines of research and focus more on the more promising projects being undertaken in the group.

- **Recommendations:**

The experts committee recommends focusing on developing the PGD2/male germ cell project in the future, which appears to be generating more publications and external grant income than the 'SOX9 target sequences' line of investigation.

The proposed collaboration with team 20 to provide expertise in translation and RNA biology is strongly encouraged, and a similar collaboration with experts in epigenetics will be highly beneficial for the prostaglandin signalling project.

The current PI should remain as sole leader of this team.

Team 16: Neurogenetics and Memory

Name of team leader: Mr Jean-Maurice DURA

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	2
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)		
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**2**	**2**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	1	
Theses defended	1	
Postdoctoral fellows having spent at least 12 months in the unit		
Number of Research Supervisor Qualifications (HDR) taken	1	
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The research topic is centred on the investigation of the molecular processes involved during *Drosophila* brain development, and the long-term and short-term memory processes. For this, several key molecules are being studied, including ftz-f1, Hr39, TGF-b signaling and Wnt/APPL signaling. This is a very interesting topic, and the *Drosophila* model seems appropriate for the questions being addressed.

Taking into account the very small size of the team (only one researcher), the team publication rate is absolutely excellent, as it published 6 original articles during the period. Some of these papers have been published in top-impact journals such as Nature Neurosciences, Current Biology and PLoS Biol. Another paper is in revision in Science.

Assessment of the unit's academic reputation and appeal

The PI is invited as a speaker in international prestigious meetings (EMBO meeting, Janelia Farm Conference..) and labs (such as MRC). He has organized national meetings on Invertebrate Neurobiology. He is reviewer for both international and national grants and is referee for peer-reviewed top journals (PNAS, Development..). The team has developed international collaborations. The team has welcomed a senior researcher in the lab (6 months).

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

The PI contributes to education of high school students. He has participated to open days towards high school audience and "Science en fête".

Assessment of the unit's involvement in training through research

The team leader highly participates in teaching (License, Master) and regularly supervises Master and PhD students.

Assessment of the strategy and the five-year plan

The project is in the continuity of the previous work, and is based on solid results (both published and unpublished). Due to the small size of the team, the project has been restricted to few items and mainly focuses on the role of Wnt in axon guidance, thus it is feasible although ambitious. As mentioned in the SWOT analysis, the PI has to recruit middle- (post-doc) and long- (tenure) term researchers to increase the critical mass of the team.

Conclusion

- **Strengths and opportunities:**

Excellent PI mastering the technologies and tools required for conducting the project, that is very original.

- **Weaknesses and threats:**

The very small size of the team and uncertainty on financial support.

- **Recommendations:**

The team should put all its efforts to get funding in order to hire a post-doc and/or recruit a tenure researcher to increase its critical mass. Hopefully, upcoming publications should be exploited to obtain such funding.

Team 17: Cell Cycle and Myogenesis

Name of team leader: Ms Anne FERNANDEZ and Mr Ned LAMB

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	3	3
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	3	3
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**7**	**7**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students	3	
Theses defended		
Postdoctoral fellows 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	3	3

• Detailed assessments

Assessment of scientific quality and outputs

The 'Cell cycle and myogenesis' team is co-headed by two team leaders and works on a broad list of subjects that includes the investigation of the role played by protein phosphatases in cell cycle regulation, insulin signalling and Akt kinases, muscle stem cells and c-AMP signalling in insulin secretion.

A clear rationale for an apparent dispersion of themes is missing, likely reflected in the average scientific contributions by the team over the evaluation period : 11 papers in average to good journals (HMG, J Cell Physio, PLoS One). This is in sharp contrast with the publications in JCB, MBC and MCB between 1998-2008.

Assessment of the unit's academic reputation and appeal

The team is and has been involved in national projects and is currently funded until 2015 for a specific branch of their research program. The team has long term national and international collaborations and has been able to attract PhD students and one post-doc. The team is responsible for maintaining GeneStream and Cell Biology unit servers, the former still highly accessed and used as a remote international platform open to the community. There is extensive participation in national meetings but limited exposure to an international environment that could foster new collaborations and dissemination of the work. One of the team leaders is on the Editorial board of World Journal of Stem Cells and both leaders review regularly for specialized journals and grant agencies (FP7, AXA and AERES). At the moment, the team lacks international projection, also reflecting the limited participation in international meetings.

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

The team has been involved in outreach activities with high school students in coordination with other public bodies. The team also collaborated with a start-up company Cisbio to perform pilot experiments using microinjection, but the contract was withdrawn.

Assessment of the unit's involvement in training through research

The number of PhDs was rather low for the whole 2008-2013 period, considering the presence of 4 full time researchers in the unit. However, this has been improved by the recent enrolment of several students in PhD programs (1 in 2011 and 2 in 2012). One post-doc works in the team. The team is also involved in the training program for Medical students from Université Montpellier 1.

Assessment of the strategy and the five-year plan

The proposed project is in the continuity of the previous work with 3 aims on phophastases in the cell cycle and on muscle stem cells. This last research line has a strong potential and the research strategy seems adequate, but needs focus. This is reflected in the SWOT analysis of the team, meaning that they are aware of their own weaknesses, which is always a first step towards a solution, which might open up other opportunities for public and private funding, given the translational value of the research line involving muscle stem cells.

Conclusion

- **Strengths and opportunities:**

Scholar level of team leaders with strong background in cell cycle regulation and multidisciplinary nature of the team. Promising line of research involving muscle stem cells with cardiac regeneration potential.

- **Weaknesses and threats:**

The team has limited resources and the research program appears too dispersed. Publication record and impact is declining over the years. There is no clear added-value of a double leadership in a team of a relativly small size.

- **Recommendations:**

The most promising research line seems to be the multipotency and regeneration potential of adult muscle derived stem cells with pacemaker properties, which have been isolated and characterized by this team and is the main source of funding from a private foundation. The high potential of this research will be achieved only by in depth analysis of the events triggering the therapeutical properties of these cells at cellular and molecular levels. Given the limited resources the team should focus their research on the project that can earn the highest possible gain and for which they have secured funding. The existence of two team leaders is not justified, in this case leading to loss of focus of the team.

Team 18: Tubulin Code

Name of team leader: Mr Krzysztof ROGOWSKI

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	1
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	1	2
N6: Other contractual staff (without research duties)		
TOTAL N1 to N6	**3**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended	1	
Postdoctoral fellows 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		

• Detailed assessments

Assessment of scientific quality and outputs

This group was established at IGH in January 2011. As a post-doc at CRBM in Montpellier, the PI published 7 scientific papers from 2008-2011, two of these were first author papers that were both published in a top quality journal (Cell). These two Cell papers identified the enzymes responsible for polyglycylation and deglutamylation of tubulin, and each represented a major breakthrough in the field of tubulin post-translational modification. After being independently established, this group is focused on the biochemical identification of tubulin modifying enzymes and functional characterization of their in vivo roles using Drosophila and mammalian tissue culture systems. The ongoing research is highly competitive and timely at the international level and focuses on the investigation of the role of tubulin polyglutamylation in the cell cycle and sperm development and on the identification of tubulin carboxipeptidase, an enigmatic enzyme whose existence has been postulated but has not yet been isolated. Tubulin post-translational modifications are now more and more being seen as key hallmarks that regulate microtubule

function in several key processes, including a growing list of evidence that they might regulate the association and function of motor proteins and MAPs. This is therefore a 'hot' topic of research. The group has not yet published independent work, which is not unexpected given the relatively short period between the establishment of this team and the AERES evaluation. Importantly, the research strategy is thoughtful, laborious and centred in the high-risk/high-gain principle. The questions that are being addressed by this team are important for the microtubule/cytoskeleton field, and the genetic approaches and results that the team has generated suggest that post-translational modification of tubulin is important for different aspects of development and disease. The team is using multiple systems (cell culture, Drosophila) and approaches (biochemistry, cell biology, developmental genetics) to analyse different aspects of tubulin post-translational modification, and the resulting ongoing program of work is impressive. The extent of progress across a range of projects, all of which have the potential for publication in good/high impact factor journals bodes well for the future of this group. In particular, the identification of tubulin carboxipeptidade, when fully validated, will have a major and broad impact that will extend beyond the immediate field of research. Overall, this is a very strong team with excellent potential and should be supported at the highest level.

Assessment of the unit's academic reputation and appeal

The team is and has been involved in national projects and is currently funded until 2016. The team is part of a post-doc exchange project at the international level, but participation in larger scale international projects (e.g. ERC, Horizon 2020) should remain a goal to pursue in the future after consolidation of the research program. The team is also collaborating internationally (e.g. Stanford University) on scientific aspects concerning the purification of tubulin carboxypeptidase. The team has also been able to attract apparently very talented post-docs and students, albeit in a limited number. There is also participation in international meetings, both in the form of oral and poster presentations.

Given the short time period between the PI establishing his team (Jan 2011) and this evaluation it is difficult to assess the team's reputation and appeal. Clearly with two major breakthrough publications from his post-doc, the PI has potential to become a leader in his field. The team's success in securing grants (e.g. ANR JC and ATIP) shows that he has a very good reputation nationally.

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

The team is involved in the isolation of a tubulin carboxypeptidase inhibitor compound, active in the nM range, which might have commercial value in the near future. The major strength of the team is on basic research of very high quality, which has the potential for high impact and wide dissemination in top ranked journals.

Assessment of the unit's organisation and life

The team is well organized and focused on 3 main goals, all of exceptional value and supported by a coherent research program. Presently, the team has 2 post-doc fellows, 1 research scientist, which might be a limiting factor for the scope of the research being carried out, and the range of expertises involved. There is some frequency of national and international meetings, limited in number due the prime focus in consolidating research.

Assessment of the unit's involvement in training through research

The high quality of research nurtured by this small team offers an excellent environment for mentoring and training. One PhD student graduated already from this team and one post-doc is actively involved in teaching at the Université Montpellier 2. The team is also involved in an international post-doc exchange program.

Assessment of the strategy and the five-year plan

The research project is based on a high-risk/high-gain premise and focused on 3 major research lines. The strategy is well conceived and the team is surrounded by all necessary expertise to achieve the goals. The research questions being addressed are important and exploit breakthroughs that the team leader made during his post-doc. The multi-disciplinary approach being undertaken by this newly formed group is impressive. The scope of the research being undertaken, in combination with the new lines of research that are emerging from their ongoing work, suggests that the team might need to focus their efforts over the next few years. The plan to follow up the identification of tyrosine carboxypeptidase could provide more focus to the team's research. The suggestion to use

EUCOMM-derived mouse ES cells to assess TCP function during ES-derived neural differentiation needs some clarification. The team leader expressed his concern that the paradigm shift in basic research funding at the national level could represent a serious threat to the success of this excellent team, as highlighted in their own SWOT analysis.

Conclusion

- **Strengths and opportunities:**

Excellent track record of the team leader with strong expertise in biochemistry. Excellent and ambitious research plan, with high potential for major breakthroughs that will extend beyond the research field. The identification of tubulin carboxypeptidase is quite timely and should be published, when validated, as soon as possible. This will open doors for other funding opportunities. The significant progress that has been made by the team across a range of projects in a short period of time is impressive. This team has the opportunity to exploit these advances and make significant progress in the field.

- **Weaknesses and threats:**

The team has limited resources, especially at the human level, to achieve an internationally competitive research program.

- **Recommendations:**

Publication of the tubulin carboxypeptidase in a top-ranked journal as soon as technically possible. Soon after, the team leader should apply for ERC funding which would protect the team from the change in funding policy at the national level. The team should also take advantage from the expertise in *Drosophila* to look for/generate mutant alleles for TCP, as well as invest in mouse models, since KO ES cells are already available. This team should be supported internally and externally at the highest level. Strategies to allow either focusing of the team's research, or expansion of the team through external funding should be developed.

Team 19: Systemic Impact of Small Regulatory RNAs

Name of team leader: Mr Hervé SEITZ

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	1	1
N3: Other permanent staff (without research duties)		
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	1	1
N6: Other contractual staff (without research duties)	1	1
TOTAL N1 to N6	**3**	**3**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended		
Postdoctoral fellows 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	1	1

• Detailed assessments

Assessment of scientific quality and outputs

During his post-doctoral work, The PI made seminal contributions in small RNA biology and acquired a reputation of expert in systems biology and statistics. Micro-RNAs have been involved in numerous biological processes. Each miRNA has the potential to target the silencing of many mRNAs through imperfect base complementarity. However, the biological significance of many predicted miRNA-mRNA interactions remain unclear, as most of these interactions result in only a 1.5 to 2-fold repression of the targets. The team is built on the “pseudo-target” hypothesis (Curr Biol, 2009) upon which most of miRNA targets would actually be pseudo-targets whose function is to buffer/quench miRNAs and thus to modulate the repression of real miRNA targets. The main idea is that real targets would be genes sensitive to the ~2-fold repression by miRNAs, and therefore would tend to be haploinsufficient, whereas pseudo-targets would accommodate fluctuations higher than 2-fold. Over the past years, the hypothesis was refined to make predictions, which were tested through high-throughput, genome-wide analyses

and systems biology approaches. Three of these predictions (the most abundant mRNAs bear the most conserved miRNA binding sites; the most dose-sensitive mRNAs bear the most conserved miRNA binding sites; many predicted microRNA targets are insensitive to microRNA-mediated repression) are now well supported. Considering that the team was created only 2 years ago, the limited number of publications is understandable. The pseudo-target theory has the potential to produce major insights. The team has implemented original systems biology approaches and has expertise in big data analyses, bioinformatics and statistics that should benefit to the IGH.

Assessment of the unit's academic reputation and appeal

The team leader has published a number of scientific articles in highly rated journals (Science, Nat Struct Mol Biol, Curr Biol) before starting his group at IGH. The expertise of the team in bioinformatics and statistics is well established and highly valuable for IGH. The PI was a member of the organization committee of the "Journées Ouvertes en Biologie, Informatique et Mathématiques", this illustrates well this reputation. The team leader has been invited to many prestigious international meetings in the field. A post-doc in the team has given a talk at a Cold Spring Harbor Symposium. The team leader has been reviewer for many journals (Biochimie, BioEssays, Biophysical Journal, Cell Research, Current Biology, EMBO Reports, Genome Biology, Genome Research, Genomics, Nucleic Acids Research, PLoS One, RNA and Silence).

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

The team leader has been referee for the "Deep-sequencing" call for proposals of the GIS IBiSA (Génoscope and Centre national de séquençage, France) (2010) and for French grant agencies "ARC Alsace" (2011) and "ANR" (program "ANR Blanche", 2012). The team is supported by an ATIP-Avenir grant sponsored by Sanofi and has established contacts with this company. The team leader had consulting activities for Medesis Pharma, S.A. The team published an article in "Pour la Science" (Les petits ARN entrent dans l'arêne), accessible to the lay public.

Assessment of the unit's organisation and life

The team is relatively small, being composed of 1 staff scientist, 1 Assistant-Engineer and 1 or 2 post-docs in addition to the PI. On the one hand, the lack of perspectives for publications in high standard journals in the short term is worrying. One the other hand, the Systems Biology projects for the next 5 years are very ambitious and will require a reinforcement of the team personnel.

Assessment of the unit's involvement in training through research

There is no PhD student currently in the team. The team leader participates in teaching in different Master programs in Toulouse, Rennes, Lyon and Paris, and was member of 6 theses and 1 HDR committees.

Assessment of the strategy and the five-year plan

Ongoing and future works are essentially aimed at testing various predictions from the pseudo-target theory. This implies the precise quantification of miRNAs, mRNA targets and pseudo-targets in Drosophila cells, data that is clearly missing in the field. Potential competitions between pseudo-targets will also be addressed, with the perspective of identifying new regulatory networks. Last, additional pseudo-targets will be searched through the identification and characterization of long non-coding RNAs in Drosophila. The research plan is very ambitious, requiring important manpower and funding as well as diversity of expertise (mouse and Drosophila models, genetics, high-throughput genomics, bioinformatics & computational biology).

Conclusion

- **Strengths and opportunities:**

The team has a renowned expertise in miRNA systems biology and carries on very high profile science with an original angle in a competitive field. Its bioinformatics and statistics skills open real opportunities for collaborations in the community.

- **Weaknesses and threats:**

The approaches of the team are strongly driven by the pseudo-target theory. This is a risk because the theory, although not formally demonstrated, is generally accepted and used by the community; making a breakthrough under those conditions seems difficult. In addition, the strong focus of the lab generates a risk of neglecting other possible explanations for the lack of impact of miRNAs on many predicted targets (site-accessibility, required multiplicity of binding sites on the same RNA, etc).

- **Recommendations:**

The team has very strong potential and should quickly establish solid ground by publishing in order to be able to move forward. Mentoring by senior scientists in the field would be beneficial.

Team 20: mRNA Regulation and Development

Name of team leader: Ms Martine SIMONELIG

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	3	2
N3: Other permanent staff (without research duties)	1	1
N4: Other professors (PREM, ECC, etc.)		
N5: Other EPST or EPIC researchers (DREM, Postdoctoral fellows, visitors, etc.)	4	4
N6: Other contractual staff (without research duties)	1	2
TOTAL N1 to N6	**9**	**9**

Team workforce	Number as at 30/06/2013	Number as at 01/01/2015
Doctoral students		
Theses defended	1	
Postdoctoral fellows having spent at least 12 months in the unit	2	
Number of Research Supervisor Qualifications (HDR) taken		
Qualified research supervisors (with an HDR) or similar positions	2	2

• Detailed assessments

Assessment of scientific quality and outputs

The team continues to produce outstanding work in two areas: translational control during oogenesis and early embryogenesis; and pathology of the genetic disease OMPD. Both approaches use Drosophila as sole model.

The team showed that piRNAs, previously thought to function only in repressing transposition, also regulate certain important maternal RNAs. The lab has also made very nice progress in developing important new observations in both projects.

Publications were outstanding during the first part of period under review, although productivity has dropped off somewhat since. Highlights include Development 2008, HMG 2009, Nature 2010, EMBO Mol Med 2011, plus several reviews/commentaries. Overall the PI has 457 citations from 2009-2013 (WoS). It was very encouraging to hear of the

recent Stem Cell Reports publication, plus that an additional manuscript is under review at Developmental Cell. It is recommended to make a priority of publishing the other two manuscripts listed in the report as soon as feasible.

Several grants have been awarded. The laboratory has ample funding.

Assessment of the unit's academic reputation and appeal

The PI organizes a biannual national workshop, serves on several national science committees and serves also as head of the department of Genetics and Development at IGH. She coordinates one European AFM network and is a member of other collaborative ones.

The ability to recruit scientists is excellent. The lab has maintained a steady state of approximately 10 staff mostly postdocs. Turnover was 11 members out and 13 new recruits in.

The PI lists several important national research awards. She is also frequently invited to speak at national and international conferences, and was also invited to write 4 reviews and 2 highlight articles.

The team leader has reviewing activities for European as well as French organizations (ERC, MRC, AFM, ANR, Genoscope, etc), has sited in 6 committees of PhD/HDR and is member of the evaluation committee of ANR Blanche (Biologie et Santé). The team leader has reviewed scientific manuscripts for high-standard international journals.

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

The projects on OMPD were performed in EU and AFM networks and are by essence translational with potential outputs in medicine and human health care. The team leader was coordinator of the AFM “Projet Stratégique eOPMD” (2010-2013). Since 2011, the team is member of the Laboratory of Excellence EpiGenMed.

Assessment of the unit's organisation and life

Each aim lists one or more team members and the theme of the lab is clear and consistent.

The accessibility of pooled resources is outstanding.

Assessment of the unit's involvement in training through research

Only 1 student was in a PhD program, who is now a pharmacist. Four L3/M1 students carried out an internship in the lab during the evaluation period.

The team leader teaches Master’s students at University of Montpellier and Paris 11. Several lab members also teach, some with an extensive involvement (100 hr/yr in one case).

Assessment of the strategy and the five-year plan

The team has competed successfully in two fields, namely gene regulation by piRNAs and OPMD. The future plan follows up on these themes, with three aims devoted to each area for a total of six aims. Aims 1-3 pursue the piRNA angle. Overall these aims are ambitious but definitely focused on key questions and generally doable. Aims 4-6 focus on OPMD. One point of interest in aim 4 is that deregulation of silencing is linked to OPMD progression. Is there any way to test causality? The opportunity for therapeutic approaches to OPMD is very exciting and the lab will use its expertise in Drosophila to partner with other labs using mice or performing clinical trials. One minor concern with personnel allocation is that one member of the lab appears to be solely or primarily responsible for all three aims on the OPMD project. This is much for one person.

The strategy is generally feasible. The team stands a very good chance of continuing to impact this field of research.

There is an excellent track record of adapting to changes in both areas of research, and to developing new approaches that make an impact. The focus on Drosophila is highly appropriate for the piRNA work because work on flies is far ahead in the field. For the OPMD work, it is important to maintain network contacts with labs using other models, such as mice, to optimize the relevance of the fly work.

From the SWOT analysis, the team leader has very clear picture of the current situation. She proposes to build on the team strengths and to take advantage of new developments such as super-resolution microscopy. Presumably the PI will continue to apply for and attract extramural funding. The major concern stated in the report is recruitment of postdocs and staff.

Conclusion

- **Strengths and opportunities:**

- strong track record of publication in excellent journals;
- continued leadership in competitive fields;
- intriguing unpublished developments that can mature into high-impact projects;
- excellent self-sense;
- outstanding leadership contributions.

- **Weaknesses and threats:**

- drop-off in publication of research articles since 2011, although the situation is improving;
- a few aspects of the future plan appear unevenly allocated among lab personnel.

- **Recommendations:**

- focus on publishing research articles;
- keep up the successful attraction of extramural funding;
- keep up the OPMD network connections.

5 • Conduct of the visit

Visit dates:

Start: Wednesday, February 5th 2014 at 9.00 am

End: Friday, February 7th 2014 at 4.15 pm

Visit site: Montpellier

Institution: Institut de Génétique Humaine

Address: 141 rue de la Cardonille, 34396 Montpellier

Conduct or programme of visit:

Wednesday February 5th 2014

09.00-09.30 am	Preliminary meeting of the experts committee (closed hearing) *Attending: expert committee members and AERES Scientific Delegate (DS)*
09.30-09.45 am	Presentation of AERES evaluation and of expert committee members (Mr Pierre COUBLE)
09.45-10.45 am	Presentation of the research unit by Mr Giacomo CAVALLI and Mr Monsef BENKIRANE (including questions) *Attending: expert committee members, DS, representatives of institutions and unit members*
10.45-11.45 am	Meeting with representative of Institutions *Attending: expert committee members, DS, representative of CNRS and Université Montpellier*
11.45-01.00 pm	Lunch
01.00-01.50 pm	Scientific presentation by Mr Monsef BENKIRANE *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
01.50-02.40 pm	Scientific presentation by Mr Angelos CONSTANTINOU *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
02.40-03.30 pm	Scientific presentation by Mr Pierre CORBEAU *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
03.30-03.45 pm	*Break*
03.45-04.35 pm	Scientific presentation Ms Marie-Paule LEFRANC *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
04.35-05.25 pm	Scientific presentation Mr Domenico MORAIANO *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
05.25-06.15 pm	Scientific presentation Mr Philippe PASERO *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*

Thursday February 6th 2014

08.00-08.15 am	Closed-door Committee meeting
08.15-09.05 am	Scientific presentation Mr Giacomo CAVALLI *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
09.05-09.55 am	Scientific presentation Ms Séverine CHAMBEYRON *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
09.55-10.45 am	Scientific presentation Mr Bernard DE MASSY *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
10.45-11.00 am	*Break*
11.00-11.45 am	Meeting with technical and administrative personnel (sub-committee 1)
11.00-11.45 am	Meeting of the experts committee with thesis students and post-docs (sub-committee 2)
11.00-11.45 am	Meeting of the experts committee with researchers (sub-committee 3) *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
11.45-12.00 am	Meeting with the director of doctoral school
12.00-01.00 am	Lunch
01.00-01.50 am	Scientific presentation by Mr Jérôme DEJARDIN *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
01.50-02.40 am	Scientific presentation by Ms Reini Fernandez DE LUCO *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
02.40-03.30 am	Scientific presentation by Ms Rosemary KIERNAN *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
03.30-03.45 am	*Break*
03.45-04.35 am	Scientific presentation by Mr Marcel MECHALI *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
04.35-05.25 am	Scientific presentation by Ms Brigitte BOIZET *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
05.25-06.15 am	Scientific presentation by Mr Jean-Maurice DURA *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*

Friday February 7th 2014

08.00-08.15 am	Closed door committee meeting
08.15-09.05 am	Scientific presentation by Ms Anne FERNANDEZ *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
09.05-09.55 am	Scientific presentation by Mr Krzysztof ROGOWSKI *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
09.55-10.45 am	Scientific presentation by Mr Hervé SEITZ *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
10.45-11.35 am	Scientific presentation by Ms Martine SIMONELIG *Attending: expert committee members, DS, director of unit, representatives of institutions and team members*
11.35-01.00 pm	Lunch-discussion with the heads of research unit
01.00-04.00 pm	Deliberation of the experts committee (closed hearing) *Attending: expert committee members and DS*
04.15 pm	Thanks and leave of the experts committee

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 28 avril 2014

Référence : G. CAVALLI/M. BENKIRANE : S2PUR150008541 – IGH – Institut de Génétique Humaine - 04342321N

Messieurs,

Je tiens à remercier le comité de visite AERES pour la qualité de son rapport d'évaluation concernant l'Institut de Génétique Humaine dirigé par M. Giacomo CAVALLI.

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 actuel et le futur directeur, M. Monsef BENKIRANE, de cette structure de recherche.

Vous trouverez ci-joint les commentaires du directeur de l'unité de recherche auxquels je n'ai rien à rajouter.

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

Philippe AUGE
Président
Université Montpellier 1

Observations de portée générale - rapport d'évaluation de l'unité « Institut de Génétique Humaine »

In general, we find this report balanced and well thought out. We are happy to see that the committee highlighted the outstanding quality of this Institute, defined as "flagship for life sciences in France" and as "world-class institute" and we would like to thank the committee and all its members for their important contribution to our institute assessment and future developments.

We also saw that interesting inputs were given in the report and as a result of the visit.

We can already say that, concerning office space, an open space office area will be kindly provided by Genopolys and made accessible to IGH staff under an online booking system. We are aware of the lack of office space for IGH PIs and will make every effort to attribute office space to those PIs who have none.

Concerning the need to take care of communication from the directorship, the Institute director will start next month holding regular seminars open to all IGH staff reporting on news and updates, on results of discussions and votes held at the PI meetings and "conseils de laboratoires", and on any other items as necessary.

Finally, one remark on the need to set up accompanying services for foreign students, post docs and researchers was raised and we have already solved the problem by contacting a company called "Get settled (www.getsettled.fr)" which will assist foreign collaborators in all paper works needed to establish in Montpellier, plus follow them up during the first months in order to solve for them any administrative troubles.

Therefore, we thank the committee for the visit and, as always, we used their inputs in order to improve our management and we will struggle to keep steadily improving our management.

Below, we would like to list below two comments written by the PIs of two teams concerning their evaluation

Team 20: Martine Simonelig

Concerning Team 20 (Martine Simonelig), we have been surprised by the comment that the productivity has dropped in the second part of the period, since it was our understanding that the period should be evaluated as a whole. This team has published, among others, a key publication on gene regulation and genome evolution in Nature (2010). Since 2012, the team has published five Reviews or Highlights, one research article in Stem Cell Reports which made the cover of the journal (2013) and has now a major publication in revision at Developmental Cell.
In addition, we note that a few important facts have been omitted in the report, as follows:
- The team leader has been session chair at five major international meetings (EMBO Conference, Jacques Monod Conference, European Drosophila Conference).
- The team leader is a member of the INSERM Scientific Committee CSS3.
- The team leader is coordinator of the new AFM European network "Projet Stratégique eOPMD" 2014-2017.

Team 17 "Cell Biology" (leaders Anne FERNANDEZ and Ned LAMB)

Most of the criteria other than relating to scientific production --□responded in the factual errors section above--□ seem to have been under--□considered in the detailed assessment and translated in complete discredit in the "conclusion" page 54. Indeed there is a surprising disregard of the achievements and strengths of the team.

For instance concerning the "Training through research" criteria, the evaluation comments appears to be skewed by negativity stating that *"the number of PhDs was rather low for the whole 2008--2013 period"*, whereas our teams has the highest ratio of HDR to researchers and PhD students per lab members, and the general comment made on this criteria for the IGH unit underlines the need for more researchers with HDR and for the recruitment of more PhD students. In addition, we also had one PhD student, Nabil Khouya, in our team from 2010 to 2011. This student chose to end his training because of a significant health problem in 2011, but still has co--□authored a publication in our group in 2011.
As for the "academic reputation and appeal" criteria, the AERES evaluation comments ignored completely 1) that our server for genomic resources "Genestream" is still accessed and used more than 100 times a day worldwide, 2) that our team has kept publishing and collaborating with well--□known teams in the USA (Derek Leroith, a world specialist in insulin signaling and diabetes, formerly in Washington, now at the Mont. Sinai School of Medicine, NY) and in Switzerland (Brian Hemmings, FMI in Basel; a leading scientist in the field of protein kinases and particularly Akt--□PKB).

For the last criteria the "strategy and next 5 year plan" and conclusions, a major criticism raised in "weaknesses and threats" (in addition to the claim that our "publication record and impact is declining over years", which is totally wrong as detailed in the section on factual errors) was that *"the research program appears too dispersed"*. We had mentioned ourselves that the diverse research themes addressed in the team, although complementing each others, could be a potential weakness because of a slower way to publication (regrettably, with the pressure to publish fast rather than right, a pressure that has now reach French science, it is always harder to

publish scientific results that carry more than one result, from one angle). However, multi--□disciplinarity is continuously encouraged at all levels and our diversity is also a strength as stated in the report's conclusion recognizing the *"multidisciplinary nature of the team",* thereby contradicting the criticism on diversity of research themes.

As a result of this systematic negativity and ignoring (or even down--□grading) the team's size, strengths and achievements on all criteria, the report purports to conclude and recommend that the dual leadership of the team, that has been the effective management of our team for more than 20 years, has "no clear added value" and "is not justified".