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

Research Units Department

AERES report on unit:

Ingénierie Moléculaire & Physiopathologie Articulaire

IMOPA

Under the supervision of the following institutions and research bodies:

Université de Lorraine

CNRS

March 2012

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

Research Units Department

President of AERES

Didier Houssin

Research Units Department

Department Head

Pierre Glaudes

Unit

Name of unit:	**I**ngénierie **Mo**léculaire et **P**hysiopathologie **A**rticulaire
Acronym of unit:	**IMoPA**
Label requested:	UMR
Present no.:	UMR 7561 & UMR 7214
Name of Director (2009-2012):	Mr Jacques MAGDALOU & Ms Christiane BRANLANT
Name of project leader (2013-2017):	Mr Jean-Yves JOUZEAU

Members of the committee of experts

Chair:	Mr Philippe ORCEL, Paris
	Ms Catherine ROYER, Montpellier
Experts:	Ms Magali CUCCHIARINI-MADRY, Homburg, Germany
	Mr Denis LAFONTAINE, Brussels, Belgium
	Ms Claudine MAYER, Paris (CNU representative)
	Mr Antoni PLANAS, Barcelona, Spain
	Mr Francois RANNOU, Paris
	Ms Heidy SCHMID-ANTOMARCHI, Nice (CNRS representative)

Representatives present during the visit

Scientific Delegates representing AERES:

Mr Jacques BARATTI

Mr Bernard DASTUGUE

Representative(s) of the unit's supervising institutions and bodies:

Mr Jean-Claude MICHALSKI, CNRS (INSB)

Mr Pierre MUTZENHARDT, Université de Lorraine

Ms Florence NOBLE, CNRS (INSB)

Mr Pascal SOMMER, CNRS (INSIS)

Report

1 • Introduction

Date and conduct of visit: March 2012

The visit took place on March 15, 2012. An international team of 8 scientists, with expertise in the research areas of the 5 teams of the IMoPA, conducted it. The visit started with a closed-door meeting of one hour of the committee. This was followed by a presentation of the activity of the two UMR over the past period, UMR 7214 and UMR 7561. Next the five teams of the proposed unit presented their projects and answered questions from committee members (lunch was served between the presentations by teams 2 and 3). The committee next met with the supervising institutions and bodies (CNRS and Université de Lorraine, UdL). The committee questioned the CNRS and UdL representatives about the place given to the laboratory in their respective scientific policy as well as its importance in the regional and national context. Three committee subgroups then met concurrently with students and postdocs, technical staff, and research staff in absence of the team leaders. Finally, the committee met with new management team during a closed-door meeting. The next morning the committee gathered for the final deliberation and the preparation of the present report.

History and geographical location of the unit, and overall description of its field and activities:

Historically, C. BRANLANT, specialist in the field of RNA biology, and her husband, specialist in enzymology, had created the UMR 7214. By their successive managements of UMR and IFR ("Institut Fédératif de Recherche"), they contributed significantly to the improvement of the knowhow in these fields in Nancy. The strong specialization of the research they developed – chemistry of enzyme reactions based on the knowledge of enzyme 3D- structure determination, and determination of RNA structures and structure-function relationships – is rather unique in France and in Europe and widely acknowledged as such. The UMR 7561 developed an original research program aiming at better understanding the biology, structure and function of joint tissues (cartilage, synovial membrane, tendons) in injured or diseased conditions. The research is based on a multidisciplinary approach of bioengineering (CNRS Institutes INSIS & INSB), bolstered by expertise in biochemistry, chemistry, cell and molecular biology, and use of animal models.

Through their participation since 2009 to IFR111 (Federative Research Institute) and then to FR3209 (Research Federation) and through a common Bioengineering program in the framework of the government-region plan contract, the two previous research units had participated for some time in the establishment of common technological platforms and initiated shared brain-storming meetings aimed at defining how research in the field of biology and health should be organized in Nancy in order to increase its international visibility and recognition. The managers of the UMR 7214 and 7561 had considered for some time that they should join their complementary strengths in molecular and structural biology (UMR 7214) and cellular and more integrated analysis (UMR 7561) and they successfully combined their energy to obtain a common new building, the Biopôle, in order to create a high-level new research center. This new institute in which the two UMRs are now settled also includes all the high-level technical platforms of FR 3209. It will play a key role in the local organization of the research in the field of health and biology in the context of the national program call "plan campus". Therefore, the fusion between UMRs 7214 and 7561 into a unique research unit IMoPA (Molecular Engineering and Articular Pathophysiology) results from a long-term common wish to join complementary expertise in the same geographical location. This location is also going to facilitate collaborations within the FR3209. In this new building, the future IMoPA research unit will home all the technical platforms that are coordinated by the FR3209, some of them functioning as core facilities of the university.

Management team:

Mr Jean-Yves JOUZEAU will be the director of the new IMoPA unit. Mr Bruno CHARPENTIER will act as deputy director. The IMoPA is constituted of 5 distinct research teams, each having one to three leaders, according to the subgroups in each team. The IMoPA teams directly derive from the teams of the former units with only one major change in team 3, which will be headed by a high profile scientist recruited in 2010 and integrated very efficiently into the unit. Thus, the global management structure of the IMoPA appears quite conservative but will undoubtedly lead to a new management style. This is expected from many of the researchers, students and technicians, as pointed out very strongly during the discussions with the committee members.

Unit workforce:

Workforce	**Number** on 06/30/2011[Φ]	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	11 + 17	27	27
N2: EPST or EPIC researchers	6 + 9	14	11
N3: Other professors and researchers	Teach : 0 + 1 Resear : 0 + 1	Teach : 3 Resear : 4	3
N4: Engineers, technicians and administrative staff *on a permanent position	13 + 18[§]	33[§§]	
N5: Engineers, technicians and administrative staff * on a non-permanent position	4 + 2		
N6: Postdoctoral students having spent at least 12 months in the unit	4 + 4		
N7: Doctoral students	17 + 13		
N8: PhD defended	11 + 19		
N9: Number of Habilitations to Direct Research (HDR) defended	3 + 1		
N10: People habilitated to direct research or similar	10 + 13	21[¶]	
TOTAL N1 to N7	**54 + 65**[§]	**81**[§§]	**41**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.
Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

[§]: including 7 “shared services” personnel (“Services communs”)

[§§]: including 9 “shared services” personnel (“Services communs”)

[¶]: including 1 PREM and 1 PUPHEM (“Professor Emeritus”)

2 • Assessment of the unit

Overall opinion on the unit:

The overall proposed unit would result from a fusion of two well-established CNRS UMRs, namely UMR 7214 (AREMS, Ms C. BRANLANT) and UMR 7561 (PPIA, Mr J. MAGDALOU), into a new UMR entitled IMoPA "Ingénierie Moléculaire et Physiopathologie Articulaire" (Mr J.-Y. JOUZEAU, Mr B. CHARPENTIER). The scientific production from the two separate units has been very strong, although quite heterogeneous between the two UMRs (47 publications in peer-reviewed international journals for UMR 7214 *vs.* 155 for UMR 7561) and among teams within UMR 7561 (100 for the team working on bioengineering). The two laboratories attract a large number of PhD students (30 during the current term), but fewer postdoctoral associates (8 in the same period). The research training effort is important (30 PhD theses defended during the period) but this capacity could be even reinforced by increasing the number of researchers habilitated to direct research (currently 22; only 4 HDR defended durign the previous term for both UMRs). The unit has obtained a significant level of financial support via national granting agencies (with a focus on the ANR, ANRS, and PHRC) and European funding (including the creation of two virtual LEA European laboratories).

Strengths and opportunities:

The committee recognized the strong science in all teams, the importance of the very good platform facilities and of the new building, the convergence between certain teams and nascent collaborations that should lead to new, unique programs and knowledge.

The fusion of the two units into one should homogenize and normalize the managerial aspects among the teams and favour career building and recognition of the young scientists and of the technical staff in the unit.

The new direction team has the potential to conduct a harmonious fusion but this will require the full support and input from all members of the units, in particular from the more experienced ones. The existence of a steering committee will be important. In addition, ongoing discussions and the creation of a laboratory council will bring all unit members, including students, postdocs and technical staff on board in the project.

Weaknesses and risks:

Despite the overall strengths of the project, some of the teams do not have the critical mass (team 2 and to a lesser extent teams 3 and 4) or the international attractiveness (team 3 and to a lesser extent team 4) required to be competitive at the international level. This could jeopardize access to funds and recruitment of researchers and students. Moreover, the polyketone synthetic biology project, while very strong and innovative scientifically, is not particularly linked to the other projects of the unit. This is not necessarily a weakness, but could become one.

The committee was also concerned about the translational aspects of the project, in particular the small number of MDs working with the unit.

Recommendations:

Develop translational research programs; attract more MDs as PhD students or postdocs.

Increase the mentoring force for young researchers and students by stimulating young senior researchers and teaching resaerchers to become "habilitated to direct research" (HDR).

Stimulate interactions between the teams in order to evolve toward more integrated programs between the five teams, especially between those coming from the two previous UMRs or from outside. Encourage the teams to make applications for grants on common projects.

3 • Detailed assessments

Assessment of scientific quality and production:

The scientific contributions of the five teams of the two UMRs are quite distinct. The two teams of the UMR 7214 develop basic research in the fields of RNA biology and enzymology. This research is of very important biological relevance and the quality of the research is nationally and internationally acknowledged. The three teams of UMR 7561 have a long-term expertise in pharmacology, pathophysiology, and engineering of the cartilage, from the molecular to the tissue level. These teams have developed important translational research in the fields of proteoglycan synthesis, pathophysiological analysis of joint diseases, tissue engineering of cartilage and blood vessels.

The unit overall has a strong level of research productivity, although the committee notes a certain heterogeneity among the different teams. The large majority of faculty and research staff published multiple papers in the last period. The majority of their publications have appeared in well-respected international journals, albeit specialty publications for the most part. The trends in the bibliometry of the unit are difficult to assess, given the broad based scientific activities of the different teams, from the molecular to the clinic. Overall the quantity and quality of the publications is very good, with a total of 202 publications over the period of assessment, and 105 in the last 3 years.

Whatever the level of publication, the scientific quality and competence of all of the teams is strong. Individually the teams are all strong and some convergence is occurring between teams, but the enzymology group despite its high quality, appears to be a stand-alone group. For the unit's coherence, it will be important to establish collaborations between this team and the others. In a nutshell : within IMoPA, the former UMR 7214 will bring strong molecular and cellular biology to the former UMR 7561, and reciprocally, the former UMR7561 will bring access to whole animal models to the former UMR 7214.

In conclusion, by designing of IMoPA the 5 teams have created an "interface" with the stated purpose of interacting with each other, developing novel, cutting-edge and *trans*-disciplinary research (chemistry, molecular medecine, molecular and cellular biology, bioengineering etc). This common project was initiated several years ago informally. For example, with the identification of microRNAs involved in chondrogenesis. The teams have clearly stated to the committee experts that they do not intend to weaken their internationally recognized scientificic identity. Rather, they have explained that they are willing to acquire, in addition, a novel 'shared identity'. We believe that this is a good approach to the fusion into IMoPA. To be succesful, IMoPA now needs to nourish and further develop and extend this "novel scientific interface".

Assessment of the unit's integration into its environment:

The unit has been well-funded, receiving nearly 1.5 M€ per year in recent years. The funds have been obtained from four different sources: Université de Lorraine and CNRS (approx. 13-15% each); grants obtained as three- or four-year applications from national program calls supported by the government, such as ANR (National Research Agency) or ANRS (National Research Agency on AIDS) (approx. 27%); funds obtained as application grants from international program calls (approx. 10%); funds raised through national program calls supported by charitable foundations (AFM: French Association against Myopathy, Sidaction: research foundation against AIDS, FRM: Foundation for Medical Research, ARC: Association for Research against Cancer, Courtin Arthritis Foundation). Additional funds were obtained at a regional level (Bonus Quality – Research [BQR] in the context of a partnership between University and "Région Lorraine", Clinical Research Project Contracts [CPRC] with Nancy University Hospital) or at inter-regional level (League against Cancer, Hospital Clinical Research Program [PHRC] with partners from other university hospitals). Funds were also obtained from scientific collaborations with private companies.

Thus, the global funding for high level scientific research activities is very good and the distribution between the different funding bodies is also very good. It is also important to emphasize the ability of the leaders of the UMRs and of each constitutive research team to secure recurrent funds, especially through a sustained effort in grant applications to national and international programs, the most prominent being the ANR.

The technology transfer in terms of patents should be improved.

Assessment of the research unit's reputation and drawing power:

The international reputation of both UMRs is very strong, as exemplified by the high level of international funding and by some international collaborations, such as the two "Laboratoires Européens Associés", or LEAs. One of them, LEA n°546 entitled "An integrated experimental approach to the structure of the spliceosome and regulation of alternative splicing" headed by C BRANLANT, originates from the UMR 7214 and is supported by UL, the CNRS, the

University of Montpellier and the Max Planck Institute at Gottingen, Germany. The other one, LEA SFGEN for "SulFo and Glycosyltransferase Enzymes : tools and targets in bioengineering and medical sciences" headed by S FOURNEL-GIGLEUX, originates from the UMR 7561 and is supported by UL, the CNRS and the University of Dundee, UK. The UMR 7214 also contributes, through the coordination of one workpackage, to an European Network of excellence on alternative splicing of pre-mRNA which includes 35 teams. These partnerships include exchanges of students between partner universities. A partnership with Chinese teams also exists, with an agreement between the schools of medicine of Wuhan and Nancy. However, given the high level of research produced in these laboratories, international collaborations and attractivity could be stronger. There are few international postdoctoral associates for example, attracted to these groups. Moreover, invitations to international meetings and involvement in international societies and journals are limited.

Overall the quality of the recruitment is good as the unit has consistently recruited high-profile staff member.

Assessment of the unit's governance and life:

The fusion of two units into a single unit with five research teams is a very important turning point in the lives of these teams. The committee first focused its evaluation on the real integration of the two former UMRs into the common project for the future IMoPA unit. The new building in which the UMRs had moved in July 2011, the brand-new platform of equipment have stimulated a real fusion project and not just an opportunist rapprochement. Shared research projects have already started and others are planned, with increased interactions between teams and researchers. During the discussions, it clearly appeared that the creation of the new unit will definitely impulse a strong dynamic and will trigger new projects and stimulate scientific activity. In addition, the committee felt that the preparation of the onsite visit by the AERES has clearly participated to this dynamics. The elements required to develop a novel 'shared identity' are thus well in place both physically (new building "Biopôle") and scientifically (about half a dozen of new converging projects uniting the two former UMRs around single scientific questions).

The governance and scientific animation policy of the new unit has been the subject of several discussions among the team members these last months. The foreseen director for the new unit has a clear vision of the scientific and human evolution of the teams for the coming years. His strong involvement in teaching activities in the Université de Lorraine, including his former position as Director of one of the eight local Doctoral Schools, gives him a good legitimacy, which is well-recognized by the members of the unit. The choice to have a deputy director originating from the other constitutive UMR is well accepted, and even welcomed by the whole staff. The deputy director should play progressively an important role in managing human resources (especially for student and postdoc recruitment) and career development, as well as in the scientific animation (grant applications) of the IMoPA. The committee felt that the projected creation of a laboratory council (in accordance with national CNRS policy) is extremely important, and should be done immediately upon creation of the new unit.

Assessment of the strategy and 5-year project:

In the next period, the fusion of the two units into one proposes five teams which have complementary expertise and will be in a good position for developing a high quality multi-scale engineering and pathophysiology project, from genetic engineering to regenerative medicine, through structural biology, protein engineering, cell biology, and imaging. This strategy is very comprehensive and original, though it is not particularly risk-taking given the expertise and competence of the research staff. Also, the composition of the five new teams appears very conservative and close to a juxtaposition of the former teams coming from the previous UMRs: the committee encouraged strongly the team leaders to develop more interactions between the research fields in order to evolve towards a more integrated global project. To strengthen IMoPA, it would also be very useful in the future to recruit permanent staff with declared interest and renowned expertise in the science of the two former UMRs (RNA biology and regeneration medicine); i.e. to develop a strategy of communal recruitment. Currently, this has been done at the level of the equipment (core facilities), which is a good start, and on some novel and quite innovative projects, but full integration within IMoPA requires that novel teams (i.e. new PIs) to fully develop at the interface between the two former UMRs.

Teams 1 and 3 come from the former UMR 7214 and teams 2, 4 and 5 from the UMR 7561. Team 1 is recognized internationally for its work on RNA and RNP structure, function, and maturation and will develop 3 axes of research: ribosome and RNP biognenesis in archea and eucaryotes; transcribed non coding sequences; and development of new technologies applicable to RNAs and RNPs. Team 2 is involved in molecular pharmacology, structure and function of glycosyl transferase and aims at elucidating the structure/function and regulation of GT enzymes in order to understand the molecular mechanisms leading to altered GAG synthesis and assembly in pathophysiological conditions and to develop GAG-based therapeutic and bioengineering strategies. Team 3 has centred its work and project on

molecular and structural enzymology and the project, driven by a recently recruited PI, will continue previous lines of research but also initiate a new avenue of study, especially on polyketide synthases (PKSs), multienzyme systems which have important medical implications. Team 4 which focused its research on inflammation and cartilage will develop projects to study the phenotypic deregulation of joint cells that occurs during osteoarthritis by evaluating the contribution of adipokines in the onset and progression of OA and the role of PPi/Pi balance on the control of the chondrocyte phenotype and by developing translational research potential of new targets for anti-inflammatory strategies. Team 5 has a strong activity on 3 axes: cell and tissue engineering by using stem cells to create bio-tissues for use in joint or vascular engineering; vectorization for enabling drug delivery to its target using a biocompatible vehicle; multiscale imaging to monitor the development, biocompatibility and bio-integration of the resulting bio-tissues.

While the competence and objectives of each of the individual teams are strong and clearly stated, there was no clear strategy presented that would lead to convergence of these five separate teams.

Assessment of the unit's involvement in training:

Several members of the teams have a major involvement in the training of master and doctoral students, as well as in the academic training at the master (Life and Health Sciences) and PhD (Biology, Health & Environment) levels. There is a project to develop an international master with other universites of the "Grande Région". This training program will favor exchanges between research laboratories and offer opportunities to foreign students to come to Nancy. The new management of the IMoPA is expected to improve the visibility on the career development of young researchers and technical staff members. The attractivity for postdoc positions should be developed and the potential for coaching students and yound researchers improved by increasing the number of researchers habilitated to direct research (currently too low). A training policy is clearly stated in the project and the mainlines are shared between the governance of the unit and the researchers and technicians staff. Three member of the committee met the PhD students of the unit. All were funded, many were coming from abroad (french speaking northern african countries and China), all were fully satisfied by the organization and support they are receiving from 'Ecole doctorale'. All are followed by an efficient 'Comité d'accompagnement' and their progress is assessed on a regular basis.

4 • Team-by-team analysis

Team 1: RNA, RNP Structure-Function-Maturation

Team leader: Ms Christiane BRANLANT, Mr Bruno CHARPENTIER, and Mr Yuri MOTORIN

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	4	5□	5□
N2: EPST or EPIC researchers	5	4	2
N3: Other professors and researchers	0	0	0
N4: Engineers, technicians and administrative staff * on a permanent position	8 + [1 SC]	7 + [2 SC] + 1 recruitment & [1 SC] recruitment in 2012	
N5: Engineers, technicians and administrative staff * on a non-permanent position	2 + [2 SC]		
N6: Postdoctoral students having spent at least 12 months in the unit	4		
N7: Doctoral students	13		
N8: PhD defended	7		
N9: Number of Habilitations to Direct Research (HDR) defended	1		
N10: People habilitated to direct research or similar	5	4	
TOTAL N1 to N7	**36 + [3 SC]**	**16 + [2 SC] + 2 recruitments & [1 SC] recruitment in 2012**	**7□**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.
Definition and downloading of criteria:
http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

□ including 1 to be recruited in 2012, not yet identified.

SC: "shared services" personnel ("Services Communs").

• Detailed assessments

Assessment of scientific quality and production:

The work of team 1 is concerned with the function and structure of RNA, including ribosome synthesis, the regulation of alternative splicing in health and disease, RNA modification enzymes, and the role of transcribed non-coding RNAs. Team 1 forms a group specialized in the analysis of the structure-function relationships in RNA and ribonucleoprotein particles (RNPs). Team 1 has a strong international position and is recognized for highly relevant work in the field of RNA biology. This group has consistently addressed the most essential and fundamental aspects of gene expression and has consistently shown interest into biomedical and applied research. For example, they have recently contributed to the elucidation of a new mechanism of assembly of small nucleolar RNPs (snoRNP) and suggested that it is applicable to other classes of RNAs, and they have discovered that a cryptic splicing site in lamin A is implicated in the human disease progeria, characterized by premature aging (work published in J. Cell. Biol and Human Mol Genetics, respectively). Over the years, the work of team 1 has had a good impact on the RNA community.

In total, team 1 has produced 25 papers, 6 reviews and 2 book chapters. Considering the large size of the group (10 PIs, corresponding to 3 leaders plus 7 staff scientists and a large technical staff) the productivity in terms of publications, although of good quality, is lower than expected. While they publish in high quality and internationally respected journals in their fields, there had few very high level publications in more high profile general journals.

Assessment of the research team's integration into its environment:

The team has demonstrated its ability to secure outside funding for most of their research, both at the national and international levels, including the creation of a European virtual laboratory with the top scientists in the field of pre-mRNA splicing (MaxPlanck Institute). The team is also involved in a start-up called Splicos in collaboration with a group in Montpellier. In the context of the EURASNET, they have participated in the dissemination of their results to a large international audience. For many years, the team has been a driving force in the organisation of the scientific community in Nancy and has consistently implemented cutting-edge technologies directly relevant to molecular medicine and molecular biology. The team participates strongly in teaching at the university and is instrumental in the organization of the IFR and general structuring of the biohealth sciences in Nancy.

Assessment of the research team's reputation and drawing power:

The team has good qualification in terms of national and international recognition. The group leaders received several distinctions and were active as invited speakers to international meetings (EMBO conference, Wilhelm Bernhard Workshop) and also to multiple French conferences. Over the last 15 years, this team has consistently recruited young and very active high-profile permanent scientists whom despite their young age had already achieved some level of international recognition. The group attracts a large number of Ph.D. students, which also speaks in favour of the drawing power of their work, and also 4 postdoctoral associates. They have recruited during this period 1 junior faculty and 1 permanent research staff (CR1) to the team. However, their international drawing power is somewhat limited.

Assessment of the strategy and 5-year project:

Within IMoPA, the reorganization of the research into three main projects (Ribosome biogenesis and RNP assembly, Transcribed non-coding sequences, and Engineering of RNA and RNP), with one well-identified and well-qualified responsible PI for each project, should help to better focus their work and improve international competitiveness and scientific production. This is a very positive evolution. The existence, relevance and feasibility of the long-term project are apparent. The team has the manpower, the equipment, the expertise and the funding to carry out these projects. Some of the projects, such as the involvement of SMN in SRP maturation, are calculated risks, but well worth the effort and likely to succeed and lead to provocative contributions. Their participation in internal platforms, including the deep sequencing effort represents a long-standing commitment to improve local productivity.

Conclusions:

• *Overall opinion on the team:*

This team is highly active, carrying out relevant work, with a strong international position in modern molecular and cellular biology (gene expression). This is a truly solid group that has contributed and will continue to contribute significantly to the field of RNA biology.

• *Strengths and opportunities:*

The team has deep knowledge and competence in the field of RNA biology, including very precise technical expertise, in particular worldwide recognized expertise in the chemical and enzymatic mapping in solution of the secondary structure of RNAs. They are sought out for this. In line with this, they are currently developing new protocols for the engineering of artificial RNAs. They have consistently published in good impact factor journals in the field of RNA biology. Over the last 15 years, young researchers trained in this team have populated laboratories throughout the country, often developing their own vigorous independent research.

• *Weaknesses and risks:*

In the previous period the large number of projects has somehow dispersed their efforts and diminished their productivity. Some of the dispersion is linked to the necessity of obtaining research contracts to the level required to function as a team. It is important to note however that the dispersion is less than might be apparent, because important conclusions reached on one class of RNA molecules have classically been expanded on other classes owing to a certain level of communalities within the RNA world.

• *Recommendations:*

The team needs to really focus on completing and publishing their very good work in a timely fashion. The organisation and clarification of their work into 3 main subject areas should help in this effort. The high quality of their results merits more recognition and high level publication than is currently the case. In particular, the young members of the group, with very innovative and interesting projects need to gain better visibility. Now that much reorganisation and local structuring is behind them, they should be able to better concentrate their efforts.

Team 2: Molecular, Cellular, Therapeutic Engineering & Glycosyl Transferases (MolCelTeG)

Team leader: Ms Sylvie FOURNEL GIGLEUX et Mr Mohamed OUZZINE

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	2	2	2
N2: EPST or EPIC researchers	3	3	3
N3: Other professors and researchers	0	0	0
N4: Engineers, technicians and administrative staff * on a permanent position	3 + [1 SC]	2 + [1 SC]	
N5: Engineers, technicians and administrative staff * on a non-permanent position	2		
N6: Postdoctoral students having spent at least 12 months in the unit	3		
N7: Doctoral students	2		
N8: PhD defended	3		
N9: Number of Habilitations to Direct Research (HDR) defended	0		
N10: People habilitated to direct research or similar	3	3	
TOTAL N1 to N7	**15 + [1 SC]**	**7 + [1 SC]**	**5**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

SC: "shared services" personnel ("Services Communs").

• Detailed assessments

Assessment of scientific quality and production:

The team is recognized for their highly relevant work on structure-function relationships of glycosyltransferases (GTs) and the identification of dysfunctions in GTs involved in glycosaminoglycans (GAGs) biosynthesis. As reported, they are addressing well-focused issues on the biological significance of selected GTs by using molecular approaches. The scientific approach and models are relevant of a clinical problem (arthritis, drug design and metabolism) and inserted in the evolution of the concepts, evolving towards more translational research. The topic is original and the two group leaders are nationally and internationally recognized.

The productivity (together with the scientific quality) is good, with 34 original articles and 3 reviews published in very good level speciality journals (FASEB J, J Biol Chem, Cancer Res, Arthr Rheum, PLoS One, FEBS Lett), and 13 oral communications with a good ratio according to the number of researchers. All researchers do publish and there are 5 ongoing theses (2 with joint supervision) and 3 theses completed during the contract period.

Assessment of the research team's integration into its environment:

The team has accomplished a considerable effort in contracting for research funds, with high number of grants of high quality (3 ANR, 2 FRM, 1 ACI, 2 LCC). Of note is also a grant, as coordinating investigator, from the Clinical Research Hospital Program (PHRC), emphasizing the willingness for developing translational research. The recurrent grant attribution from ANR and FRM is also a particular strength of the team. The tech transfer of the research should be achieved through a planned partnership with the Cognis-BASF Company for a screening programme of molecules of potential clinical interest. One team member is the head of the Licence Pro degree program at the University.

Assessment of the research team's reputation and drawing power:

There is a good national and international recognition with several participations as invited speaker, nationally (5) and internationally (7). The group attracts Ph.D. students (5) and postdocs (2, from abroad), and have recruited during this period 2 permanent research staff (MCF) to the team. However, there is not a strong international attraction at the postdoctoral level.

One team leader has been instrumental in the creation of a french-british European Associated Laboratory (LEA SFGEN with the University Dundee, UK), has been appointed as Honorary professor of the Dundee University, and has developed a network of other European collaborations to apply for joint EU grants. One PI of the team has developed close collaboration, exchanges of PhD and postdocs, and collaborative international grants applications with Wuhan University (China) and Beirut University (Lebanon).

Assessment of the strategy and 5-year project:

Projects will move to focus on GAG biosynthesis and bioengineering strategies for GAG-associated pathologies. Therefore, a former project on glucuronosyltransferases will be less prioritized. Their projects are well focused and relevant, and show an increasing interaction and collaboration with other groups in the framework of the new IMoPA unit. The group will be structured in two main axes, headed by one PI each. The team plans to implement a multidisciplinary approach on GAGs biology, combining molecular approaches for structure/function studies of GTs, and cell biology and animal models for establishing physiological roles of GTs and bioengineering approaches for GAG-associated pathologies. The project is strong, in continuum and development of the previous work (translational evolution). New building and facilities will be facilitating in developing the project, especially through improved interactions with other teams of the new unit. The project is ambitious and fit harmoniously with the new unit project and to be able to have strong arguments in the international competition.

Conclusion:

- *Overall opinion on the team:*

High quality work, expertise in the field, but rather small group, that may lack critical mass. Despite its size the team presents a high level of scientific excellence, with nice developments from a basic to a more translational approach. Their interaction with the other teams is strong and they are able to secure funding for their projects.

- *Strengths and opportunities:*

The team has very strong and recognized expertise and relevant international position in GAGs biology. They implement an innovative multidisciplinary approach from molecular enzymology to physiological studies in cell and animal models. Of note is the plan to seize on opportunities for closer collaborations with other teams of the new unit, testifying to a scientific and human adaptation to the fusion project.

- *Weaknesses and risks:*

The translation towards animal models of osteoarthritis will be difficult and the small size of the team may be a handicap.

- *Recommendations:*

The team is encouraged to increased contacts with clinicians in order to attract MD students in the scientific curriculum and to increase their forces.

Team 3: Molecular and Structural Enzymology

Team leader: Ms Kira WEISSMAN

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	7	7	7
N2: EPST or EPIC researchers	1	1	1
N3: Other professors and researchers	0	1	1
N4: Engineers, technicians and administrative staff * on a permanent position	4	4 + [1 SC]	
N5: Engineers, technicians and administrative staff * on a non-permanent position	0		
N6: Postdoctoral students having spent at least 12 months in the unit	0		
N7: Doctoral students	4		
N8: PhD defended	4		
N9: Number of Habilitations to Direct Research (HDR) defended	2		
N10: People habilitated to direct research or similar	5	5¶	
TOTAL N1 to N7	**16**	**13 + [1 SC]**	**9**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

SC: "shared services" personnel ("Services Communs").

¶ including 1 PREM (Professor Emeritus).

• Detailed assessments

Assessment of scientific quality and production:

The work of team 3 has previously been concentrated on the mechanistic enzymology of sulfur containing proteins. The team has worked hard to place their results in a biological context. They have produced high quality work resulting in good and numerous publications (22 papers + 4 reviews), representing strong productivity for a rather small team. The papers are published in good quality international journals in their field. This team is recognized for their very serious and strong competence in mechanistic enzymology, and their commitment to fundamentals.

Assessment of the research team's integration into its environment:

Despite their strength and high quality, the international visibility of the team is rather low, although their recent recruitment should help changing this situation. Even within the unit, the team seems to be a stand-alone group, and the other teams do not profit via collaborations from their strengths. In the past, the team has had few invitations to speak at international conferences and few collaborations. Of note, the team has actively participated in the creation of a thematic enzymology group in the French Biochemical Society.

Assessment of the research team's reputation and drawing power:

The team was able to recruit three permanent staff, including one high-level international scientist. This will open new perspectives. The team has a reasonable number of Ph.D. students, but no postdocs either locally or from abroad. They have been able to secure 2 ANR grants in the last period. This is rather limited and should be improved.

Assessment of the strategy and 5-year project:

The team will be reorganized in the next period, with a new group working on synthetic biology of polyketides. This is a highly novel and interesting project, but rather unrelated to the existing projects within the team and the unit. The integration of this group into the new unit will take place via shared approaches, rather than shared scientific interests. This situation is not necessarily problematic, but could become so. The PI will need to take care to foster this technical integration into the unit.

Conclusion:

- *Overall opinion on the team:*

This is a medium size team, carrying out basic research with a reasonable publication record. The science is good, albeit highly specialized, but with few applied projects. They have very strong expertise in fundamental enzymology and biophysical techniques (in charge of FR3209 platform). The past lack of internationalization is reflected by few collaborations and insufficient invitations to international congresses. However, building on their strong competence in fundamental enzymology by adding the new polyketide synthase project in synthetic biology is highly innovative and should increase the international recognition and draw of the team.

- *Strengths and opportunities:*

Overall, the team possesses complementary expertise from protein biochemistry, structural enzymology to structure determination using several techniques (NMR and crystallography). It builds on the existing know-how of the team concerning methodology and biological systems while extending towards ambitious biological questions, like multienzyme systems, which have important medical implications.

- *Weaknesses and risks:*

The team is strategically rather stand-alone within the new proposed unit. This situation could weaken them in terms of their positioning within the unit for future recruitment of research and technical staff. The rate of publication over the 5 past years was quite low for some researchers.

- *Recommendations:*

The team needs to offer (up to a possible extent) their expertise in enzymology to the other teams of the unit via collaborative efforts (for example, much of the work on RNA involves enzymes). They need to extend their international collaborations and visibility and improve their funding.

Team 4: Inflammation, Phenotypic Dysregulation & Abnormal Articular Remodeling (IPeDAAR)

Team leader: Mr Pascal REBOUL and Mr Jean-Yves JOUZEAU

Workforce

Workforce	**Number** on 06/30/2011	**Number** on 01/01/2013	2013-2017 **Number of producers****
N1: Professors or assistant professors	4 + 1 shared with team 3 UMR 7561	4 + 1 shared with team 5 UMR IMoPA	4 + 1
N2: EPST or EPIC researchers	3	3	2
N3: Other professors and researchers	0	2	0
N4: Engineers, technicians and administrative staff * on a permanent position	3 + [1 SC]	3 + [1 SC]	
N5: Engineers, technicians and administrative staff * on a non-permanent position	0		
N6: Postdoctoral students having spent at least 12 months in the unit	0		
N7: Doctoral students	1		
N8: PhD defended	2		
N9: Number of Habilitations to Direct Research (HDR) defended	0		
N10: People habilitated to direct research or similar	3	3	
TOTAL N1 to N7	**11 + [1 SC] + 1 shared with team 3 of UMR 7561**	**12 + [1 SC] + 1 shared with team 5 of UMR IMoPA**	**6 + 1**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

SC: "shared services" personnel ("Services Communs").

• Detailed assessments

Assessment of scientific quality and production:

The work of team 4 is concentrated in inflammation, phenotypic dysregulation and abnormal articular remodelling. This team is presently in a transition period with the recent arrival of one of the two leaders of the group. Several research approaches are original, but others might be points of discussion. A stronger feedback from clinicians might be necessary to strengthen the questions of interest.

The scientific production includes 34 articles, published generally in good level journals (Arthr Rheum, J Bone Miner Res, J Biol Chem, Arthr Res Ther, J Cell Physiol). The group made 13 oral presentations and 12 invited talks. It should be noted the team includes an outstanding technical staff.

Assessment of the research team's integration into its environment:

The funding of the team is important to secure the long-term research, with grants from the FRM (4), PHRC (1), Arthritis Foundation Courtin (1), PIR (1) and from the bureau quality research of the University (2). Collaborations are established with French groups (bone imaging, microcrystal-induced inflammation), as well as in Canada and Switzerland. The teaching responsibility of several members of the team is very important. This could be used for attracting more students (MDs especially) to the team.

Assessment of the research team's reputation and drawing power:

The group has a good recognition with 9 participations as invited speaker. The attraction of Ph.D. students and of postdocs could be improved, especially trough the high involvement of its members in teaching activities at the University, and also by trying to attract MDs on translational research projects. During this period, the group has recruited 3 postdocs and 3 permanent research staff (2 full time researchers and 1 teaching researcher as team leader) to the team. The team leader was recruited on a 'Chair of Excellence' of the CNRS.

Assessment of the strategy and 5-year project:

The project was redesigned with the arrival of a new team leader, who brought innovative research topics. It is specially the case for the galectin-3 axis, which has a strong potential of collaborations (internal and international: Canada), discovery and publication. Consequently, the number of research topics appear a bit too dense and some of them should be rethought for being too competitive and risky (leptin/adipokin axis) or deleted for being less innovative (PPAR axis). The continuation of the Ank axis appears to be promising and valuable.

Conclusion:

- *Overall opinion on the team:*

Medium size team, performing basic and translational research with average publication record. It shows a good expertise in pathophysiological approaches of cartilage degradation with relevant animal models (although other models could be envisaged) and efforts to develop translational approaches. The international positionning in a competitive field should be carefully taken into consideration. The research projects and approaches are in a transition period.

- *Strengths and opportunities:*

Relevance of the topic with new themes; good potential due to arrival of one new group leader with high potential of publication; development of emerging international collaborations.

- *Weaknesses and risks:*

There is insufficient interaction with clinicians and absence of industrial partnership with no patents.

- *Recommendations:*

Increase the number of HDR people to increase the opportunity for student supervision and consequently attract more students in particular MDs); translational approaches to be emphasized; improve the capacity for funding (ANR).

Team 5: Cell & Tissue Engineering, Vectorization, Imaging (CeTVI)

Team leader: Mr Pierre GILLET et Mr Patrick MENU

Workforce

Workforce	Number on 06/30/2011	Number on 01/01/2013	2013-2017 Number of producers**
N1: Professors or assistant professors	10 + 1 shared with team 1 of UMR 7561	8 + 1 shared with team 4 UMR IMoPA	8 + 1 shared with team 4 UMR IMoPA
N2: EPST or EPIC researchers	3	3	3
N3: Other professors and researchers	2	2	2
N4: Engineers, technicians and administrative staff * on a permanent position	8 + [2 SC]	7 + [3 SC]	
N5: Engineers, technicians and administrative staff * on a non-permanent position	0		
N6: Postdoctoral students having spent at least 12 months in the unit	1		
N7: Doctoral students	10		
N8: PhD defended	14		
N9: Number of Habilitations to Direct Research (HDR) defended	1		
N10: People habilitated to direct research or similar	9	7	
TOTAL N1 to N7	**34 + [2 SC] + 1 shared with team 1 of UMR 7561**	**20 + [3 SC] + 1 shared with team 4 UMR IMoPA**	**13 + 1 shared with team 4 UMR IMoPA**

* **If** different, indicate corresponding FTEs in brackets.

** Number of producers in the [01/01/2007-06/30/2011] period who will be present in 2013-2017.

Definition and downloading of criteria:

http://www.aeres-evaluation.fr/Evaluation/Evaluation-des-unites-de-recherche/Principes-d-evaluation.

SC: "shared services" personnel ("Services Communs").

• Detailed assessments

Assessment of scientific quality and production:

The work of team 5 is concentrated in cell and tissue engineering, vectorization and imaging. The general theme of research – regenerative medicine – is original and the group has several approaches (some are innovative, in particular the preparation of multi-layer biomaterials by cells and matrix spraying), though certain aspects could be re-evaluated (broader panel of scaffolds employed). Both groups of the team (cartilage/ligament and blood vessels) expressed a clear clinical vision of the prerequisite of such research for clinical applications. The integration in the clinical environment is excellent for the vascular part, but could be improved for the cartilage/ligament part: it is unfortunate not to have an orthopaedic surgeon in the group (though it was the case in the UR 7561).

The scientific production is outstanding in quantity (68 peer-review articles during the period), very good in quality (one third of the papers in journals with IF > 5 and 3 papers with IF > 10 : J Am Coll Cardiol, Nano Lett, Adv Mater). The productivity ratio amongst researchers is very good and rather homogenous within the team. The scientific training is also very good with 19 PhD theses defended during the period and 12 in progress.

Assessment of the research team's integration into its environment:

The research produced by the group is highly valorized with 5 patents obtained during the period as well as several industrial collaborations (Danone Research, Genévrier, Separex–Stanipharm Nancy and Symatese Biomatériaux). The grant application success is remarkable (20 grants over the 4 yr period, including 5 ANR grants) with a very strong ability to generate recurrent funding.

Assessment of the research team's reputation and drawing power:

Research and training collaboration is established between University de Lorraine and University of Wuhan (China), with a so-called "laboratory without walls". Three students are in-training with joint supervision; one teaching researcher of the team 5 is coordinating the medical French-speaking branch of the University of Wuhan and there is a contract with a Cell Therapy Lab of this University (Hôpital Calmette, Kunming). A higher level of recognition would be expected in coutries with a record of scientific excellence (US, Europe, Japan). There is also a partnership for a PhD student fellowship with the University of Beirut (Lebanon). There is a good recognition with 14 participations as invited speaker.

Assessment of the strategy and 5-year project:

The project presented for the new contract has a good clinical relevance, a very good feasibility, and is original without risk. The general strategy is to develop bio-tissues using stem cells; the tissues will mainly be used for joint or vascular engineering. In addition, vectorization of biotherapy and therapies will be used to address dedicated active principles to the joint site and bio-tissues, and multi-scale biomedical imaging will be developed to monitor the development, biocompatibility and bio-integration of the resulting bio-tissues. This comprehensive approach is original, mainly by the use of mesenchymal stem cells as a source of bio-tissue.

Conclusion:

- *Overall opinion on the team:*

The team performs high quality research and the great quality of the management is acknowledged.

- *Strengths and opportunities:*

Beside the good management and the very good production of original articles by the team, all components for a project on regenerative medicine are present (cells, scaffolds, experimental models, biomechanical testing).

- *Weaknesses and risks:*

Publication quality could be stronger (try to access other journals in the field like eCM and Tissue Engineering). Although already employed in the clinics, the biomaterial used here might not be the unique option for cartilage engineering and others could be manipulated for the same purposes.

- *Recommendations:*

To deevelop translational approaches in more relevant animal models, to improve industrial valorization and interactions with clinicians.

5 • Grading

Once the visits for the 2011-2012 evaluation campaign had been completed, the chairpersons of the expert committees, who met per disciplinary group, proceeded to attribute a score to the research units in their group (and, when necessary, for these units' in-house teams).

This score (A+, A, B, C) concerned each of the four criteria defined by the AERES and was given along with an overall assessment.

With respect to this score, the research unit concerned by this report (and, when necessary, its in-house teams) received the overall assessment and the following grades:

Overall assessment of the unit "**I**ngénierie **Mo**léculaire et **P**hysiopathologie **A**rticulaire » **IMoPA**:

Unité dont la production, le rayonnement et le projet sont très bons. L'organisation et l'animation sont excellentes.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A	A	A+	A

Overall assessment of the **team 1** "RNA, RNP Structure-Function-Maturation" (JOUZEAU-CHARPENTIER):

Équipe dont la production, le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A	A	-	A

Overall assessment of the **team 2** "Molecular, Cellular, Therapeutic Engineering & Glycosyl Transferases (MolCelTeG)" (JOUZEAU-FOURNEL):

Équipe dont la production, le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A	A	-	A

Overall assessment of the **team 3** "Molecular and Structural Enzymology" (JOUZEAU-WEISSMAN):

Équipe dont la production, le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A	A	-	A

Overall assessment of the **team 4** "Inflammation, Phenotypic Dysregulation & Abnormal Articular Remodeling (IPeDAAR)" (JOUZEAU-REBOUL):

Équipe dont la production, le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A	A	-	A

Overall assessment of the **team 5** "Cell & Tissue Engineering, Vectorization, Imaging (CeTVI)" (JOUZEAU-GILLET) :

Équipe dont la production est excellente. Le rayonnement et le projet sont très bons.

Grading table:

C1 Scientific quality and production.	**C2** Reputation and drawing power, integration into the environment.	**C3** Laboratory life and governance.	**C4** Strategy and scientific project.
A+	A	-	A

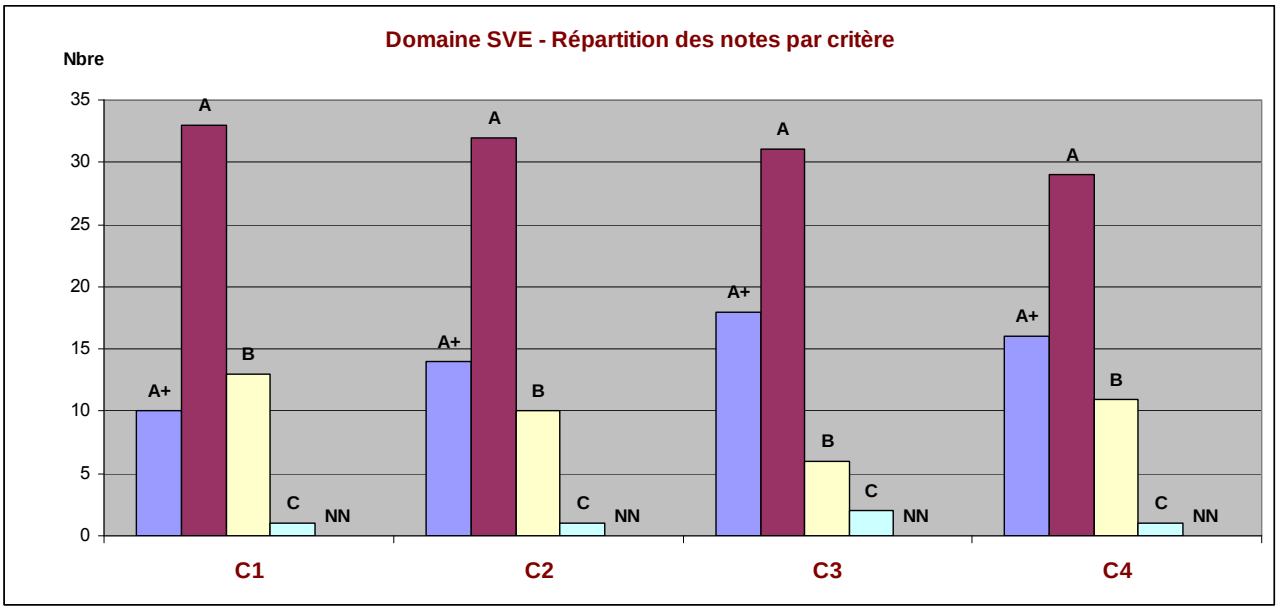
6 • Statistics per field

Notes

Critères	C1	C2	C3	C4
	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Gouvernance et vie du laboratoire	Stratégie et projet scientifique
A+	10	14	18	16
A	33	32	31	29
B	13	10	6	11
C	1	1	2	1
Non noté	-	-	-	-

Pourcentages

Critères	C1	C2	C3	C4
	Qualité scientifique et production	Rayonnement et attractivité, intégration dans l'environnement	Gouvernance et vie du laboratoire	Stratégie et projet scientifique
A+	18%	25%	32%	28%
A	58%	56%	54%	51%
B	23%	18%	11%	19%
C	2%	2%	4%	2%
Non noté	-	-	-	-



7 • Supervising bodies' general comments

UNIVERSITÉ DE LORRAINE

Date 06/05/2012

L'Administrateur Provisoire
Jean-Pierre Finance

à

Monsieur Pierre GLAUDES
Directeur de la section des unités de l'AERES
20 rue Vivienne
75002 PARIS

Objet : rapport d'évaluation de l'UMR IMOPA
Référence du document : C2013-EV-0542493S-S2PUR130004837-RT

Monsieur le Directeur,

Vous m'avez transmis le 5 avril dernier le rapport d'évaluation de l'UMR « Ingénierie Moléculaire et Physiopathologie Articulaire (IMOPA) » et je vous en remercie.

Je vous prie de trouver ci-dessous les éléments de réponse de Monsieur J.Y. Jouzeau, directeur de l'unité, ainsi que celles de Madame M.C. Lafarie-Frenot, Directrice Adjointe Scientifique de l'INSIS et de Monsieur P. Piéri, Délégué Régional Centre-Est du CNRS, cotutelle de cette structure.

En tant que tutelle du laboratoire nous n'avons pas de remarque particulière à émettre sur le rapport du Comité d'évaluation. Nous prenons bonne note de ses recommandations qui nous semblent tout à fait recevables à ce jour.

Je vous prie d'agréer, cher collègue, l'expression de mes sentiments distingués.

L'Administrateur Provisoire

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Observations de la tutelle CNRS

L'avis définitif du CNRS sur ce projet d'unité sera formalisé à l'issue de la prochaine session du comité national. A ce stade, l'INSIS-CNRS ne communique donc pas de remarque particulière sur le rapport. Philippe Piéri n'a pas d'observation à formuler. MC.Lafarie-Frenot souligne néanmoins l'argumentation détaillée fournie par les responsables des anciens laboratoires et porteur du projet IMoPA au rapport d'évaluation de l'AERES.

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Vandœuvre-Lès-Nancy, le 17 avril 2012

General comments of the management team on the IMoPA unit assessment:
Project leader Jean-Yves Jouzeau
Deputy-director Bruno Charpentier

The AERES committee evaluated the project of fusion between UMR 7214 CNRS-UL (AREMS, headed by Ms Christiane Branlant) and UMR 7561 CNRS-UL (PPIA, headed by Mr Jacques Magdalou) into a new research unit entitled IMoPA ("Ingénierie Moléculaire et Physiopathologie Articulaire") on 15 & 16 March, 2012. The new unit will be attached to the INSIS department of CNRS. As the committee was composed of 8 experts including two foreigners and 2 AERES scientific delegates, all presentations and discussions were made in English. The management team was informed of the composition of the committee on 28 February, 2012 and was given no opportunity to reject any of its members.

We acknowledge the members of the AERES committee for their accurate comments on the overall project and their encouragements to the management team for developing a "novel scientific interface" inside IMoPA.

Our feeling concerning the AERES evaluation of the IMoPA project is as follows. As indicated in the first part of the evaluation report, the scientific fields covered by the five research teams are very large, ranging from molecular, structural and functional biology of ARNs (team 1) to cell and tissue engineering from cell progenitors for articular or vascular regenerative medicine (team 5), through molecular and structural studies of sulphur containing enzymes or modular polyketides synthases (team 3), molecular and therapeutic engineering of glycosyl transferases (team 2), and studies of molecular mechanisms supporting altered joint cells phenotype or joint tissue remodeling (team 4). Although some research projects have already been initiated between teams, such as those on the pathophysiological role of microRNAs in the regulation/dysregulation of chondrocyte phenotype and some structure-function studies on glycosyltransferases, the management policy proposed for the new unit is to maintain the expertise of each team in its own research field but to promote the onset of common projects at the interface (the so-called "shared entity" which has been judged as a good approach to the fusion although being "quite conservative"). We feel that the apparent scientific scattering generated by such organization may have been puzzling for committee members, and may have contributed to an underrating of the performance of the teams which are the more involved in basic science.

Jean-Yves JOUZEAU

Bruno CHARPENTIER

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UMR 7214 « ARN, RNP structure-fonction-maturation, Enzymologie Moléculaire et Structurale»

Vandœuvre-Lès-Nancy, le 17 avril 2012

I. Response to the overall assessment of the achievements of UMR 7214

Members of UMR 7214, thank committee members for the important work done to evaluate our unit, but respectfully express their disappointment that among the eight committee members, only one specialist in RNA and no expert in the chemistry of enzyme catalysis were present, as these are the two main research areas of teams 1 and 3.
Although we greatly appreciate the generally positive comments of the assessors on the two previous units, members of UMR 7214 would like to respond to some concerns of the committee which suggested: 1) a lack of evolution of the teams during the evaluation period and the absence of convergence between them (e.g. "the composition of the five new teams of IMOPA appears to be conservative", "there was no clear strategy presented that would lead to convergence of these five separate teams" and "the enzymology group despite its high quality, appears to be a stand-alone group"), and 2) the need to "improve the visibility on career development of young researchers and technical staff members" .
We feel that the strong managerial effort that was made with the support of the Lorraine University, in order to ensure the future of the two teams of UMR 7214 was under-evaluated by the committee. This is likely due to the absence of discussion by the committee with the UMR director.

Point 1: To address this issue we would like to point out that all along the evaluation period, together with the senior scientists of the lab, the present director:
- i) Prepared the future leadership of the two teams, as recommended by the previous AERES committee. This included reshaping of the two teams in order to preserve their competitiveness in the future and to transfer significantly more responsibilities to the younger scientists (recruitment a high profile Pr to direct team 3, reorganization of team 3 in two sub-groups, and independence granted to scientists of team 1 and its reorganization in 3 sub-groups),
- ii) Orchestrated a progressive shift of the research themes toward more biological aspects and subject of medical interest, in order to prepare the integration of the unit in its new context, the Faculty of Medicine and FR3209 (which includes two INSERM units). This has included defining new subjects to be developed with teams of UMR 7561, and an expansion of the scientific approaches used. Notably also, the move to this new site necessitated the resolution of numerous financial and technical problems.
-iii) Initiated the fusion of the two units by discussion with managers of UMR 7561, and prepared members of UMR 7214 for the transition, via in-deep discussions to make clear the advantages of creating the IMOPA unit which incorporates a larger spectrum of approaches and themes.
Thus, we do not agree with the committee that our management strategy is "quite conservative" as we have made all changes necessary to favor the future success of the IMOPA unit.
In addition, members of UMR 7214 would like to point out that their enthusiasm for IMOPA is not motivated by dissatisfaction with the present governing structure as suggested by the report, but by the fact that the fusion is scientifically attractive. The new unit will benefit enormously from the significant investment by its senior leaders over the last decade in building a strong biology institute in Nancy and, from the synergy between the collected expertise available in the institute, as well as the advanced research platforms.

Point 2: Concerning career building and recognition of technical staff, we would like to emphasize that each technician and engineer has clearly defined general responsibilities in UMR 7214 and this will continue to be the case in IMOPA. Furthermore, a major effort is made to provide them with opportunities to maintain their specific expertise at the highest level and to apply it to one or several challenging subject(s), both of which are requirements for career progression within the CNRS or the University. Every year individualized strategies for each ITA/IATOS are developed via in-depth discussions with both his/her direct supervisor and lab head, and

we invest significant effort in producing annual reports and applications for promotion. The quality of the reports is particularly critical for technicians and assistant-engineers who are not judged on the basis of their publications (though the policy in the lab is to include technicians as co-authors when they have made a significant contribution). Engineers, on the other hand, are co-authors on papers which directly result from their work. We would also like to point out that all our technical staff and engineers are young compared to other candidates at Lorraine University and the Nord-Est CNRS delegation, a factor which impedes promotion as age is an important selection criteria. In this context it is worth emphazing the promotion this year of an engineer from IR2 to IR1 and a member of the secretarial staff from AI to IE.

In response to the comments on our younger scientists, we have made a major effort to promote them during the last four years, as will be detailed in the response to the committee's assessments of team 1.

Finally, concerning the identification of team 3 as stand-alone, we would like to point out that team 3 has already published on a collaborative project with team 2 during the evaluation period. Furthermore, the numerous fruitful discussions between members of teams 1 and 3 concerning catalysis have and will continue to be helpful for the development of studies on RNA modification enzymes and snoRNP catalysis by team 1. Team's 3 advices on protein purification protocols and methods to determine protein quality by biophysical approaches have also been valuable for team 1. Conversely, team 3 has benefited from team's 1 expertise on molecular biology methods. In fact, we believe that team 3 represents an important resource for all members of IMOPA interested in the detailed analysis of enzymes, as well as of macro-complexes with catalytic properties through the newly-acquired expertise on polyketide synthases. The team members can also provide critical support to other teams working on oxidative stress (teams 1, and 4). This is one reason why team 1 started to work on the impact of oxidative stress on splicing. Therefore, depending on the willingness of other teams to collaborate, team 3 will become even better integrated into the overall research effort of the unit. In addition, as noted in the response to the assessment of team 3, the team already has strong international recognition in its field of research, and this will be reinforced by the high profile of the newly-recruited PI.

II. Answer to the detailed assessments on team 1:

Point 1: The committee indicates that "considering the large size of the team 10 PIs (3 leaders plus 7 staff scientists and a large technical staff) the productivity in terms of publications although of good quality, is lower than expected" and also that, "the high quality of the results merits more recognition and high level publication than currently the case", "in particular the young members of the group, with innovative and interesting project need better visibility". We agree that we have a delay in publication and that "now that much reorganization and local structuring is behind" us we will be able to focus on publishing.
However, we would like to point out that the publications produced during the evaluation period correspond to 8 PIs and not 10 as mentioned in the report (3 Pr and 5 CNRS scientists). One member was recruited in September 2010 on a "Chaire d'excellence" and thus he could not contribute to papers published before July 2011. For this reason his publications during the evaluation period were given separately in the report. The 10th PI (MC) has yet to be recruited (September 2012). It should also be taken into account that the two female CR1 scientists took two maternity leaves each during the evaluation period. In addition, in the absence of a permanent member of secretarial staff for 1.5 years, several of the permanent scientists from team 1 had to invest heavily with the lab head in preparing to move the UMR and its platforms to the new building. It is also notable that, in addition to her scientific activities, the head of lab assumed many local, national and international responsibilities.

Another important consideration in evaluating the team is the low average age of its members. We have made every effort to help them earn their "habilitations", but the qualification criteria at Nancy University were strict and

therefore difficult to satisfy. For example, candidates must have published at least once as last author, and must have in addition closely co-supervised one or preferably two PhD students. Thus, to help our young scientists meet these criteria, we provided them with students and technical staff, and offered continuous advises to obtain funding, to supervise students and to drive original research which can be published in high impact journals. They have indeed succeeded, as noted by the committee. Nonetheless, it has taken some time for them to be fully productive while developing new subjects. During the period, the CR1 CNRS in charge of structural biology introduced with success co-expressions of recombinant proteins for structural analyses and NMR 3D structure analyses of vertebrate proteins (1 paper in revision for *NAR*, 1 almost ready for submission to *Structure*). Despite her two maternity leaves (one of which was extended due to health issues), one of the CR1 scientist obtained as noted by the committee, important original data on an unexpected role of the SMN complex in SRP assembly (she published 1 JBC paper as last and corresponding author in the period and 1 paper where she is also last author was submitted to PNAS, several additional experiments were requested, these have been carried out and a revised manuscript is ready for submission). Hence, she should not be considered as a "non-producer scientist" as indicated in the table on page 10. The other female CR1 scientist who was recruited at the beginning of the evaluation period initiated a new field on the link between splicing and genetic diseases. She too was highly successful in spite of two maternity leaves (3 papers published in this new field). Another CR1 scientist has developed new approaches for *in silico* SELEX experiments (several papers published on previous work and attainment of an HDR). Therefore, in contrast to the committee's statements, we made substantial effort to promote young scientists. This was a "passage obligé" which carried a price in terms of the time required for publication.

Noticeably, also, in addition to their heavy teaching responsibilities, during the last two years the 3 Professors made substantial investments in conceiving new teaching curricula in biology in the framework of the fusion of Nancy's and Metz's Universities. In addition, they made efforts to introduce fresh approaches and themes into the laboratory. More specifically following a 6 month sabbatical abroad, one of the professors established a new field of research on RNA engineering, the second developed a new theme on the machinery of snoRNP assembly that he co-discovered with E Bertrand, and the third initiated studies on a field which was also new to us: long coding RNA and epigenetics. Furthermore, in addition to the high-level papers they published, several manuscripts by these Prs are either in revision or nearing submission.

Point 2: The committee wrote "that we published in high quality internationally respected journals in our fields, but there had few high level publications in more high profile general journals". We would like to point out that we were leaders or co-leaders of the work published in several high IF factor journals: 1 *PLoS Biology* (IF 13), 1 *J. Cell. Biol.* (IF 9.6), *1 PLoS pathogen* (IF 9), 1 *Human Mol. Genet.* (IF 8) and 8 *Nucleic Acids Res.* (IF 7.5). These are not specialized journals. Original and high level general data in the DNA or RNA fields is required for publication in these journals.

Answer to the detailed assessments on team 3:

The committee points out that the team has produced high quality work representing strong productivity (although this is noted one paragraph below as a reasonable publication record and in rather specialized journals). However, it considers that the team 1) rather lacks international visibility and attractiveness; 2) has had few invitations to speak at international conferences; 3) has few collaborations, in particular at the international level; 4) needs to improve its funding; 5) has introduced a new line of research on PKS which is somewhat unrelated to the existing projects; and 6) is rather stand-alone within the new unit.

UMR 7214 « ARN, RNP structure-fonction-maturation,
Enzymologie Moléculaire et Structurale»

Points 1 and 2: The team is one of the world leaders (top 4) in the area of methionine sulfoxide reductases, the study of which is critical to advancing a central theme in biology, that of ageing. The team is highly recognized within the enzymology community in France, Europe and the US. For example, we were in 2008, among ten leading teams to be invited to contribute to a special issue of *A.B.B.* devoted to enzymology in Europe. Furthermore, one of the PIs (GB) has been invited as a "Professor invité" for a sabbatical year in the NIH lab of Dr. Levine (Bethesda). Finally, the team recruited a high profile scientist in 2010.
We are usually invited as speakers to present talks (4) at biannual conferences in our domain of expertise (e.g. TINE and carbonyl meetings; see for instance the TINE congress in June).
There is consistent interest from Academic institutions and pharmaceutical and biotechnology companies in recruiting researchers in enzymology from the team. Over the last 12 years, all of the graduating PhDs have found a job in their speciality, many of them in academia.

Points 3 and 4: The team has established six fruitful collaborations with French labs who are leaders in their respective fields (including team 2; Tolédano, CEA, redox biology; Van Dorsselear, Strasbourg, proteomics; Ruiz-Lopez, Nancy, theoretical chemistry…), as well as a collaboration with a private company, COGNIS/BASF. International collaborations, while desirable, are not an end in themselves when the required expertise is available in France. Nonetheless, the newly recruited PI already has several international collaborations. Finally, the team is able to secure funding for its projects (two ANR, as coordinators; one from LCC, 2011; and two BQR from the University).

Points 5 and 6: We believe that the PKS project can easily integrate into the existing projects not only on the basis of shared technical approaches, but also via common scientific interest (for example, the enzymology of PKS ketoreductases, which belong to the short chain dehydrogenase/reductase superfamily of which the AREMS team is expert).
We are the only team in the new unit to have established a fruitful collaboration with team 2 (resulting in two publications in *Biochem. J.*). Thus, the team has already and can continue to offer its expertise to the other teams, provided that the collaborations are beneficial to each partner.

To conclude, as indicated in the team self-evaluation, the team has strong international recognition and is attractive, as demonstrated by the recruitment of a high-level PI. Our team can improve the number of invitations to conferences, of ANR contracts and international collaborations (where appropriate), but in any case, these points should not be considered as a lack of attractiveness and visibility.

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UMR 7561 « Physiopathologie, Pharmacologie et Ingénierie Articulaires »

Vandœuvre-Lès-Nancy, le 17 avril 2012

As the head of UMR 7561 CNRS-UL, which comprises the teams 2, 4 and 5 of the future IMoPA unit, I acknowledge the members of the AERES committee for their comments on the scientific reports and projects of its constitutive teams. As mentioned in the AERES guidelines, team leaders take opportunity to provide some comments concerning the evaluation of their scientific activity by the committee:

Comments on the detailed evaluation of team 2 (MolCelTeG):
Leaders Sylvie Fournel-Gigleux and Mohamed Ouzzine

We gratefully acknowledge the members of the AERES committee for their positive comments concerning the activity of our team.
We would like to highlight that we are currently actively implicated in efforts to bolster the size of the team: 1) Through the recruitment of post-doctoral fellows from France and abroad, 2) through strongly promoting the application of former PhD students currently trained as post-doctoral fellows at CNRS and INSERM positions, and 3) through the recruitment of technical staff required to replace personal retired over the last contract (as stated in the document). This technical staff will be more specifically dedicated to the implementation of osteoarthritis mice models that are planned in our programme. These actions should undoubtedly be rewarded in a next future.
Furthermore, the team has already reinforced its links with medical staff via two “Contrats Hospitaliers de Recherche Translationnelle” (M. Ouzzine and J. Magdalou). These active collaborations are testified by recent common publications with clinicians of the UMR (Venkatesan *et al*. PlosOne, 2012). In the recent past, we also hosted several MD trainees and these contacts with clinicians will be reinforced, as recommended by the committee.

Comments on the detailed evaluation of team 4 (IPeDAAR):
Leaders Jean-Yves Jouzeau and Pascal Reboul

We gratefully acknowledge the members of the AERES committee for their comments concerning the activity of our team, which resume most of the strengths and weaknesses identified by the team itself in its SWOT analysis.
We wish to underline that the team leaders have still begun to reinforce to links with rheumatologists both in the context of team projects and, more generally, by promoting a monthly meeting between unit members and physicians at the unit level. Efforts will be made to attract more MDs in basic science trainings and this has already begun through a one year post-doctoral position for a rheumatologist and three “stage d’initiation à la recherche [SIR]” for MD students. The main limitation is to retain them in such research training, due to the local heavy clinical duties compared to human resources availability. However, the development of translational research programs could be a good option, as recommended by the committee. We agree globally with the comments of the committee relative to the scientific themes to be developed in the future but wish to underline that the PPAR axis will be deleted only when the ongoing programs will have been completed. Indeed, despite the recent withdrawal of several marketed drugs for safety concerns in diabetic patients, the unique ongoing collaboration on PPARgamma deficient mice is prone to clarify the underlying mechanisms of their anti-arthritic potential.

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UMR 7561 « Physiopathologie, Pharmacologie et Ingénierie Articulaires »

Comments on the detailed evaluation of team 5 (CeTEVI):
Leaders Pierre Gillet and Patrick Menu

The team 5 agrees with most of the comments of the Expert panel but wishes to provide the following comments for seeking clarity:

- Concerning the Scaffolds employed, an effort will be made to use new/original matrixes:
  - In collaboration with Paris XIII (Collagen grafted with heparin) and local collaborations with ENSIC (electrospinning, in collaboration with D Rouxel).
  - Original scaffolds are also developed with X Wang for ligament engineering. In addition, the "Nacre" project is very original.
  - Concerning vascular Tissue Engineering, the aim for the next 5 years is to develop bio-compatible polymers authorized by AFSSAPS, *i.e.* Chitosan and hyaluronic acid. Thanks to our collaborations with Strasbourg, we have just optimized these molecules arrangement (2nd generation) to have better stability in biological medium, with an adequate Young modulus for good cells behavior.
  - We also have collaboration with IJL (Institut Jean Lamour – UMR CNRS 7198) to develop a piezoelectric nanoparticles copolymer based scaffold that involves the use of acoustic waves. These copolymers are sensitive to stretching and piezoelectric deliver electrical stimulation. The Integration of nanomaterial in vascular substitute and in vivo stimulation by stretching promote stem cells differentiation.
- Please note that the Cartilage/Ligament part the team includes 2 orthopedic surgeons: Prof D Mainard (half time) and Prof L Galois (associate researcher).
- The follow-up of vascular studies is submitted to the expertise of vascular surgeons (Dr B. Lehalle and Pr S. Rinckenbach) that belong to team 5 as associate professors. Moreover a PhD student, young cardiovascular surgeon from Wuhan (Chine) will join the team in September, in order to assess the cellularized graft firstly in rabbit, and then in mini-pig.
- Concerning animal models, an effort will be made to develop more relevant experimental models, *e.g.* in the mini pig, in collaboration with the school of surgery in the Faculty of Medicine (N. Tran). This is a main point of the ANR project MACSIPIG which is actually undergoing expertise.
- Interactions with Clinicians will be pursued: Pierre Gillet is a clinician, both Rheumatologist and Pharmacologist; several collaborations are in progress with the Departments of Rheumatology (Pr D Lœuille), Orthopedics (Prs D Mainard & L Galois), Cell Therapy (Pr D Bensoussan) and Radiology (Pr J Felblinger). Additionally the Pharmacovigilance Center (Head Pr P Gillet) is an important actor in Clinical Research in our CHU (expertise and help in the redaction of each Protocol submitted, especially in the Field of Pharmacology & Therapeutics). Besides 2 contracts of Interface INSERM are in progress in the team for translational research.
- As mentioned in the project an effort will be made in the next contract to publish in the top ranked papers in the field of Biomaterials and Tissue Engineering.

Jacques MAGDALOU

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