LBCMCP - Laboratoire de biologie cellulaire et moléculaire du contrôle de la prolifération

Rapport Hcéres

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

Section des Unités de recherche

AERES report on the research unit

Laboratoire de Biologie Cellulaire et Moléculaire du Contrôle de la Prolifération

Cellular and Molecular Biology of the Control of Cell Proliferation

From the

University Paul Sabatier, Toulouse

CNRS

May 2010

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Le Président de l'AERES	Section des unités de recherche
	Le Directeur
Jean-François Dhainaut	**Pierre Glorieux**

May 2010

Research Unit

Name of the research unit : Laboratoire de Biologie Cellulaire et Moléculaire du Contrôle de la Prolifération, Cellular and Molecular Biology of the Control of Cell Proliferation Laboratory

Requested label :

N° in the case of renewal : UMR5088

Name of the director : M. Didier TROUCHE

Members of the review committee

Committee chairman

M. Jonathan WEITZMAN, University Paris 7, France

Other committee members

M. Rob de BRUIN, MRC Laboratory for Molecular Cell Biology, London, UK

M. Cayetano GONZALEZ, Institut de Recerca Biomedica (IRB), Barcelona, Spain

Mrs Anja GROTH, Biotech Research & Innovation Centre (BRIC) Copenhagen, Dennmark

Mrs Sarah LAMBERT, Institut Curie, France

M.Yvan DE LAUNOIT, Univ. Lille, Institut Pasteur Lille, France

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

M. Olivier COQUERET, University of Angers, CNU member

M. Vincent PEYROT, University Aix-Marseille 2, CoNRS member

Observers

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M. Jean-François ARNAL, University Toulouse 3

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M. Bernard KNIBIEHLER, University Toulouse 3

Report

1 • Introduction

- Date and execution of the visit

The visit took place on the 27-28th January 2010 at the premises of the Laboratoire de Biologie Cellulaire et Moléculaire du Contrôle de de la Prolifération (LBCMCP) on the campus of the Université Paul Sabatier - Toulouse III. The preparation of the evaluation visit by the current Director and future Director was excellent. The committee was provided with full written documentation and printed copies of all the slides for the different presentations. This professional organisation was much appreciated by the committee and allowed them to work effectively and efficiently. The visit was organised over one-and-half days, allowing ample time for discussion with the Director, group leaders and staff. The visit included presentations by each group leader, as well as meetings with technical personnel, researchers/lecturers, and students/postdocs. In addition, there was a poster session at lunch time; this was much appreciated by the committee members and gave them time to discuss the projects in more depth with students, postdocs and research staff. Members of the committee also visited the laboratories to assess the conditions under which research is performed. Although there were six research teams in the UMR for the last four years, three of them will not apply for renewal and did not present their work. The presentations focused on the four groups that will form the UMR for the next four years and the group of the departing Director. On the second day, the committee also met with the future Director to discuss strategic issues for the future unit and with members of the management of the Université Paul Sabatier and the CNRS.

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

The LBCMCP labratory is a joint research unit (Unité Mixte de Recherche, UMR5088) supported by the CNRS and the Université Paul Sabatier - Toulouse III. The laboratory was founded in 1999 and the founding director has served as a dynamic head for the last 12 years as the unit has grown to incorporate new groups. The laboratory is located on the university campus in a building of the UFR des Sciences de la Vie et de la Terre (SVT) which houses other groups working on developmental and molecular biology. These groups and others in adjacent buldings form an Institut Fédératif de Recherche (IFR109) called the "Institut d'Exploration Fonctionnelle des Génomes" (IEFG) which was created in 2001 and brings together researchers with common scientific interests, encouraging them to collaborate and allowing them to support shared technology platforms. The UMR5088 currently occupies about 800 m2 spread out over five floors in the building. The renewal of the unit will see a change of direction and likely a shift in research emphasis.

The current research teams of the UMR are focused on studying the molecular mechanisms that control cell proliferation, cell cycle progression and cell division. They are particularly interested in checkpoint control mechanisms and their importance for disease pathologies such as cancer. Several of the projects are directed at understanding the role of epigenetic modifications in cell cycle control. The unit is characterised by the use of diverse biological models and the development of sophisticated technological innovation to address important biological questions related to cell cycle control.

- Management team

For the last four years the UMR5088 has been under the management of its founding director. The UMR has been organised into six research teams that are thematically independent. Each team is managed by a dynamic and active group leader. The unit is supported by a general secretariat and central "laverie". In addition, the unit supports technical platforms in Imaging and Cellular Pharmacology. The laboratory council meets every two months and is actively involved in the decision making of the unit. The committee was impressed by the leadership skills of the outgoing Director and commends him for his drive and enthusiasm, which has fostered the emergence of young groups and created strong ties with industry. The committee was equally impressed by the leadership potential of the future Director and his clear vision for development in the future. Finally, based on the different meetings (with research staff, technical personnel, postdocs and students), the committee had the clear impression that people were happy to work in the unit and appreciated the supportive atmosphere and the strong emphasis on training.

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	2
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	9	12
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	2	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	8	8
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	1	2
N6: Number of Ph.D. students (Form 2.7 of the application file)	8	12
N7: Number of staff members with a HDR or a similar grade	7	10

2 • Overall appreciation on the research unit

- Summary

The Laboratoire de Biologie Cellulaire et Moléculaire du Contrôle de la Prolifération (LBCMCP) UMR5088 is a dynamic research unit focused on investigating important questions related to the control for cellular proliferation, the epigenetic mechanisms that modulate cell fate and the checkpoint machineries that regulate the cell cycle. The research carried out in the unit is of a high quality and is generally published in high-impact journals. The unit has invested heavily in technological innovation and has developed expertise in microscopy imaging and genome-wide analysis. The unit is at a pivotal point of change, as the founding Director and many of the staff are to leave this year. The new UMR will be built around four groups with strong potential for collaborative synergies. The younger group leaders are emerging as major players in their field at the national level, with potential to create international reputations. All the group leaders are ambitious and enthusiastic and they have created an excellent environment for training and the exchange of ideas. The unit is committed to nurturing young talent and should be able to attract first-rate new groups with complementary interests in epigenetics and cell proliferation. The committee was impressed by the quality of the scientific discussion, the coherence of the projects and the energetic environment during the visit.

• Strengths and opportunities

- The UMR has benefited from strong charismatic leadership since its creation and has a future Director with an enthusiastic vision for the next four years.

- The unit has strong interdisciplinary expertise and complementary approaches. These need to be fostered in the future.

- The departure of several teams will provide free space to allow the recruitment of new teams through an international search. This momentary instability should be turned to an advantage to recruit new talent, creating both scientific diversity and enhanced synergies.

- The unit is one of the founding members in the creation of the new Fédération de Recherche en Biologie de Toulouse. This is an exciting opportunity to build a new centre for integrated biology and the study of complex living systems. The creation will be accompanied by enhanced scientific activity, support for shared technology platforms and the eventual move into a new building on the university campus.

- The unit has nurtured the emergence of young talent and has created high standards for student training and mentoring.

• Weaknesses and threats

- The biggest immediate problem that the Unit faces is the exceedingly poor quality of the premises and the appalling research conditions. The committee was shocked by the state of the labs and offices and hopes that the assurances offered by the Senior Managment of the Université Paul Sabatier during the visit will be honoured. The building is in need of urgent attention to ensure that the conditions for the next few years comply with Health and Safety regulations.

- The management of external research funds by the university is another serious problem that must be addressed. The unit is loosing the confidence of a number of suppliers of reagents due to delays in paying bills etc. This is seriously compromising their ability to do timely, competitive research.

- The third issue is personnel: the departure of a large chunk of the personnel, including many technical and support staff will create serious Human Resources challenges over the next year or so. It will be critical that the CNRS and the Université Paul Sabatier commit to replacing lost positions, particularly those linked to the support of technology platforms (Cellular Imaging, Bioinformatics). The committee was assured by the two 'Tutelles' that the UMR would be a priority for future allocation of permanent positions. It may also be necessary to 're-deploy' technical personnel to support emerging groups and ensure balanced distribution. This will be challenging and will require tact and open communication.

• Recommendations to the head of the research unit

- The committee recommends the establishment of a search committee to assist in the selection of new research groups when space becomes available. It will be important to define criteria for recruitment and ensure thematic balance and complimentarity.

- The committee recommends frequent meetings with the individual group leaders to help them remain focused on their most promising research projects. This mentoring role should help in increasing quality of the journals that they publish in.

- The committee recommends that the members of the unit become more involved in campus life and university affairs in order to increase the local visibility of the unit that is critical for negotiating space and technical staff.

- There is an urgent need to assure the replacement of technical staff to support technology platforms (Cellular Imaging) and the emergence of a Bio-informatics facility.

- The committee recommends the creation of a mentoring/tutorship program for PhD students, post-docs and young researchers.

- The committee recommends that the Director meets regularly with technical staff (during the transition period) to reassure them about the changes associated with the new UMR and the consequences for their professional development.

- The committee recommends that the Director reports to CNRS regularly about the progress in terms of critical improvements in the quality of the premises and the management of external funds by the University.

• Production results

A1: Number of permanent researchers with or without teaching duties (recorded in N1 and N2) who are active in research	14
A2: Number of other researchers (recorded in N3, N4 and N5) who are active in research	7
A3: Ratio of members who are active in research among permanent researchers [(A1)/(N1 + N2)]	1
A4: Number of HDR granted during the past 4 years	5
A5: Number of PhD granted during the past 4 years	7

3 • Specific comments on the research unit

• Appreciation on the results

The research at the LBCMCP UMR5088 is innovative and of high quality. The individual group leaders are dynamic and enthusiastic and are developing international reputations for their work. The projects are well funded (over 800 KEuros per year mainly from national cancer sources such as INCa, La Ligue Nationale Contre le Cancer, l'Association contre le Cancer…) and the groups have developed strong international collaborations and close ties with industrial partners (e.g. GSK, Pierre Fabre). The unit has published almost 80 papers over the evaluation period, many in good and very good journals (Molecular Cell, EMBO Journal, J Cell Biol). The Unit has also filed four patents. The level of training and mentoring (in terms of quantity and quality) is high and 7 PhD students have defended their thesis.

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

The atmosphere and intellectual environment at the LBCMCP make it an attractive place to work. Indeed, the unit currently houses 14 post-docs and 15 PhD students from around the world and the unit has been remarkably successful in recruiting young scientists to permanent positions at CNRS or Inserm. Members of the unit are often invited to participate in international meetings and they play active roles in local and national committees and editorial boards. There is an active seminar series and the members of the unit organised a major international conference on Cell Cycle and Cancer. The unit also has close ties with industry and has several projects of 'translational research'.

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

The UMR5088 has been organised into six independent research groups over the last four years. Several of these are to leave this year. The new UMR will consist of four founding groups, each led by a dynamic and enthusiastic researcher. The laboratory council meets every two months and is actively involved in the decision making of the unit. The committee was impressed by the leadership qualities of both the outgoing Director and the future Director. The committee assessed that they have successfully created a supportive atmosphere with a strong emphasis on training and mentoring. For example, the committee was impressed by the ability of the unit to nurture the emergence of new groups, either those that have stayed and become independent or those that have set up elsewhere. The unit also successfully combines technological innovation (microscopy platforms, mathematical modeling, drug screening) with important biological questions. Many of the staff are involved in teaching and the unit contributes to local training and transmission of expertise through its technology platforms (particularly microscopy and imaging, cell pharmacology). Finally, the unit pools some research grant funding to generate a common funding source which could be critical to support emerging groups and new research themes.

- Appreciation on the project

The projects proposed by the individual teams are ambitious, yet realistic. The groups will need to define milestones and keep focused in order to compete internationally. They should also be encouraged to explore more common ground for collaborative synergies. This will be aided greatly by the re-structuring locally to create the exciting Federation initiative. In general, the projects are cutting-edge and innovative. The next four years will be a challenging time for the unit in terms of applying the technological expertise they have developed, recruiting new groups to generate additional dynamism and building innovative interdisciplinary opportunities in the fields of cell proliferation and cell cycle control.

4 • Appreciation team by team

Team : CELL CYCLE CONTROL

Project leader: M. Bernard DUCOMMUN

- Staff members

N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	4
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	3
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	3
N7: Number of staff members with a HDR or a similar grade	2

- Appreciation on the results

The Cell Cycle Control group has worked for many years on the CDC25 phosphatase family that play key roles in the progression from S phase to mitosis. Their work has mainly focused on three aspects : (i) regulation of the CDC25B protein - by studying splice variants, post-translational phosphorylation using mass-spectrometry and the kinases involved in its regulation: (ii) function of the CDC2B protein - by studying its intracellular localization, its links with the PLK1 and Aurora-A kinases, and its role at the centrosomes during mitosis and in the DNA damage response: and (iii) attempts to develop inhibitors to target CDC25 phosphatases and their regulators. Given the importance of this phosphatase in cancer, the group leader has develop several successful collaborations with academic or industrial groups to study the activity of potential drugs targeting CDC25B in a therapeutic context. These include strong collaborations with IPSEN, GSK and Pierre Fabre.

The Cell Cycle Control group is considered an important research laboratory in the field of cell cycle research in France. The group leader is well known, both nationally and internationally (as evidenced by invitation to meetings and participation in committees). His work on CDC25B is original, competitive and internationally recognized, as illustrated by a recent review in Nat Rev Cancer on this topic. The group has published 39 publications over the past four years, 25 of which represent work done directly in this laboratory. Many of these publications appear in high quality journals in the field, such as Oncogene or Cancer Research. The group has also submitted two international patent applications. Over the evaluation period, five PhD students defended their theses and eight post-docs worked in the laboratory. Several of these came from abroad, demonstrating the international visibility of the group. Notably, many of the past members of the lab were subsequently recruited to permanent positions in France and abroad.

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

The importance of work performed in the Cell Cycle Control group is demonstrated by invitation to many international meetings and the ability to attract funding and staff from across Europe. The group leader has participated in international workshops on cancer and organised the Cell Cycle and Cancer meeting in Toulouse in 2008, which attracted 400 participants from around the globe. He is also president of the Société de Biologie Cellulaire de France (SBCF) and partipates actively in regional and national scientific committees (LLNCC, INCa, Pôle de Compétitivité, etc).

Eight post-docs have been trained in the laboratory. Several of these came from abroad and have returned to positions in Canada, Spain and Australia. One of these was also successfully recruited by the CNRS and three others are still present in the lab.

The Cell Cycle Control group has an impressive track-record of funding and grants, mostly from national cancer sources and industrial partnerships. Notably, the team is an 'Equipe labellisée' of La Ligue Nationale Contre le Cancer. Projects in the lab also received funding from INCa and from Innabiosanté which corresponds to a very competitive call.

Some projects in the Cell Cycle Control group are directly linked to the discovery of anti-cancer drugs, in particular those developped with IPSEN Beaufour. Some of these products are currently being tested in a clinical context. This group has two international patent applications and is actively involved in translational research relevant to industry. Furthermore, the group participates actively in the ONCO-SP-IM project by developing cancer models for imaging and drug discovery.

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

The team leader has demonstated a commitment to fostering young talent and catalysing innovative technological development in the form of an imaging platform. He is a professor at the Toulouse Medical School and actively participates in teaching.

- Appreciation on the project

Just before the site visit, the committee was informed that group will leave the LBCMCP and will therefore not participate in the the future activities of UMR5088. They will continue to collaborate with colleagues in the unit. The future projects of this group are not therefore evaluated.

- Conclusion :

  – Summary

This team is well established in the field of cell cycle research and has produced many interesting and innovative results on the biology of CDC25B phosphatase. The past projects in the laboratory were extremely well funded and innovative and have generated strong ties with industrial partners. This team has attracted many talented young researchers and the research output of the team in terms of publications and patents has been prolific.

  – Recommendations:

As the group will be leaving the UMR5088 and will not participate in the future plans, the committee makes no formal recommendations concerning their projects. The committee hopes that this team will continue to maintain collaborative contact with the unit in order to maximize transfer of skills and expertise to remaining groups.

Team: CHROMATIN AND CELL PROLIFERATION

Project leader: M. Didier TROUCHE

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	1	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	6	5
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	2
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	4	3
N7: Number of staff members with a HDR or a similar grade	3	4

- Appreciation on the results

The Chromatin and Cell Proliferation group studies cell proliferative events with respect to chromatin and chromatin modifying enzymes. The research is focused on two aspects: (i) chromatin modifying enzymes in proliferation programs, and (ii) chormatin modifications in DNA repair and double-strand break (DSB) signalling. The former is a long-standing interest of the group leader and the latter is a newer research direction. The cell proliferation studies are focused on the E2F-regulated program and the function of the Tip60 histone acetyl-transferase complex, areas in which they have published extensively in recent years. The DNA repair studies integrate Tip60 expertise and chromatin around DSB sites.

The work of this team is of a high quality and the group leader has a strong reputation in this field; he is a national leader in the chromatin field with established international credentials. The committee was impressed by the leadership skills and charisma of the group leader and repeatedly heard favourable reports from students and staff in his group. The group is extremely dynamic attracting post-docs and established scientists and nurturing young researchers towards independence. Over the evaluation period, two PhD students defended their thesis and three post-docs were successful in obtaining CNRS/Inserm positions. The group published 14 papers over the past four years in good quality journals (such as Oncogene, EMBO Journal, Molecular Cell and Mol. Cell. Biol.) as primary and senior authors. Researchers joining the group have similarly good track records. The committee felt that the team could do even better in terms of top-impact publications and urges the team to set higher publishing ambitions for the unit. The group is very well supported by national cancer funding (significant grants from INCa, ANR, LLNCC) and has establised a large number of productive collaborations at the national and international level.

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

Members of the Chromatin and Cell Proliferation group participate actively in regional and national committees and are invited to international meetings (e.g. Plenary lecture at the Young Scientist Forum, FEBS meeting). The attractiveness of the group is largely related to the charisma of the group leader and his ability to create a stimulating environment for training and nurturing young talent. Post-docs who joined the group have often subsequently obtained permanent positions and the group leader has managed to allow them to become independent, either within the group or outside. He has also attracted a number of permanent researchers and scientists returning from abroad.

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

The group leader clearly feels that nurturing young ones is one of his missions and he has attracted and promoted young researchers, providing them with an environment in which they can explore their potential to emerge as independent group leaders. The management style is informal, yet professional; friendly and supportive, yet challenging and critical. This was clearly appreciated by students and research staff alike.

Although several group members are involved in teaching, it remains somewhat limited. The committee urges researchers in the group to become more involved in teaching in order to enhance integration into university life on campus and to attract good students.

- Appreciation on the project

Over the next years the group plans to develop several projects related to cell proliferation and DNA repair. The projects are diverse but integrate well with each other and share technological approaches. More specifically:

One exciting project aims at elucidating the function of the JMJD2A lysine demethylase and its role in removing the H3K9me repressive mark on E2F-regulated promoters. The group has identified a short isoform of JMJD2A which is induced during muscle differentiation. They will also explore post-translational modifications and substrate specificity of the JMJD2A demethylase. This project is innovative and builds on past expertise.

The group has a long-standing interest in the Tip60-p400 complex. They are performing genome-wide studies of the Tip60 and p400 functions looking at transcriptional regulation and roles in the DNA damage response. Experiments with knockout mice and cell lines will explore their roles in tumorigenesis and cell fate decisions.

Another line of research is investigating the role of the Tip60 complex and other chromatin modifyers in DNA DSB repair. This project will be in collaboration with the Chromatin and DNA Repair group and will incorporate biochemistry, cellular assays and genome-wide technologies.

A recently-recruited young scientist will develop another project on the role of widespread antisense transcription. The aim is to explore antisense transcription in mammalian cells. It will be important quite quickly to define a clear experimental strategy for this project and how it integrates with other interests of the unit (such as antisense transcritional regulation during senescence).

- Conclusion :

  – Summary

This is a strong established team which has a proven track-record of scientific productivity combined with nurturing young research talent. It is a leading lab in the field of chromatin modification during cellular proliferation.

  – Strengths and opportunities

The group combines genome-wide technologies with a strong background in cellular biology and chromatin. The emergence of new teams will open up additional opportunities for collaborative synergies. The group leader has created a stimulating environment for intellectual growth.

  – Weaknesses and threats

The team will have to ensure that it remains focused on its key expertise areas and leverages these to access high-impact journals. The sheer mass of genome-wide data will require an in-house expertise in bio-informatics.

  – Recommendations

The committee encourages the team to recruit qualified bio-informatics personnel and integrate them into the genomics projects.

The committee recommends that attention be paid to the development of new projects and overlap with those of emerging groups. Maintaining focus and key core competences should enable the group to have higher publication ambitions.

Team: SPATIO-TEMPORAL CONTROL OF CELL DIVISION

Project leader: Mme Sylvie TOURNIER

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	1
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	2	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	1	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	1	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	3	3
N7: Number of staff members with a HDR or a similar grade	2	3

- Appreciation on the results

The Spatio-temporal Control of Cell Division group studies chromosome dynamics using a powerful combination of yeast genetics, video-microscopy imaging techniques and mathematical modelling. The group has focused their efforts on the study the spatio-temporal control of cell division in S. pombe. They investigate proteins involved in the control of chromosome segregation, attachment of chromosomes to the microtubules (MT) and mitotic spindle positioning during cytokinesis. They have made a major contribution by uncovering mechanisms that control spindle postioning and kinetochore capture and chromosome attachment. These mechanisms underlie the formation of aneuploid cells seen in cancer and genetic diseases. Since 2005, this team has been led by a dynamic CR1–CNRS who was joined by another CR1-CNRS at the end of 2006. Altogether, the group now comprises two CR1, three Ph.D. students and two post-docs. The productivity of this small group during the reviewed period has been excellent, with 8 articles (first and last authorship) published in high profile journals such as J. Cell Biol., Mol. Biol. Cell, Dev. Cell, and J. Cell Sci. The research activity of this group has a clear interdisciplinary and technology-driven nature which was much commended by the committee.

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

This group is undoubtedly attractive as it combines an interdisciplinary approach and cutting-edge technology to address fundamental questions regarding chromosome dynamics during cell division. An optical physicist and a technical assistant have recently joined the group. The group has already established collaborations with national and international laboratories in their field. The committee felt that the technological skills that the lab has developed offer a strong basis for extending collaboration and funding. In the future, they should be encouraged to continue their efforts to develop new national and international collaborations. The group was initially supported by a CNRS ATIP and also has national cancer funding (ARC, LLNC); they should also be encouraged to seek international funding. Unfortunately, several attempts to recruit candidates through CNRS/Inserm concours for permanent positions have not yet been successful.

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

This team has developed an ambitious program requiring the development of major interdisciplinary and innovative techniques. They have created user-friendly microscopy platforms on which they can acquire 3D time lapse data, as well as carrying out FRAP and laser ablation. These tools have given them a valuable edge in their research.

For such a small group, co-leadership does not seem justified, although PhD students acknowledged the contribution of both group leaders to directing their projects. Both team leaders have teaching duties at M2R Biologie-Santé-Biotechnologies de Toulouse. One of the co-leaders is also a member of the CoNRS.

- Appreciation on the project

Over the next years the group plans to focus on the mechanism and regulation of kinetochore/MTs capture. More specifically:

They will investigate the role of key mitotic players such as EB1, Prc1, Dis1/Alp6 and the spindle checkpoint components. They will examine the role of the actin cytoskeleton in the efficiency of kinetochore capture. They plan to test the possibility that the MTs required for kinetochore recapture are in fact bundles of MTs. To address this point they will perform electron tomography in collaboration with international groups at the EMBL, Heidelberg.

Another objective is to develop mathematical modelling of mitosis. Mathematical and computational models which integrate experimental results will help the team to identify which mechanisms are important to control chromosome movement. To achieve this project, the team hope to recruit a physicist who is already integrated into the laboratory.

They will study the mechanisms controlling the anisotropy of MT formation during kinetochore capture.

The modelling project is very exciting and the first results are extremely promising. In general, the projects are focused on highly relevant questions and the team has the required know-how and tools to succeed and to compete internationally. The group is widely recognised and well integrated into the S. pombe research community.

- Conclusion :

– Summary

The results obtained by this small team have already demonstrated an impressive capacity to integrate experimental biology with mathematical modelling. These achievements are excellent and the proposed projects are particularly promising.

– Strengths and opportunities

The objectives set by the team are ambitious, yet realistic, given the track-record of the team leadership and the context of the unit to which they belong. Their strategy of technology innovation gives them a leading edge that they should continue to exploit in the future as they have done effectively over the last few years.

– Weaknesses and threats

The only issue of concern could be the relatively small size of the team that might not yet have reached the necessary critical mass.

– Recommendations:

To achieve their full potential, the committee recommends that the team be encouraged to grow and to request stronger support from the Université Paul Sabatier in terms of the recruitment of permanent staff members.

Identifying common research interests with other laboratories in the UMR and at the University might help strengthen internal and local links. The committee encourages the team to seek more collaborative opportunities to exploit the technological innovation that they have developed.

Team : EPIGENETIC FUNCTION OF POLYCOMB AND MML IN CELLULAR MEMORY AND CELL CYCLE

Project leader: M. Malek DJABALI

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	1	3
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	0
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	1	2
N7: Number of staff members with a HDR or a similar grade	1	2

- Appreciation on the results

This group studies the regulation of key cell cycle events (such as senescence and replication) focusing on chromatin modifying machineries. These issues are important for understanding development and pathologies such as cancer. Previous research work by the group leader has contributed to the current understanding of the role of Polycomb in the regulation of gene expression during development in mammalian cells. The group strength lies in studying polycomb mutant mice. Their scientific approach has been straight-forward and the results solid. This is undoubtedly a very competitive field, in which they have been only modestly productive; 4 publications in the last 4 years, and in some publications (e.g. Cell) his contribution seems to have been minor. They have, however, been able to build strong collaborations with leaders in the field, which allowed him to contribute to high-impact work.

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

The team is led by an experienced group leader who is working on important questions in a very competitive field. Even though the team was able to secure reasonable funding over the past 4 years (INCa-Daad, ARC, FdF), the impact of the work done by this group has been modest. Previous members of the lab were successful in finding permanent positions and the two previous PhD students are currently doing post-docs abroad. The group has not been able to attract sufficient numbers of high level scientists, post-docs and and students. Clearly this is an area that needs developing. However, the investigator has built strong links with international and national partners, which have created potential to significantly improve the profile and attractiveness of the team. The group leader recently moved to Toulouse to join the LBCMCP and this will undoubtedly contribute to the enhancing attractiveness of the team. One of the priorities should be to work on local integration.

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

The committee felt that the group research projects are somewhat fragmented and encouraged to prioritise and to find a research niche in this very competitive field, in order potentially to develop into a leader in the field. To become competitive the team will need to grow considerably and keep a tight research focus. While international collaborations are a strength of the team, the group leader should be encouraged to develop stronger projects that are mainly driven by work done in his own laboratory to ensure that he is the main contributor. His expertise in the characterisation of animal mouse models should contribute to research projects at the local level.

- Appreciation on the project

The group works on the understanding of the epigenetic function of Polycomb and MLL in cellular memory and cell cycle. Based on the current size of the team, the committee felt that the proposed projects are too ambitious and lack a clear overall direction. The inability to prioritise is evident from both the written description and oral presentation by the group leader. However, the group is addressing important questions and brings new expertise to the unit. It is therefore imperative to focus on projects with the most potential to create original research results to compete in the future. More specifically:

Involvement of Polycomb repressive complexes in Ink4a/Arf repression during senescence: This is a follow-up to research carried out by the group leader in recent years. However, several of the observations made by this team have been published in recent high-profile papers by other groups, so it is questionable whether they will be able to develop a competitive edge with this project.

Role of the regulatory domain RD-INK4a/Arf element in the expression of the INKa/Arf locus during development: The coupling of DNA replication and Polycomb silencing is an exciting line of research. The initial observation of this regulation, was published in a high-profile paper by a group now collaborating with the team. With the RD knock-out mouse already in the pipe-line and the strong collaboration with one of the leaders in the field, the team is well positioned to turn this into a very successful project.

Cellular senescence as a cell-intrinsic tumor suppression mechanism: This project proposed to investigate senescence as an efficient brake on tumor progression. As there was no discussion of this project in the oral presentation, we conclude that this study should and will not have priority.

The group leader is highly qualified to carry out the work proposed in Project 2 and the team is well positioned to be competitive in this field. Additional experiments to characterize the role of Cyp33 and MLL inhibition at the INK4a/Arf locus could be integrated and developed into a feasible, cutting-edge project. Based on the small size of the team, the majority of their efforts should go into this project with little or no priority given to the other two.

- Conclusion :

  – Summary

This group is led by an experienced researcher and works on important biological questions. However, the lack of focus in the past has prevented the team from making significant contributions to this competitive field. Now, the group leader has built strong links with international and national partners, and they are well-positioned to become competitive on some of the research proposed.

  – Strengths and opportunities

The group leader brings expertise in animal models to address important biological questions at the molecuar level. He has developed strong international collaborations which should enable him to find a competitive niche.

  – Weaknesses and threats

The lack of focus in the past may have diluted the impact of the work of the team. It will be important to focus on one clear line of research in which the team can be competitive in the future.

  – Recommendations

The committee recommends that the team be encouraged to grow by the recruitment of students and perhaps permanent staff in order to achieve the critical mass necessary.

The committee urges the team to adopt a tight research focus, concentrating on Project 2, that will could allow them to develop a competitive niche.

Team: CHROMATIN AND DNA REPAIR

Project leader: Mme Gaelle LEGUBE

- Staff members (on the basis of the application file submitted to the AERES)

	Past	Future
N1: Number of researchers with teaching duties (Form 2.1 of the application file)	0	0
N2: Number of full time researchers from research organizations (Form 2.3 of the application file)	0	2
N3: Number of other researchers including postdoctoral fellows (Form 2.2 and 2.4 of the application file)	0	1
N4: Number of engineers, technicians and administrative staff with a tenured position (Form 2.5 of the application file)	0	1
N5: Number of other engineers, technicians and administrative staff (Form 2.6 of the application file)	0	0
N6: Number of Ph.D. students (Form 2.7 of the application file)	0	2
N7: Number of staff members with a HDR or a similar grade	0	2

- Appreciation on the results

The Chromatin and DNA Repair group is an emerging team that proposes to study the relationships between chromatin modifications and double-strand break signalling and repair. Over the past 4 years, the group leader has produced high-quality results published in very good international journals (Genes Dev., EMBO Journal, Mol. Cell) as first or last author. Moreover, she recently established a powerful and original system to induce multiple double-strand breaks (DSBs) at defined loci in mammalian cells.

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

The group leader has a strong background in mammalian cell biology, DDR and genome-wide analysis. The team includes a PhD student and a first post-doc. The present scientific program is strong and innovative. Start-up funding is provided by a competitive and prestigious 'ANR Jeunes Chercheurs' grant. Key collaborations and transfer technology have already been established by this novel team which should rapidly attract students and post-docs at the national and international level.

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

This research team is newly created, so it is not relevant to comment on management of the team.

- Appreciation on the project

The group aims to study the chromatin landscape around DSBs, including changes in chromatin induced upon damage and the effects of chromatin environment on repair (choice of repair pathway, 3D organization and efficiency). They have developed an innovative system, in which multiple breaks are rapidly introduced at specific locations in the genome, allowing high-resolution genome-wide analysis. Based on this assay, the project will focus on four areas: (i) the characterisation of chromatin landscape around DSBs, (ii) the influence of chromatin organization on choice of repair pathway,(iii) the 3D-organization of DSBs, and (iv) the effects of chromatin organization on DNA repair efficiency. The project is quite ambitious, including cutting-edge approaches and raises conceptually interestingly biological questions that should open new avenues of research (especially the part concerning the chromatin landscape around DSBs that may reveal new players and histone marks involved in DSBs signalling and repair). However, the system has some potential caveats: for example, chromatin organization may affect cutting efficiency and thus DSBs signalling. Also, it is not clear what will be the read-out for repair efficiency, as the system is not reversible and breaks will undergo continuous repair-cut cycles. Finally, to get an initial assessment of whether chromatin organization contributes to differences in repair efficiency between cell types and during aging, it could be an advantage to use ES cells or differentiation models rather than Drosophila or mice model organisms. Collaborations instrumental for success of the project are already established and funding will likely be secured.

- Conclusion :

– Summary

This team appears as a very promising young group with potential for excellence, and the group leader has already produced exciting results. There is no doubt that combining the original system established to induce rare DSBs with genome-wide analysis has great potential to bring novel insights into mechanisms of DSB signalling and repair in the context of the chromatin.

– Strengths and opportunities

The approaches are innovative and the group leader has an excellent background and the necessary skills to supervise the project. Project 1 (chromatin lanscape around DSBs) is particularly promising with possibility of high impact and opening new biological questions to follow in the future.

– Weaknesses and threats

This is an ambitious project with many different and complex techniques/models. The size of the group may be below the critical mass necessary for high productivity.

– Recommendations

This is an exciting project in a competitive research area. The committee recommends that the group prioritize the various sub-projects in order to define milestones and a rational progress plan for the different aspects of the project to be achieved in 4 years.

The committee encourages the group to grow by recruiting a post-doc and a student as proposed. The committee also agrees about the necessity to recruit bioinformatics expertise in the near future.

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

Team: CHROMATIN AND CELL PROLIFERATION

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

Team: SPATIO-TEMPORAL CONTROL OF CELL DIVISION

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

Team: EPIGENETIC FUNCTION OF POLYCOMB AND MML IN CELLULAR MEMORY AND CELL CYCLE

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

Team: CHROMATIN AND DNA REPAIR

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

Université Paul Sabatier
TOULOUSE III

Direction de la Recherche

Toulouse, le 20 avril 2010

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Le Président

au

Président du comité d'experts de l'AERES

Objet : Observations de portée générale sur le rapport d'évaluation de l'unité
« Laboratoire de Biologie Cellulaire et Moléculaire du Contrôle de la Prolifération » - UMR 5088 CNRS/UPS
portée par **Didier Trouche**

We would like to thank the AERES committee for their excellent work. We are pleased to note that the committee praized the projects of the unit as a whole and of the four groups individually. All comments, either during the visit or in the written report, are very constructive, and the written report is a very good basis for driving future developments of the unit. In particular, we will strengthen our links with the University through the allocation of professor or assistant professor positions. The committee points to a number of weaknesses and threats and made some recommendations concerning the life of the unit. The future director largely agrees with the committee's comments and will do his best to cope adequately with the various recommendations.

Since the visit, we were able to obtain new information about two main concerns of the committee :

1) Quality of the premises : It was recently announced that the construction of a new building has been funded by the so called « Plan Campus ». This building will house the Center of Integrative Biology (CIB), a new institute that will bring together three laboratories housed in the current building (destined for destruction). The construction of the CIB should be achieved between 2014 and 2018, and will solve the committee's concerns about the state of our current building.

2) The issue of personnel for technological platforms: Obviously, this is a critical point since efficient technological platforms are required to allow groups to perform innovative research and to envision high impact publications. Since the aéres visit, we secured the development of the two platforms : Indeed, the CNRS has opened a position of Research Engineer for the cellular imaging platform and selection of candidates is sheduled July 2010. For the Bioinformatics platform, we have already recruited a bioinformatician on a two year contract (from a caritative agency) ; during these two years, we will carry out major efforts to obtain a permanent position on this topic.

The AERES committee also raised some points about the team « epigenetic function of polycomb and MLL in cellular memory and cell cycle » and its contribution to this research domain. First, it has to be noted that the group leader had stopped recruiting people more than two years ago, in order to be able to move to Toulouse. This had obviously some impact on the levels of achievements. Moreover, despite the strong competition in the field, this group recently demonstrated that members of the replication complex were interacting with the polycomb complex to maintain the Ink4a locus in a late replicating state. This function of polycomb in regulating DNA replication was never described by other groups. The projects of this team were very well evaluated by the committee and we agree that focusing on the two main projects will be an improvment. Moreover, the installation of the group leader has been very successful, since in six months time he has secured a technician position from the CNRS and he has attracted an experienced researcher as well as a post-doctoral scientist. Finally, its local integration is excellent (with some collaborative projects being set up with other groups of the unit). Therefore, we feel, in agreement with the committee's recommendations, that this group undoubtedly deserves to be strongly supported.

Finally, we would like to stress that the future director and all group leaders are particularly committed to publishing in high impact factor journals. We will of course consider all recommendations from the committee to reach this goal (increasing groups size, developping efficient technological platforms, mentoring,…). We also would like to point out that since the AERES visit, the « Chromatin and Cell proliferation » group had a manuscript accepted in a high profile journal.

Gilles FOURTANIER

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Toulouse, le 10 Avril 2010

Objet : Observations de portée générale sur le rapport d'évaluation
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Porteur du projet LBCMCP 2011-2014